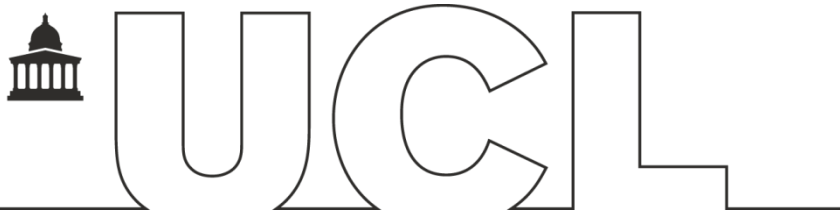

The Role of Alcohol Consumption on Physical Functioning in Middle-aged and Older Adults in Central and Eastern Europe

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DECLARATION

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

ABSTRACT

Background: Among middle-aged and older adults, light-to-moderate drinkers appear to have better physical functioning than non- and heavy drinkers. The cross-sectional association may be confounded by former drinking. Longitudinal evidence on alcohol consumption and future changes in physical functioning is sparse.

Objective: To investigate the role of alcohol consumption and physical functioning in Central and Eastern Europe (CEE), a region characterised by relatively poor health status and high alcohol consumption.

Study design: Cross-sectional and longitudinal analyses of a study of 28,783 men and women aged 45–69 years randomly selected from population registers in Novosibirsk (Russia), Krakow (Poland) and seven towns of Czech Republic, with approximately 10 years of follow-up.

Methods: At baseline, alcohol consumption in the past 12 months was measured by a graduated frequency questionnaire, and problem drinking was assessed by the CAGE questionnaire. In the Russian cohort, past drinking behaviour was also assessed. Physical functioning at baseline and at three subsequent occasions was measured by the PF-10 subscale of the Short-Form-36 (SF-36) instrument.

Results: In cross-sectional analyses of the baseline data, the odds of physical limitations (PF-10 score<75% of maximum) were highest among non-drinkers, decreased with increasing drinking frequency, drinking volume and average drinking quantity, and were not associated with problem drinking. In the Russian cohort with data on past drinking, increased odds of physical limitations were found in subjects who stopped or reduced drinking for health reasons. In longitudinal analyses, using 10-year follow-up data, alcohol consumption and problem drinking at baseline was not consistently associated with the rate of decline in physical functioning.

Conclusions: The excess risk of physical limitations in non-drinkers at baseline was partly explained by 'sick quitters', and the apparently protective effect of heavier drinking was partly due to less healthy former heavy drinkers moving to lower drinking categories. The lack of longitudinal association between alcohol consumption indices and the rate of decline in physical functioning may be due to methodological limitations; however, the possibility cannot be excluded that my findings reflect a genuine absence of an effect.

DEDICATION

This thesis is dedicated to my loving parents, Hu Shijun and Luo Min, for their unreserved love, their unending support, and their continuous encouragement in my life for pursuing my education, all of which make me who I am.

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ABBREVIATIONS

ACT	Adult Changes in Thought study
ADH	Alcohol dehydrogenase
ADL	Activities of daily living
AHEAD	Health Dynamics Among the Oldest Old
ALDH	Aldehyde dehydrogenase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUDIT	Alcohol Use Disorders Identification Test
BAC	Blood alcohol concentration
BMI	Body mass index
CAPI	Computer Assisted Personal Interview
CDT	Carbohydratedeficient transferrin
CEE	Central and Eastern Europe
CES-D	Center for Epidemiologic Studies Depression Scale
CHD	Coronary heart disease
CI	Confidence interval
CIDI-SAM	Composite International Diagnostic Interview Substance Abuse Module
CRP	C-reactive protein
CVD	Cardiovascular disease
DALY	Disability-adjusted life year
ELSA	English Longitudinal Study of Ageing
EtG	Ethyl glucuronide
EtS	Ethyl sulphate
EU	European Union
FAEE	Fatty acid ethyl esters
FCS	Full conditional specification
FFQ	Food frequency questionnaire
FIML	Full-information maximum likelihood
FMI	Fraction of missing information
FSU	Former Soviet Union
GF	Graduated frequency
GGT	Gamma-glutamyl transpeptidase
GMM	Growth mixture modelling
HAPIEE	Health, Alcohol and Psychosocial factors In Eastern Europe study
HDL-C	High-density lipoprotein cholesterol
HED	Heavy episodic drinking

HIAA	Hydroxyindole-3-acetic acid
HRS	Health and Retirement Study
HTOL	Hydroxytryptophol
IADL	Instrumental activities of daily living
ICF	International Classification of Functioning, Disability and Health
ICIDH	International Classification of Impairments, Disability and Handicap
IL-6	Interleukin 6
IOM	Institute of Medicine
JHFT	Jebsen Hand Function Test
KLoSA	Korean Longitudinal Study of Aging
LDL-C	Low-density lipoprotein cholesterol
MAR	Missing at random
MAST	Michigan Alcoholism Screening Test
MCH	Mean corpuscular haemoglobin
MCV	Mean corpuscular volume
MI	Multiple imputation
MICE	Multiple imputation by chained equations
MLM	Multilevel modelling
MLR	Maximum likelihood estimation with robust standard errors
MOS	Medical Outcome Study
MrOS	Osteoporotic Fractures in Men study
NIAAA	National Institute on Alcohol Abuse and Alcoholism
OR	Odds ratio
PDI	Physical Disability Index
PEth	Phosphatidylethanol
PF-10	Physical functioning subscale
PMM	Predictive mean match
PPF	Performance-based physical function
PQ2009	Postal questionnaire follow-up 2009
PQ2012	Postal questionnaire follow-up 2012
PYLL	Potential year of life lost
QF	Quantity-frequency
QoL	Quality of life
SCRAM	Secure continuous remote alcohol monitor
SE	Standard error
SEM	Structural equation modelling
SEP	Socioeconomic position
SF-36	Short-Form-36 Health Survey
SPPB	Short Physical Performance Battery

SRMI	Sequential regression multivariate imputation
TAS	Transdermal alcohol sensor/recorder
TLFB	Timeline follow-back
TNF-α	Tumor necrosis factor-alpha
TUG	Timed Up and Go test
WHO	World Health Organization
YLD	Year of lost due to disability

CHAPTER 1 INTRODUCTION

Central and Eastern Europe (CEE) is ageing rapidly.[1] This is particularly challenging for CEE countries owing to the inadequacies of health services, long-term social care and private savings in this region.[2,3] Compared with Western Europe, CEE also has a higher level of alcohol consumption,[4,5] shorter life expectancy,[6-10] and a higher health burden attributable to alcohol.[4,11-13]

Physical functioning is a key indicator of older adults' health status and strongly related to their quality of life.[14,15] Decline in physical functioning in late-life is, to a great extent, a consequence of physiological changes and onset of diseases related to ageing, modified by medical care, socioeconomic, psychosocial and behavioural factors.[16,17] Preventing disability, keeping independent on daily self-care and domestic-related tasks, and identifying factors associated with physical functioning, are imperative for older adults, for public health and for social care systems.[18]

Despite the lack of evidence, older adults' physical functioning in CEE also appears to be poorer than their counterparts in Western Europe.[19,20] Older adults are more sensitive to the harmful effects of alcohol than younger persons because of ageing-related changes (e.g., increased body fat, decreased body water, ageing organs, and gradually breakdown of the blood-brain barrier),[21,22] and negative interactions between alcohol and medications.[23,24] Considering the high alcohol consumption and high alcohol-attributable health burden in CEE, it is plausible that alcohol also plays a role in physical functioning in this region.

Previous cross-sectional studies on alcohol consumption and physical functioning have revealed that, compared with light-to-moderate drinking, non-drinking and/or heavy drinking was associated with poorer physical functioning among middle-aged and older adults.[25-36] However, cross-sectional studies are subject to reverse causation and 'sick quitters' bias[37] caused by the failure to separate former drinkers who quit drinking because of health reasons from never drinkers. 'Sick quitters' may lead to an overestimation of the protective effect of alcohol consumption on mortality and cardiovascular disease (CVD).[37,38] This bias may also apply to alcohol

consumption and physical functioning. Evidence from longitudinal studies with clear temporal structure is mixed and inconclusive. Some studies have found no association,[39-51] while other studies have shown an L-/J-shaped relationship that non-drinking and/or heavy drinking was associated with (incident) functional limitations and disability at follow-up.[52-64] The majority of these studies, both cross-sectional and longitudinal, have been conducted in the US and a few from European and Asian populations, where the level of alcohol consumption is lower than CEE. None of these studies have examined alcohol consumption and physical functioning in populations from CEE.

The overall aim of this thesis therefore is to investigate the role of alcohol consumption on physical functioning in middle-aged and older adults in three CEE countries–Czech Republic, Russia and Poland–using cross-sectional and longitudinal data from the multi-centre prospective HAPIEE (Health, Alcohol and Psychosocial factors In Eastern Europe) study. In particular, this thesis will examine: 1) the cross-sectional association between alcohol consumption and physical limitations in the Czech, Russian and Polish cohorts, using data from the baseline survey of the HAPIEE study; 2) how past drinking behaviour prior to the baseline survey (including 'sick quitters') affects the cross-sectional association of alcohol consumption with physical limitations in the Russian cohort; 3) the trajectories of physical functioning in the three cohorts over 10-year follow-up of the HAPIEE study; and 4) the longitudinal association between alcohol consumption at baseline, past drinking behaviour (in the Russian cohort) and the rate of change in physical functioning over time.

This thesis uses data from 28,783 men and women aged 45–69 years at baseline of the HAPIEE study, who were randomly selected from population registers in seven towns of Czech Republic and Krakow (Poland) and from electoral lists in Novosibirsk (Russia). The cohorts were re-examined in 2006–2008, and assessed by a postal questionnaire in 2009 and 2012, respectively. By using invaluable data on alcohol consumption at baseline and repeated measurements of physical functioning at baseline and three subsequent occasions, this thesis offers some important insights into the associations of alcohol consumption with physical functioning at baseline

and with the trajectories of physical functioning over time in CEE. The data on past drinking behaviour in the Russian cohort provide a unique opportunity to address the 'sick quitters' bias directly in this thesis.

This thesis is composed of seven themed chapters. **CHAPTER 2** begins by laying out the ageing phenomenon in Europe, the importance of physical functioning and alcohol consumption to ageing populations, the health gap between Eastern and Western Europe, and the alcohol-attributable health burden in CEE. It then introduces the conceptual models, definitions and measures of disability and physical functioning, and their determinants and risk factors. The measures of alcohol consumption, health consequences of alcohol consumption, and a comprehensive literature review of previous cross-sectional and longitudinal studies on alcohol consumption and physical functioning are also included in this chapter.

CHAPTER 3 presents the overall aims, specific objectives and hypotheses of this thesis. **CHAPTER 4** is concerned with the methodology used in this thesis, including study design and data collection, ethical issues, study subjects and analytical samples, study variables, missing data, and statistical analyses. Multiple imputation by chained equations, growth curve modelling and their applications in the HAPIEE study are detailed in this chapter. **CHAPTER 5** reports the results of statistical analyses, focusing on the sample characteristics of the Czech, Russian and Polish cohorts, the comparison between the non-missing and imputed data, the cross-sectional and longitudinal findings on the relationship between alcohol consumption and physical functioning, and the results of sensitivity analyses.

CHAPTER 6 draws upon the entire thesis, summarising the cross-sectional and longitudinal findings, discussing methodological issues, and interpreting the findings in the context of existing literature. Several strengths, limitations such as non-response, measurement error in study variables and residual confounding, as well as other crucial methodological issues including reverse causation and multiple imputation of missing data are presented in this chapter. Possible explanations of the findings in this thesis are also provided. **CHAPTER 7** gives the implications for future research and policy and the conclusions of this thesis.

CHAPTER 2 BACKGROUND

This chapter describes the literature relevant to the main themes of this thesis. In particular, it reviews up-to-date evidence on the association between alcohol consumption and physical functioning among middle-aged and older populations. Four sections compose the body of this chapter, seeking to provide a picture of: 1) the importance of physical functioning and alcohol consumption to ageing populations; 2) the health gap between Eastern and Western Europe, and alcohol-attributable health burden in CEE; 3) frameworks, measures, and determinants of disability and physical functioning; and 4) measures of alcohol consumption and health consequences of alcohol consumption, including a comprehensive literature review on alcohol consumption and physical functioning.

2.1 Ageing, Physical Functioning, and Alcohol Consumption

There is a growing ageing population in Europe.[1,65] Physical functioning, a central component of older adults' health, is determined by genetics, lifestyle and environment factors.[16,17] Older adults are more sensitive to the harmful effects of alcohol than younger persons, owing to the age-related physiological changes[21,22] and potential negative interactions between alcohol and medications[23,24].

2.1.1 Ageing in Europe

Population ageing is a global phenomenon, and Europe is not an exception.[65,66] At present, the median age of the population in Europe is already the highest in the world.[67] By 2050, the proportions of older adults (≥65 years) and the oldest of old (≥80 years) in the population of the whole Europe are forecasted to reach 29% and 10%, respectively.[65] In European Union (EU) countries, older adults are projected to account for 29% of the EU population in 2060 compared with 16% in 2010; meanwhile the proportion of the oldest of old is expected to increase from 4% to 12%.[1]

Within Europe, countries with the median population age above the EU average will shift from the North and West to South and CEE after 2040.[1] The rapid population ageing challenges the societies on how they allocate social resources, such as social security system, health services, and long-term social care and support.[18,66,68,69] Considering the inadequacies of these social sources provided to the public alongside low private savings, population ageing is a particular concern in the CEE region.[2,3]

2.1.2 Physical functioning and ageing

Successful ageing has drawn substantial interest from academia, the general public, and policy makers. The ideal goal of successful ageing is to maintain and optimise physical, social, and mental wellbeing, independence of living, and quality of life in late-life for as long as possible.[18,70-72] Physical functioning is one of the key indicators of older adults' health status,[15,18] and is strongly related to their quality of life.[14,18]

In 1997, Kalache and Kichbusch[73] proposed a conceptual framework of functional capacity over the life-course: an individual's functional capacity develops steeply and then hits a peak in early adulthood, afterwards it declines linearly with age increasing.[73-75] Apart from genetic factors, the decline in functional capacity is determined by lifestyle and environment factors (e.g., diet, smoking, socioeconomic position, and psychosocial factors);[74] thus at population level, a fitness gap emerges with increasing age.[17,74,75] In consequence, individuals who have a lower peak and/or faster rate of decline in functional capacity, reach the disability threshold at an earlier age.[74,75]

Compared with younger persons, older adults are at an increased risk of disability,[15,66,76] mirroring an accumulation of risk over the life-course.[66,68] Preventing disability, keeping independent on daily self-care and domestic-related tasks, and identifying factors associated with physical functioning, are imperative for older adults themselves and for public health and social care systems.[18]

There is some evidence that the prevalence of disability declines among older adults in Europe.[18,77] The decrease seems to relate to more severe disability, while less severe disability appears to become more common.[69] In an international comparison, the prevalence of at least one limitation in instrumental activities of daily living (IADLs) among adults aged 50–74 years was 8.3% in Europe and 11.8% in England; whilst the prevalence of at least one limitation in mobility was 44.3% and 53.7% in Europe and England, respectively.[78]

Despite the lack of reliable evidence, older adults' physical functioning in CEE appears to be poorer than their counterparts in Western Europe,[19,20] in addition to the shorter life expectancy and higher mortality in CEE due to the epidemic of CVD.[20] Findings from a cross-sectional comparison between Sweden and Russia showed that, after reaching an age of 40–50 years, physical functioning in Russia declined much more steeply with increasing age than in Sweden.[19]

2.1.3 Alcohol consumption and ageing

Alcohol consumption is the third leading global risk factor for disease and disability.[5] Alcohol intake per occasion tends to decrease with increasing age, but this does not always hold for frequency of drinking.[79-81] By comparing 35 countries, Wilsnack *et al.*[81] found that, the proportion of frequent drinkers (≥5 times per week) was consistently the highest in the oldest age group; European and English-speaking countries showed a greater decline in high annual alcohol intake (>8468 g/year) and heavy episodic drinking (>60 g/day) with increasing age.

Older adults are more sensitive to alcohol than younger persons.[21,22,80,82-85] Body fat increases by 100% and 50% in older men and women respectively, resulting in reduced body water and interstitial fluid volume.[85] These changes lead to a higher blood alcohol concentration (BAC) in older adults compare with younger ones, when they consume a similar dose of alcohol.[21,22,80,82-85] Other age-related physiological changes (e.g., ageing organs and gradual breakdown of the blood-brain barrier), which affect older adults' ability to recover from damages, increase the risk of diseases in older adults who consume even a relatively small quantity of

alcohol.[21,86,87] Furthermore, alcohol use, at a moderate amount, negatively interacts with many medications and increases the risk of possible side effects; this is particularly relevant to older adults.[23,24,88]

2.2 Alcohol-attributable Health Burden in Central and Eastern Europe

The health gap between Eastern and Western Europe has been recognised and observed for a long time, and it hitherto persists.[6-10,89,90] One of the leading modifiable causes of the gap and health losses in CEE is alcohol use.[6-9,91-93]

2.2.1 East-west health gap

Since the fall of communism in 1989, CEE and Former Soviet Union (FSU) countries have witnessed profound political, social, and economic changes. These changes had influences on population health. Divergences in mortality and life expectancy between CEE, FSU and Western Europe before 1989 have not been universally reversed during the post-communist transition.[6-10,89,90] While Western European countries have continuously seen a gain in life expectancy since 1970s; life expectancy in Central European countries stagnated until the end of 1980s and began to increase in 1990s, and the positive trend has been sustained to date.[6-9] During Gorbachev's reforms that included anti-alcohol campaign, a short-lived growth of life expectancy took place in FSU countries between 1985 and 1987, following by a sharp drop until 1994/5; afterwards an overall improvement occurred in FSU, except in Russia where the life expectancy declined again between 1998 and 2005, after that it has been improving.[6-10]

In 2002, the probability of premature death (<65 years old) in men was 31% in CEE, 54% in Russia, and only 16% in Western Europe; a similar pattern was also seen in women.[13] In 2010, compared with Western European countries, CEE countries, in general, had 2–3 years lower life expectancy in both genders; the lowest life expectancy was seen in Russia while it was slightly higher in other FSU countries (except the life expectancy among women in Moldova).[10] The changes of life expectancy observed in FSU and CEE countries, are largely attributed to injuries and

violence, cancer, and CVD, in which alcohol plays an important role, particularly in FSU countries.[6-9,91,92]

2.2.2 Health burden attributable to alcohol in Central and Eastern Europe

Powles *et al.*[93] identified three clusters of leading modifiable causes of health losses in CEE: nutritional/physiological risk factors (e.g., low consumption of vegetables and fruits, body mass index, and blood cholesterol), tobacco, and alcohol.

Europe has the highest level of alcohol consumption in the world.[4,5,94] In 2005, the average adult per capita consumption in Europe (47 countries excluding Israel, Monaco, Montenegro and San Marino) was 9.2 litres; more than 20% of the population aged 15 years and over reported heavy episodic drinking (≥5 drinks per occasion, or 50 grams of pure alcohol per occasion) at least once a week.[94] Eastern European countries and their neighbours have the highest consumption and the most risky pattern of drinking in Europe.[5] According to the data in 2009, the average adult per capita consumption was 12.5 litres (1.6 litres unrecorded) in EU, 14.5 litres (2.5 unrecorded) in CEE and 15.7 litres (4.7 unrecorded) in Russia, respectively.[4] Russia also has the most hazardous pattern of drinking.[4]

In 2002, alcohol misuse accounted for an estimated 25% and 6% of the East-West gap in life expectancy in men and women aged 20–64 years, respectively.[13] Alcohol also contributed to a higher proportion of premature deaths in CEE than the West.[4,11] In 2004, 19% of premature deaths in men and 9% in women were attributable to alcohol in CEE, with the EU average of 14% in men and 8% in women.[4]

Comparing other commonly-used public health indicators, in 2004, 22% of potential years of life lost (PYLL), 18% of years of life lost due to disability (YLD), and 20% of disability-adjusted life years (DALYs) were attributed to alcohol in men in CEE, all of which were approximately 5% higher than the EU average.[4] The proportions were much smaller in women, and the disparity between CEE and EU average was about 1%.[4] In the Global Burden of Disease Study 2010, alcohol use was the fourth leading risk factor of the disease burden in Central Europe, and the first leading risk

factor in Eastern Europe.[12] Pooling men and women together, 8% of DALYs were attributed to alcohol in Central Europe; whilst the alcohol-attributable DALYs was as much as 24% in Eastern Europe, an increase of about 5% compared to 1990.[12]

2.3 Disability and Physical Functioning

Loss of human functioning (disablement) is a dynamic process which is determined by biological, psychological and social factors.[95-97]

2.3.1 Conceptual models of disability

Disability is a complex, dynamic, and multidimensional concept.[98,99] The conceptual models of disability are usually categorised into medical, social, and bio-psycho-social models.[98,100] Medical models view disability as a consequence of disease, trauma or other health conditions, which can be 'corrected' or 'compensated' by medical interventions and rehabilitation.[100-104] In contrast, social models consider disability as a social construct created by societies that fail to provide an accommodating and flexible environment to enable disabled people.[100-103] Bio-psycho-social models, a hybrid of medical and social models, perceive disability to originate from health problems, and be influenced by psychological and social factors, as well as the interactions between them.[100-102] The bio-psycho-social models acknowledge disability as a dynamic process; both directions of the process, disablement and recovery, are affected by biological, psychological, and social factors.[100]

Four influential conceptual models of disability will be briefly introduced below: 1) the Nagi model and its revisions;[95,96,105,106] 2) the International Classification of Impairments, Disability and Handicap (ICIDH);[107] 3) the International Classification of Functioning, Disability and Health (ICF);[101] and 4) the late-life disablement process.[97]

2.3.1.1 Nagi model and its revisions

In 1965, Nagi[105] proposed a model to describe the disablement process, from active pathology, impairment, functional limitation, to disability, and he revised his original model in 1991.[106] In the revised version, Nagi[106] defined active pathology as 'result[ing] from infection, trauma, metabolic imbalance, degenerative disease process, or other etiology' (p.313). Impairment is 'a loss or abnormality of an anatomical, physiological, mental or emotional nature' (p.314).[106] Functional limitation is impairments manifesting 'at the level of the organism as a whole' (p.314).[106] Disability is 'an inability or limitation in performing socially defined roles and tasks expected of an individual within a sociocultural and physical environment' (p.315).[106] Although the Nagi model is usually presented with linear links between consecutive stages, Nagi[106] clarified that the disablement process is not necessarily a causal pathway, and impairments and functional limitations do not inevitably result in disability. The disablement process is influenced by one's own and others' perceptions towards his/her situation and the characteristics of environment.[106]

Verbrugge and Jette[95] introduced risk factors as well as intra- and extra-individual factors into the Nagi model, which theoretically can accelerate or decelerate the disablement process. Risk factors are an individual's characteristics (e.g., demographic, biological, behavioural, psychosocial and social characteristics), pre-existing before or at the onset of the disablement process.[95] Intra-individual factors stem from or work within an individual, whilst extra-individual factors are those from outside of an individual.[95] Both intra- and extra-individual factors act after the disablement process has initiated, by hastening or retarding the process.[95]

Brandt and Pope[96] extended the Nagi model substantially and named it the Institute of Medicine (IOM) model. The IOM model views disablement as a dynamic process between an individual and the environment, and three dimensions are identified: the person, environment, and interaction between the person and environment.[96] At the dimension of 'the person', disablement is a bi-directional process of disabling and enabling; enabling is a reversal of disabling due to interventions and rehabilitation.[96] A stage of no disabling condition is added to indicate a beginning and/or end of the

enabling-disabling process; the process is influenced by transitional factors including biology, environment (physical, social, and psychological), and lifestyle and behaviours.[96] Disability, defined as the interaction between a person and environment, is determined by the magnitude of the person's potential disabling conditions and by how supportive the physical and social environment is.[96] An individual experiences a greater level of disability in a less supportive environment, compared with those in a more supportive environment, given the same level of impairment or functional limitation.[96]

2.3.1.2 International Classification of Impairments, Disability and Handicap (ICIDH)

The World Health Organization (WHO)[107] published the International Classification of Impairments, Disability and Handicap (ICIDH) in 1980. Three levels of consequences of diseases are identified: impairment, disability, and handicap. Impairment is defined as 'any loss or abnormality of psychological, physiological or anatomical structure or function' (p.27).[107] Disability is 'any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being' (p.28).[107] Handicap is 'a disadvantage for a given individual, resulting from an impairment or a disability, that limits or prevents the fulfilment of a role that is normal (depending on age, sex, and social and cultural factors) for that individual' (p.29).[107]

The ICIDH has been widely criticised for: 1) being a medical model of disability;[99] 2) implying a rigid causal path between the three levels of consequences of disease;[98,108,109] and 3) the ambiguous definitions of disability and handicap.[108]

2.3.1.3 International Classification of Functioning, Disability and Health (ICF)

Subsequent revision of the ICIDH took two decades. In 2001, it was renamed to the International Classification of Functioning, Disability and Health (ICF). One of the fundamental differences between the ICIDH and ICF is that the ICF is a classification of components of health instead of consequences of diseases.[110] The ICF is a bio-psycho-social model of disability, encompassing two parts: 1)

functioning and disability; and 2) contextual factors.[101] In the first part, two components are classified: 1) body functions and structures; and 2) activities and participation. Similarly, contextual factors comprise of environmental and personal factors.[101]

Functioning is defined as 'an umbrella term encompassing all body functions, activities and participation' (p.3).[101] Disability, a negative term of functioning, is defined as 'an umbrella term for impairments, activity limitations or participation restriction' (p.3), corresponding to dysfunctioning at the three levels of functioning, respectively.[101] The ICF acknowledges that every individual can experience a decline in health, and in consequence, undergo some levels of disability.[110] At the body and body part level, impairments are defined as abnormalities in body functions or structures.[101] At the person level, activity limitations are the difficulties for an individual to accomplish a task or action.[101] At the societal level, participation restrictions refer to an individual's problems of involvement in life situation.[101]

Contextual factors are broadly defined as an individual's entire background.[101] Environmental factors comprise the physical, social and attitudinal environment; whilst personal factors include an individual's characteristics other than health and the his/her particular background of life and living.[101]

In addition, the ICF distinguishes 'capacity' and 'performance'. 'Capacity' indicates 'the highest probable level of functioning that a person may reach in a given domain at a given moment' (p.15).[101] 'Performance' describes 'what an individual does in his or her current environment' which involves 'the lived experience of people in the actual context in which they live' (p.15).[101]

The ICF views disability as an interaction between an individual's health condition and contextual factors, without implying a causal pathway.[101] However, the ICF fails to distinguish activities and participation clearly[15,104,109] or incorporate quality of life[15]; it is inherently a classification system rather than a dynamic model.[15]

One common feature of the Nagi model and the ICF is that they both classify the disablement process from the body level, whole organism level, and societal level.[111] Describing functioning and disability as an umbrella term in the ICF causes some confusion.[104] Additionally, the ICF fails to separate physical, cognitive, and emotional functioning from activities, and accomplishment of activities is built upon these functioning domains.[104]

2.3.1.4 Late-life disablement process

Schoeni *et al.*[97] conceptualised the disablement process in late-life using a life-course perspective. The three stages of disability in late-life are borrowed directly from the Nagi model. Accommodation, which can moderate or modify disability in late-life, is 'actions that people take in response to their limitations, such as changing their behaviour, using assistive or mainstream technology, or relying on personal care' (p.53).[97] Medical, behavioural, economic, social, and environmental factors have a reciprocal relationship with health in early-life, mid-life, and late-life; these factors contribute to form biological and social 'chains of risk'.[97] In other words, factors in early, middle, and late stages of life, directly or indirectly influence the disablement process in late-life through forming a chain of risk. Schoeni and colleagues[97] urged formal assessments and tests of the late-life disablement framework, especially in terms of early-life and mid-life factors and environmental factors.

Although these models of disability presented above differ in important aspects, they aim to describe the process of loss of human functioning. Despite disparities in the categorisation of human functioning, physical functioning is the one key domain in common to all models.[104,112,113] The models of disability, therefore, are useful for understanding the process of loss of physical functioning and its determinants and risk factors.

2.3.2 Physical functioning and its building blocks

Due to the ambiguous and confused definition of functioning in the ICF, it is important to clarify the concept of physical functioning in more detail.

2.3.2.1 Defining physical functioning

Halter and Reuben[112] defined physical functioning, in a strict sense, as voluntary motor function. Because of the absence of a clear universal definition, researchers' understanding of physical functioning depends considerably on the measurement instruments they choose.[113] Various labels of physical functioning are used in literature, such as physical capacity/ability, functional capacity/ability, physical fitness, physical performance, and functional status.[114]

There are a number of definitions. For example, Nagi[105] defined physical functioning as 'sensory-motor functioning of the organism as indicated by limitations in such activities as walking, climbing, bending, reaching, hearing, etc.' (p.441). Stewart and Kamberg[115] described physical functioning as 'the performance of or the capacity to perform a variety of physical activities normal for people in good health. Such physical activities include bathing, dressing, walking, bending, climbing stairs, and running' (p.86). Painter[116] argued that the best definition of physical functioning is a person's 'ability to perform activities required in their daily lives' (p.219). Rantz *et al.*[113] concluded that physical functioning 'represents a person's current abilities to participate in daily activities relating to different social roles' (p.6).

According to these various definitions, physical functioning has been commonly interpreted as a person's ability to perform simple physical movements (e.g., walking and standing), activities of daily living (ADLs, e.g., dressing, bathing and toileting), and instrumental activities of daily living (IADLs, e.g., shopping, cooking and handling money).[113]

2.3.2.2 Building blocks of physical functioning

Built upon the Nagi model, Rikli and Jones[117] proposed a functional performance framework, in which physical functioning is in a hierarchical nature from physical parameters to functions and activity goals. Activity goals require functions to accomplish; likewise functions require physical strength, endurance, flexibility, and motor ability to be carried out effectively. Dysfunctioning in terms of physical

parameters, functions, and activity goals, reflects physical impairment, functional limitations, and physical disability/independence, respectively.[117]

Halter and Reuben[112] further dissected physical functioning by increasing levels of integration that tasks and activities require to accomplish. This framework not only overlaps with current conceptual models of disability, but also is in harmony with existing measures of physical functioning.[112] Along with increasing levels of integration, physical functioning is divided into: basic components (strength, balance, coordination, flexibility and endurance), specific physical movements, goal-oriented activities (ADLs and IADLs), and personal choices of role. The five basic components of physical functioning are not functional tasks per se; instead, they are essential elements necessary for activities to be completed at higher levels of integration.[112] Besides physical capacity, several other determinants such as cognitive functioning, physical environment, and perceived self-efficacy, can moderate how basic components integrate into higher levels of physical functioning.[112] Dysfunctioning in terms of basic components, specific physical movements, and goal-directed activities, roughly corresponds to impairments, functional limitations, and physical disability, respectively. Inability to perform activities at the highest level of integration, indeed represents limitations in role functioning rather than pure physical functioning.

2.3.3 Measuring physical functioning

Measures of physical functioning are usually categorised into self-reports and performance-based tests.[15,111,113,118-121] To be consistent with the Nagi model, measures of physical functioning will be introduced in the following order: 1) measuring impairments and functional limitations; 2) measuring disability; and 3) measuring general health status. Several important issues should be kept in mind. First of all, since physical components, to a varied extent, are required in most of activities of life, in theory all activities could be included to measure physical functioning.[114] Second, most measures of physical functioning are based on the Nagi model, viewing functional limitations as linking impairments and disability.[122] It is not always straightforward to identify which specific concept is captured by a given

item or measurement instrument.[118] Third, due to the definitions described above, impairments and functional limitations can be measured within individuals; however, disability cannot be measured solely within an individual because disability involves social roles and expectations towards tasks and activities.[121]

2.3.3.1 Measuring impairments and functional limitations

In the light of the functional performance framework, impairments are defined as abnormalities or deviations in physical parameters. Impairments can be detected by testing range of motion, maximal oxygen consumption, muscle strength, balance and so on, and are usually measured by physical performance tests.[111,120,121,123,124] For example, grip strength is usually measured by a dynamometer.[111,119] Maximal oxygen consumption can be measured by a cycle ergometer.[124,125] Balance can be measured by standing tandem, semi-tandem, and side-by-side.[126]

Functional limitations involve a person's ability to perform basic actions (e.g., walking, climbing stairs and reaching; they are necessary for daily living tasks),[104] but do not indicate the real environment of the person's functioning.[118] Functional limitations can be measured by both self-report and performance-based tests,[118,123] and items included in various scales vary widely.[122]

As discussed above, it is difficult to differentiate impairments and functional limitations unequivocally; in fact, many instruments measure both. For instance, the Berg Balance Scale[127] assesses balance by tasks capturing impairments (e.g, tandem stand, stand unsupported and single-leg stand) and functional limitations (e.g., transfer from chair to chair, sit to stand, and reach forward with outstretched arm). The Physical Disability Index (PDI)[128] contains tasks of impairments such as range of motion (e.g., elbow/knee extension and flexion, shoulder flexion and rotation), muscle strength (e.g., grip strength and strength of specific groups of muscles with certain poses), balance, as well as tasks of functional limitations such as chair stand, chair transfer, and roll over the bed.

Regarding self-reported measures of functional limitations, the Physical Performance Scale includes questions relating to difficulties in lifting/carrying weight of 10 pounds, using hands and fingers, reaching with either/both hands, standing for long periods, going up/down stairs, walking, stooping, and bending/kneeling.[105] The Late-Life Function and Disability Instrument requires respondents to report their difficulties on comprehensive tasks and activities of upper and lower extremity functions, attempting to capture a full spectrum of gross and fine motor function.[129]

Performance-based tests of functional limitations can be in the form of individual tests and batteries of tests.[118] Most of the batteries measure functional limitations as well as impairments and disability.[118] For example, the 6-minute walk can be regarded as a test of exercise tolerance reflecting impairments rather than functional limitations; simulated eating and putting on a shirt, when measured in a standardised way (diminishing possible adaptions provided by home environment) assess functional limitations instead of disability.[118]

Individual tests can be grouped by assessing upper extremity function (e.g., pegboard test, picking up an object, and lifting 10 pounds), and assessing lower extremity function (e.g., gait speed, chair rise, and up-and-go test).[118] Gait speed is measured by walking a relatively short distance without factoring in endurance.[130] The distance walked varies in studies,[111,131] such as 8 foot,[126] 4 meters,[132] 9 meters,[125] and 9.8 meters.[133] Factoring in endurance, 2-minute, 6-minute, and 12-minute walking tests are also applied in studies.[111,131,134,135] Chair rise is used to evaluate lower body strength,[111] such as 5 chair stands[126] and 30-second chair stand[136]. The Timed Up and Go test (TUG)[137] combines chair rise and gait speed;[118] the time a subject spends to complete a series of movements is recorded: stand up from an armchair, walk 3 meters, turn, walk back to the chair, and sit down.

The Jebsen Hand Function Test (JHFT)[138] is a standardised battery of hand function, covering tasks of writing short sentences, turning over cards, picking up small objects, simulated eating, and moving empty/weighted large cans. Guralnik *et al.*[126] developed a Short Physical Performance Battery (SPPB) to measure lower extremity function by testing standing balance (tandem, semi-tandem and side-by-side), 8-foot

walking, and 5 chair rises. SPPB is recommended in use of older populations given its high validity, reliability, and responsiveness, compared with other batteries.[139]

2.3.3.2 Measuring disability

Since the nature of disability involves role participation and interaction between the person, cultural expectations and environment,[104,121] disability is most commonly assessed by limitations to perform activities of daily living and instrumental activities of daily living.

2.3.3.2.1 Activities of daily living (ADL) scales

ADLs are 'basic personal care tasks of everyday life',[140] with characteristics of being: universal to all people, performed almost every day, and tend not to vary between men and women or different lifestyles.[15] The Index of ADL,[141,142] an early developed ADL scale, included six activities of bathing, dressing, toileting, transfer, continence and feeding (with a descending order of complexity), to represent human's 'primary biological functions'. The Index of ADL was developed based on a theoretical judgement that loss of physical functioning is in a hierarchical order starting with complex functions to basic ones.[141,142] Most of ADL scales have been created after the Index of ADL, in spite of some variation, commonly include bathing, dressing, going to toilet, transfer, feeding, plus mobility (e.g., walking and going outside).[140] In the US national surveys, five ADLs are usually included: eating, dressing, bathing, transfer from bed to chair, and using the toilet.[143] McDowell[144] criticised most ADL scales on the basis of not being developed on a theoretical judgement and lacking tests of validity and reliability; among them, the Index of ADL, Physical Self-Maintenance Scale,[145] and Medical Outcome Study (MOS) Physical Functioning Measure[115] were advisable for population surveys.

Since ADLs capture only severe disability and do not include the full range of activities necessary for living independently;[111,123,143,144,146,147] ADLs are less able to capture variations of physical functioning in the general population.[111,129] A ceiling effect is usually reported when applying ADL scales in the general population living in the community.[144] To address these weaknesses, the MOS Physical Functioning

Measure assesses a range of activities.[115,144] It encompasses three parts: 1) physical function (PF-10); 2) satisfaction of own physical ability; and 3) use of public transport and travel around the community.[115] The PF-10 is comprised of 10 items regarding vigorous and moderate activities, light activities, mobility, and self-care tasks, allowing the evaluation of a wider spectrum of physical functioning.[115,144] Limitations in these items included in the PF-10 reflect both functional limitations and disability. McDowell[144] concluded the MOS Physical Functioning Measure as a 'well-established set of ADLs and mobility', and it tends to measure relatively 'pure' physical functioning independently from different life situations.

2.3.3.2.2 Instrumental activities of daily living (IADL) scales

To capture the activities necessary for people living in the community, Lawton and Brody[145] proposed to measure IADLs, including activities of cooking, shopping, housekeeping, doing laundry, using transport, taking medications, handling money, and using a telephone. IADLs are household activities,[15,111,148] whereas ADLs are self-care activities.[140]

A number of IADL scales have been developed to satisfy specific research interests; the majority of them cover cooking, followed by doing housework, shopping and doing laundry, while few of them include taking medications, work or using a telephone.[148] Fillenbaum[149] claimed that being able to cook, shop, do housework, handle money, and get to places out of walking distance, meet the criterion of living independently in the community. McDowell[144] concluded that the Functional Assessment Questionnaire[150], and scales combined ADLs and IADLs such as Lambeth Disability Screening Questionnaire[151] and Disability Interview Schedule[152], were suitable for most population survey purposes.

Compared with ADLs, IADLs are more complex, able to capture less severe disability, and most importantly, they do not purely mirror physical functioning but also reflect cognitive functioning.[111,140,144,148] For example, handling money and using telephone require higher cognitive functioning than ADLs.[148] In addition, IADLs tend to be influenced by social, cultural and environmental factors;[15,123] for

instance, cooking and doing housework involve social role besides physical functioning.[144]

2.3.3.3 Measuring general health status

Instruments of general health status, also known as instruments of health-related quality of life (QoL) have been growingly used in research, which at least measure physical, emotional and social dimensions of health.[144] Amidst a number of general health status/QoL instruments, McDowell[144] recommended the Sickness Impact Profile,[153] Nottingham Health Profile,[154] Short-Form-36 Health Survey (SF-36),[155] Health Utilities Index,[156] and European Quality of Life[157] for use in population surveys.

The SF-36 is a leading instrument of general health status in research, consisting of eight commonly measured dimensions of health: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health.[155,158] The former four comprise a summary measure of physical health; the latter four make up a summary measure of mental health. The PF-10 in the MOS Physical Functioning Measure is kept entirely as the subscale of physical functioning in the SF-36.

2.3.3.4 Self-reports versus performance-based tests

Performance-based tests of physical functioning have evident advantages over self-reports; for instance, they are more objective, sensitive and accurate,[113] are able to capture the full spectrum of both gross and fine motor function, have better reproducibility and responsiveness,[121,129] are sensitive to changes over time,[120,159] and diminish the influences of cognitive functioning, culture, language and education.[159] However, performance-based tests are also more time consuming, require special equipment and trained examiners, and may cause potential injuries.[159] Self-reported measures have been shown to be reliable and accurate,[129] less costly, easier to administer and do not need trained examiners[120]. According to Myers *et al.*[131], performance-based tests do not appear to be superior to self-reports in terms of psychometric properties, acceptance by respondents or interpretation.

In fact, the two types of measures usually capture different aspects of physical functioning: self-reports involve an individual's own perception on his/her ability to perform physical activities in their real environment, which are affected by various factors ('perform' in the ICF); performance-based tests do not measure physical functioning in real-life context ('capacity' in the ICF).[120] When measuring the same concept in the Nagi model, the two types show a moderate to strong correlation.[120]

2.3.4 Determinants and risk factors of disability and physical functioning

Decline in physical functioning in late-life is, to a great extent, a consequence of physiological changes and onset of diseases related to ageing, modified by medical care, socioeconomic, psychosocial and behavioural factors.[16,17] Diseases, acting independently or together, are established risk factors for physical disability: about half of disability in late-life develops progressively over time depending on the underlying severity of disease, comorbidity and frailty; the other half develops acutely related to catastrophic clinical events such as hip fracture or stroke.[16,160]

Although physical functioning is conceptualised to decline linearly with increasing age,[73] Guralnik *et al.*[161] found the risk of mobility loss doubled with every 10-year age increase. Similarly, Peeters *et al.*[75] reported a non-linear decline in the PF-10 scores among women: the rate of decline did not vary among women aged 45–75 years, but it doubled among those aged 76–81 years and tripled among those aged 82–90 years; the PF-10 score declined more rapidly in women with lower physical functioning. In contrast, Nelson *et al.*[25] showed that physical functioning, measured by both self-report and performance tests, was associated with age linearly.

Stuck *et al.*[162] reviewed 78 longitudinal studies published between 1985 and 1997 on factors associated with decline in functional status (defined by ADLs and IADLs) among community-dwelling older adults. They identified chronological age as the most important factor of functional decline, which was supported by other studies.[43,52,163] Manini[164] argued that it is challenging to estimate the effect of age on physical functioning independent of chronic diseases, since the disablement process is closely related to both age and chronic diseases.

Compared with men, reported by Beckett *et al.*[165], women had lower physical functioning and a faster decline with increasing age. A meta-analysis of eight cohorts also demonstrated that physical performances declined with age, and men performed better in grip strength, chair rise and balance than women.[166] A similar gender difference was found in the Health and Retirement Study (HRS) and Health Dynamics Among the Oldest Old (AHEAD) study as well.[54]

Stuck and colleagues[162] also reported a number of factors other than age which were associated with functional decline, including cognitive impairment, depression, chronic diseases (or comorbidity), change of body mass index (BMI), lower extremity functional limitations, poor social contacts, physical inactivity, non-drinking, poor self-rated health, smoking, and vision impairment. A more recent systematic review by Tas *et al.*[167] synthesised evidence on prognostic factors of disability among the elderly (defined as limitations in ADLs and IADLs). They reported strong evidence on increasing age and cognitive impairment with disability; moderate evidence on poor self-rated health and visual impairment; and limited evidence on income, marital status, social networks, BMI, physical activity and hospitalisation.[167]

To date, numerous studies have documented that poor and/or loss of physical functioning is associated with female gender,[39,52,54] smoking (former or current smoking),[25,31,36,40,41,46,47,52,56,60,62,168,169] unhealthy diet,[31,40,46,169] higher BMI or obesity,[27,31,34,40,41,43,47,52,56,62,168] physical inactivity,[25,27,31,33,35,39,40,46,47,52,55,60,62,168-171] CVD,[31,36,43,52,55,161,170] hypertension,[52] musculoskeletal diseases or joint complaints,[31,43] hip fracture,[52,161,170] chronic bronchitis/emphysema or poorer lung function,[31,39] arthritis,[43,52] diabetes,[52,55] cancer,[52,161] chronic kidney disease,[36] number of comorbid medical conditions,[33,43,161,170] use of medications,[43] depression,[33,43,52,55,170] hearing impairment,[52] cognitive impairment,[43,52,171] worse social networks,[27,52,170] widowhood or being unmarried,[27,31,54] lower emotional support,[39] and lower socioeconomic position (SEP)[33,36,39,41,52,56,60,161,170].

Independent of medical conditions (e.g., CVD, cancer, hypertension, diabetes, arthritis, bronchitis and asthma), Ebrahim *et al.*[172] found smoking, obesity, physical

inactivity, and heavy drinking in mid-life were predictive of locomotor disability in late-life. Abbott *et al.*[64], however, reported that only stroke and past drinking were strongly associated with developing limitations in ADLs in older Japanese adults; no association was observed for smoking, BMI, total cholesterol, diabetes, blood pressure or myocardial infarction.

Using data from the HRS, Freedman *et al.*[173] showed that ADL and IADL limitations in late-life were related to age, education, lifetime occupation during mid-life, as well as late-life factors including income and wealth, smoking, and a number of medical conditions (e.g., hypertension, diabetes, cancer, lung disease, heart disease, stroke, psychiatric disorder, arthritis, obesity, vision and hearing impairment).

Ferrucci *et al.*[160] summarised these potential risk factors and determinants of physical functioning into: 1) behavioural risk factors and individual characteristics (including heavy and no alcohol consumption, low physical activity, smoking, high/low BMI, increased age, low SEP, high medication use, poor self-rate health and reduced social contacts); and 2) chronic conditions (including CVD, osteoarthritis, hip fracture, diabetes, chronic obstructive pulmonary disease, cancer, visual impairment, depression, cognitive impairment and comorbidity). Urbano-Marquez and Fernandez-Sola[174] reported in their review that high alcohol intake was associated with acute alcoholic myopathy (mainly among men with heavy episodic drinking) and chronic alcoholic myopathy (among both men and women with long-term high alcohol intake). The damages to muscle fibres caused by heavy drinking may directly impair an individual's muscle strength, as well as physical functioning at higher integration level such as walking, climbing stairs, lifting or carrying heavy objects, and dressing and bathing (see Section 2.3.2.2).

2.4 Alcohol and Health

Among health behaviours, alcohol plays a major role in many health outcomes. The relationship between alcohol and health is complex and multidimensional.[175,176] Alcohol consumption has been documented to be adversely associated with more than 60 health outcomes.[177-181] However, a J-shaped relationship has been reported

between alcohol consumption and all-cause mortality and CVD.[177-181] In spite of plausible biological mechanisms, the J-shaped relationship is subject to several methodological issues.[182,183] An apparently L-/J-shaped relationship has also been observed between alcohol consumption and physical functioning, and the methodological problems are likely to be similar.

2.4.1 Terminology related to alcohol consumption

The WHO defined abstinence as 'refraining from drinking alcoholic beverages, whether as a matter of principle or for other reasons' (p.4).[184] In population surveys, current abstainers, often are defined as individuals who have 'not drunk an alcoholic beverage in the preceding 12 months' (p.4).[184]

Moderate drinking is an often ill-defined term. It is used to describe a pattern of drinking that does not cause problems compared with heavy drinking.[181] The term of 'low-risk drinking' may be preferred.[181] According to the US National Institute on Alcohol Abuse and Alcoholism (NIAAA), moderate/low-risk drinking is defined as: ≤4 drinks on any single day and ≤14 drinks per week for men; ≤3 drinks on any single day and ≤7 drinks per week for women.[185] In the US context, a standard drink contains 14 grams (g) of pure alcohol.[186]

Heavy episodic drinking (HED), defined by the WHO, is 'drinking at least 60 grams or more of pure alcohol on at least one occasion in the past seven days' (p.16).[5] Another widely used cut-off of HED is ≥5 drinks for men and ≥4 drinks for women on a single occasion.[187] A similar term, binge drinking, is also used frequently in literature. According to NIAAA, binge drinking is a pattern of drinking that brings blood alcohol concentration to 0.08 g/dL in about 2 hours, which, for a typical adult, corresponds to ≥5 drinks for men and ≥4 drinks for women.[188]

The WHO defined alcohol dependence as a cluster of physiological, behavioural, and cognitive phenomena, in which the use of alcohol takes on a much higher priority for a person than other behaviours that once had greater value.[189] A central descriptive characteristic of alcohol dependence syndrome is the desire to drink alcohol.[189]

According to the WHO recommended diagnostic criteria for research,[190] dependence syndrome is diagnosed by at least three of following manifestations together for at least one month: 1) 'a strong desire or sense of compulsion to take the substance'; 2) 'impaired capacity to control substance-taking behaviour in terms of onset, termination or level of use'; 3) 'a physiological withdrawal state when substance use is reduced or ceased'; 4) 'evidence of tolerance to the effects of the substance'; 5) 'preoccupation with substance use'; and 6) 'persisting with substance use despite clear evidence of harmful consequences' (p.70). The term, 'alcohol abuse', should be used as a residual category when alcohol dependence is not applicable but alcohol intake is above recommended limits.[181]

2.4.2 Measuring alcohol consumption

At individual level, alcohol consumption can be assessed by self-reported and objective measures; self-reports are further divided into measuring 'customary/usual drinking habits' and measuring 'recent drinking occasions'.[191] Different measures may give systematically different estimates of mean alcohol consumption.[192] Given the diverse research objectives and interests in studies, there is no consensus on the 'best' measure of alcohol consumption.[193,194]

2.4.2.1 Self-reported measures

Self-reported measures of alcohol consumption are generally reliable,[194-197] correlated with 'true' alcohol consumption,[195] relatively inexpensive, non-invasive, and acceptable to respondents.[196] Rehm[194], however, criticised the widely used self-reported measures for lacking formal tests of reliability. Survey estimates of alcohol consumption usually cover only about 50% of sales data of alcohol, probably due to under-reporting.[192,198]

Measures of 'customary/usual drinking habits' assess an individual's 'central tendency' of drinking behaviour in terms of his/her customary drinking quantity and customary drinking frequency.[191] Measures of 'recent drinking occasions' capture both 'central tendency' and 'variability' of drinking, by asking respondents to report their quantities consumed on recent occasions.[191] Measures of 'customary drinking

habits' require respondents to average their drinking frequencies and quantities;[191,196,198] the same task is done by researchers using measures of 'recent drinking occasions'.[191]

2.4.2.1.1 Measuring customary drinking habits

This approach is also known as summary measures of alcohol consumption.[198,199] Both quantity-frequency and graduated frequency measures fit in this category.

Quantity-frequency

The quantity-frequency (QF) measure, in the basic form, is composed of two questions: respondent's usual drinking frequency and usual drinking quantity per occasion or per day during a given reference period (e.g., 1 week, 1 month, or 12 months); total drinking volume is obtained by multiplying usual frequency with usual quantity.[191,196,200] Extended forms of the QF vary: beverage-specific (wine, beer and spirits); work days and weekend separately; different drinking situations (e.g., at home and at a bar); inclusion of an additional question on risky single occasion drinking (≥5, ≥8 or ≥12 drinks per occasion or day);[191] or additional questions of maximum quantity and corresponding frequency.[201] Food frequency questionnaires (FFQ), commonly used in studies the primary research interest of which is not alcohol, include questions relating to the frequency of consuming a predefined typical drink (beverage-combined or beverage-specific).[191]

The QF is simple and easy for respondents to complete,[202] and is a useful tool when a quick measure of drinking is needed.[196,201] However, the basic QF is not able to capture within-individual variability of drinking,[191,196,197,200,201,203] although the extended QFs may do it to a limited extent.[191,203] For both quantity and frequency, respondents tend to report the mode instead of the mean.[191,196,200,202-204] Respondents may over-report their drinking by not taking non-drinking periods into account.[191,196] Under-report may also occur.[191,202,205,206] The usual drinking quantity tends to be under-reported because heavy drinking occasions are likely to be disregarded by respondents.[202,205] The usual drinking frequency is also possibly underestimated

when drinking frequency is positively skewed (e.g., more periods with lower frequencies versus higher frequencies).[191,206] Reporting alcohol intake accurately using the QF is especially problematic for infrequent drinkers.[191,203] Knibbe and Bloomfield[198] argued that the unreliability of the QF is greater in those whose drinking pattern is not on a daily basis compared to regular/mostly daily drinking.

Graduated frequency

The graduated frequency (GF) measure includes questions that ask respondents to report their drinking frequency over several bands of drinking quantity in a descending order starting from the heaviest.[191,196,204] In essence, the GF attempts to obtain a series of QFs at various levels of drinking quantity.[202] Drinking volumes at each quantity level are summed to derive the total drinking volume. The GF is widely used, especially in North America.[204] Three types of the GF are commonly used in research: beverage-combined, beverage-specific, and paper-and-pencil GF.[202] The GF can capture the within-individual variability of drinking,[191,203,206] and assess drinking pattern directly.[202,206]

The GF works better among light drinkers and among respondents with adequate cognitive skills.[204] Some respondents may not intend to or not be able to convert their actual drinks to the defined standard drink.[196] The GF provides the frequency of risky single drinking occasion directly.[204,206] Compared with the QF and weekly drinking recall, the GF performs better in identifying harmful/hazardous drinking because it is more effective at capturing heavy drinking occasions.[201,203,205] For drinkers whose heaviest drinking quantity is greatly over the presumed mid-point of the highest level of quantity in the GF, Dawson[193] advocated asking an additional question about the largest number of drinks and corresponding frequency.

The GF suffers from several drawbacks: 1) much longer administration time than the QF;[201] 2) relatively high response burden as respondents are required to remember all their drinking occasions over a long-period, usually 12 months, and distribute their total drinking days correctly over different levels of drinking quantity;[191,203,204] 3) annual drinking days may be over 365 (e.g., due to poor math or double-

counting).[191,193,202-204,206] This can be corrected by capping (accept drinking days beginning with the heaviest level of quantity until 365 days are reached);[191,206] 4) difficult for respondents to understand that the various levels of drinking quantity are mutually exclusive;[203] and 5) some respondents tend to report frequency to only one level of quantity.[203]

The measures of 'customary drinking habits', as retrospective measures, are prone to recall bias caused by forgetting or confusing drinking events.[197] Since asking about beer, wine and spirits separately aids respondents to recall their drinking, the beverage-specific approach usually yields higher drinking volume than beverage-combined.[191,193,194,202] However, neither total drinking days nor average quantity per occasion/drinking day is derivable by the beverage-specific approach, because the combination of beverages in a given occasion is unknown.[191,193,203] In general, for societies and countries dominated by a regular drinking pattern, the 'customary drinking habit' approach should yield a mean drinking volume close to the 'true' volume, since the individual distribution of drinking quantity across occasions is almost constant.[191]

In addition to the QF and GF, owing to the great interest of heavy episodic drinking, some 'binge drinking' measures have been developed, such as the frequency of risky single occasion drinking (e.g., ≥5 drinks for men and ≥4 drinks for women), frequency of drunkenness, and maximum amount drunk in any day during the reference period.[202]

2.4.2.1.2 Measuring recent drinking occasions

This approach is also known as actual consumption measures[198] and short-term recall measures[194]. Recent drinking occasions can be measured by: 1) most recent drinking occasions approach by listing drinking quantity in the last few occasions, usually 1–4 occasions; 2) survey period approach by listing drinking quantity in all drinking occasions over a specific period, usually one week; the period can be individually varied by allowing 4–5 occasions to occur; 3) retrospective and prospective diaries, usually in a short period (e.g., 1 week); and 4) timeline follow-back (TLFB) which

requires respondents to recall their daily drinking with a calendar and memory aids provided.[191] The prospective diary is often used to validate retrospective measures;[191] but it has a high response burden and lacks compliance from respondents when a longer study period is adopted,[197] and respondents' drinking behaviour may change as a result of the measurement.[196] The retrospective diary can be viewed as a series of 24-hour recall.[194]

The measures of 'recent drinking occasions' are easy to administer and for respondents to understand,[204] and have greater face validity than the 'customary drinking habits' measures.[196] They diminish recall bias by using a short reference time,[196] and minimise under-reporting therefore have a higher coverage of sales data.[204] On the other hand, the short reference period may not be long enough for infrequent drinkers to report any drinking occasions, resulting in an overestimation of abstinence and less indicative of long-term drinking behaviour.[191,193,194,196-198,204] This issue can be addressed by applying individually varied recall period, but differential errors may occur because less frequent drinkers have a longer recall period and may suffer larger slips of memory.[191,194] In fact, Rehm[194] argued that recall may only be reliable for 2–3 days, and a short reference period of even one week is subject to some magnitude of recall error. Rare and periodical heavy drinking occasions are also likely to be overlooked within a short period.[191]

2.4.2.2 Objective measures of alcohol consumption

Laboratory tests of alcohol-related biomarkers, as the objective measures of alcohol consumption, are mainly applied in clinical and primary care settings for screening of alcohol use disorders and chronic heavy drinking.[191] Alcohol concentration from blood, breath or urine measures alcohol directly.[207,208] They are easy to perform and widely used in screening and follow-up of abstinence, particularly for possible alcohol intoxication.[191,209] By reason of fast metabolism of alcohol in human body system, blood alcohol concentration (BAC) is only a good marker of recent alcohol use.[191,210,211] Moreover, it is not suitable for large-scale surveys which require high compliance from respondents to take regular samples.[191]

Many other biomarkers and objective measures of alcohol consumption have also been used: 1) traditional biomarkers: liver enzymes such as gamma-glutamyl transpeptidase (GGT), alanine aminotransferase (ALT) and aspartate aminotransferase (AST); abnormalities related to blood cell such as mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH); and carbohydratedeficient transferrin (CDT); 2) less well established biomarkers such as acetaldehyde adducts, 5-hydroxytryptophol (5-HTOL)/5-hydroxyindole-3-acetic acid (5-HIAA) ratio, ethyl glucuronide (EtG), ethyl sulphate (EtS), phosphatidylethanol (PEth), and fatty acid ethyl esters (FAEE); and 3) alcohol sensor devices such as secure continuous remote alcohol monitor (SCRAM) and transdermal alcohol sensor/recorder (TAS).[207-209,212] Gmel and Rehm[191] advocated to use TAS as it is non-invasive and able to monitor recent alcohol consumption for a long time, but they also acknowledged that transdermal ethanol is affected by many other factors besides BAC.

2.4.2.3 Measures of alcohol abuse and dependence

Several instruments have been developed to identify alcohol dependence; for instance, the AUDIT (Alcohol Use Disorders Identification Test)[213], CIDI-SAM (Composite International Diagnostic Interview Substance Abuse Module)[214], and shorter questionnaires such as the 5-item AUDIT,[215] CAGE (cut-down, annoyed, guilt, eye-opener),[216] MAST (Michigan Alcoholism Screening Test),[217] B-MAST (Brief MAST)[218], SMAST (Short MAST)[219], and TWEAK (tolerance, worry, eye-opener, amnesia, kut down)[220]. In older populations, the CAGE is the most widely used instrument,[221,222] following by MAST and its variants, then AUDIT and its variants.[222]

Bloomfield *et al.*[204] recommended the CIDI as a diagnostic instrument for alcohol dependence and the AUDIT as a screening instrument. The AUDIT contains questions about binge drinking, dependence symptoms, alcohol-related problems, and the quantity and frequency of alcohol use, seeking to detect a broad spectrum of alcohol disorders.[213] The CAGE includes four questions about cutting down on drinking, being annoyed by others' criticisms, feeling guilty, and having a drink first

thing in the morning (eye-opener).[216] The MAST includes questions about both drinking behaviour and alcohol-related problem.[217,223]

A systematic review by Fiellin *et al.*[224] revealed that the AUDIT outperformed the CAGE, the single risky drinking occasion (≥5 drinks) and even some biomarkers, to accurately detect less severe alcohol problems (e.g., at-risk, harmful and hazardous drinking), with a sensitivity of 57%–97% and specificity of 78%–96%. However, the CAGE is useful for its brevity and simplicity.[221] Fiellin *et al.*[224] showed that the CAGE performed better in detecting alcohol abuse and dependence than the AUDIT and SMAST, with a sensitivity of 43%–94% and specificity of 70%–97%. In contrast, Reid *et al.*[223] reported a better sensitivity but worse specificity of the MAST (sensitivity: 90%–98%; specificity: 57%–82%), compared with the CAGE when using a cut-off of ≥2 positive responses (sensitivity: 73%–81%; specificity: 89%–96%). According to a meta-analysis, using the recommended cut-off of ≥2 positive responses, the CAGE had a limited diagnostic value for alcohol abuse and dependence.[221]

2.4.3 Consequences of alcohol consumption on health

Detrimental effects of alcohol consumption have been found on many health outcomes,[177-181] via both average volume and patterns of drinking.[175,176] As a known toxic substance, alcohol causes organotoxicity, carcinogenicity, teratogenicity, hepatotoxicity, neurotoxicity, and exerts adverse effects on immunological system, through ethanol, its metabolites, and reactions with constituents of the body.[177,225]

A number of studies have demonstrated that alcohol consumption is associated with intentional and unintentional injuries (e.g., violence, drinking and driving, and suicide), mental and behavioural disorders (e.g., alcohol dependence, anxiety, depression and epilepsy), gastrointestinal conditions (e.g., liver cirrhosis, pancreatitis, and gall bladder and bile duct disease), cancers (e.g., liver cancer and breast cancer), CVD (e.g., hypertension, coronary heart disease, stroke, and cardiomyopathy), immunological disorders (increased susceptibility to pneumonia and tuberculosis), lung diseases (e.g., acute respiratory distress syndrome), skeletal and muscular

diseases (e.g., fracture), reproductive disorders (impaired fertility) and pre-natal harm (e.g., prematurity and low birth weight), most of which are in a dose-response relationship that the risk increases with increasing dose of alcohol.[175,177-179,181,226-230] The few exceptions that alcohol shows some beneficial effects on are coronary heart disease (CHD), ischaemic stroke, diabetes, dementias, and cholelithiasis.[175,181]

Rehm *et al.*[176] conceptualised the pathway from alcohol consumption to its long-term health and social consequences. Three intermediate mechanisms are identified: direct biochemical effects, intoxication, and dependence. Independent of alcohol intoxication and dependence, direct biochemical effects are mainly associated with chronic diseases, covering all the toxic and beneficial effects of alcohol on organs or tissues. Intoxication is mainly linked to acute outcomes. Dependence plays an important role in both acute and chronic consequences via maintaining alcohol consumption.[176,179] In a revised model, Rehm *et al.*[175] added the quality of alcoholic beverages as it may affect health and mortality, although it seems to have less impact from a public health perspective.

All-cause mortality is the best single health indicator for severe consequences of alcohol consumption.[231,232] Several meta-analyses of prospective studies have been reported a J-shaped relationship between alcohol consumption and all-cause mortality.[231-236] This dose-response relationship reflects a balance between the beneficial effects of light-to-moderate drinking on CHD and ischaemic stroke and the detrimental effects of alcohol consumption on other 50 diseases.[232,233] A meta-analysis by Di Castelnuovo *et al.*[236] showed a J-shaped curve between alcohol consumption and all-cause mortality in both men and women: drinking ≤25 g of alcohol per day in women and ≤42 g of alcohol per day in men were associated with a lower relative risk of all-cause mortality, compared with non-drinking; the maximum risk reduction was 17% in men and 18% in women, respectively.

White *et al.*[234] found that the shape of the curve between alcohol consumption and all-cause mortality was modified by age: a linear curve appeared at young age and a J-shaped curve was seen at age of 35–55 years. Gronbæk *et al.*[237] examined the relationship between change of alcohol consumption over approximately 5 years and

all-cause mortality and reported: 1) a J-shaped curve among subjects with stable drinking behaviour; and 2) a higher risk of death among subjects who transited towards heavy drinking compared with stable subjects, mainly contributed to cancer mortality. Rehm *et al.*[231] argued that pattern of drinking is usually not examined in studies and this may moderate the association between alcohol consumption and all-cause mortality.

A number of meta-analyses also have been carried out to synthesise evidence on alcohol consumption and CVD, and they have reported a J-shaped relationship.[38,226,229,238-240] By pooling results from 28 high-quality cohort studies, Corrao *et al.*[226] derived a J-shaped curve between alcohol consumption and relative risk of CHD: the nadir was 20 g/day, the protective effect was shown up to 72 g/day, and the harmful effect emerged at 89 g/day. In the meta-analysis by Ronksley *et al.*[240], compared with non-drinking, drinking 2.5–14.9 g/day was consistently associated with a 14%–25% reduction in the risk of CVD mortality, incident CHD, CHD mortality, incident stroke, and stroke mortality; the nadir was lower for stroke (2.5–14.9 g/day) than CVD and CHD (25–29.9 g/day). The protective effect of light drinking was found on ischaemic stroke but not on haemorrhagic stroke.[240]

Studies have investigated the plausible biological mechanisms of these J-shaped relationships. A review reported that light-to-moderate alcohol intake was associated with increased high-density lipoprotein cholesterol (HDL-C), decreased low-density lipoprotein cholesterol (LDL-C), decreased plasma apolipoprotein(a), increased plasma apolipoprotein AI, reduced blood clotting and platelet aggregation (e.g., decreased plasma fibrinogen concentration and reduced blood platelet aggregability), reduced insulin resistance and increased insulin sensitivity, reduced blood pressure, and increased serum paraoxonase.[241]

In the meta-analysis by Rimm *et al.*[242] of experimental studies on alcohol consumption and changes in biomarkers, 30 g of ethanol a day raised the levels of HDL-C by 3.99 mg/dl, apolipoprotein AI by 8.82 mg/dl, and triglyceride by 5.69 mg/dl; no significant change on fibrinogen concentration, tissue-type plasminogen activator antigen concentration, or apolipoprotein(a) was found. In a recent meta-

analysis of experimental studies, Brien *et al.*[243] reported that, compared with the levels of biomarkers during no drinking, during drinking, the levels of HLD-C increased by 0.09 mmol/L, apolipoprotein AI increased by 0.10 g/L, and adiponectin raised by 0.56 mg/L; no difference was shown on the levels of LDL-C, total cholesterol, triglycerides, inflammatory factors (C-reactive protein, interleukin-6, and tumour necrosis factor-α), or haemostatic factors (plasminogen activator inhibitor-1 and tissue plasminogen activator).

There is also evidence on the relationship of CVD with poor physical functioning and disability.[160,162,164] In fact, among the elderly, CVD and osteoarthritis are the top two diseases causing physical disability.[164] It is possible that, compared with light-to-moderate drinkers, non- and heavy drinkers are more likely to develop CVD which may then result in their poorer physical functioning. In other words, CVD may be on the pathway between alcohol consumption and physical functioning. Furthermore, since the above evidence is based on observational studies, the cardio-protective effect of light-to-moderate drinking has been criticised by suffering from several methodological issues (Section 2.4.4 in more detail).[37,182,183] The same methodological issues may also underlie findings that alcohol consumption protects against mortality and morbidity from other diseases,[182] and physical functioning may not be an exception. For these reasons, previous findings on alcohol consumption and CVD have been described and the related methodological concerns will be outlined below.

2.4.4 Methodological issues regarding the J-shaped curve

The methodological issues include 'sick quitters' bias, problems with respect to abstainers, possible effects of drinking pattern, measurement error in alcohol consumption, residual confounding, and the appropriate reference group to compare with.[37,182,183]

2.4.4.1 'Sick quitters'

The misclassification of non-drinkers is one major methodological concern.[37,38,182,183,232,244-247] In 1988, Shaper *et al.*[37] proposed a 'sick quitters'

hypothesis that non-drinkers may include former drinkers who quit drinking due to health reasons. Failure to separate former drinkers from never drinkers may partly contribute to the J-shaped relationship between alcohol consumption and mortality or morbidity found in observational studies.

Some evidence exists to support the notion that the failure to separating former drinkers from never drinker seems not distort the association of alcohol consumption with CVD outcomes and all-cause mortality, and the relationship remains essentially unchanged after excluding former drinkers.[228,236,239,240,244] However, in a meta-analysis of studies free of 'sick quitters' bias, instead of a J-shaped relationship, no protective effect of alcohol on death or CVD was reported.[38] Despite the great importance, unfortunately, studies continuingly examine the relationship between alcohol consumption and health outcomes without separating former drinkers, including 'sick quitters', from lifetime abstainers.[175]

2.4.4.2 Abstainers

Evidence on cardio-protective effect of alcohol consumption mainly comes from Western societies, where abstainers are an atypical, deviant, and marginalised group.[183,245] Abstainers tend to have a less healthy diet, unfavourable lifestyle and poorer social networks, and tend to be less physically active, less educated, depressed and unmarried.[183,228,248]

A related issue is that alcohol consumption is dynamic and time-varying. Moderate and heavy drinkers tend to drift towards light drinking or abstinence with increasing age,[88,182,245,249-252] and this drift is often due to accumulated ill health and medication use.[250,251] In a meta-analysis by Fillmore *et al.*[253], former male drinkers were more likely to be heavier smokers, depressed, less educated, unemployed and with lower SEP; former female drinkers were more likely to be heavier smokers, with poorer health and unmarried. Majority of the studies have used alcohol consumption (usually drinking volume) at baseline,[175,245] which assumes people's drinking is stable and time invariant.[232] It may introduce unsystematic errors in prospective

studies, [232] and may cause an overestimation of the protective effect of light-to-moderate drinking on CVD and all-cause mortality.[250]

2.4.4.3 Pattern of drinking

Pattern of drinking (e.g., heavy episodic drinking and occasional drinking to intoxication), usually not explored in studies, is important in explaining the relationship of alcohol consumption with morbidity and mortality.[180,182,231,247] To consume 100 g of alcohol a week in total, a person may drink 20 g of alcohol on 5 separate days or 100 g of alcohol in a single day, which are two very different patterns of drinking. Drinking pattern can be associated with certain diseases independent of drinking volume, or in some cases mediate the effects of drinking volume; for example, heavy episodic drinking largely mediates the dose-response relationship of alcohol intake with injures and CVD.[181,254]

As previously mentioned, the theory of a protective effect existing for low to moderate intake of alcohol is largely drawn from studies in Western societies where regular moderate drinking is the dominant pattern of drinking.[182,183] Abstinence and heavy episodic drinking may accordingly be less covered and less investigated in studies.[182] In addition, because people with alcohol dependence tend to be under-represented in studies, it is possible that the health risk of harmful and hazardous drinking may be underestimated.[228]

2.4.4.4 Other issues

Several additional methodological concerns are also noteworthy. For instance, as mentioned earlier, alcohol consumption is usually measured by self-report in population surveys, which is prone to recall error and under-report.[182,233,239,245,247] Since both alcohol consumption and health outcomes are associated with many factors, it is unlikely that they are entirely controlled for, and there may be residual confounding.[182,247,250,251] Because non-drinkers consist of lifetime abstainers and former drinkers, non-drinkers are not an appropriate reference group to compare with when estimating the association between alcohol consumption and health

outcomes.[249,251,255] These methodological issues are closely related to this thesis and will be discussed in detail in the Discussion Chapter (see Section 6.2).

2.4.5 Alcohol consumption and disability and physical functioning

As the main focus of this thesis, literature on the association between alcohol consumption and physical functioning has been reviewed more systematically. Literature was searched for in the databases of MEDLINE and EMBASE, limited to studies: 1) published between 1990 and May 2014; and 2) in middle-aged and older populations.

Several terms related to physical functioning were used in the literature search, including functional limitations (e.g, functional status, functional/physical impairment, functional/physical limitation, physical performance, hand strength, walking and mobility), disability (e.g., ADLs, IADLs and disabled persons), health status and geriatric assessment (Appendix A). Several terms of alcohol consumption were included as well, such as alcohol drinking, alcohol consumption, drinking pattern, heavy/binge/risky/hazardous drinking, alcohol abuse and alcoholism (Appendix A).

Titles and abstracts of over 2,700 papers were examined and 228 full-text articles were read. A few additional papers were identified through searching reference lists of extracted papers. All papers needed to meet the following criteria to be included in the literature review: 1) focus on middle-aged and older adults; 2) not restricted to populations with presence of specific medical conditions; and 3) adjusted at least for basic potential confounders (e.g., age and sex). In total, 43 papers were included, among which 12 were based on cross-sectional studies (Appendix B)[25-36] and 31 were based on longitudinal studies (Appendix C)[39-64,168,169,172,256,257].

2.4.5.1 Cross-sectional findings

Among the 12 papers based on cross-sectional studies, the majority of which were conducted in the US, five have found an L-shaped relationship that only non-drinkers are at a higher risk of functional limitations and/or disability than drinkers.[25,28,33,34,36]

Other seven have reported a J-shaped relationship that light-to-moderate drinking is associated with better physical functioning than non-drinking and heavy drinking.[26,27,29-32,35]

Only Moore *et al.*[29] investigated the effect of binge drinking (defined as ≥3 drinks per occasion for women; ≥4 drinks per occasion for men) in a sample of drinkers, and reported a higher risk of IADL impairments among binge drinkers compared with light-to-moderate drinkers. Only the Study of Osteoporotic Fracture[25] and the Osteoporotic Fractures in Men (MrOS) study[32] used physical performance tasks to measure physical functioning, all other studies adopted self-reported measures, including the SF-36, ADLs, IADLs, and mobility limitations. In the study by Moore *et al.*[29], a timeline calendar of recent drinking in the last 30 days was used to measure recent drinking occasions. Other studies assessed alcohol consumption relatively crudely using the FFQ or basic QF within a reference time of 3 or 12 months, or only asked number of drinks in the past week or 3 months. About half of the studies employed non-drinking as the reference group to compare with; whilst the other half used light-to-moderate drinking, although the definitions of light-to-moderate drinking varied from study to study.

Only 3 papers attempted to separate former drinkers from never drinkers.[25,28,36] Nelson *et al.*[25] found that, compared with light-to-moderate drinkers, former drinkers had poorer physical functioning (measured by self-reported mobility, ADLs, IADLs and physical performances); but among former drinkers, lifetime alcohol intake was not associated with physical functioning. Green *et al.*[28] also reported a lower PF-10 score among former drinkers than light-to-moderate drinkers. Similarly, Canavan *et al.*[36] showed that, independent of CVD, diabetes and serum cholesterol, former drinking was associated with a higher risk of limitations in ADLs and IADLs compared with non-drinking.

Green *el al.*[30] found a similar J-shaped relationship of the PF-10 score across different indices of alcohol consumption: in both men and women, drinking 2–3 times per week, 1–2 drinks per occasion, 15–29 drinks per month, and regular light-to-moderate drinking were related to the highest PF-10 score.

2.4.5.2 Longitudinal findings

Findings from the longitudinal studies, with 2–22 years of follow-up, are less consistent. Among the 31 papers based on longitudinal studies, 13 have reported no association between alcohol consumption and physical functioning at follow-up.[39-51] Tabbarah *et al.*[42] found no association between alcohol consumption at baseline and the change in performance of physical tasks during 7-year follow-up of older adults aged 70–79 at baseline. Similarly, based on a sample of Dutchs aged 55 years and over at baseline with 6-year follow-up, Tas *et al.*[45] showed no association between alcohol consumption at baseline and either recovery from or progression of disability at follow-up. Using the Korean Longitudinal Study of Aging (KLoSA) of older adults with 2 years of follow-up, Lee *et al.*[48] found that transitions relating to heavy drinking (e.g., developed heavy drinking 2 years later and quit heavy drinking) were not associated with a transition related to disability; either recovery from or development of. Artaud *et al.*[46] followed older French adults over 12 years with 6 repeated measurements of physical functioning combining mobility, ADLs and IADLs, and reported no association between alcohol consumption at baseline and incident disability at follow-up.

Among the 13 papers that reported no association, only Seeman *et al.*[39], Tabbarah *et al.*[42] and Stenholm *et al.*[51] investigated physical performance. The former two papers used data from the MacArthur Research Network on Successful Aging Community Study in the US; the latter one followed the grip strength in a general Finnish population for 22 years. Other studies adopted self-reported physical functioning or disability. It is also worth noting that alcohol consumption was measured by weekly alcohol intake, FFQ, basic QF, or asking about only frequency of drinking in these studies. Except the study by Lee *et al.*[48], all studies only measured alcohol consumption once at baseline.

Four papers examined possible effect modifiers.[168,169,256,257] Stratified by obesity and follow-up years (first 2 years vs. 2–6.5 years), Koster *et al.*[169] found no association between baseline alcohol consumption and late onset of mobility limitations (2–6.5 years of follow-up) among community-dwelling older adults free of limitations in

mobility and ADLs at baseline. Early onset of mobility limitations (first 2 years) was only positively associated with former drinking among non-obese subjects.

Maraldi *et al.*[256] showed a gender difference between alcohol consumption at baseline and development of mobility limitations at follow-up. No association was found in women, and no association between drinking and severe mobility disability (reported mobility limitations in two consecutive follow-up assessments) was showed in either women or men. Male former and light drinkers (1–7 drinks/week) were more likely to develop mobility limitations than those who drank less than 1 drink per week in the past 12 months.

Stratified by sex and self-rated health, Karlamangla *et al.*[257] reported a lower risk of incident disability at follow-up among female light-to-moderate drinkers than occasional drinkers in the strata of women with good or better self-rated health. No association was found either among women with fair or worse health or among men. Stratified by presence of chronic diseases, LaCroix *et al.*[168] found that, compared to light-to-moderate drinking, non-drinking was associated with a higher risk of mobility loss only among older adults with presence of at least one chronic disease at baseline; no association was observed among those without any chronic disease at baseline. In contrast, Ebrahim *et al.*[172] showed that, independent of CVD and other medical conditions at baseline, compared with no heavy drinking, heavy drinking was related to an increased risk of disability.

In the remaining 13 papers, an L-/J-shaped relationship between alcohol consumption and physical functioning at follow-up has been reported.[52-64] Only the Adult Changes in Thought (ACT) study[55] used performance-based physical function (PPF: 10-foot timed walk, 5 chair stands, standing balance and grip strength), a performance-based battery, together with self-reported ADLs and IADLs to measure physical functioning. Wang and colleagues[55] showed that, drinking 5 drinks or more in the last 12 months without problem drinking had a decreased age-adjusted rate of decline in ADLs, IADLs, and PPF. This was the only study which investigated alcohol consumption and the rate of change in physical functioning during follow-up.

However, alcohol consumption was measured very crudely in this study by only one question on whether participants drank 5 drinks or more in the last 12 months or not.

Almost all these studies measured alcohol consumption only at baseline and used it to predict physical functioning at follow-up. Changes in alcohol consumption over time were examined by Lin *et al.*[61], and subjects were categorised into consistent abstainers, consistent low-risk drinkers, consistent high-risk drinkers, recent quitters and other patterns. Only consistent low-risk drinkers had a lower risk of incident IADL and functional limitations than consistent abstainers, and this protective effect was larger among those aged 50-65 years than among older age groups.

In a comparison between the AHEAD/HRS in the US and the English Longitudinal Study of Ageing (ELSA), an L-shaped relationship was found: only non-drinkers were at a higher risk of ADL and IADL limitations 4 years later in both studies; the association did not change after exclusion of 'sick quitters' and former drinkers.[59]

Four papers separated former drinkers from never drinkers;[46,64,256,257] two of them reported no association between former drinking and disability at follow-up.[46,257] Maraldi *et al.*[256] found an increased risk of incident mobility limitations among male former drinkers but not among female former drinkers; whilst Abbott *et al.*[64] reported a higher risk of developing ADL limitations among former drinkers compared with abstainers.

Similar to the cross-sectional studies, the majority of the longitudinal studies were conducted in the US, few from Europe and Asia. Nine papers employed non-drinkers as the reference group; others used light-to-moderate drinking, occasional drinking or non-heavy drinking, the definition of which varied across studies. In addition, these longitudinal studies applied the QF, weekly alcohol consumption, FFQ, and crude measures such as the number of drinks or drinking frequency in the past 7 days. Almost all of the longitudinal studies evaluated physical functioning or disability by self-reported ADLs, IADLs and mobility, or other self-reported instruments of general health such as the SF-36 and Stanford Health Assessment Questionnaire. Most of these studies examined the risk of (incident) functional limitations and

disability. Nineteen papers used data from two time points: alcohol consumption and physical functioning at baseline, and one follow-up assessment of physical functioning. Only one study employed three repeated measures of physical functioning and investigated the rate of change in physical functioning over time. Very few papers assessed the relationship between drinking pattern and physical functioning at follow-up.

2.4.5.3 Problem drinking

Only four reports, two based on cross-sectional data and two based on the longitudinal HRS/AHEAD, examined the effect of alcohol abuse or dependence on physical functioning.[26,32,53,54] Among the two cross-sectional studies, one found that subjects with alcohol dependence had a lower PF-10 score than those with alcohol abuse, but there was no difference between subjects with alcohol abuse and those with no alcohol abuse disorder.[26] The other cross-sectional study reported that problem drinkers did worse in performance tasks and were more likely to have IADL impairments and mobility limitations than those without problem drinking.[32]

By analysing the longitudinal HRS data (wave 1–4), Perreira *et al.*[53] reported no association between problem drinking at wave 1 and development of at least two ADL limitations at follow-up; whereas Ostbye *et al.*[54] showed, in the same data, that problem drinkers at wave 1 had an increased risk of developing at least one limitation in ADLs as well as mobility limitations (climbing one flight of stairs and walking several blocks) during follow-up. Findings in the AHEAD cohort, an older cohort than the HRS, were different: problem drinking was not associated with ADL limitations, IADL limitations or the difficulty in walking several blocks but only with the limitation in climbing stairs.[54]

2.4.5.4 Summary of the literature review

Overall, findings from previous longitudinal studies on the association between alcohol consumption and physical functioning are more inconsistent than findings from cross-sectional studies. Many studies, both cross-sectional and longitudinal, have reported an L-/J-shaped relationship between alcohol and physical functioning;

but still, over one third of papers based on longitudinal studies have shown no association. Considering the drawbacks of cross-sectional studies in assessing temporality, longitudinal studies with clear temporal structure are advantageous, and should therefore be viewed as more reliable.

A number of methodological issues may help explain the inconsistency between studies. They will be briefly summarised here and discussed in more detail in the Discussion Chapter (Section 6.2).

Firstly, the majority of the studies are from Western countries, mainly the US and Western Europe. None of these studies included populations from CEE, a region with high alcohol consumption and apparently low physical functioning. This is a major limitation of existing research. In addition, only few studies have investigated alcohol consumption as the primary research interest; in fact, some studies have focused more on the joint effects of health behaviours (including smoking, alcohol consumption, physical activity and diet).

Secondly, since non-drinkers are a typically 'contaminated' group, with inclusion of former drinkers (partly include 'sick quitters') alongside never drinkers, non-drinkers may not be an ideal reference group.[255] However, 14 out of 43 studies in total adopted non-drinkers as the reference group, which may result in an overestimation of the detrimental effect of non-drinking on physical functioning.

Thirdly, the majority of these studies used self-reported alcohol consumption and physical functioning, by which reporting bias is likely to be present. People may under-report their drinking and over-report their physical functioning due to the shame or stigma attached to drinking and being unhealthy or physically limited/disabled.[258] Alcohol consumption, in particular, has been often measured crudely by the QF, FFQ and weekly alcohol intake. These measures do not allow the assessment of drinking pattern. Moreover, most of the longitudinal studies relied on alcohol consumption at one time point. Over two thirds of longitudinal studies assessed physical functioning only twice, at baseline and one follow-up assessment, which did not allow the estimation of trajectories of physical functioning over time.

Quite a few studies used IADLs to measure physical functioning/disability, however, as mentioned previously, IADLs tend to reflect role functioning alongside physical functioning.

Fourthly, the follow-up time of longitudinal studies ranges from 2 to 22 years. On one hand, it is likely that a short time period may not be long enough to allow the differences in the rate of decline in physical functioning or onset of disability by drinking categories to be observed. On the other hand, with one assessment of alcohol consumption, the misclassification error is likely to increase with increasing follow-up years.

Finally, adjustments for potential confounders vary across studies, including age, sex, smoking, BMI, physical activity, medical conditions (e.g., CHD, stroke, hypertension, diabetes, arthritis, or number of diseases), cognitive functioning, depression, marital status, SEP (e.g., education, income and employment), and social networks. Some studies attempted to control for more variables than others, but none included all these variables. Even if above named variables are entirely controlled for, it is unlikely to eliminate residual confounding, since the potential confounders are often not fully understood or measured.[182]

2.5 Summary

Physical functioning, a central component of health and quality of life for older adults, represents an individual's ability to perform activities required in their daily living. It is related but not identical with the concept of disability. Decline of physical functioning in late-life is a consequence of physiological changes and the onset of diseases related to ageing, modified by medical care, socioeconomic, psychological and behavioural factors. To achieve the ideal goal of successful ageing, optimising physical functioning, maintaining independence of living, and identifying modifiable factors related to physical functioning, are imperative for older adults.

Alcohol consumption, the third leading global risk factor of disease and disability, could be more harmful to older adults than younger ones due to age-related

physiological changes and increasing medication use. Previous studies have suggested an apparently protective effect of light-to-moderate drinking on physical functioning, but the evidence is inconclusive, particularly from longitudinal studies. The majority of the studies conducted to date have been in the US, Western Europe and Asia, where the level of alcohol consumption is lower than CEE. Given the high alcohol intake, harmful drinking pattern, and the high estimated burden of disease attributable to alcohol in CEE, it is possible that alcohol also plays a role in determining physical functioning in CEE, even though there is lack of evidence.

Shared with studies on alcohol and CVD, besides plausible biological mechanisms, several methodological concerns should be considered that they may explain the apparently protective effect of light-to-moderate drinking on physical functioning, including 'sick quitters' bias, problems regarding abstainers, possible but less well studied effect of drinking pattern, measurement error in alcohol consumption, residual confounding and the reference group. In addition, CVD may be on the pathway (if any) between alcohol consumption and physical functioning.

In the light of the gaps in the literature highlighted above, I analysed data from the multi-centre prospective HAPIEE study conducted in the Czech Republic, Russia and Poland, to provide original evidence on: 1) physical functioning and its decline over time in CEE; 2) cross-sectional and longitudinal associations between alcohol consumption and physical functioning in CEE, by examining several aspects of alcohol consumption including drinking pattern; and 3) effect of 'sick quitters' on alcohol consumption and physical functioning.

Several features of this thesis distinguished this study from previously published reports. First, unlike the vast majority of previous studies, this investigation included several different aspects of alcohol consumption (average drinking frequency, annual drinking volume, average drinking quantity per drinking day, drinking pattern and problem drinking). Crucially, drinking pattern was captured by a GF questionnaire in this thesis, an aspect of alcohol consumption which has rarely been examined in relation to physical functioning in previous studies. In addition, drinking pattern has been suggested to play an important role in health status in CEE, particularly in

Russia. This feature therefore is a major improvement over previous studies. Second, most previous studies have not taken into account the potential 'sick quitters' bias, mainly due to the lack of data on past drinking. With these data available in the Russia cohort, 'sick quitters' could be separated from never drinkers in this thesis. This enabled a direct test of 'sick quitters' bias and an assessment of the extent to which it affected the cross-sectional association between alcohol consumption and physical functioning. Third, to my knowledge, only one previous longitudinal study examined alcohol consumption and rate of change in physical functioning over time. No study did investigate alcohol consumption and individual trajectories of physical functioning over time as a primary research question. This was addressed by using data from four repeated measurement occasions in the HAPIEE study. Finally, this is the first study of physical functioning in CEE. Although associations of physical functioning and risk factors are likely to be similar in different populations, it is critical that regional results are available.

Most findings in this thesis should be generalizable to populations outside of CEE. Alcohol consumption is common in most societies, although drinking pattern may differ. Physical functioning is one of the fundamental attributes of healthy ageing and is important for all populations. Given the absence of previous studies on alcohol consumption and individual trajectories of physical functioning in ageing populations, this thesis provides original and generalizable insights on future research in populations from other regions. One characteristic specific to CEE is that these societies have undergone the rapid and profound political, social and economic changes since the fall of communism in 1989. These changes have influenced, even until now, socioeconomic, psychosocial, lifestyle and behavioural factors, as well as physical and mental health in populations in Central and Eastern Europe. This may affect the structure of factors that may confound the association between alcohol consumption and physical functioning; if anything, studies in different populations are important to assess the consistency of observational results across studies and populations.

CHAPTER 3 AIMS, OBJECTIVES AND HYPOTHESES

Aim

The overall aim of this thesis is to investigate the role of alcohol consumption in physical functioning in middle-aged and older adults in three CEE countries–Czech Republic, Russia and Poland–using cross-sectional and longitudinal data from the multi-centre HAPIEE study.

Objectives

In order to achieve the overall aim, the thesis will address the following specific objectives:

1. To explore the cross-sectional association between alcohol consumption (including average drinking frequency, annual drinking volume, average drinking quantity per drinking day, drinking pattern, and problem drinking) and self-reported physical functioning in the Czech, Russian and Polish cohorts, using data from the baseline survey of the HAPIEE study;

2. To examine the role of past drinking behaviour prior to the baseline survey in the cross-sectional association between alcohol consumption and physical functioning at baseline in the Russian cohort (for which data on past drinking behaviour are available);

3. To investigate the trajectories of self-reported physical functioning throughout 10-year follow-up of the three cohorts, using longitudinal data from the baseline survey and three subsequent measurement occasions of the HAPIEE study;

4. To assess the association of alcohol consumption at baseline (including average drinking frequency, annual drinking volume, average drinking quantity per drinking day, drinking pattern, and problem drinking) with the trajectories of physical functioning throughout follow-up; and to examine the

relationship between past drinking behaviour prior to the baseline survey and the trajectories of physical functioning in the Russian cohort.

Self-reported alcohol consumption measured by a GF questionnaire was used in this thesis. Self-reported alcohol consumption generally underestimates the absolute level of intake (by approximately one half), but it is reasonably reliable to rank persons in terms of their 'true' alcohol consumption. Unlike measures of alcohol consumption applied in previous studies (e.g., QF and FFQ), the GF allows capturing drinking pattern, an aspect of alcohol consumption which has scarcely been examined in previous studies. In particular, heavy episodic drinking appears to play a critical role in affecting various health outcomes in Eastern Europe. Furthermore, there are no perfect biomarkers of alcohol consumption. Most biomarkers of alcohol consumption are not specific for alcohol, only reflect recent drinking, and cannot distinguish between regular vs. episodic drinking. The GF used in the HAPIEE study had a reference period of 12 months; compared with biomarkers of alcohol consumption, it is able to assess long-term drinking behaviour. For these reasons, the use of GF was considered to be appropriate.

As described in the literature review, previous cross-sectional studies have consistently shown that abstaining and/or heavy drinking were associated with poorer physical functioning compared with light-to-moderate drinking. However, the evidence from previous longitudinal studies is far less consistent; about one third of longitudinal studies have reported no association between alcohol consumption and physical functioning during follow-up. One major methodological concern with cross-sectional studies is the 'sick quitters' bias, which most existing cross-sectional studies failed to take into account. The baseline data of the HAPIEE study were therefore important to examine: 1) whether a similar finding of such cross-sectional association between alcohol consumption and physical functioning will be replicated in ageing cohorts in CEE; and 2) whether the 'sick quitters' bias affects the cross-sectional association and, if so, how important is this bias for the interpretation of cross-sectional studies. Such careful assessment is also crucial for the interpretation of longitudinal studies and particularly for the clarification of discrepancies in findings between cross-sectional and longitudinal studies.

Hypotheses

In the light of the literature review on alcohol consumption and physical functioning, I formulated the following hypotheses related to the specific objectives:

1. In cross-sectional data, non-drinkers and heavy drinkers have a higher risk of low physical functioning in comparison with regular and/or light-to-moderate drinkers (J-shaped relationship);

2. In cross-sectional data, former drinkers, particularly those who quit drinking for health reasons, have lower physical functioning than those who maintained their alcohol consumption ('sick quitters' hypothesis);

3. In longitudinal data, physical functioning at the population level declines over the 10 years of follow-up;

4. In longitudinal data, non-drinkers and/or heavy drinkers have a faster decline in physical functioning than regular and/or light-to-moderate drinkers (L-/J-shaped relationship with faster decline); lifetime abstainers and former drinkers who quit drinking have a faster decline in physical functioning over time than drinkers who maintained their alcohol consumption.

CHAPTER 4 METHODOLOGY

This chapter lays out the methodology applied to this thesis, including study design and data collection, ethical issues, study subjects and analytical samples, study variables, missing data, and statistical analyses.

4.1 Study Design and Data Collection

In this thesis, data from the HAPIEE study were used. The HAPIEE study is a multi-centre prospective cohort study aiming to investigate the effect of alcohol consumption, dietary factors and psychosocial factors on health in Central and Eastern Europe. The HAPIEE study is conducted in seven towns in the Czech Republic (Havířov/Karviná, Jihlava, Ústí nad Labem, Liberec, Hradec Králové, and Kroměříz), Novosibirsk (Russia), Krakow (Poland) and Kaunas (Lithuania). The Czech towns, Novosibirsk and Krakow took part in the study from the baseline survey (2002–2005), and Kaunas joined in at re-examination (2006–2008). Follow-up assessments by postal questionnaire were carried out in 2009 and 2012 respectively in all countries and in 2013 in the Czech Republic.

The Czech towns with varied social profiles and economic development levels were selected to recruit participants, in order to optimise the representativeness of the target population. Novosibirsk (Russia) and Krakow (Poland) are large industrial cities and regional centres. Two districts of Novosibirsk and four districts of Krakow with different social profiles were selected. Kaunas is a major city in Lithuania.

Samples of local residents aged 45–69 years were randomly selected from population registers in the Czech towns, Krakow (4 city districts) and Kaunas (whole city) and electoral lists in Novosibirsk (2 city districts), stratified by sex and 5-year age bands. A total of 36,121 participants were recruited, with an overall response rate of 60% (Czech towns: 55%, Novosibirsk: 61%, Krakow: 61%, and Kaunas: 65%).[259]

As the study started 4 years later in Kaunas than in the other three research centres and the follow-up time is much shorter so far, only data from the Czech towns,

Novosibirsk and Krakow were used in this thesis. The data collection procedures described below are restricted to these three research centres.

Baseline data were collected via a structured questionnaire and a short medical examination in 2002–2005. In the Czech towns and Krakow, participants were paid a home visit first by trained nurses, and then they were invited to attend a short medical examination in a clinic. The questionnaire was left for Czech participants to fill out during the home visit, and it was checked for completeness and collected by the trained nurses few days later. Polish participants completed the questionnaire during the home visit with help from the trained nurses in case they had difficulties on the questionnaire. Since the short medical examination was carried out in a clinic after the home visit, 1,576 Czechs and 1,436 Poles did not go to the clinic and attend the medical examination. All Russian participants completed the questionnaire and medical examination simultaneously in a clinic, and the questionnaire was filled out by the participants together with the trained nurses.

The structured questionnaire gathered information on demographic factors, health status, medical conditions, physical functioning, quality of life, health behaviours, socioeconomic position (SEP, including education, number of household amenities during childhood and adulthood, and current economic activity), and psychosocial factors (including depressive symptoms, perceived control, social networks, and job control/demand and effect/reward imbalance among working participants). The questionnaire was translated into local languages and back-translated into English to ensure accuracy and cross-cultural comparability, and it was piloted in a separate sample.[260]

During the medical examination, height, weight, trunk length, waist and hip circumference, blood pressure, heart rate, lung function and cognitive functions (memory, concentration and verbal skills) were measured under a standardised protocol. Blood samples were taken, and information on biomarkers such as blood lipids, inflammatory markers and markers of glutose metabolism, homocysteine and vitamins were obtained.

A re-examination of the Czech, Russian and Polish cohorts was conducted in 2006–2008. Face-to-face Computer Assisted Personal Interview (CAPI) was employed to collect data on ageing-related outcomes (chronic diseases, cognitive functions, self-reported and objective physical functioning, quality of life and social participation) and economic circumstances (characteristics of retirement and pensions, income, materials and composition of household).

A postal questionnaire was used for further follow-up of the cohorts on chronic diseases (e.g. CVD, hypertension and diabetes), physical functioning, SEP, social networks, depressive symptoms, self-rated health and dental health, sleep, smoking and care giving. Two postal questionnaire follow-up assessments were completed in 2009 and 2012, and another follow-up in 2013–2014 is still ongoing.

A detailed description of the study design and data collection procedures are provided in Peasey *et al.*[259]. Figure 4.1 shows the timeline of the measurement occasions of the HAPIEE study included in this thesis, alongside the study variables included in the data analyses.

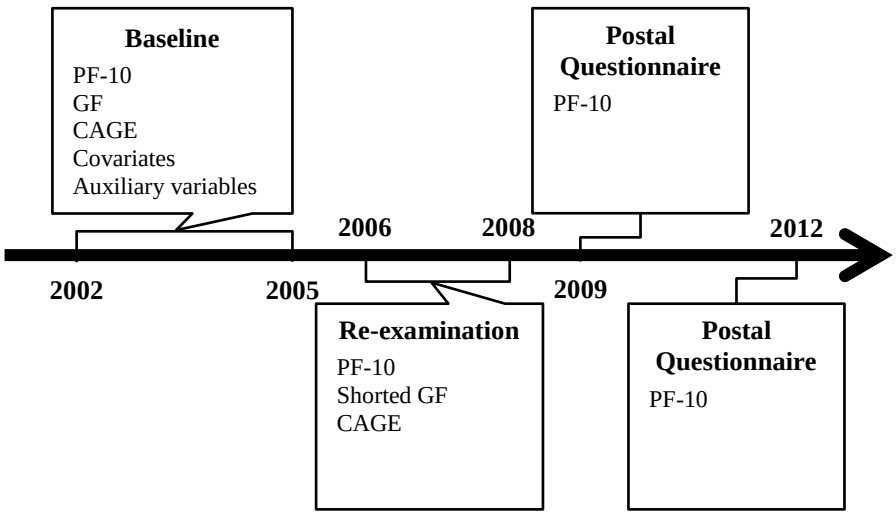


Figure 4.1. Timeline of the HAPIEE study

4.2 Ethical Issues

The HAPIEE study has been approved by the ethics committees at University College London, UK; National Institute of Public Health, Prague, Czech Republic; Russian Academy of Medical Sciences, Novosibirsk, Russia; Jagiellonian University, Krakow, Poland; and Kaunas University of Medicine, Kaunas, Lithuania. Written informed consent was obtained from all participants.

4.3 Study Subjects and Analytical Samples

At baseline, 8,857 Czechs, 9,360 Russians and 10,728 Poles were recruited to take part in the HAPIEE study. Among them, 162 were excluded because they were outside of the target age range (<44.5 and ≥70.5 years) at baseline. To maximise the analytical samples, participants aged 44.5–44.9 years (46 Czechs and 18 Russians) and 70.0–70.4 years (73 Czechs, 59 Russians and 102 Poles) were moved into the age groups of 45–49 and 65–69 years, respectively. As a result, the total available analytical sample size is 28,783, including 8,773 Czechs (46% men and 54% women), 9,301 Russians (46% men and 54% women) and 10,709 Poles (49% men and 51% women).

Physical functioning is the outcome of interest. It was measured repeatedly by the same PF-10 subscale of the SF-36 questionnaire (Figure 4.1), the longitudinal samples based on non-missing PF-10 score in the Czech, Russian and Polish HAPIEE cohorts are described in Table 4.1. In all three cohorts, the number of participants with non-missing PF-10 score dropped approximately by 40% between baseline and re-examination. A further fall of approximately 20% in the Russian cohort and 30% in the Polish cohort occurred between the postal questionnaire follow-up in 2009 (PQ2009) and in 2012 (PQ2012).

Table 4.1. Longitudinal samples of the HAPIEE study, based on non-missing PF-10 score

	Czech Republic		Russia		Poland		Total
	Men	Women	Men	Women	Men	Women	
Total	4070	4703	4239	5062	5219	5490	28783
Non-missing PF-10 score							
Baseline	4019 (98.7%)	4612 (98.1%)	4239 (100.0%)	5062 (100.0%)	5185 (99.4%)	5449 (99.3%)	28566 (99.3%)
Re-examination	2326 (57.2%)	2833 (60.2%)	2699 (63.7%)	3448 (68.1%)	3194 (61.2%)	3415 (62.2%)	17915 (62.2%)
PQ2009	2304 (56.6%)	2891 (61.5%)	2738 (64.6%)	3706 (73.2%)	3402 (65.2%)	3799 (69.2%)	18840 (65.5%)
PQ2012	2017 (49.6%)	2581 (54.9%)	1826 (43.1%)	2790 (55.1%)	1730 (33.2%)	1955 (35.6%)	12899 (44.8%)
Non-participation of medical examination	790 (19.4%)	786 (16.7%)	N/A	N/A	708 (13.6%)	728 (13.3%)	3012 (10.5%)

N/A: not applicable

Table 4.2 presents the pattern of missing PF-10 score in the HAPIEE study, where 0 denotes non-missing and 1 denotes missing. Only 35.4% of participants had complete information on the PF-10 score at all four measurement occasions. 23.3% of participants dropped out after baseline and never returned to the study. 16.8% of participants were observed again after they failed to attend one or more measurement occasions. This is a non-monotone missing pattern (Section 4.5.1 in detail). On account of the relatively large proportion of missing data, multiple imputation by chained equations was applied to handle missing data in this thesis, the method of which will be described below in more detail (Section 4.5).

As shown in Table 4.2, 35.4% of participants had complete information on the PF-10 scores *at all four measurement occasions*; 60.4% had valid score values at three or more occasions, and 76.3% had valid score values at two or more occasions. The comparison of baseline health status by missing patterns of the PF-10 scores suggested that participants with better health were more likely to stay in the study (and have fewer missing values) than those with less good health (Appendix D). The PF-10 scores at missing measurement occasions were imputed. The health selection was taken into account in the imputation process, since the imputation models

included many auxiliary variables related to baseline health status, such as self-reported health, presence of long-term health problems, history of CVD, etc. (see Section 4.5.4).

Table 4.2. Pattern of missing PF-10 score in the HAPIEE study

	Patterns of missing PF-10 score				
N	Baseline	Re-examination	PQ2009	PQ2012	%
10200	0	0	0	0	35.4
6701	0	1	1	1	23.3
4919	0	0	0	1	17.1
2202	0	1	0	1	7.7
1903	0	0	1	1	6.6
1722	0	0	1	0	6.0
495	0	1	0	0	1.7
424	0	1	1	0	1.5
93	1	1	1	1	0.3
46	1	0	0	0	0.2
26	1	0	0	1	<0.1
22	1	1	0	1	<0.1
18	1	0	1	1	<0.1
6	1	0	1	0	<0.1
5	1	1	0	0	<0.1
1	1	1	1	0	<0.1
	Valid (non-missing) PF-10 score			**Simple %**	**Cumulative %**
10200	All 4 time points			35.4	35.4
7182	3 out of 4 time points			25.0	60.4
4566	2 out of 4 time points			15.9	76.3
6742	1 out of 4 time points			23.4	99.7
93	None			0.3	100.0

0: non-missing; 1: missing

4.4 Study Variables

Aside from physical functioning as the outcome of interest and alcohol consumption as the exposure, several covariates were included in this thesis as potential confounders. Additional auxiliary variables (those were not part of the data analysis but correlated with other variables included in the analysis[261,262]) were used to deal with missing data.[261-264]

4.4.1 Physical functioning

Physical functioning was measured using the physical functioning subscale (PF-10) of Short-Form-36 (SF-36) questionnaire (see Section 2.3.3) throughout data collection in the HAPIEE study. The SF-36 has been validated in numerous countries, including those examined in this thesis.[144,265] The PF-10 assesses 10 items regarding vigorous activities (e.g., running and participating in strenuous sports), moderate activities (e.g., moving a table and pushing a vacuum cleaner), lifting/carrying a bag of groceries, mobility (climbing one and several flights of stairs, walking 2 kilometres, 1 kilometres and 100 metres, and bending, kneeling or stooping) and self-care tasks (bathing and dressing). Participants provided an answer for each item using a Likert scale with options of 'limited a lot', 'limited a little' and 'not limited at all' (coded as 1, 2 and 3 respectively). Based on their responses, a score ranging from 0 to 100 was constructed. The PF-10 score was calculated using the formula below (Equation 1):[266]

$$PF = \left(\frac{PF_{sum} - PF_{num}}{2 \times PF_{num}}\right) \times 100 \quad (1)$$

Where, PF_{sum} is the sum of the responses on the 10 items; PF_{num} is the total number of items subjects responded to. The score of 0 indicates poor physical functioning with severe limitations of activities, whilst 100 indicates optimal physical functioning with no limitation of activities at all.

It is recommended to calculate the PF-10 score when ≥5 items are answered by the respondent, and the missing responses are substituted by the respondent's mean response to the non-missing items (person mean substitution).[266] In the HAPIEE study, missing response to each item of the PF-10 subscale was further inspected. At re-examination, 11,979 participants (3,541 Czechs, 3,476 Russians and 4,962 Poles) skipped the item of 'climbing one flight of stairs' after they responded 'not limited at all' to the item of 'climbing several flights of stairs'. Similarly, 14,404 participants (4,403 Czechs, 4,568 Russians and 5,433 Poles) who answered 'not limited at all' to 'walking 2 km' omitted the item of 'walking 1 km'. 1,052 participants (250 Czechs,

435 Russians and 367 Poles) who reported ‘not limited at all’ to ‘walking 1 km’ did not respond to the item of ‘walking 100 m’. At PQ2009 and PQ2012, few hundreds participants also skipped items of the PF-10 subscale with a similar pattern.

The items of ‘climbing several flights of stairs’ and ‘climbing one flight of stairs’ in the PF-10 subscale are in a hierarchical nature that respondents who are not limited in climbing several flights of stairs, in theory, are not limited in climbing one flight of stairs either. The same rationale can be applied to the items of ‘walking 2 km’, ‘walking 1 km’ and ‘walking 100 m’ as well. In this thesis, participants who reported ‘not limited at all’ to the item of ‘climbing several flights of stairs’ but skipped the item of ‘climbing one flight of stairs’ thereby were recoded to be ‘not limited at all’ on the item of ‘climbing one flight of stairs’. The same recoding was also done to the items of ‘walking 2 km’, ‘walking 1 km’ and ‘walking 100 m’. In other words, The recoding was done on the basis of a logical judgement that participants who were able to perform more vigorous activities (climbing several flights of stairs, and walking 1 or 2 km) were also able to carry out less physically demanding activities (climbing one flight of stairs, and walking 100 m).

The recoding consequently reduced the missing responses to the items of ‘climbing one flight of stairs’, ‘walking 1 km’ and ‘walking 100 m’, and increased the completeness of the PF-10 subscale. Downey and King[267] advocated to use the person mean substitution when the proportion of respondents with any missing items and the proportion of missing items for a given respondent are both less than 20%. In the HAPIEE study, after the recoding, few participants had at least one missing item of the PF-10 subscale (1.8% at baseline, <0.1% at re-examination, 6.6% at PQ2009, and 8.7% at PQ2012). Furthermore, among participants who answered ≥1 item of the PF-10 subscale, at the four measurement occasions, 97.9%-99.9% of them had responses to ≥8 items. The PF-10 score therefore was calculated in participants with responses to ≥8 items, instead of ≥5 items.

4.4.2 Alcohol consumption

Alcohol consumption and problem drinking were evaluated at baseline.

4.4.2.1 Drinking indices derived from the graduated frequency questionnaire

Alcohol consumption in the past 12 months was assessed by a graduated frequency (GF) questionnaire. Six levels of drinking quantity during one day (≥10, 7–9, 5–6, 3–4, 1–2, and about 0.5 drink) were asked topdown starting from the heaviest. For each level of drinking quantity, 9 categories of drinking frequency (every day or almost every day, 3–4/week, 1–2/week, 2–3/month, 1/month, 6–11/year, 3–5/year, 1–2/year and never in the past year) were provided. One standard drink was defined as 0.5 litre of beer, 2 decilitres of wine, or 5 centilitres of spirits, which roughly equals 20 g of ethanol.

Four drinking indices were derived from the GF: average drinking frequency in the past 12 months, annual drinking volume, average quantity per drinking day, and drinking pattern. In the Polish cohort, a filter question was asked prior to the GF that whether participants had drunk alcohol in the past 12 months. Polish participants who reported no drinking to the filter question and skipped the GF were classified as non-drinkers.

Average drinking frequency

First, annual drinking days were calculated by summing drinking days over all levels of drinking quantity using middle points (Table 4.3). Annual drinking days were then categorised into average drinking frequency (0, 0.1–2.9, 3.0–5.9, 6.0–11.9, 12.0–23.9, 24.0–51.9, 52.0–155.9, 156.0–259.9, ≥260.0 days corresponding to never, 1–2/year, 3–5/year, 6–11/year, 1/month, 2–3/month, 1–2/week, 3–4/week, ≥5/week, respectively).

Annual drinking volume

Drinking volume at each level of drinking quantity was calculated by multiplying the middle point of drinking quantity with corresponding drinking days (Table 4.3). The sum of these drinking volumes was the annual drinking volume.

Average drinking quantity per drinking day

Average drinking quantity per drinking day was obtained by dividing annual drinking volume by annual drinking days. It was further categorised into non-, light, moderate and heavy drinking using gender-specific thresholds proposed by Rehm *et al.*[176] (0, 0.1–19.9, 20.0–39.9, ≥40.0 g/day for women; 0, 0.1–39.9, 40.0–59.9, ≥60.0 g/day for men).

Table 4.3. Middle points used for calculation of the GF

Drinking quantity	Middle point (drinks)	Drinking amount (g ethanol)
10 drinks	10	200
7-9 drinks	8	160
5-6 drinks	5.5	110
3-4 drinks	3.5	70
1-2 drinks	1.5	30
0.5 drink	0.5	10
Drinking frequency	Middle point	Drinking days/year
Every day or almost every day	6/week	312
3-4/week	3.5/week	182
1-2/week	1.5/week	78
2-3/month	2.5/month	30
1/month	1/month	12
6-11/year	8.5/year	8.5
3-5/year	4/year	4
1-2/year	1.5/year	1.5
Never in the past year	0	0

Drinking pattern

Drinking pattern was derived from the GF directly, by combining drinking quantity and drinking frequency (Table 4.4). Light-to-moderate drinking was defined as ≤4 drinks during one day among men, while ≤2 drinks was used for women; higher intakes were considered as heavy drinking. Regular drinking was defined as ≥1/week; less than that was considered irregular drinking. Due to the small number of women who drank >2 drinks during one day (heavy drinking), when categorising regular

versus irregular heavy drinking among women, ≥1/month was used as the cut-point of drinking frequency instead of ≥1/week.

Table 4.4. Categorisation of drinking pattern among drinkers

Drinking pattern	Men	Women
Irregular light-to-moderate	≤4 drinks a day, <1/week	≤2 drinks a day, <1/week
Regular light-to-moderate	≤4 drinks a day, ≥1/week	≤2 drinks a day, ≥1/week
Irregular heavy	>4 drinks a day, <1/week	>2 drinks a day, <1/month
Regular heavy	>4 drinks a day, ≥1/week	>2 drinks a day, ≥1/month

4.4.2.2 Problem drinking

The CAGE questionnaire[216] was used to evaluate problem drinking. The CAGE consists of 4 questions on cutting down on drinking, getting annoyed by others' criticisms on drinking, feeling guilty on drinking, and having a drink first thing in the morning ('eye-opener'). Problem drinking was classified by using the recommended cut-off of having ≥2 positive responses to the 4 questions.[224,268]

4.4.2.3 Past drinking behaviour

Past drinking behaviour was assessed in the Russian cohort. Participants were asked whether they used to drink more alcohol than they did during the past year, and if yes, they were asked to provide detailed reasons (health and non-health) why they cut down drinking. Health reasons comprised of several medical conditions including CVD, gastrointestinal diseases, neurological and cerebrovascular diseases, respiratory diseases, urological diseases, rheumatic diseases, injury and other illness. Non-health reasons covered age, work, family circumstances, difficulty to get hold of alcohol and other reasons.

Based on the response to cutting down on drinking, current non-drinkers identified by the GF were further divided into lifetime abstainers and former drinkers. Likewise

current drinkers were grouped into those who had reduced their consumption versus 'continuing' drinkers. Based on the reasons of cutting down on drinking, former drinkers and reduced drinkers were further divided into: due to health reasons versus due to other reasons (Table 4.5).

Table 4.5. Categorisation of past drinking behaviour in the Russian cohort

GF	**Cut down on drinking**		
	No	Yes	
		Health reasons	Non-health reasons
Non-drinkers	Lifetime abstainers	Former drinkers, health reasons	Former drinkers, non-health reasons
Drinkers	Continuing drinkers	Reduced drinkers, health reasons	Reduced drinkers, non-health reasons

4.4.3 Covariates and auxiliary variables

In the light of the literature review reported in the Background Chapter, several covariates measured at baseline were included in the data analyses to control for possible confounding. Some other variables were used as auxiliary variables in the process of handling missing data.

4.4.3.1 Socio-demographic variables

Age at baseline was divided into 5-year groups, to allow a potential non-linear age effect on physical functioning. Education, number of household amenities, and current economic activity were selected to reflect participants' socioeconomic position (SEP). The highest educational attainment was grouped into university, secondary school, and less than secondary school. Twelve currently owned household amenities (e.g., microwave, mobile phone, washing machine, television and car), which are comparable across the three countries, were assessed and the sum score was used in the analyses. Current economic activity was categorised into

working, pensioner but still employed, pensioner without employment, and unemployed. Marital status was dichotomised into married/cohabiting or not (single, divorced or widowed).

4.4.3.2 Health-related and behavioural variables

Participants reported whether they had been diagnosed or hospitalised for a disease of the spine or joints. BMI (kg/m^2) was calculated by objectively measured height and weight, and further categorised according to the WHO cut-points (underweight<18.5, normal weight: 18.5–24.9; overweight: 25.0–29.9; obese: ≥30.0). Due to the very small number of underweight participants (15 Czechs, 79 Russians and 45 Poles), this group was combined with the normal weight category. Smoking status was grouped into never, former and current smoking.

4.4.3.3 Auxiliary variables

Except drinking behaviour at re-examination, all other auxiliary variables used in this thesis were measured at baseline, including self-rated health, long-term health problem, injury, CVD, cancer, hypertension, physical activity, number of household amenities in childhood, depressive symptoms and social networks.

At re-examination, a shorter version of the GF with 3 levels of drinking quantity (≥5, 3–4 and 0.5–2 drinks) and the same 9 categories of drinking frequency was used to assess participants' alcohol consumption in the past 12 months. Drinking indices were derived based on the same rationale and mathematical algorithms as the GF at baseline. Problem drinking was evaluated again using the CAGE questionnaire. Data regarding drinking behaviour at re-examination were used as auxiliary variables to handle missing data in the longitudinal dataset, but not included in the main analyses.

At baseline, participants rated their health over the past 12 months as very good, good, average, poor or very poor, and reported whether they had any long-term health problems that they sought medical treatment in the past 12 months. Information on injury was obtained by the question that whether they had been injured or had an accident serious enough to contact a doctor in the past 12 months.

Presence of CVD combined self-reports on whether participants had been diagnosed or hospitalised for heart attack/acute myocardial infarction, angina/ischaemic heart disease and stroke. Hypertension was based on objectively measured blood pressure (systolic pressure≥140 mmHg and diastolic pressure≥90 mmHg), and self-reported medication use for hypertension in the past two weeks. Physical activity was assessed by the hours per week participants spend on physically demanding activities (e.g., housework, gardening and maintenance of the house) and on sports, games, or hiking. Participants were asked about six amenities that their household had when they were aged approximately 10 years, including cold and hot tap water, owning a radio, a fridge, having their own kitchen and toilet. Depressive symptoms were measured using the 20-item Center for Epidemiologic Studies Depression Scale (CES-D)[269], and a continuous score ranging 0–60 was used. Social networks combined the frequency of participants contact with friends and with relatives.

4.5 Missing Data

Handling missing data inappropriately leads to biased estimates of parameters and standard errors, unreliable confidence intervals and significance tests, and larger Type I and Type II error rates.[263,270] In a longitudinal context, missing data are of a greater concern in how they affect the estimates of rate of changes over time along with their confidence intervals and significance tests.[271] For these reasons, a particular attention was paid to missing data.

4.5.1 Missing data patterns

Schafer and Graham[272] classified three patterns of missing data: univariate, monotone, and non-monotone pattern. In a dataset, if only Y (a single variable or a variable derived from a set of variables, e.g., from a scale or questionnaire) is missing; this is a univariate pattern. If the variables are ordered in a way that, when Y_j is missing, all variables after it (Y_{j+1}, Y_{j+2}, $\ldots Y_p$) are missing, the missing pattern is monotone. Any variable from any participant can be missing and it is defined as a non-monotone or arbitrary missing pattern.

In a longitudinal setting, a monotone missing pattern is caused by dropout or permanent attrition (participants not returning after they fail to attend one measurement occasion of the study); in contrast, when participants are observed again, this is a non-monotone missing pattern.[273-275] According to this classification, the missing data pattern in the HAPIEE study is non-monotone (see Table 4.2).

4.5.2 Missing data mechanisms

Missing data mechanisms, originally proposed by Rubin[276], are crucial for researchers to choose a proper method to analyse data at hand, since certain statistical techniques are valid under specific assumptions of particular missing data mechanisms.[261,271,272,275,277,278]

In descending restrictiveness, the missing data mechanisms are: missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR).[271,272,274,277-279] Let R denote the missing data indicator of a variable Y, in which 0 indicates observed and 1 indicates missing. Given R, Y is composed of observed Y (Y^o) and missing Y (Y^m). X denotes a set of covariates related to Y. Under MCAR, the distribution of R does not depend on either Y^o or Y^m.[271,279] A crucial implication of MCAR is that completers are a random sample of the target population and there is no systematic difference between observed and missing data; as a consequence, complete-case analysis yields unbiased estimates of parameters and confidence intervals, in spite of larger standard errors and loss of statistical power.[272,277,279-281]

Under MAR, the distribution of R depends on Y^o but not on Y^m, implying that any systematic differences between observed and missing data can be explained by differences in the observed data.[271,279] In other words, completers are a biased sample of target population under MAR.[271,279] The key difference between MAR and MNAR is whether the distribution of R is related to Y^m or not; if so, the missingness is MNAR.[271,279] Under MNAR, systematic differences between observed and missing data remain after accounting for observed data.[271,279]

Since the distribution of R does not depend on Y^m under MCAR and MAR, the missing data mechanism does not need to be modelled which considerably simplifies the computation of estimating parameters of interest; in contrast, under MNAR, the missing data mechanism must be modelled.[271,277,278,280] Because of this, MCAR and MAR are '**ignorable**' missingness, while MNAR is '**non-ignorable**'.[271,277,280] Given a dataset, it is impossible to test MAR versus MNAR simply because the values of Y^m are unknown, therefore whether the distribution of R is related to Y^m or not is unknown.

The plausibility of MAR can be improved by collecting data on X and incorporating them in data analysis.[263] Although researchers should expect MNAR in real-life research, Graham[261] argued that missingness should be seen as lying somewhere on a continuum between MAR and MNAR. Using statistical techniques valid under MAR in a MNAR circumstance, especially when incorporating more X, may influence the estimates of parameters and standard errors slightly.[272,280] Even when MNAR statistical techniques (e.g., selection models and pattern-mixture models) are adopted, the estimates are sensitive to the assumption researchers make on the missing process because the assumption itself is specified in modelling (expanded on further in Section 6.2.5).[277]

In the HAPIEE study, the possibility of MCAR was ruled out, since the missingness of the PF-10 score, as the outcome variable, was related to many other variables (e.g., age, sex, SEP, health conditions, depressive symptoms and smoking). Although MAR versus MNAR is untestable, there were extensive data on participants' characteristics (X variables, e.g., SEP, self-rated health, medical conditions, health behaviours and psychosocial factors) collected in the HAPIEE study, which were associated with the missingness. Incorporating these data into the data analyses supported the possibility of MAR in the HAPIEE study.

4.5.3 Statistical techniques to handle missing data and multiple imputation

Traditional statistical techniques to handle missing data, for example, complete-case analysis, available-case analysis, replacing missing values with a specific value as a

separate category, and single imputation, generally yield unbiased estimates only under MCAR (see details in Appendix E).[272,277] Modern statistical techniques, such as multiple imputation (MI) and full-information maximum likelihood (FIML), outperform traditional methods and single imputation because (if correctly specified) they yield unbiased estimates under **ignorable** missingness (i.e., MCAR and MAR) and they are more powerful without loss of statistical power.[261,264,282]

In essence, MI is a data-based technique that handles missing data before analysis; FIML is a model-based technique that deals with missing data during model estimation.[261,264,272] MI and FIML give similar estimates of parameters, when the imputation model and analysis model in MI are identical and the same analysis model is fitted in FIML.[264,272] However, incorporating covariates in MI is much more straightforward and simpler than in FIML.[261,273] Using FIML, cases with incomplete covariates are conventionally excluded from analysis in most commonly used statistical packages.[282] On account of the possibility of MAR (especially by incorporating data on the *X* variables) and incomplete covariates in the HAPIEE study, MI was chosen to deal with missing data in this thesis.

4.5.3.1 Basic concepts and steps of multiple imputation

Multiple imputation takes into account the uncertainty of imputed values by generating several imputed datasets.[279] The core of MI is to replace missing values by values based on the distribution of observed data; once the multiply imputed datasets are obtained, standard methods for complete-case analysis are applicable.[271,280]

There are three steps to perform MI: 1) replace missing data by plausible values from random draws of posterior predictive distribution of missing data conditional on observed data. The procedure is repeated *m* times to generate *m* imputed datasets; 2) analyse each of the *m* imputed datasets separately by standard complete-data methods; and 3) combine the separate *m* estimates of the parameter of interest into an overall estimate alongside variances and confidence intervals.[263,273,278,279] Rubin's

rules[283] are applied to combine estimates of the parameter from *m* imputed datasets in the third step of MI.

MI can be carried out by assuming a joint multivariate normal distribution or by using a set of univariate conditional distributions (also known as full conditional specification).[264,273,278,280] The first approach is not appropriate for non-monotone missing pattern,[273,284] and a joint normal distribution is unlikely for a large dataset with various types of variables (e.g. continuous, binary, nominal and count variables).[264,284,285] Under those circumstances, the second approach is more applicable and practical.[263,286]

4.5.3.2 Multiple imputation by chained equations

Considering the non-monotone missing pattern, large sample size, and various types of study variables in the HAPIEE study, full conditional specification (FCS) was used to perform multiple imputation. FCS is also known as multiple imputation by chained equations (MICE) and sequential regression multivariate imputation (SRMI).

MICE completes the first step of MI using the following steps:[263,285,287]

1. Replace missing values by random sampling from the observed values;
2. Variables with missing values are ordered in a form from those with the least missing values to with the most (y_1, y_2,…, y_k). Observed y_1 is regressed on y_2,…, y_k, and then missing y_1 is replaced by simulated draws from the posterior predictive distribution of observed y_1. Similarly, observed y_2 is regressed on complete y_1 (observed and imputed y_1), y_3,…, y_k, and missing y_2 is replaced by simulated draws from the posterior predictive distribution of observed y_2. This process carries on until all the variables with missing values are imputed, and it is called a cycle (or an iteration);
3. Several cycles (e.g. 10 or 20) are performed to stabilise imputations, and the imputations are renewed by each cycle. The imputations from the final cycle are used to generate one single imputed dataset;

4. Steps are repeated to generate *m* imputed datasets.

Various models can be specified for different types of variables: linear regression and predictive mean matching (PMM) for continuous variables; logistic regression for binary variables; ordered logistic regression for ordinal variables; and multinomial logistic regression for nominal variables.[263,284] PMM is advisable for non-normally distributed continuous variables which cannot be transformed to achieve normality or those with a range of observed values.[263,284]

To perform MICE appropriately, several caveats on selecting variables have been highlighted.[263,264,278,279,285] First, all variables in the analysis model must be included in the imputation model, and the outcome variable must be included in the imputation model of covariates. Second, variables which predict missingness and/or values of the variable being imputed should be included in the imputation model, to maximise the plausibility of MAR, to ameliorate the imputations, and to reduce the standard errors of estimates in the analysis model. These variables are auxiliary variables. It is considered wiser to include more variables than needed rather than less in the imputation model, because over-inclusion may reduce the precision of the final estimates but it will not lead to biased estimates, whereas the exclusion of crucial predictive variables causes bias.[263,278]

Another issue is how many imputations are adequate. Graham *et al.*[288] and White *et al.*[263] argued that *m* depends on the unknown fraction of missing information (FMI). A rule of thumb is that *m* should be equal or greater than the proportion of incomplete cases.[263,289] However, this rule is not equally applicable to all settings,[263] and *m* is also depends on the size of dataset and computational resources in practice.[285]

4.5.4 Multiple imputation by chained equations in the HAPIEE study

The missingness in study variables in the Czech, Russian and Polish cohorts is provided in Table 4.6. The main source of missingness comes from the PF-10 scores at follow-up (30.7%–65.6%) and alcohol consumption at re-examination (33.9%–

48.6%). The proportion of Polish participants with missing data on the CAGE at baseline was 20.4%, which was higher than their Czech and Russian counterparts. Since some Czech and Polish participants did not attend the medical examination at baseline (see Section 4.1), 18.0% of Czechs and 13.5% of Poles did not have data on BMI.

Table 4.6. Missingness in study variables

Study variables	Missing (N, %)		
	Czech Republic	**Russia**	**Poland**
Total	8773	9301	10709
PF-10 score			
Baseline	142 (1.6)	0	75 (0.7)
Re-examination	3614 (41.2)	3154 (33.9)	4100 (38.3)
PQ2009	3578 (40.8)	2857 (30.7)	3508 (32.8)
PQ2012	4175 (47.6)	4685 (50.4)	7024 (65.6)
Alcohol consumption			
Baseline GF	311 (3.5)	1 (<0.1)	60 (0.6)
Baseline CAGE	450 (5.1)	1 (<0.1)	2186 (20.4)
Covariates			
Socio-demographic factors			
Age	0	0	0
Sex	0	0	0
Marital status	38 (0.4)	0	26 (0.2)
Education	47 (0.5)	0	11 (0.1)
Household amenities in adulthood	534 (6.1)	45 (0.5)	166 (1.6)
Current economic activity	102 (1.2)	0	25 (0.2)
Health-related and behavioural factors			
Spine/joint problems	224 (2.6)	0	37 (0.4)
BMI	1579 (18.0)	1 (<0.1)	1449 (13.5)
Smoking	117 (1.3)	0	31 (0.3)
Auxiliary variables			
GF at re-examination	3612 (41.2)	3154 (33.9)	4102 (38.3)
CAGE at re-examination	3612 (41.2)	3155 (33.9)	5209 (48.6)
Household amenities in childhood	493 (5.6)	58 (0.6)	330 (3.1)
Self-rated health	54 (0.6)	0	19 (0.2)
Long-term health problem	117 (1.33	0	66 (0.6)
Injury	66 (0.8)	0	197 (1.8)
CVD	392 (4.5)	0	98 (0.9)
Hypertension	1593 (18.2)	10 (0.1)	1481 (13.8)
Cancer	438 (5.0)	0	96 (0.9)
CES-D score	585 (6.7)	2435 (26.2)	230 (2.2)
Social networks	56 (0.6)	1 (<0.1)	20 (0.2)
Non-participation of medical examination at baseline	1576 (18.0)	0	1436 (13.4)

N: number of participants

Based on the variables included in the analysis model (the PF-10 score, baseline alcohol consumption and covariates), Table 4.7 shows the completeness of the three HAPIEE cohorts. Using the rule of thumb previously described, *m*=25 imputations and *m*=70 imputations were generated for the cross-sectional dataset and longitudinal dataset, respectively. The imputed datasets, cross-sectional and longitudinal, contain both non-missing data and imputed data.

Table 4.7. Completeness of variables in the analysis model

	Completeness (N, %)			
	Czech Republic	**Russia**	**Poland**	**Total**
Total	8773	9301	10709	28783
Completeness				
Cross-sectional dataset	6234 (71.1)	9255 (99.5)	7219 (67.4)	22708 (78.9)
Longitudinal dataset	2891 (33.0)	3645 (39.2)	2326 (21.7)	8862 (30.8)

N: number of participants

The specification of imputation models for the cross-sectional dataset and longitudinal dataset are summarised in Table 4.8 and Table 4.9, respectively. Several auxiliary variables (see Section 4.4.3.3) were added into the imputation models because they are predictive of the missingness and/or values of variables in the analysis model. Another variable, attendance of medical examination at baseline, was also included because it may be related to the missing process, as 1,576 Czechs (18.0%) and 1,436 Poles (13.4%) did not attend the medical examination after the home visit. It is likely that some of them did not make it because of their poor health or poor mobility, which is directly associated with physical functioning. Non-participation in the medical examination in the Czech and Polish cohorts was less relevant to the PF-10 score at baseline than to scores at subsequent occasions. Among Czechs and Poles who did not attend the medical examination, 96.5% of Czechs and 99.2% of Poles reported PF-10 score at baseline. Compared with participants who attended the medical examination at baseline, those who did not attend the examination reported lower PF-10 scores at all four measurement

occasions in both cohorts. As a result, inclusion of attendance of medical examination as an auxiliary variable improves the imputation, and makes sure that the imputed values of the PF-10 scores in the Czech and Polish cohorts reflect the participants' health status. Age, sex and attendance of medical examination were complete for all participants and acted as predictors for all variables with missing values.

In the imputation of the cross-sectional dataset, the PF-10 score, drinking indices derived from the GF, and problem drinking at baseline were used (Table 4.8). In the imputation of the longitudinal dataset, since the PF-10 scores at baseline and follow-up were correlated with each other, the PF-10 scores from baseline, re-examination, PQ2009 and PQ2012 were entered into the imputation models as predictors for each other (Table 4.9). Information on the PF-10 scores from other measurement occasions makes the imputed values of the PF-10 score more plausible. Likewise drinking behaviour at re-examination was used to impute baseline alcohol consumption in the longitudinal dataset. The imputation models of covariates and auxiliary variables in the cross-sectional dataset were basically the same as in the longitudinal dataset (Table 4.8–4.9). Except, in the longitudinal dataset, the PF-10 scores at all measurement occasions and drinking behaviour at re-examination were used as predictors in the imputation models of covariates and auxiliary variables (Table 4.9).

PMM was specified for all the continuous and semi-continuous (e.g., CES-D score) variables except BMI, because they were not normally distributed and had a restricted range of values that could be possibly observed (e.g., it is impossible for drinking indices to be negative). Linear regression was used for the normally distributed BMI. Logistic regression was employed for binary variables. Ordered logistic regression was specified for categorical variables with an order in nature; otherwise multinomial logistic regression was used (e.g., current economic activity).

Here, two important terms, **completers** and **complete cases**, need to be clarified. Throughout this thesis, **completers** in the HAPIEE study refer to participants whose PF-10 scores were non-missing at all four measurement occasions. **Complete cases**,

however, refer to participants with complete information on all variables including the PF-10 score, alcohol consumption and covariates. It is worth noting that the complete cases in the cross-sectional dataset are different from those in the longitudinal dataset. Complete cases in the cross-sectional dataset are participants with no missing data on the baseline PF-10 score, baseline alcohol consumption and baseline covariates. In the longitudinal dataset, they are those with no missing data on the PF-10 scores at baseline and throughout follow-up, baseline alcohol consumption or baseline covariates.

Table 4.8. Imputation models for cross-sectional dataset

Study variable	Model	Predictors
Baseline PF-10 score	PMM	Baseline drinking pattern and problem drinking, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Average drinking frequency	Ordered logistic regression	Baseline PF-10 score, baseline problem drinking, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Annual drinking volume	PMM	Baseline PF-10 score, baseline problem drinking, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Average drinking quantity/day	PMM	Baseline PF-10 score, baseline problem drinking, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Drinking pattern	Ordered logistic regression	Baseline PF-10 score, baseline problem drinking, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Problem drinking	Logistic regression	Baseline PF-10 score, baseline drinking pattern, baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Baseline covariates		
Marital status	Multinomial logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Education	Ordered logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Household amenities in adulthood	PMM	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Current economic activity	Multinomial logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Spine/joint problems	Multinomial logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
BMI	Linear regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Smoking	Multinomial logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, all other baseline covariates, auxiliary variables, age, sex and attendance of medical examination
Auxiliary variables		
Household amenities in childhood	Ordered logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Self-rated health	Ordered logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Long-term health problem	Logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Injury	Logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
CVD	Multinomial logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination

Table 4.8 continued

Study variable	Model	Predictors
Hypertension	Logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Cancer	Logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Physical activity	PMM	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
CES-D score	PMM	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination
Social networks	Ordered logistic regression	Baseline PF-10 score, baseline drinking pattern and problem drinking, baseline covariates, all other auxiliary variables, age, sex and attendance of medical examination

Table 4.9. Imputation models for longitudinal dataset

Study variable	Model	Predictors
PF-10 score		
Baseline	PMM	All other PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Re-examination	PMM	All other PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
PQ2009	PMM	All other PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
PQ2012	PMM	All other PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Baseline alcohol consumption		
Average drinking frequency	Ordered logistic regression	All PF-10 scores, average drinking frequency at re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Annual drinking volume	PMM	All PF-10 scores, annual drinking volume at re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Average drinking quantity/day	PMM	All PF-10 scores, average drinking quantity per day at re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Drinking pattern	Ordered logistic regression	All PF-10 scores, drinking pattern at re-examination, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Problem drinking	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Baseline covariates		
Marital status	Multinomial logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Education	Ordered logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Household amenities in adulthood	PMM	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Current economic activity	Multinomial logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Spine/joint problems	Multinomial logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
BMI	Linear regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Smoking	Multinomial logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, all other baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination

Table 4.9 continued

Study variables	Model	Predictors
Auxiliary variables		
Alcohol consumption at re-examination		
Average drinking frequency	Ordered logistic regression	All PF-10 scores, average drinking frequency at baseline, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Annual drinking volume	PMM	All PF-10 scores, annual drinking volume at baseline, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Average drinking quantity/day	PMM	All PF-10 scores, average drinking quantity per day at baseline, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Drinking pattern	Ordered logistic regression	All PF-10, scores drinking pattern at baseline, problem drinking at baseline and re-examination, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Problem drinking	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline, baseline covariates, baseline auxiliary variables, age, sex and attendance of medical examination
Baseline auxiliary variables		
Household amenities in childhood	Ordered logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Self-rated health	Ordered logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Long-term health problem	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Injury	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
CVD	Multinomial logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Hypertension	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Cancer	Logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Physical activity	PMM	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
CES-D score	PMM	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination
Social networks	Ordered logistic regression	All PF-10 scores, drinking pattern at baseline and re-examination, problem drinking at baseline and re-examination, baseline covariates, all other baseline auxiliary variables, age, sex and attendance of medical examination

4.6 Statistical Analyses

Different statistical methods were adopted to analyse the cross-sectional dataset and longitudinal dataset.

4.6.1 Cross-sectional analyses

The distribution of the PF-10 score at baseline is asymmetrical in the three HAPIEE cohorts, as seen in Figure 4.2. A considerable proportion of participants had the highest possible PF-10 score of 100 (16.0% Czechs, 21.1% Russians and 21.4% Poles), suggesting a ceiling effect of the PF-10 subscale.

Normality of the PF-10 score could not be achieved by transformation (e.g., log transformation, inverse transformation, square and square-root transformation). To deal with the non-normality of the PF-10 score, the score was first categorised into quartiles. Initially, ordered logistic regression was estimated, but its fundamental assumption of proportionality of odds (the odds of an independent variable are constant at each cumulative split of the ordinal dependent variable) was violated. Multinomial logistic regression, as an alternative, provided a lot of statistical information which was difficult to integrate and interpret.[290] Moreover, since previous studies have very rarely applied multinomial logistic regression, its use in this thesis would constrain the comparability of findings with previous studies.

In order to address the non-normality of the scores derived from the SF-36 (each of the eight subscales has a score ranging 0–100), Rose *et al.*[291] proposed an indicator of being impaired (at the specific health dimension captured by each subscale) by having a score less than the lowest quartile in the population. According to this, the PF-10 score at baseline was dichotomised (lowest quartile in the three cohorts: PF-10 score<75). Participants with the PF-10 score less than 75 were considered having physical limitations in the data analyses. As a result, multivariable logistic regression, despite its limitations, emerged as the most appropriate, practical and comparable statistical technique to examine the associations of alcohol consumption and past drinking behaviour with physical limitations at baseline.

The data analyses were performed in men and women separately, since gender may be a possible effect modifier,[256,257] and a considerable gender difference in both alcohol consumption and physical functioning was seen in the HAPEIE study. Two models were used for the multiply imputed cross-sectional datasets: 1) adjusted for age. Age-adjusted models are presented separately because age is the single most important influence on physical functioning and its decline in middle-aged and older adults (Section 2.3.4); and 2) additionally adjusted for marital status, education, current economic activity, household amenities, spine/joint problems, BMI and smoking status.

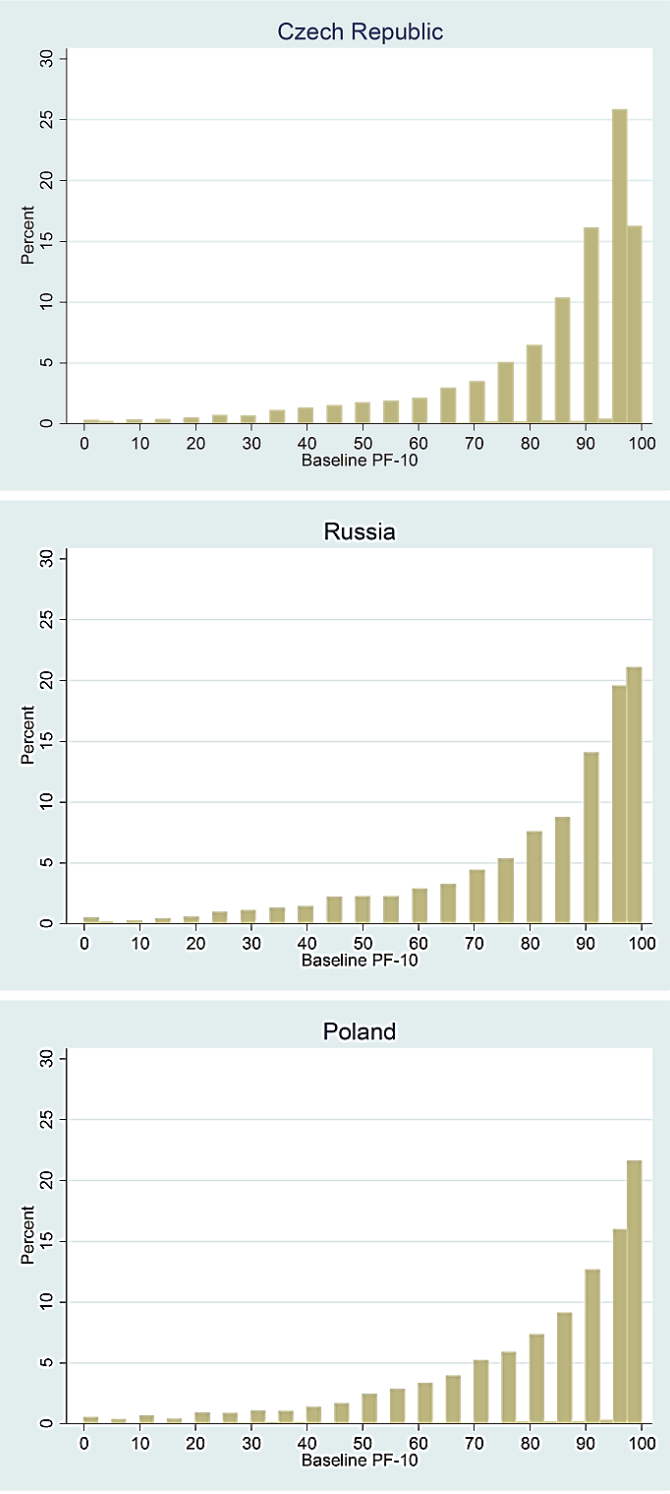


Figure 4.2. Distribution of the PF-10 score at baseline

4.6.2 Longitudinal data analyses

Proceeding to the data analyses of the longitudinal dataset, several issues relating to the PF-10 score at re-examination and missing follow-up time had to be addressed. The trajectories of the PF-10 score over time in the three HAPIEE cohorts were estimated by multilevel modelling, along with the relationships of alcohol consumption at baseline and past drinking behaviour with the trajectories.

4.6.2.1 Adjustment of the PF-10 score at re-examination

Among participants with complete PF-10 scores at all measurement occasions (completers: 3,488 Czechs, 3,656 Russians and 3,056 Poles), the mean PF-10 score at re-examination were higher at all ages and in both sexes than at baseline among Czechs and Poles but not Russians (Appendix F.1). The most likely explanation for the observed increase is the change in the mode of data collection between baseline and re-examination (see Section 4.1). In Russia, participants completed the questionnaire together with trained nurses at both measurement occasions. In the Czech Republic and Poland, by contrast, participants largely self-completed the questionnaire at baseline, while at re-examination, they completed the questionnaire during the interview with trained nurses. Consequently, it is likely that, compared with baseline, Czech and Polish participants over-reported their physical functioning at re-examination in the presence of trained nurses, possibly due to the shame or stigma attached to being unhealthy (social desirability bias).[258] This issue will be discussed in detail in the Discussion Chapter (see section 6.2.2.4).

The PF-10 score at re-examination in the Czech and Polish cohorts were therefore adjusted. In the two cohorts and both sexes, the trends of the PF-10 score over age at baseline, PQ2009, and PQ2012 were fairly straight and clustered (Appendix F.1), suggesting that the PF-10 score declined over both age and follow-up time linearly. This linear decline assumption was used to adjust the PF-10 score at re-examination by using a scaling factor (Equation 2).

$$y' = y - (\alpha_1 - \alpha_2) \times d \qquad (2)$$

Where, y' is the adjusted PF-10 score at re-examination; y is the observed PF-10 score at re-examination; α_1 is the average rate of change in the PF-10 score *per day* between baseline and re-examination; α_2 is the average rate of change in the PF-10 score *per day* between baseline and PQ2012; d is the follow-up days between baseline and re-examination.

There are several technical notes for this adjustment procedure. Firstly, α_1 and α_2 were calculated among completers (i.e., participants with the PF-10 score observed at all measurement occasions), in order to keep the samples from which to derive α_1 and α_2 the same. Secondly, the adjustment was applied to all observed PF-10 scores at re-examination. Finally, the adjustment was done by cohort, sex, and every year of age separately. Table 4.10 compares the observed and adjusted PF-10 score at re-examination among completers. The figures of the adjusted PF-10 score at re-examination alongside the PF-10 scores measured at other occasions over age is provided in Appendix F.2.

Table 4.10. Comparison between observed and adjusted PF-10 score at re-examination among completers

PF-10 score	**Czech Republic** (mean, S.D.)		**Poland** (mean, S.D.)	
	Men	Women	Men	Women
Baseline	88.44 (14.14)	84.73 (16.86)	86.87 (17.07)	80.09 (19.72)
Re-examination				
Observed	91.17 (13.81)	87.85 (15.67)	88.60 (16.58)	81.94 (18.28)
Adjusted	86.27 (14.00)	83.11 (15.93)	80.02 (16.77)	73.77 (18.79)
PQ2009	84.93 (18.16)	81.78 (19.28)	78.04 (23.67)	68.15 (25.22)
PQ2012	83.59 (19.46)	80.84 (20.92)	73.40 (25.06)	64.51 (26.34)

S.D.: standard deviation

4.6.2.2 Follow-up time

Due to the non-response at re-examination, PQ2009 and PQ2012, follow-up days were missing for those who did not take part in these data collections. Follow-up

days were not imputed by multiple imputation as they did not depend on observed data. Instead, the following approach has been used. Let f_1, f_2, f_3 denote the follow-up days between baseline and re-examination, between baseline and PQ2009, and between baseline and PQ2012, respectively. Missing f_1, f_2, f_3 were substituted by random numbers generated from normal distributions of non-missing f_1, f_2, f_3 (distributions see Appendix G) and for each cohort separately, with the condition of $f_1 \leq f_2 \leq f_3$. Table 4.11 compares the non-missing and substituted follow-up years.

Table 4.11. Comparison of observed and substituted follow-up years

Follow-up years	**Non-missing**		**Substituted**	
	Mean (min, max)	Total	Mean (min, max)	Total
Czech Republic				
Baseline-Re-examination	3.63 (1.82, 5.49)	5162	3.61 (2.14, 4.95)	3611
Baseline-PQ2009	5.80 (3.76, 7.49)	5246	5.87 (4.32, 7.47)	3527
Baseline-PQ2012	8.43 (6.71, 9.90)	4637	8.39 (6.78, 9.82)	4136
Russia				
Baseline-Re-examination	3.11 (1.08, 5.87)	6148	3.09 (1.13, 5.72)	3153
Baseline-PQ2009	5.34 (3.62, 7.54)	6958	5.37 (3.64, 7.24)	2343
Baseline-PQ2012	8.24 (6.74, 10.68)	3667	8.38 (6.75, 10.64)	5634
Poland				
Baseline-Re-examination	3.99 (2.52, 5.39)	6614	3.99 (2.75, 5.26)	4095
Baseline-PQ2009	6.24 (5.02, 8.55)	7979	6.24 (5.12, 7.65)	2730
Baseline-PQ2012	8.89 (7.87, 9.83)	3735	8.87 (7.87, 9.83)	6974

4.6.2.3 Growth curve modelling

Growth curves of longitudinal data can be estimated via two approaches: 1) multilevel level modelling (MLM); and 2) structural equation modelling (SEM).[292-299] MLM and SEM share the same basic rationale when modelling growth curves.[293,294,296,298,299] In MLM, time is modelled as a fixed explanatory variable (univariate approach), whilst time is introduced via factor loadings in SEM (multivariable approach).[293-295,297,300,301] MLM and SEM yield similar results across a

wide range of models, including linear growth models and some non-linear ones.[294,297-299] Both of them are commonly estimated by standard maximum likelihood and FIML.[298]

Given the central role of time in growth curve modelling, it is important to specify the types of longitudinal data that may be available. Three types of longitudinal data can be identified:[298]

1. *Type I: balanced on time with complete data*: time interval between two adjacent measurement occasions is fixed (time is discrete), and every subject is observed at each measurement occasion.

2. *Type II: balanced on time with data missing at random*: time interval between two adjacent measurement occasions is fixed, but not every subject is observed at every measurement occasion and the missingness is MAR;

3. *Type III: unbalanced on time*: every subject is observed at a potentially different set of time points. For example, longitudinal data are collected in continuous time.

The MLM approach is able to handle *type III* longitudinal data, whereas conventional SEM is only able to handle *Type I* and *Type II* longitudinal data.[295,297-299]

In the HAPIEE study, the follow-up time is continuous and varies between participants (Appendix G). Since the growth curves of the PF-10 score are a function of time, it is crucial to specify the time metric correctly. Fixed factor loadings in SEM represent discrete time interval between measurement occasions (e.g., if using mean follow-up years, the factor loadings for baseline, re-examination, PQ2009 and PQ2012 are 0, 3.6, 5.8 and 8.6, respectively). By doing so, it implies that, for all participants, their PF-10 scores were measured at the same time at each measurement occasion, which is not the case in the HAPIEE study and therefore not appropriate. In contrast to SEM, MLM which allows modelling individually varying follow-up time is more appropriate and practical to estimate the PF-10 trajectories over time in the HAPIEE study.

To put it more simply, two participants, for example, had the same PF-10 scores at all measurement occasions (e.g., 100, 95, 90 and 85 at baseline, re-examination, PQ2009 and PQ2012, respectively). The follow-up time differed between them: one participant was observed 3.6 (re-examination), 5.8 (PQ2009) and 8.6 (PQ2012) years after the baseline survey, while the corresponding follow-up years were 4, 6 and 10 respectively for the other participant. Employing SEM approach, these two participants would have the same rate of decline in the PF-10 score per year (if the factor loadings of 0, 3.6, 5.8 and 8.6 were used). Clearly, the genuine rate of decline in the PF-10 score per year was slower in the latter participant than the former one. As a result, standard SEM may not accurately estimate the rate of change in the PF-10 score in the HAPIEE cohorts; instead, MLM approach is more suitable.

In the context of longitudinal data, two-level models (i.e., repeated measures are nested within individuals) are usually adequate to represent growth trajectories. Level 1 captures the shape of intra-individual growth trajectories (Table 4.12, Equation 3), while level 2 captures inter-individual differences in growth parameters (Table 4.12, Equation 4).[292-294,298,302] In other words, level-1 equations describe the growth trajectories over time for each individual; level-2 equations represent the population-level trajectories together with the deviation of individual trajectories from the population average. Based on the work of Wu *et al.*[298], Bollen and Curran[296], and Singer and Willett[302], the equations of conditional linear MLM are presented in Table 4.12. The first parenthetical term in Equation 5 represents fixed effects which are constant across individuals; the second parenthetical term represents random effects which vary across individuals.

MLM assumes that: 1) the repeat measure *y* is normally distributed, and ε_{ij}, ζ_{0i}, and ζ_{1i} have a multivariate normal distribution with a mean of 0; 2) ζ_{0i} and ζ_{1i} are independent of ε_{ij}; 3) ε_{ij} are uncorrelated across individuals and time; and 4) ζ_{0i} and ζ_{1i} are uncorrelated between individuals.[296,299,302] Moderate violations of the normal distribution assumption do not largely affect the estimation of fixed effects; however, violations of independence assumptions (uncorrelated residuals) can lead to biased estimates of parameters, standard errors and test statistics.[298,303] Given the proximally

autocorrelated structure of longitudinal data that adjacent measurement occasions correlate to a larger extent than non-adjacent ones and the correlation decreases with increasing interval between measurement occasions,[303] when fitting MLM, covariance of ε_{ij} between two adjacent measurement occasions should be included in the models.

Covariates can be introduced in both level-1 and level-2 equations, which are known as time-varying covariates (level-1) and time-invariant covariates (level-2).[295] Time-invariant covariates (Z_i) are either background characteristics that do not vary over time (e.g., sex) or covariates that are only measured at the first wave of the study.[295,299,304] $Z_i \times Time_{ij}$ in Equation 5 is a cross-level interaction, and γ_{11} represents the difference of individual slopes across different levels of Z; in other words, the effect of $Time$ on y differs across levels of Z.[299,302] Since only covariates measured at baseline in the HAPIEE study were modelled, all of them were time-invariant covariates. Depending on the primary research interest, the time variable ($Time_{ij}$) can be: 1) follow-up time (or measurement occasions for balanced data); or 2) chronological age.[296,304] In the first application, the effect of other time metrics (e.g., age at first occasion) can be controlled for in the prediction of the intercept and slope (level-2).[296]

Table 4.12. Equations of conditional linear multilevel model

Equations

Level 1 $$Y_{ij} = \pi_{0i} + \pi_{1i} Time_{ij} + \pi_{2i} X_{ij} + \varepsilon_{ij},\ \varepsilon_{ij} \sim N(0, \sigma^2) \quad (3)$$

Level 2 $$\pi_{0i} = \gamma_{00} + \gamma_{01} Z_i + \varsigma_{0i},\ \pi_{1i} = \gamma_{10} + \gamma_{11} Z_i + \varsigma_{1i}$$

$$\begin{bmatrix} \varsigma_{0i} \\ \varsigma_{1i} \end{bmatrix} \sim MVN\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, G = \begin{bmatrix} \tau_{00} \tau_{01} \\ \tau_{10} \tau_{11} \end{bmatrix} \right) \quad (4)$$

Combined $$Y_{ij} = (\gamma_{00} + \gamma_{01} Z_i + \gamma_{10} Time_{ij} + \gamma_{11} Z_i Time_{ij} + \pi_{2i} X_{ij}) + (\varsigma_{0i} + \varsigma_{1i} Time_{ij} + \varepsilon_{ij}) \quad (5)$$

Where

i	Individuals, $i=1, 2, \ldots, N$
j	Time points of repeated measurement occasions
y_{ij}	Repeated measures y for individual i at time j
π_{0i}	Intercept of the individual linear growth trajectory for individual i
π_{1i}	Slope of the individual linear growth trajectory for individual i
π_{2i}	Effect of time-varying covariates
$Time_{ij}$	Time of measurement occasion for individual i at time j
X_{ij}	Time-varying covariates for individual i at time j
ε_{ij}	Residuals of predicted individual growth trajectory for individual i at time j
γ_{00}	Predicted population mean intercept of the linear growth trajectory
γ_{10}	Predicted population mean slope of the linear growth trajectory
γ_{01}	Effect of time-invariant covariates on population mean intercept
γ_{11}	Effect of time-invariant covariates on population mean slope
Z_i	Time-invariant covariates for individual i
ς_{0i}	Deviation of intercept for individual i from population mean intercept
ς_{1i}	Deviation of slope for individual i from population mean slope
τ_{00}	Variance of intercepts
τ_{11}	Variance of slopes
τ_{01}	$= \tau_{10}$, covariance of individual intercepts and slopes
MVN	Multivariate normal distribution
G	Between-individuals covariance matrix of intercepts and slopes

The PF-10 scores in the HAPIEE study are not normally distributed (Figure 4.2). However, according to the rule of thumb proposed by Kline[305], the PF-10 scores are not extremely non-normally distributed (skewness≤3 and kurtosis≤10), which allows the use of maximum likelihood methods (i.e., the estimation employed in this thesis). The assumption of normality for residuals is more important than the normality of the PF-10 scores, but when the sample size is large (e.g., >400), the violation of normality assumption of residuals does not seem to influence conclusions largely.[306]

In this thesis, MLM was applied in the longitudinal data analyses: 1) the PF-10 scores at the four measurement occasions were modelled as outcome y_{ij} ; 2) individually varying follow-up years were entered into the model as $Time_{ij}$, since the primary research aim is to investigate how alcohol consumption is associated with the rate of change in the PF-10 score at follow-up; 3) time at baseline was coded as zero. Centring time of the baseline survey as 0 facilitates interpretation of the intercept (π_{0i}) as initial PF-10 score at the beginning of HAPIEE study and the slope (π_{1i}) as the rate of change in the PF-10 score per year of follow-up;[302] and 4) drinking behaviour at baseline along with age and other covariates measured at baseline were entered into the model as time-invariant variables (Z_i).

Due to the change of the data collection procedure in the HAPIEE study, the measurement error of the PF-10 subscale is likely to be different between the first two measurement occasions (baseline and re-examination) and the latter two occasions (PQ2009 and PQ2012). Taking it into account, residual variances of the PF-10 score at baseline and re-examination were constrained to be the same in the longitudinal data analyses. The same constraint of residual variances was also done between PQ2009 and PQ2012. In addition, on account of the proximally autocorrelated structure of longitudinal data, residual covariance of the PF-10 scores between two adjacent measurement occasions was estimated in all models.

All random effects were estimated to take into account the differences of individual PF-10 trajectories over time. The shape of growth curves, linear or non-linear, was determined first, and then the effect of alcohol consumption on the PF-10 trajectories

was examined. Non-linear models were also fitted in the Czech and Polish cohorts to validate the assumption of linearity made for the adjustment of the PF-10 score at re-examination.

The same as in the cross-sectional data analyses, the longitudinal data analyses were conducted for each cohort and in men and women separately. Two models were also estimated in the longitudinal data analyses: 1) adjusted for age; and 2) fully adjusted for age, marital status, SEP (education, current economic activity and household amenities), spine/joint problems, BMI and smoking status.

4.6.3 Sensitivity analyses

Two sets of sensitivity analyses were carried out in both the cross-sectional and longitudinal datasets, restricting the samples to be: 1) participants without CVD or cancer at baseline in the multiply imputed datasets, to examine the potential role of CVD and cancer in the association between alcohol consumption and physical functioning; and 2) complete cases (i.e. subjects with complete PF-10 score, alcohol consumption and covariates), to assess the possible influence of missing data.

As previously mentioned in Section 2.4.3, non-drinkers and heavy drinkers may be more likely to develop CVD than light-to-moderate drinkers prior to the baseline survey of the HAPIEE study, which may be directly related to their poorer physical functioning reported at baseline (if any). In turn, heavy drinkers who developed CVD before the baseline may then have cut down their alcohol intake or even abstain from alcohol before baseline considering their health conditions. As a result, non-drinkers and less heavy drinkers at baseline may disproportionately include participants who developed CVD and/or cut down their drinking before baseline; these subjects may be more likely to have reported poor physical functioning at baseline. In addition to it, their changes in physical functioning over time may be different from non-drinkers and less heavier drinkers who were free of CVD at baseline. As for participants with cancer at baseline, their physical functioning may be poorer than the general population and deteriorate much more quickly and dramatically over time;[52,160,161] hence they were excluded in the sensitivity analyses as well.

4.6.4 Statistical packages

Stata 13 (StataCorp, 2013) and M*plus* 6.12 (Muthén & Muthén, 1998–2011) were used for the data analyses. Multiple imputation was performed separately for the cross-sectional dataset and longitudinal dataset using MICE in Stata (using *mi impute chained*). The multiply imputed cross-sectional datasets were directly analysed in Stata using the command of multivariable logistic regression for imputed datasets (using *mi estimate: logistic*). Multiply imputed longitudinal datasets were transferred from Stata to M*plus* and analysed in M*plus*.

Maximum likelihood estimation with robust standard errors (MLR) in M*plus* was used in the longitudinal analyses owing to the non-normality of the PF-10 score.[307] The MLR standard errors are computed using a sandwich estimator.[307] Individually varying follow-up years were specified using the TSCORE option in M*plus*.[307] Chi-square test of model fit is not available with TSCORE in M*plus*, because the variance of outcome variable changes as a function of time, then no constant covariance matrix is derivable.[308] Instead, the log-likelihood is given as a model fit statistic.

4.6.5 Statistical power of data analyses

Statistical power of cross-sectional analyses using multivariable logistic regression was calculated using G*Power 3.1[309]. With the probability of a Type I error (α) set at 0.05, the cross-sectional analyses achieved the power of over 90% when the odds ratio (OR) reached 1.15 and over, as presented in Table 4.13.

Table 4.13. Power of multivariable logistic regression by effect size

OR	Czech Republic		Russia		Poland	
	Men	Women	Men	Women	Men	Women
1.10	60.6%	77.0%	60.5%	87.8%	79.1%	91.1%
1.15	90.5%	97.7%	90.4%	99.6%	98.2%	99.8%
1.20	99.0%	99.9%	98.9%	>99.9%	>99.9%	>99.9%

Power analysis of MLM is more complex due to the hierarchical nature of data.[310-312] PinT 2.1.2 (Power in Two-level design, available on http://www.stats.ox.ac.uk/~snijders/multilevel.htm#progPINT)[310,313] was used to calculate the power of longitudinal analyses. PinT gives standard errors of regression coefficients in multilevel linear models (two-level).[314] Power (1-β, β is the probability of a Type II error) was calculated based on the equation of *Effect size/standard error* $\approx (Z_{1-\alpha} + Z_{1-\beta})$.[314] Here, $Z_{1-\alpha}$ and $Z_{1-\beta}$ are Z-scores at levels of given 1-α and 1-β. Given an α level of 0.05 and two-tailed, the power of the longitudinal analyses with estimated rates of change in the PF-10 score in all three cohorts was very high (Table 4.14).

Table 4.14. Power of longitudinal analyses

	Czech Republic		**Russia**		**Poland**	
	Men	Women	Men	Women	Men	Women
Estimated slope (year)[a]	-0.699	-0.621	-2.023	-2.262	-1.556	-1.747
Standard error of slope[b]	0.081	0.080	0.118	0.117	0.097	0.101
Power	>99.9%	>99.9%	>99.9%	>99.9%	>99.9%	>99.9%

[a] estimated slope of change in the PF-10 score over time by M*plus*;
[b] standard error of slope by PinT on the basis of output in M*plus* of variance of intercept, variance of slope, covariance of intercept and slope, and residual variance of the PF-10 score

4.7 Summary

In this chapter, I described the analyses of data from 28,783 Czech, Russian and Polish men and women aged 45–69 years at baseline in the HAPIEE study. Participants were randomly selected from population registers in the seven Czech towns and Krakow (Poland) and from electoral lists in Novosibirsk (Russia), stratified by sex and 5-year age bands. Physical functioning was measured by the same PF-10 of the SF-36 instrument at baseline, re-examination, PQ2009 and PQ2012. Based on participants' responses to the PF-10, a score ranging 0–100 was constructed. Alcohol consumption in the past 12 months prior to baseline was measured by the GF, from which average drinking frequency, annual drinking

volume, average drinking quantity per drinking day, and drinking pattern were derived. Problem drinking at baseline was identified by having ≥2 positive responses to the CAGE questionnaire. In the Russian cohort, past drinking behaviour was also assessed.

Two sets of analyses were performed: first, in the baseline data and second, in the longitudinal data collected at all four measurement occasions. MICE was applied to handle missing data in both datasets. Multivariable logistic regression was adopted to examine the cross-sectional association between alcohol consumption and physical limitations (PF-10 score<75) at baseline. Growth curve modelling by MLM approach was implemented to investigate the individual trajectories of the PF-10 score during follow-up, and whether alcohol consumption was associated with these trajectories. Two models were estimated in both cross-sectional and longitudinal datasets: 1) adjusted for age; and 2) additionally adjusted for marital status, education, current economic activity, household amenities, spine/joint problems, BMI and smoking status. Two sets of sensitivity analyses were also carried out in both cross-sectional and longitudinal datasets with samples to be: 1) participants without CVD and cancer at baseline; and 2) complete case analyses (among participants with complete information on the PF-10 score, alcohol consumption and covariates).

CHAPTER 5 RESULTS

This chapter reports the results of statistical analyses, including a description of the sample characteristics, a comparison between the non-missing and imputed data, and cross-sectional and longitudinal findings on the association between alcohol consumption and physical functioning in the Czech, Russian and Polish HAPIEE cohorts.

5.1 Sample Characteristics

The characteristics of analytical samples for the cross-sectional dataset and longitudinal dataset were summarised separately. Both the cross-sectional and longitudinal datasets consist of 4,070 men and 4,703 women in the Czech cohort, 4,239 men and 5,062 women in the Russian cohort, and 5,219 men and 5,490 women in the Polish cohort.

5.1.1 Baseline dataset

Physical limitations and alcohol consumption at baseline are displayed in Table 5.1. In all three cohorts, fewer men than women had physical limitations (PF-10 score<75) at baseline.

Compared with Czechs and Russians, a higher proportion of Poles reported no drinking in the past 12 months prior to baseline, possibly due to the filter question asked before the GF in the Polish cohort. A gender difference was also seen in alcohol consumption. As expected, men drank more frequently and more heavily than women. The possible influence of the filter question on the classification of non-drinkers in the Polish cohort is discussed in detail in Section 6.2.2.3. According to the WHO European Status Report on Alcohol and Health 2010[94], the proportion of non-drinkers among Poles aged 15 years and over was 16% in men and 34% in women in 2005. In the HAPIEE study, at baseline (2002–2005), the proportion of Polish non-drinkers was 22% in men and 46% in women. These proportions were higher than in the WHO estimates but, taking into account the fact that older persons

drink less alcohol than younger adults, the data on non-drinkers in the Polish cohort are not implausible.

Among men, more Czechs drank at least once per week than their Russian and Polish counterparts. Only 10.4% of Polish men drank more than 8,000 g of alcohol annually, the proportion of which was much lower than in Czech men (28.4%) and Russian men (22.7%). The four drinking categories of average drinking quantity per drinking day (non-drinkers, light drinkers, moderate drinkers, and heavy drinkers) were categorised based on gender-specific thresholds proposed by Rehm *et al.*[176] (0, 0.1–19.9, 20.0–39.9, ≥40.0 g/day for women; 0, 0.1–39.9, 40.0–59.9, ≥60.0 g/day for men; see Section 4.4.2.1). A considerably higher proportion of Russian men (44.4%) were categorised as heavy drinkers, compared with Czech men (16.9%) and Polish men (12.4%). Over half of Czech and Polish men were light drinkers. As a result, combining drinking frequency and quantity into drinking pattern, fewer Polish men were identified as irregular or regular heavy drinkers than their Czech and Russian counterparts. Here, heavy drinking was defined as >4 drinks during one day among men (>2 drinks for women); lower intakes were considered as light-to-moderate drinking. Regular drinking was defined as ≥1/week; less than that was considered irregular drinking. The cut-off of female regular vs. irregular heavy drinking was 1/month (see Section 4.4.2.1).

Among female drinkers, drinking less than once per week (<1/month and 1–3/month) was the most prevalent average drinking frequency in all three cohorts. More Czech women drank more than 1,500 g of alcohol annually than Russian and Polish women. With regard to average drinking quantity per day, more female drinkers engaged with light and moderate drinking than with heavy drinking in all three cohorts. Regarding drinking pattern, 37.9% Czech women, 58.7% Russian women and 33.1% Polish women consumed alcohol in light-to-moderate quantity irregularly (<1/week). A higher proportion of Czech women were categorised as irregular and regular heavy drinkers than Russian and Polish women.

Consistent with drinking indices derived from the GF, a larger proportion of men than women were identified as problem drinkers (based on ≥2 positive responses to

the CAGE questionnaire). More Russian men (19.2%) were problem drinkers in comparison to Czech men (8.9%) and Polish men (8.8%). Only 92 Czech women, 72 Russian women, and 52 Polish women were classified as problem drinkers.

Table 5.2 presents the characteristics of covariates at baseline. Age was distributed almost evenly across cohorts and in both sexes. The proportion of participants in the youngest group (45.00–49.99 years) was slightly lower than in other age groups. More women than men were not married or cohabiting with a partner. Compared to Russians and Poles, a higher proportion of Czechs had an educational attainment lower than secondary school; however, Czechs had more household amenities. In all three cohorts, more men than women were working at baseline, while more women were unemployed or pensioners. In the Czech and Russian cohorts, spine or joint problems in the 12 months prior to baseline were more common in women; the opposite was seen in the Polish cohort. Overweight participants were the largest BMI group in all cohorts and both sexes, except in the Russian cohort that half of the female participants were obese. 25%–30% of male participants reported never smoking; the proportion was about 50% in Czech and Polish women and 85% in Russian women.

Overall, Czechs and Poles reported better health than Russians in terms of self-rated health, long-term health problem, CVD, hypertension and depressive symptoms (Appendix H). Czechs spent fewer hours per week on physical activity than their Russian and Poles counterparts. Poles had less frequent contact with their friends and relatives, compared to Czechs and Russians.

Table 5.1. Physical limitations and alcohol consumption at baseline

	Czech Republic		**Russia**		**Poland**	
	Men	Women	Men	Women	Men	Women
Total	4070	4703	4239	5062	5219	5490
Physical limitations						
No (PF-10 score≥75)	3376 (83.0%)	3605 (76.7%)	3596 (84.9%)	3501 (69.2%)	4129 (79.1%)	3659 (66.7%)
Yes (PF-10 score<75)	643 (15.8%)	1007 (21.4%)	643 (15.2%)	1561 (30.8%)	1056 (20.2%)	1790 (32.6%)
Missing	51 (1.3%)	91 (1.9%)	0	0	34 (0.7%)	41 (0.8%)
Alcohol consumption						
Average drinking frequency						
0	258 (6.3%)	832 (17.7%)	571 (13.5%)	901 (17.8%)	1140 (21.8%)	2533 (46.1%)
<1/month	557 (13.7%)	1263 (26.9%)	587 (13.9%)	2327 (46.0%)	753 (14.4%)	1241 (22.6%)
1-3/month	675 (16.6%)	1149 (24.4%)	1090 (25.7%)	1411 (27.9%)	1216 (23.3%)	1036 (18.9%)
1-4/week	1207 (29.7%)	934 (19.9%)	1630 (38.5%)	399 (7.9%)	1485 (28.5%)	558 (10.2%)
≥5/week	1261 (31.0%)	326 (6.9%)	360 (8.5%)	24 (0.3%)	592 (11.3%)	95 (1.7%)
Missing	112 (2.8%)	199 (4.2%)	1 (<0.1%)	0	33 (0.6%)	27 (0.5%)
Annual drinking volume (g)						
0	258 (6.3%)	832 (17.7%)	571 (13.5%)	901 (17.8%)	1140 (21.8%)	2533 (46.1%)
1-1500[a]/1-250[b]	1256 (30.9 %)	1313 (27.9%)	1194 (28.2%)	1567 (31.0%)	2036 (39.0%)	1364 (24.9%)
1501-4000[a] /251-500[b]	703 (17.3%)	544 (11.6%)	823 (19.4%)	1425 (28.2%)	970 (18.6%)	564 (10.3%)
4001-8000[a] /501-1500[b]	585 (14.4%)	730 (15.5%)	688 (16.2%)	761 (15.0%)	497 (9.5%)	559 (10.2%)
>8000[a] />1500[b]	1156 (28.4%)	1085 (23.1%)	962 (22.7%)	408 (8.1%)	543 (10.4%)	443 (8.1%)
Missing	112 (2.8%)	199 (4.2%)	1 (<0.1%)	0	33 (0.6%)	27 (0.5%)
Average drinking quantity per day						
Non-drinker	258 (6.3%)	832 (17.7%)	571 (13.5%)	901 (17.8%)	1140 (21.8%)	2533 (46.1%)
Light	2634 (64.7%)	1519 (32.3%)	1016 (24.0%)	962 (19.0%)	3037 (58.2%)	1636 (29.8%)
Moderate	377 (9.3%)	1711 (36.4%)	769 (18.1%)	2500 (49.4%)	361 (6.9%)	1106 (20.2%)
Heavy	689 (16.9%)	442 (9.4%)	1882 (44.4%)	699 (13.8%)	648 (12.4%)	188 (3.4%)
Missing	112 (2.8%)	199 (4.2%)	1 (<0.1%)	0	33 (0.6%)	27 (0.5%)
Drinking pattern						
Non-drinker	258 (6.3%)	832 (17.7%)	571 (13.5%)	901 (17.8%)	1140 (21.8%)	2533 (46.1%)
Irregular light-to-moderate	900 (22.1%)	1780 (37.9%)	1010 (23.8%)	2973 (58.7%)	1437 (27.5%)	1925 (33.1%)
Regular light-to-moderate	1111 (27.3%)	555 (11.8%)	740 (17.5%)	216 (4.3%)	1172 (22.5%)	397 (7.2%)
Irregular heavy	1384 (34.0%)	850 (18.1%)	1328 (31.3%)	659 (13.0%)	1259 (24.1%)	421 (7.7%)
Regular heavy	305 (7.5%)	487 (10.4%)	589 (13.9%)	313 (6.2%)	178 (3.4%)	187 (3.4%)
Missing	112 (2.8%)	199 (4.2%)	1 (<0.1%)	0	33 (0.6%)	27 (0.5%)
Problem drinking						
No	3350 (87.2%)	4320 (91.9%)	3425 (80.8%)	4990 (98.6%)	4073 (78.0%)	3941 (71.8%)
Yes	361 (8.9%)	92 (2.0%)	813 (19.2%)	72 (1.4%)	457 (8.8%)	52 (1.0%)
Missing	159 (3.9%)	291 (6.2%)	1 (<0.1%)	0	689 (13.2%)	1497 (27.3%)

[a] among men; [b] among women

Table 5.2. Distribution of covariates at baseline

	Czech Republic		**Russia**		**Poland**	
	Men	Women	Men	Women	Men	Women
Age						
45.00-49.99	642 (15.8%)	838 (17.8%)	672 (15.9%)	912 (18.0%)	907 (17.4%)	1074 (19.6%)
50.00-54.99	778 (19.1%)	957 (20.4%)	837 (19.8%)	972 (19.2%)	1034 (19.8%)	1181 (21.5%)
55.00-59.99	804 (19.8%)	870 (18.5%)	916 (21.6%)	1093 (21.6%)	1121 (21.5%)	1132 (20.6%)
60.00-64.99	904 (22.2%)	1117 (23.8%)	819 (19.3%)	951 (18.8%)	1066 (20.4%)	1064 (19.4%)
65.00-69.99	942 (23.1%)	921 (19.6%)	995 (23.5%)	1134 (22.4%)	1091 (20.9%)	1039 (18.9%)
Missing	0	0	0	0	0	0
Marital status						
Married/cohabiting	3411 (83.8%)	3200 (68.0%)	3720 (87.8%)	3011 (59.5%)	4504 (86.3%)	3644 (66.4%)
Single/divorced/widowed	640 (15.7%)	1484 (31.6%)	519 (12.2%)	2051 (40.5%)	700 (13.4%)	1835 (33.4%)
Missing	19 (0.5%)	19 (0.4%)	0	0	15 (0.3%)	11 (0.2%)
Educational attainment						
Less than secondary school	2028 (49.8%)	2316 (49.3%)	1406 (33.2%)	2029 (40.1%)	1929 (37.0%)	1572 (28.6%)
Secondary school	1284 (31.6%)	1898 (40.4%)	1479 (34.9%)	1697 (33.5%)	1713 (32.8%)	2432 (44.3%)
University	732 (18.0%)	468 (10.0%)	1354 (31.9%)	1336 (26.4%)	1572 (30.1%)	1480 (27.0%)
Missing	26 (0.6%)	21 (0.5%)	0	0	5 (0.1%)	6 (0.1%)
Household amenities						
Mean (S.D.)	7.13 (2.30)	6.63 (2.28)	6.02 (2.17)	5.42 (2.08)	6.71 (2.24)	6.14 (2.21)
Missing	238 (5.9%)	296 (6.3%)	32 (0.8%)	13 (0.3%)	73 (1.4%)	93 (1.7%)
Current economic activity						
Working	2020 (49.6%)	1898 (40.4%)	1709 (40.3%)	1642 (32.4%)	2128 (40.8%)	1980 (36.1%)
Employed pensioner	331 (8.1%)	359 (7.6%)	896 (21.1%)	824 (16.3%)	398 (7.6%)	306 (5.6%)
Unemployed pensioner	1537 (37.8%)	2274 (48.4%)	1398 (33.0%)	2455 (48.5%)	2368 (45.4%)	2956 (53.8%)
Unemployed	129 (3.2%)	123 (2.6%)	236 (5.6%)	141 (2.8%)	312 (6.0%)	236 (4.3%)
Missing	53 (1.3%)	49 (1.0%)	0	0	13 (0.3%)	12 (0.2%)
Spine/joint problems						
No	1939 (47.6%)	1819 (38.7%)	1734 (40.9%)	1481 (29.3%)	1917 (36.4%)	1345 (45.5%)
Yes, never hospitalised	1534 (37.7%)	2143 (45.6%)	2107 (49.7%)	3101 (61.3%)	2834 (54.3%)	3682 (67.1%)
Yes, hospitalised	500 (12.3%)	614 (13.1%)	398 (9.4%)	480 (9.5%)	445 (8.5%)	449 (8.2%)
Missing	97 (2.4%)	127 (2.7%)	0	0	23 (0.4%)	14 (0.3%)
BMI						
<25.00	619 (15.2%)	1139 (24.2%)	1644 (38.8%)	911 (18.0%)	1020 (19.5%)	1337 (24.4%)
25.00-29.99	1681 (41.3%)	1538 (32.7%)	1716 (40.5%)	1769 (35.0%)	2249 (43.1%)	1790 (32.6%)
≥30.00	980 (24.1%)	1237 (26.3%)	879 (20.7%)	2381 (47.0%)	1235 (23.7%)	1629 (29.7%)
Missing	790 (19.4%)	789 (16.8%)	0	1 (<0.1%)	715 (13.7%)	734 (13.4%)
Smoking						
Never	1272 (31.3%)	2529 (53.8%)	1089 (25.7%)	4318 (85.3%)	1451 (27.8%)	2781 (50.7%)
Former smoking	1548 (38.0%)	1003 (21.3%)	1047 (24.7%)	220 (4.4%)	1875 (35.9%)	1140 (20.8%)
Current smoking	1197 (29.4%)	1107 (23.5%)	2103 (49.6%)	524 (10.4%)	1876 (36.0%)	1555 (28.3%)
Missing	53 (1.3%)	64 (1.4%)	0	0	17 (0.3%)	14 (0.3%)

S.D.: standard deviation

Table 5.3 shows the distribution of past drinking behaviour in the Russian cohort. Only 1.1% of Russian men and 8.5% of Russian women were lifetime abstainers. Half of both men and women were classified as continuing drinkers who used alcohol in the past 12 months prior to baseline and did not cut down drinking compared to earlier in their life. More Russians reduced drinking (men: 37.2%, women: 26.0%) rather than stopped drinking (men: 12.4%, women: 9.3%). Among reduced drinkers, more men and women cut down their consumption for non-health reasons than for health reasons. Among former drinkers, the proportions of those who quit drinking due to health reasons and due to non-health reasons were similar.

Table 5.3. Past drinking behaviour in the Russian cohort

	Men	**Women**	**Total**
Total	4238	2844	9300
Lifetime abstainer	47 (1.1%)	432 (8.5%)	479 (5.2%)
Former drinker, health reasons	225 (5.3%)	243 (4.8%)	468 (5.0%)
Former drinker, non-health reasons	299 (7.1%)	226 (4.5%)	525 (5.7%)
Reduced drinker, health reasons	568 (13.4%)	483 (9.5%)	1051 (11.3%)
Reduced drinker, non-health reasons	1007 (23.8%)	834 (16.5%)	1841 (19.8%)
Continuing drinker			
Irregular light-to-moderate	481 (11.4%)	1975 (39.0%)	2456 (26.4%)
Regular light-to-moderate	431 (10.2%)	161 (3.2%)	592 (6.4%)
Irregular heavy	786 (18.6%)	467 (9.2%)	1253 (13.5%)
Regular heavy	394 (9.3%)	241 (4.8%)	635 (6.8%)
Total continuing drinker	2092 (49.4%)	2844 (56.2%)	4936 (53.1%)

5.1.2 Longitudinal dataset

Table 5.4 describes physical functioning throughout 10-year follow-up of the three HAPIEE cohorts. Consistently across cohorts and measurement occasions, men's physical functioning was better than women's. At the population level, the mean PF-10 score declined over time in all three cohorts and both sexes.

Because of the differences in data collection procedure at baseline between cohorts (see Section 4.1) and due to the adjustment of the PF-10 score at re-examination in

the Czech and Polish cohorts (see Section 4.6.2.1), the direct comparability of physical functioning scores over time across cohorts is limited; this, however, does not affect the within-cohort comparability. The mean PF-10 score at PQ2012 versus baseline decreased 2.59 and 1.95 points in Czech men and Czech women, respectively. The decline was 11.29 points in Russian men, 15.70 points in Russian women, 10.86 points in Polish men and 13.09 points in Polish women.

Table 5.4. Physical functioning at each assessment occasion of the HAPIEE study

PF-10 score	Czech Republic		Russia		Poland	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Total	4070	4703	4239	5062	5219	5490
Baseline						
Mean (S.D.)	85.21 (18.11)	82.00 (19.28)	86.91 (18.33)	77.47 (21.12)	83.97 (20.21)	76.99 (21.93)
Missing	51 (1.3%)	91 (1.9%)	0	0	34 (0.7%)	41 (0.8%)
Re-examination						
Mean (S.D.)	84.75 (15.72)	81.71 (17.37)	86.10 (20.03)	75.77 (22.16)	77.40 (20.25)	71.94 (20.92)
Missing	1744 (42.9%)	1870 (39.8%)	1540 (36.3%)	1614 (31.9%)	2025 (38.8%)	2075 (37.8%)
PQ2009						
Mean (S.D.)	83.18 (20.13)	80.05 (20.69)	77.60 (25.92)	64.57 (26.35)	76.88 (25.47)	67.72 (26.51)
Missing	1766 (43.4%)	1812 (38.5%)	1501 (35.4%)	1356 (26.8%)	1817 (34.8%)	1691 (29.5%)
PQ2012						
Mean (S.D.)	82.62 (20.38)	80.05 (21.43)	75.62 (26.41)	61.77 (27.40)	73.11 (25.37)	63.90 (26.58)
Missing	2053 (50.4%)	2122 (45.1%)	2413 (56.9%)	2272 (53.8%)	3489 (66.9%)	3535 (64.4%)

S.D.: standard deviation

Individual trajectories of physical functioning were inspected by spaghetti plots graphing the PF-10 scores over follow-up years. From each cohort and sex, 100 participants across all age groups were randomly drawn from completers who had no missing PF-10 scores throughout the follow-up. The individual PF-10 trajectories of these subjects are shown in Figure 5.1. An overall decline in the PF-10 score during follow-up was seen in Russians and Poles. Visually, the decline in the PF-10 score among Czechs was less obvious, and the variation of the PF-10 score increased with increasing follow-up time. This might be due to the fact that Czechs had better health at baseline than Russians and Poles, and perhaps 10 years of follow-up is not long enough to allow an overall sizeable decline to fully emerge in a relatively healthy population, such as the Czech participants.

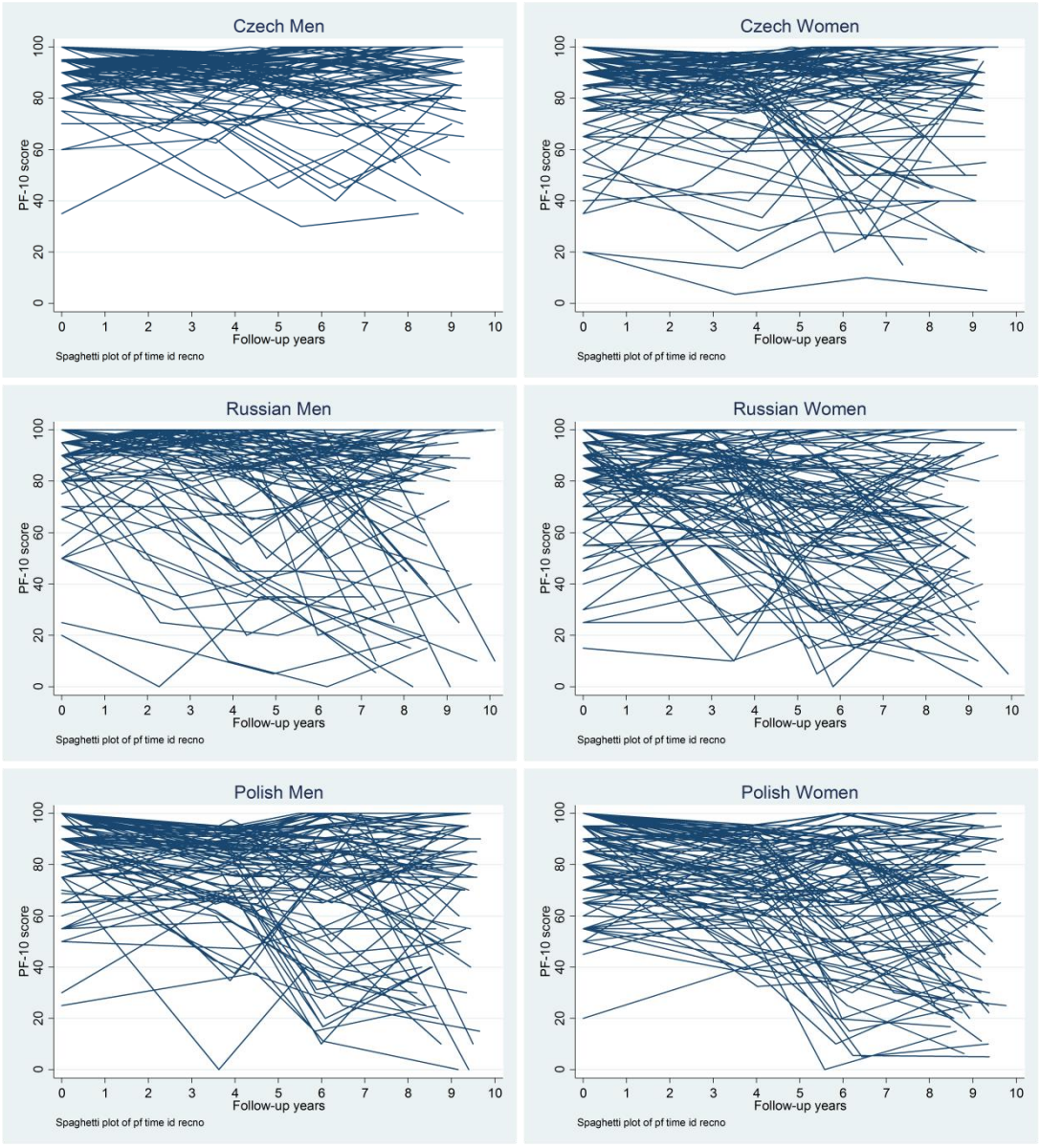


Figure 5.1. Spaghetti plots of physical functioning over follow-up years in random samples of 100 completers

Physical functioning scores throughout follow-up by drinking behaviour at baseline are presented in Table 5.5. Across cohorts, sexes and measurement occasions, physical functioning in non-drinkers was consistently the lowest. The only exception was Russian women in whom the lowest PF-10 score at baseline and PQ2012 was seen in drinkers who consumed alcohol at least once a week. A drop in the mean PF-10 score over time by drinking groups was observed in all cohorts and both sexes except Czech male non-drinkers. Among Czech male non-drinkers, the mean PF-10 score at PQ2012 versus baseline increased by 3.41 points.

Table 5.5. Mean physical functioning scores during follow-up by alcohol consumption at baseline

Mean PF-10 score	Average drinking frequency					Annual drinking volume (g)					Average drinking quantity per day				Drinking pattern					Problem drinking	
	0	<1/ month	1-3/ month	1-4/ week	≥1/ week	0	1-1500[a]/ 1-250[b]	1501-4000[a]/ 251-500[b]	4001-8000[a]/ 501-1500[b]	>8000[a]/ >1500[b]	Non-drinker	Light	Moderate	Heavy	Non-drinker	Irregular light-to-moderate	Regular light-to-moderate	Irregular heavy	Regular heavy	No	Yes
Czech men																					
Baseline	73.93	83.25	84.57	86.64	87.31	73.93	84.18	86.47	87.58	86.84	73.93	85.94	87.06	85.54	73.93	83.12	85.52	88.17	86.17	85.31	84.80
Re-examination	79.10	83.96	82.75	85.60	86.50	79.10	83.70	84.81	86.74	86.20	79.10	85.26	85.78	84.48	79.10	82.82	84.87	86.75	85.84	84.97	85.15
PQ2009	75.63	81.78	81.09	84.34	84.98	75.63	81.55	84.19	86.06	84.21	75.63	84.00	84.49	81.35	75.63	80.68	84.14	85.55	80.33	83.31	82.13
PQ2012	77.34	79.78	80.90	83.87	84.33	77.34	80.73	83.57	84.88	83.86	77.34	83.29	79.53	83.06	77.34	79.88	83.32	84.78	80.83	82.80	81.80
Czech women																					
Baseline	72.91	81.05	85.07	86.12	85.66	72.91	81.29	83.74	85.88	86.15	72.91	83.32	84.60	84.11	72.91	81.72	84.23	87.23	86.44	82.15	83.37
Re-examination	75.34	80.90	83.17	84.58	85.88	75.34	80.62	83.41	84.17	84.94	75.34	82.63	82.89	84.95	75.34	80.70	83.76	85.66	86.04	81.94	85.04
PQ2009	71.84	78.93	82.68	83.24	83.63	71.84	79.27	81.34	83.28	83.52	71.84	80.70	82.44	81.85	71.84	79.43	82.87	84.27	83.60	80.40	81.68
PQ2012	70.29	78.58	82.18	84.41	84.81	70.29	78.75	81.83	82.64	84.85	70.29	80.86	82.54	82.33	70.29	78.91	82.40	85.07	85.81	80.46	81.88
Russian men																					
Baseline	82.51	83.52	86.77	89.22	89.36	82.51	84.74	87.22	90.22	89.57	82.51	84.92	89.55	88.24	82.51	84.25	88.34	89.08	89.02	86.59	88.27
Re-examination	81.01	82.95	85.40	88.38	89.62	81.01	83.88	86.75	89.30	88.77	81.01	86.10	88.42	86.56	81.01	83.65	87.85	88.07	88.08	85.41	89.15
PQ2009	73.51	73.33	78.23	79.66	79.33	73.51	75.34	78.27	81.48	79.41	73.51	77.21	80.17	77.95	73.51	75.79	79.95	78.96	78.44	77.26	79.12
PQ2012	68.35	73.14	75.67	78.15	78.76	68.35	75.03	76.08	77.24	78.84	68.35	76.82	76.85	76.46	68.35	75.80	77.27	76.94	76.69	75.34	76.97
Russian women																					
Baseline	69.16	77.82	80.60	83.80	66.88	69.16	76.01	80.89	81.91	81.23	69.16	77.51	79.53	80.78	69.16	78.22	83.50	81.96	80.72	77.52	73.89
Re-examination	65.64	75.25	80.41	82.81	69.71	65.64	75.40	78.19	79.38	81.97	65.64	75.82	78.11	79.12	65.64	76.75	80.51	79.74	81.15	75.72	80.22
PQ2009	55.79	62.99	69.46	74.03	57.67	55.79	61.45	66.88	71.30	72.54	55.79	62.87	66.42	70.48	55.79	64.28	72.69	70.63	71.33	64.55	65.80
PQ2012	52.28	60.86	67.16	66.93	51.67	52.28	59.62	65.73	66.33	65.93	52.28	61.81	63.86	65.05	52.28	62.66	65.20	67.14	63.93	61.80	59.68
Polish men																					
Baseline	77.60	82.17	85.98	86.60	87.17	77.60	83.94	87.63	87.86	86.69	77.60	85.24	87.88	86.51	77.60	83.24	85.97	88.15	85.88	84.69	85.16
Re-examination	72.78	76.07	79.09	79.07	79.14	72.78	77.44	79.84	78.97	79.91	72.78	77.98	80.65	80.07	72.78	77.08	78.22	80.25	80.82	78.01	77.72
PQ2009	68.88	75.85	78.84	79.99	79.46	68.88	77.58	80.70	79.18	79.74	68.88	78.94	80.66	77.11	68.88	76.79	79.01	81.14	77.00	77.83	77.21
PQ2012	67.39	72.32	73.41	75.92	75.06	67.39	72.98	76.65	78.30	72.03	67.39	74.74	76.83	71.03	67.39	72.48	76.54	75.70	64.33	73.93	73.60
Polish women																					
Baseline	72.68	77.64	82.51	83.78	83.11	72.68	77.70	82.85	83.17	84.14	72.68	79.09	82.98	81.49	72.68	79.43	83.49	82.16	84.68	78.61	76.22
Re-examination	68.03	71.99	76.43	77.89	75.52	68.03	71.79	77.31	76.31	78.98	68.03	73.76	76.16	77.05	68.03	73.80	76.47	76.26	79.17	72.88	75.44
PQ2009	62.23	67.54	74.30	75.69	76.43	62.23	67.94	74.49	74.36	76.57	62.23	71.08	72.95	71.86	62.23	70.21	74.41	74.17	78.01	68.94	69.40
PQ2012	57.29	63.57	71.03	73.04	67.08	57.29	64.29	72.12	70.46	72.66	57.29	66.59	71.75	64.16	57.29	67.35	70.73	67.70	76.51	65.50	58.83

[a] Among men, [b] Among women

The Kenall's rank correlations of the PF-10 scores at all measurement occasions, alcohol consumption at baseline, and covariates at baseline were assessed. As shown in Table 5.6–5.8, in all cohorts, there were moderate to strong correlations between the PF-10 scores measured at baseline and follow-up (Czechs: 0.47–0.61; Russians: 0.36–0.52; Poles: 0.39–0.60). The PF-10 score at each measurement occasion was statistically significantly correlated with drinking indices derived from the GF (Czechs: 0.07–0.16; Russians: 0.14–0.21; Poles: 0.15–0.18). Problem drinking was statistically significantly correlated with the PF-10 scores in the Russian cohort (0.07–0.11) and Polish cohort (0.03–0.04, except PQ2012) but not in the Czech cohort (except re-examination).

Similarly, covariates at baseline were also statistically significantly correlated with the PF-10 score at each measurement occasion, as well as with baseline alcohol consumption. In the Czech cohort, however, smoking was not correlated with the PF-10 scores (except at re-examination), and most covariates were not correlated with problem drinking.

With regard to the correlations between covariates at baseline, in all the cohorts, most of the correlations were relatively weak but statistically significant. There was a moderate to strong positive correlation between age and current economic activity (Czech Republic: 0.50; Russia: 0.45; Poland: 0.36). Among Czechs, low to moderate correlations of household amenities were also seen with marital status (-0.31), education (0.26), and current economic activity (0.27). In Russians, sex was correlated strongly with smoking (-0.56), and the correlations were weaker with marital status (0.31) and BMI groups (0.28). A weak negative correlation was also observed between education and household amenities (-0.27). In the Polish cohort, a low correlation was found between sex and marital status (0.24), as well as between the three SEP variables of education, household amenities and current economic activity (0.09–0.29).

Table 5.6. Kendall's rank correlations of study variables in the Czech cohort

	PF-10 score				Alcohol consumption					Covariates								
	Baseline	Re-examination	PQ2009	PQ2012	Average drinking frequency	Annual drinking volume	Average drinking quantity/day	Drinking pattern	Problem drinking	Age	Sex	Marital status	Education	Household amenities	Current economic activity	Spine/ joint problems	BMI	Smoking
PF-10 score																		
Baseline	1																	
Re-examination	0.47*	1																
PQ2009	0.53*	0.48*	1															
PQ2012	0.52*	0.47*	0.61*	1														
Alcohol consumption																		
Average drinking frequency	0.15*	0.12*	0.11*	0.11*	1													
Annual drinking volume	0.14*	0.12*	0.10*	0.10*	0.84*	1												
Average drinking quantity/day	0.10*	0.08*	0.07*	0.07*	0.32*	0.46*	1											
Drinking pattern	0.16*	0.14*	0.11*	0.11*	0.65*	0.68*	0.54*	1										
Problem drinking	<0.01	0.02*	-0.01	<-0.01	0.21*	0.22*	0.15*	0.21*	1									
Covariates																		
Age	-0.20*	-0.28*	-0.19*	-0.21*	-0.10*	-0.12*	-0.12*	-0.19*	-0.07*	1								
Sex	-0.10*	-0.09*	-0.09*	-0.06*	-0.33*	-0.35*	-0.25*	-0.20*	-0.16*	-0.03*	1							
Marital status	-0.05*	-0.04*	-0.03*	-0.02	-0.10*	-0.09*	-0.05*	-0.06*	-0.01	0.02*	0.18*	1						
Education	0.18*	0.13*	0.16*	0.16*	0.11*	0.08*	0.02*	0.09*	-0.01	-0.04*	-0.03*	-0.04*	1					
Household amenities	0.18*	0.15*	0.15*	0.14*	0.16*	0.14*	0.09*	0.15*	<-0.01	-0.17*	-0.10*	-0.31*	0.26*	1				
Current economic activity	-0.31*	-0.33*	-0.26*	-0.27*	-0.16*	-0.17*	-0.15*	-0.22*	-0.05*	0.50*	0.09*	0.08*	-0.17*	-0.27*	1			
Spine/joint problems	-0.35*	-0.28*	-0.28*	-0.26*	-0.07*	-0.07*	-0.05*	-0.07*	-0.01	0.10*	0.08*	0.04*	-0.11*	-0.07*	0.17*	1		
BMI	-0.23*	-0.22*	-0.24*	-0.25*	-0.07*	-0.05*	<-0.01	-0.06*	-0.01	0.14*	-0.05*	<-0.01	-0.14*	-0.04*	0.15*	0.10*	1	
Smoking	0.01	0.04*	<-0.01	-0.01	0.12*	0.15*	0.15*	0.15*	0.10*	-0.11*	-0.18*	0.03*	-0.07*	-0.01	-0.07*	-0.02	-0.03*	1

* p<0.05

Table 5.7. Kendall's rank correlations of study variables in the Russian cohort

	PF-10 score				**Alcohol consumption**					**Covariates**								
	Baseline	Re-examination	PQ2009	PQ2012	Average drinking frequency	Annual drinking volume	Average drinking quantity/ day	Drinking pattern	Problem drinking	Age	Sex	Marital status	Education	Household amenities	Current economic activity	Spine/ joint problems	BMI	Smoking
PF-10 score																		
Baseline	1																	
Re-examination	0.42*	1																
PQ2009	0.38*	0.45*	1															
PQ2012	0.36*	0.43*	0.52*	1														
Alcohol consumption																		
Average drinking frequency	0.18*	0.21*	0.18*	0.18*	1													
Annual drinking volume	0.20*	0.21*	0.19*	0.18*	0.83*	1												
Average drinking quantity/day	0.17*	0.17*	0.16*	0.14*	0.53*	0.66*	1											
Drinking pattern	0.17*	0.18*	0.16*	0.14*	0.71*	0.74*	0.72*	1										
Problem drinking	0.08*	0.11*	0.09*	0.07*	0.31*	0.33*	0.31*	0.33*	1									
Covariates																		
Age	-0.16*	-0.20*	-0.22*	-0.22*	-0.12*	-0.11*	-0.07*	-0.13*	-0.06*	1								
Sex	-0.25*	-0.26*	-0.24*	-0.24*	-0.36*	-0.41*	-0.40*	-0.28*	-0.30*	-0.02*	1							
Marital status	-0.12*	-0.13*	-0.13*	-0.14*	-0.14*	-0.15*	-0.12*	-0.09*	-0.09*	0.09*	0.31*	1						
Education	0.08*	0.11*	0.11*	0.12*	0.07*	0.06*	0.02*	0.03*	0.02*	-0.06*	-0.07*	-0.05*	1					
Household amenities	0.18*	0.20*	0.19*	0.20*	0.16*	0.14*	0.08*	0.11*	0.02	-0.21*	-0.13*	-0.27*	0.19*	1				
Current economic activity	-0.25*	-0.27*	-0.26*	-0.24*	-0.15*	-0.14*	-0.11*	-0.14*	-0.04*	0.45*	0.09*	0.12*	-0.11*	-0.24*	1			
Spine/joint problems	-0.20*	-0.20*	-0.17*	-0.18*	-0.07*	-0.07*	-0.06*	-0.07*	-0.05*	0.06*	0.10*	0.04*	-0.05*	-0.04*	0.08*	1		
BMI	-0.18*	-0.20*	-0.18*	-0.20*	-0.13*	-0.12*	-0.10*	-0.08*	-0.11*	0.05*	0.28*	0.04*	-0.06*	0.01	0.07*	0.07*	1	
Smoking	0.13*	0.17*	0.14*	0.13*	0.27*	0.32*	0.31*	0.27*	0.26*	-0.11*	-0.56*	-0.14*	<0.01	0.05*	-0.11*	-0.07*	-0.25*	1

* p<0.05

Table 5.8. Kendall's rank correlations of study variables in the Polish cohort

	PF-10 score				Alcohol consumption					Covariates								
	Baseline	Re-examination	PQ2009	PQ2012	Average drinking frequency	Annual drinking volume	Average drinking quantity/day	Drinking pattern	Problem drinking	Age	Sex	Marital status	Education	Household amenities	Current economic activity	Spine/joint problems	BMI	Smoking
PF-10 score																		
Baseline PF-10	1																	
Re-examination PF-10	0.39*	1																
PQ2009 PF-10	0.39*	0.43*	1															
PQ2012 PF-10	0.39*	0.43*	0.60*	1														
Alcohol consumption																		
Average drinking frequency	0.17*	0.15*	0.18*	0.17*	1													
Annual drinking volume	0.18*	0.15*	0.17*	0.16*	0.89*	1												
Average drinking quantity/day	0.16*	0.14*	0.15*	0.14*	0.64*	0.72*	1											
Drinking pattern	0.17*	0.15*	0.17*	0.15*	0.82*	0.83*	0.77*	1										
Problem drinking	0.03*	0.04*	0.03*	0.02	0.22*	0.25*	0.21*	0.24*	1									
Covariates																		
Age	-0.19*	-0.27*	-0.20*	-0.19*	-0.14*	-0.14*	-0.15*	-0.16*	-0.07*	1								
Sex	-0.17*	-0.14*	-0.17*	-0.16*	-0.32*	-0.34*	-0.31*	-0.30*	-0.19*	-0.03*	1							
Marital status	-0.08*	-0.09*	-0.09*	-0.08*	-0.10*	-0.11*	-0.10*	-0.10*	-0.01	0.06*	0.24*	1						
Education	0.11*	0.10*	0.15*	0.18*	0.11*	0.09*	0.06*	0.09*	-0.02*	-0.05*	0.03*	<0.01	1					
Household amenities	0.18*	0.17*	0.19*	0.19*	0.18*	0.17*	0.14*	0.17*	-0.02*	-0.16*	-0.12*	-0.27*	0.29*	1				
Current economic activity	-0.26*	-0.28*	-0.26*	-0.26*	-0.18*	-0.17*	-0.15*	-0.18*	-0.02	0.36*	0.05*	0.09*	-0.27*	-0.28*	1			
Spine/joint problems	-0.32*	-0.23*	-0.24*	-0.25*	-0.08*	-0.08*	-0.06*	-0.07*	-0.02*	0.10*	0.11*	0.03*	-0.06*	-0.07*	0.15*	1		
BMI	-0.12*	-0.11*	-0.15*	-0.19*	-0.06*	-0.06*	-0.04*	-0.06*	-0.04*	0.10*	0.01	-0.01	-0.10*	<0.01	0.08*	0.05*	1	
Smoking	0.02*	0.03*	0.03*	<-0.01	0.16*	0.18*	0.18*	0.19*	0.13*	-0.14*	-0.18*	0.01	-0.07*	0.01	-0.04*	-0.01	-0.11*	1

* p<0.05

5.2 Non-missing versus Imputed Data

The multiply imputed datasets, both cross-sectional and longitudinal, contain two parts of data: non-missing and imputed data. Table 5.9–5.10 compare the non-missing and imputed values of alcohol consumption and physical functioning in the imputed cross-sectional and longitudinal datasets, respectively. In these tables, non-missing values were from participants who took part in the measurement occasion. Imputed values were generated in the process of MICE, which replaced the missing data in participants who were not observed.

In the 25 imputed cross-sectional datasets, imputed values of the PF-10 score at baseline were lower than the non-missing values (Table 5.9). This is in line with data on self-rated health showing that a higher proportion of participants with missing PF-10 score at baseline rated their health as poor or very poor than among those with no missing data.

Royston[315] did not recommend the use of MICE if the proportion of respondents with missing data in a given variable is more than 50%, although he acknowledged that there is no firm evidence base for this rule of thumb. In the HAPIEE study, the proportion of participants with missing PF-10 score was over 50% among Russians (50.4%) and Poles (65.6%) *only* for PQ2012 (i.e., not for all of the four measurement occasions). In multiple imputation, inclusion of variables which strongly correlate with the dependent variable generally reduces bias and increases power of the analysis.[261,263] This is the case for the PF-10 score at PQ2012, since the imputation model of the PF-10 score at PQ2012 included the PF-10 scores from previous three measurement occasions. The Pearson's correlations of the PF-10 scores at PQ2012 with scores from previous occasions were 0.49–0.67 in Russians and 0.51–0.76 in Poles. These strong correlations not only ameliorated the effectiveness of MICE and made the imputed values more plausible, but they also reduced the influence of the large proportion of missing data in the PF-10 score at PQ2012 among Russians and Poles.

Across cohorts, sexes and measurement occasions, compared with the non-missing mean PF-10 score in Table 5.4, the mean PF-10 score among completers in Table 5.11 was constantly higher. This suggests that healthier participants tended to stay in the study, which is supported by comparing self-rated health at baseline across major missing patterns of the PF-10 score throughout follow-up (Appendix D). As a consequence, in the 70 imputed longitudinal datasets, imputed values of the PF-10 scores across all the cohorts, sexes and measurement occasions were lower than the non-missing values (Table 5.10). The overall mean PF-10 score in the multiply imputed datasets (including both non-missing and imputed values) were 0.02–0.18, 0.35–1.54, 1.17–2.34 and 1.67–4.48 points lower at baseline, re-examination, PQ2009 and PQ2012 than the non-missing values (Table 5.10), respectively.

In both imputed cross-sectional and longitudinal datasets, imputed data of drinking behaviour at baseline were similar to the non-missing data.

Table 5.9. Comparison of non-missing and imputed cross-sectional data (*m*=25)

	Czech Republic				Russia				Poland			
	Men	N	Women	N	Men	N	Women	N	Men	N	Women	N
PF-10 (mean, SD)												
Non-missing	85.21 (18.11)	4019	82.00 (19.28)	4612	86.91 (18.33)	4239	77.47 (21.12)	5062	83.97 (20.21)	5185	76.99 (21.93)	5449
Imputed	77.68 (21.81)	51	72.84 (24.26)	91	N/A	N/A	N/A	N/A	78.65 (22.38)	34	75.57 (22.22)	41
All	85.11 (18.18)	4070	81.82 (19.43)	4703	86.91 (18.33)	4239	77.47 (21.12)	5062	83.93 (20.23)	5219	76.98 (21.93)	5490
Average drinking frequency (%)												
Non-missing		3958		4504		4238		5062		5186		5463
0	6.52		18.47		13.47		17.80		21.98		46.37	
<1/month	14.07		28.04		13.85		45.97		14.52		22.72	
1-3/month	17.05		25.51		25.72		27.87		23.45		18.96	
1-4/week	30.50		20.74		38.46		7.88		28.63		10.21	
≥5/week	31.86		7.24		8.49		0.47		11.42		1.74	
Imputed		112		199		1		N/A		33		27
0	5.82		23.28		8.00		N/A		15.52		42.22	
<1/month	14.32		29.43		12.00		N/A		16.61		20.15	
1-3/month	19.79		22.81		60.00		N/A		26.30		21.19	
1-4/week	32.79		16.56		20.00		N/A		29.70		14.17	
≥5/week	27.29		7.92		0		N/A		11.88		2.37	
All		4070		4703		4239		5062		5219		5490
0	6.50		18.68		13.47		17.80		21.94		46.35	
<1/month	14.08		28.10		13.85		45.97		14.53		22.70	
1-3/month	17.13		25.40		25.73		27.87		23.47		18.97	
1-4/week	30.56		20.56		38.46		7.88		28.64		10.23	
≥5/week	31.73		7.27		8.49		0.47		11.42		1.74	
Annual drinking volume (mean, S.D.)												
Non-missing	7272.30 (13130.43)	3958	1700.92 (5592.26)	4504	5550.84 (8474.18)	4238	569.61 (1424.52)	5062	3310.82 (9599.68)	5186	529.01 (2687.98)	5463
Imputed	7390.89 (14400.50)	112	1870.08 (5404.66)	199	5296.80 (6747.48)	1	N/A	N/A	3044.68 (7210.12)	33	1057.22 (2763.63)	27
All	7275.57 (13165.41)	4070	1708.08 (5583.96)	4703	5550.78 (8472.83)	4239	569.61 (1424.38)	5062	3309.13 (9585.56)	5219	531.61 (2688.36)	5490
Average drinking quantity per day (mean, S.D.)												
Non-missing	36.50 (33.51)	3958	21.82 (23.39)	4504	61.28 (47.65)	4238	24.78 (20.38)	5062	28.44 (33.97)	5186	11.36 (17.45)	5463
Imputed	36.32 (33.67)	112	21.69 (22.92)	199	56.54 (44.15)	1	N/A	N/A	28.56 (34.56)	33	12.36 (17.77)	27
All	36.49 (33.51)	4070	21.82 (23.37)	4703	61.28 (47.65)	4239	24.78 (20.37)	5062	28.45 (33.97)	5219	11.37 (17.45)	5490

Table 5.9 continued

	Czech Republic				Russia				Poland			
	Men	N	Women	N	Men	N	Women	N	Men	N	Women	N
Drinking pattern (%)												
Non-missing		3958		4504		4238		5062		5186		5463
Non-drinker	6.52		18.47		13.47		17.80		21.98		46.37	
Irregular light-to-moderate	22.74		39.52		23.83		58.73		27.71		35.24	
Regular light-to-moderate	28.07		12.32		17.46		4.27		22.60		7.27	
Irregular heavy	34.97		18.87		31.34		13.02		24.28		7.71	
Regular heavy	7.71		10.81		13.90		6.18		3.43		3.42	
Imputed		112		199		1		N/A		33		27
Non-drinker	9.21		21.33		20.00		N/A		20.24		39.70	
Irregular light-to-moderate	27.89		38.57		32.00		N/A		29.09		34.07	
Regular light-to-moderate	20.46		17.83		12.00		N/A		18.18		12.15	
Irregular heavy	31.32		17.47		24.00		N/A		26.18		12.15	
Regular heavy	11.11		4.80		12.00		N/A		6.30		1.93	
All		4070		4703		4239		5062		5219		5490
Non-drinker	6.59		18.59		13.47		17.80		21.97		46.33	
Irregular light-to-moderate	22.88		39.48		23.83		58.73		27.72		35.23	
Regular light-to-moderate	27.86		12.56		17.46		4.27		22.57		7.29	
Irregular heavy	34.87		18.81		31.33		13.02		24.29		7.73	
Regular heavy	7.80		10.56		13.90		6.18		3.45		3.42	
Problem drinking (%)												
Non-missing		3911		4320		4238		5062		4530		3993
No	90.77		97.91		80.82		98.58		89.91		98.70	
Yes	9.23		2.09		19.18		1.42		10.09		1.30	
Imputed		159		291		1		N/A		689		1497
No	91.67		99.08		88.00		N/A		98.27		99.75	
Yes	8.33		0.92		12.00		N/A		1.73		0.25	
All		4070		4703		4239		5062		5219		5490
No	90.80		97.99		80.82		98.58		91.02		98.99	
Yes	9.20		2.01		19.18		1.42		8.98		1.01	

N: number of participants; S.D.: standard deviation; N/A: not applicable

Table 5.10. Comparison of non-missing and imputed longitudinal data (*m*=70)

	Czech Republic				Russia				Poland			
	Men	N	Women	N	Men	N	Women	N	Men	N	Women	N
PF-10 (mean, S.D.)												
Non-missing												
Baseline	85.21 (18.11)	4019	82.00 (19.28)	4612	86.91 (18.33)	4239	77.47 (21.12)	5062	83.97 (20.21)	5185	76.99 (21.93)	5449
Re-examination	84.75 (15.72)	2326	81.71 (17.37)	2833	86.10 (20.03)	2699	75.77 (22.16)	3448	77.40 (20.25)	3194	71.94 (20.92)	3415
PQ2009	83.18 (20.13)	2304	80.05 (20.69)	2894	77.60 (25.92)	2738	64.57 (26.35)	3706	76.88 (25.47)	3402	67.72 (26.51)	3799
PQ2012	82.62 (20.38)	2017	80.05 (21.43)	2581	75.62 (26.41)	1826	61.77 (27.40)	2790	73.11 (25.37)	1730	63.90 (26.58)	1955
Imputed												
Baseline	78.13 (20.70)	51	72.55 (24.71)	91	N/A	N/A	N/A	N/A	77.65 (22.27)	34	74.34 (23.84)	41
Re-examination	81.87 (18.95)	1744	78.81 (20.67)	1870	81.86 (21.58)	1540	74.65 (24.64)	1614	75.64 (20.88)	2025	69.78 (23.17)	2075
PQ2009	78.25 (23.04)	1766	74.44 (24.80)	1812	71.00 (27.39)	1501	60.22 (28.96)	1356	70.61 (27.43)	1817	62.57 (28.93)	1691
PQ2012	76.28 (24.65)	2053	73.04 (26.03)	2122	67.75 (28.45)	2413	58.05 (29.78)	2272	67.92 (27.31)	3489	59.99 (28.43)	3535
All												
Baseline	85.12 (18.16)	4070	81.82 (19.44)	4703	86.91 (18.33)	4239	77.47 (21.12)	5062	83.93 (20.23)	5219	76.97 (21.94)	5490
Re-examination	83.52 (17.24)	4070	80.55 (18.81)	4703	84.56 (20.71)	4239	75.42 (22.98)	5062	76.72 (20.52)	5219	71.13 (21.82)	5490
PQ2009	81.04 (21.58)	4070	77.89 (22.53)	4703	75.26 (26.63)	4239	63.40 (27.14)	5062	74.70 (26.33)	5219	66.14 (27.38)	5490
PQ2012	79.42 (22.85)	4070	76.89 (23.87)	4703	71.14 (27.86)	4239	60.10 (28.55)	5062	69.64 (26.80)	5219	61.38 (27.85)	5490
Average drinking frequency (%)												
Non-missing		3958		4504		4238		5062		5186		5463
0	6.52		18.47		13.47		17.80		21.98		46.37	
<1/month	14.07		28.04		13.85		45.97		14.52		22.72	
1-3/month	17.05		25.51		25.72		27.87		23.45		18.96	
1-4/week	30.50		20.74		38.46		7.88		28.63		10.21	
≥5/week	31.86		7.24		8.49		0.47		11.42		1.74	
Imputed		112		199		1		N/A		33		27
0	6.20		24.75		11.43		N/A		13.03		40.85	
<1/month	14.89		31.52		25.71		N/A		12.90		21.59	
1-3/month	20.61		21.71		35.71		N/A		23.25		20.00	
1-4/week	32.58		16.03		22.86		N/A		33.55		13.92	
≥5/week	25.73		5.99		4.29		N/A		17.27		3.65	
All		4070		4703		4239		5062		5219		5490
0	6.51		18.74		13.47		17.80		21.93		46.34	
<1/month	14.10		28.19		13.85		45.97		14.51		22.71	
1-3/month	17.15		25.35		25.72		27.87		23.45		18.97	
1-4/week	30.55		20.54		38.46		7.88		28.67		10.23	
≥5/week	31.69		7.19		8.49		0.47		11.45		1.75	

Table 5.10 continued

	Czech Republic				Russia				Poland			
	Men	N	Women	N	Men	N	Women	N	Men	N	Women	N
Annual drinking volume (mean, S.D.)												
Non-missing	7272.30 (13130.43)	3958	1700.92 (5592.26)	4504	5550.84 (8474.18)	4238	569.61 (1424.52)	5062	3310.82 (9599.68)	5186	529.01 (2687.98)	5463
Imputed	7029.52 (12445.08)	112	1748.62 (4913.03)	199	5734.50 (9066.08)	1	N/A	N/A	4427.10 (11981.92)	33	1257.22 (3906.92)	27
All	7265.62 (13110.49)	4070	1702.94 (5564.61)	4703	5550.89 (8473.32)	4239	569.61 (1424.38)	5062	3317.87 (9616.08)	5219	532.59 (2695.55)	5490
Average drinking quantity per day (mean, S.D.)												
Non-missing	36.50 (33.51)	3958	21.82 (23.39)	4504	61.28 (47.65)	4238	24.78 (20.38)	5062	28.44 (33.97)	5186	11.36 (17.45)	5463
Imputed	37.10 (34.24)	112	21.10 (22.89)	199	66.68 (52.22)	1	N/A	N/A	30.24 (35.88)	33	13.25 (21.08)	27
All	36.51 (33.53)	4070	21.79 (23.37)	4703	61.28 (47.65)	4239	24.78 (20.37)	5062	28.46 (33.98)	5219	11.37 (17.47)	5490
Drinking pattern (%)												
Non-missing		3958		4504		4238		5062		5186		5463
Non-drinker	6.52		18.47		13.47		17.80		21.98		46.37	
Irregular light-to-moderate	22.74		39.52		23.83		58.73		27.71		35.24	
Regular light-to-moderate	28.07		12.32		17.46		4.27		22.60		7.27	
Irregular heavy	34.97		18.87		31.34		13.02		24.28		7.71	
Regular heavy	7.71		10.81		13.90		6.18		3.43		3.42	
Imputed		112		199		1		N/A		33		27
Non-drinker	8.98		22.20		11.43		N/A		15.93		39.95	
Irregular light-to-moderate	28.34		39.84		48.57		N/A		31.77		33.23	
Regular light-to-moderate	21.91		16.98		4.29		N/A		18.61		13.02	
Irregular heavy	29.86		16.07		25.71		N/A		25.76		11.32	
Regular heavy	10.91		4.91		10.00		N/A		7.92		2.49	
All		4070		4703		4239		5062		5219		5490
Non-drinker	6.59		18.63		13.47		17.80		21.94		46.33	
Irregular light-to-moderate	22.89		39.53		23.84		58.73		27.73		35.23	
Regular light-to-moderate	27.90		12.52		17.46		4.27		22.57		7.30	
Irregular heavy	34.83		18.75		31.33		13.02		24.29		7.72	
Regular heavy	7.79		10.56		13.90		6.18		3.46		3.42	
Problem drinking (%)												
Non-missing		3911		4320		4238		5062		4530		3993
No	90.77		97.91		80.82		98.58		89.91		98.70	
Yes	9.23		2.09		19.18		1.42		10.09		1.30	
Imputed		159		291		1		N/A		689		1497
No	91.88		99.11		90.00		N/A		98.18		99.79	
Yes	8.12		0.89		10.00		N/A		1.82		0.21	
All		4070		4703		4239		5062		5219		5490
No	90.81		97.99		80.82		98.58		91.00		98.99	
Yes	9.19		2.01		19.18		1.42		9.00		1.01	

N: number of participants; S.D.: standard deviation; N/A: not applicable

Table 5.11. Physical functioning at each measurement occasion among completers

PF-10 score	Czech Republic		Russia		Poland	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Total	1505	1983	1433	2223	1440	1616
Baseline						
Mean (S.D.)	88.44 (14.14)	84.73 (16.86)	90.10 (14.05)	78.99 (19.91)	86.87 (17.07)	80.09 (19.72)
Re-examination						
Mean (S.D.)	86.27 (14.00)	83.11 (15.93)	88.86 (16.56)	77.66 (20.73)	80.02 (16.77)	73.77 (18.79)
PQ2009						
Mean (S.D.)	84.93 (18.16)	81.78 (19.28)	80.79 (22.35)	64.82 (25.66)	78.04 (23.67)	68.15 (25.22)
PQ2012						
Mean (S.D.)	83.59 (19.46)	80.84 (20.92)	75.90 (25.75)	61.89 (27.06)	73.40 (25.06)	64.51 (26.34)

S.D.: standard deviation

5.3 Cross-Sectional Analyses

In order to address objectives 1 and 2, multivariable logistic regressions were conducted to examine the cross-sectional associations of alcohol consumption and past drinking behaviour with physical limitations in the multiply imputed baseline datasets. In all cohorts, men drank more frequently and heavily than women, but fewer men had physical limitations (PF-10 score<75) at baseline (Table 5.1). 643 Czech men (15.8%), 1,007 Czech women (21.4%), 643 Russian men (15.2%), 1,561 Russian women (30.8%), 1,056 Polish men (20.2%) and 1,790 Polish women (32.6%) were classified having physical limitations (Table 5.1). Considering the pronounced gender differences on both drinking behaviour and physical limitations across cohorts, data analyses were performed separately by cohort and sex.

5.3.1 Alcohol consumption and physical limitations

The cross-sectional results of alcohol consumption and physical limitations in the Czech, Russian and Polish cohorts are described in Table 5.12–5.14, respectively. These tables present results from two statistical models: model 1 adjusted for age only, and model 2 adjusted for age, marital status, SEP (education, current economic activity and household amenities), spine/joint problems, BMI and smoking.

Across cohorts and sexes, after full adjustment (model 2), non-drinking was consistently associated with higher odds of physical limitations in comparison with regular and/or light-to-moderate drinking. Compared to the models adjusted for age only (model 1), the odds ratios (ORs) among non-drinkers in the fully-adjusted models attenuated 25.6%–34.3% in the Czech cohort, 3.0%–19.5% in the Russian cohort, and 4.2%–22.6% in the Polish cohort. Furthermore, in all cohorts and both sexes, the odds of physical limitations tended to decrease with increasing drinking frequency, drinking volume and drinking quantity, and even from less to more harmful drinking pattern. Problem drinking among male drinkers was not associated with physical limitations.

Among Czech men (Table 5.12) and after full adjustment, compared with drinkers who consumed 1–1500 g of alcohol annually, the odds of physical limitations were higher in non-drinkers (OR: 1.76, 95% confidence interval [CI]: 1.24–2.50) and lower in those who drank 4001–8000 g (OR: 0.67, 95% CI: 0.48–0.94) and >8000 g (OR: 0.73, 95% CI: 0.57–0.95) of alcohol annually. Among Czech women, in comparison with regular light-to-moderate drinkers, higher odds of physical limitations were found in non-drinkers (OR: 1.85, 95% CI: 1.36–2.52) and irregular light-to-moderate drinkers (OR: 1.41, 95% CI: 1.06–1.87).

Among Russian men (Table 5.13), drinking more than 4000 g of alcohol annually was inversely associated with physical limitations, similarly as in Czech men. Lower odds of physical limitations were also found in Russian male moderate drinkers (OR: 0.57, 95% CI: 0.42–0.77) and heavy drinkers (OR: 0.58, 95% CI: 0.46–0.73) versus light drinkers. Regarding drinking pattern, compared with regular light-to-moderate drinking, the odds of physical limitations were higher in non-drinkers (OR: 1.40, 95% CI: 1.02–1.91) and lower in irregular heavy drinkers (OR: 0.72, 95% CI: 0.54–0.96).

Among Russian women (Table 5.13), drinking 251–1500 g of alcohol annually was related to lower odds of physical limitations than drinking 1–250 g of alcohol (ORs: 0.63–0.67). Russian female heavy drinkers versus light drinkers had lower odds of physical limitations (OR: 0.76, 95% CI: 0.59–0.96). In terms of drinking pattern, compared with light-to-moderate drinkers, the odds of physical limitations were

higher in non-drinkers (OR: 2.35, 95% CI: 1.59–3.46), irregular light-to-moderate drinkers (OR: 1.45, 95% CI: 1.01–2.10) and regular heavy drinkers (OR: 1.63, 95% CI: 1.04–2.54).

In Polish men and women (Table 5.14), non-drinking (ORs: 1.66–2.07) and drinking less than once per month (ORs: 1.43–1.59) were positively associated with physical limitations. Lower odds of physical functioning were found in Polish men who drank 1501–8000 g (ORs: 0.58–0.76) and in Polish women who consumed 251–1500 g of alcohol annually (ORs: 0.62–0.75). Even higher annual drinking volume (>1500 g) in Polish women was related to lower odds of physical limitations (OR: 0.74, 95% CI: 0.56–0.99). Therefore at the level of average drinking quantity per drinking day, Polish female moderate drinkers versus light drinkers had lower odds of physical limitations (OR: 0.71, 95% CI: 0.59–0.87). Similar to Russian men, the odds of physical limitations in Polish male irregular heavy drinkers were lower in comparison with regular light-to-moderate drinkers (OR: 0.68, 95% CI: 0.53–0.87).

Despite some discrepancies between cohorts and sexes, my findings revealed a persistent pattern of the cross-sectional association between alcohol consumption and physical limitations, generally suggesting a protective effect of alcohol consumption on physical limitations.

Table 5.12. Odds ratios (95% confidence intervals) of physical limitations by alcohol consumption in the Czech cohort, imputed data

	Men		Women	
	Model 1[1]	Model 2[2]	Model 1[1]	Model 2[2]
Average drinking frequency				
0	2.72 (1.95, 3.78)	1.97 (1.33, 2.91)	2.36 (1.91, 2.92)	1.55 (1.22, 1.98)
<1/month	1.22 (0.91, 1.63)	1.24 (0.89, 1.73)	1.37 (1.11, 1.68)	1.15 (0.92, 1.45)
1-3/month	1.00	1.00	1.00	1.00
1-4/week[a]	0.84 (0.64, 1.09)	0.94 (0.70, 1.27)	--	--
≥5/week[a]	0.71 (0.54, 0.93)	0.75 (0.55, 1.02)	--	--
≥1/week[b]	--	--	0.87 (0.70, 1.09)	0.90 (0.70, 1.15)
Annual drinking volume (g)				
0	2.54 (1.89, 3.42)	1.76 (1.24, 2.50)	1.79 (1.47, 2.17)	1.34 (1.07, 1.68)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	0.81 (0.63, 1.05)	0.87 (0.65, 1.17)	0.89 (0.69, 1.15)	0.93 (0.70, 1.23)
4001-8000[a] /501-1500[b]	0.65 (0.48, 0.88)	0.67 (0.48, 0.94)	0.67 (0.52, 0.85)	0.79 (0.60, 1.04)
>8000[a] />1500[b]	0.75 (0.59, 0.94)	0.73 (0.57, 0.95)	0.71 (0.58, 0.88)	0.81 (0.64, 1.03)
Average drinking quantity/day				
Non-drinker	3.17 (2.39, 4.19)	2.09 (1.50, 2.93)	2.06 (1.70, 2.50)	1.41 (1.12, 1.76)
Light	1.00	1.00	1.00	1.00
Moderate	0.89 (0.64, 1.25)	0.78 (0.53, 1.14)	0.89 (0.74, 1.07)	0.85 (0.70, 1.05)
Heavy	1.23 (0.97, 1.55)	1.07 (0.82, 1.39)	1.08 (0.82, 1.43)	1.03 (0.75, 1.41)
Drinking pattern				
Non-drinker	3.24 (2.38, 4.40)	2.16 (1.50, 3.12)	2.72 (2.07, 3.58)	1.85 (1.36, 2.52)
Irregular light-to-moderate	1.39 (1.09, 1.76)	1.29 (0.99, 1.70)	1.51 (1.17, 1.94)	1.41 (1.06, 1.87)
Regular light-to-moderate	1.00	1.00	1.00	1.00
Irregular heavy	0.84 (0.66, 1.07)	0.81 (0.62, 1.06)	0.89 (0.65, 1.21)	0.94 (0.67, 1.33)
Regular heavy	1.13 (0.78, 1.64)	1.11 (0.73, 1.70)	1.19 (0.84, 1.68)	1.21 (0.82, 1.79)
Problem drinking[c]				
No	1.00	1.00	--	--
Yes	1.27 (0.93, 1.73)	1.09 (0.77, 1.56)	--	--

[a] Among men, [b] Among women, [c] Among drinkers;
[1] Adjusted for age;
[2] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Table 5.13. Odds ratios (95% confidence intervals) of physical limitations by alcohol consumption in the Russian cohort, imputed data

	Men		Women	
	Model 1[1]	Model 2[2]	Model 1[1]	Model 2[2]
Average drinking frequency				
0	1.69 (1.30, 2.20)	1.64 (1.23, 2.18)	1.95 (1.62, 2.34)	1.78 (1.46, 2.16)
<1/month	1.29 (0.98, 1.68)	1.32 (0.99, 1.76)	1.09 (0.94, 1.28)	1.04 (0.89, 1.22)
1-3/month	1.00	1.00	1.00	1.00
1-4/week[a]	0.86 (0.69, 1.08)	1.01 (0.80, 1.29)	--	--
≥5/week[a]	0.80 (0.55, 1.17)	0.95 (0.64, 1.42)	--	--
≥1/week[b]	--	--	0.83 (0.63, 1.08)	0.90 (0.68, 1.19)
Annual drinking volume (g)				
0	1.43 (1.11, 1.84)	1.27 (0.97, 1.67)	1.53 (1.29, 1.81)	1.42 (1.19, 1.70)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	0.85 (0.66, 1.08)	0.77 (0.59, 1.01)	0.70 (0.59, 0.82)	0.67 (0.57, 0.80)
4001-8000[a] /501-1500[b]	0.64 (0.48, 0.86)	0.67 (0.49, 0.91)	0.64 (0.52, 0.78)	0.63 (0.51, 0.78)
>8000[a] />1500[b]	0.69 (0.53, 0.89)	0.73 (0.55, 0.96)	0.83 (0.64, 1.07)	0.88 (0.67, 1.15)
Average drinking quantity/day				
Non-drinker	1.30 (1.01, 1.68)	1.06 (0.70, 1.40)	1.75 (1.44, 2.12)	1.58 (1.29, 1.94)
Light	1.00	1.00	1.00	1.00
Moderate	0.54 (0.41, 0.72)	0.57 (0.42, 0.77)	0.93 (0.79, 1.10)	0.91 (0.76, 1.08)
Heavy	0.69 (0.56, 0.86)	0.58 (0.46, 0.73)	0.84 (0.67, 1.05)	0.76 (0.59, 0.96)
Drinking pattern				
Non-drinker	1.74 (1.30, 2.33)	1.40 (1.02, 1.91)	2.83 (1.95, 4.10)	2.35 (1.59, 3.46)
Irregular light-to-moderate	1.28 (0.98, 1.66)	1.17 (0.88, 1.55)	1.63 (1.14, 2.31)	1.45 (1.01, 2.10)
Regular light-to-moderate	1.00	1.00	1.00	1.00
Irregular heavy	0.85 (0.65, 1.11)	0.72 (0.54, 0.96)	1.06 (0.71, 1.57)	0.87 (0.58, 1.32)
Regular heavy	0.83 (0.60, 1.17)	0.75 (0.52, 1.07)	1.76 (1.15, 2.70)	1.63 (1.04, 2.54)
Problem drinking[c]				
No	1.00	1.00	--	--
Yes	0.94 (0.74, 1.20)	0.84 (0.65, 1.09)	--	--

[a] Among men, [b] Among women, [c] Among drinkers;
[1] Adjusted for age;
[2] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Table 5.14. Odds ratios (95% confidence intervals) of physical limitations by alcohol consumption in the Polish cohort, imputed data

	Men		Women	
	Model 1[1]	Model 2[2]	Model 1[1]	Model 2[2]
Average drinking frequency				
0	1.92 (1.57, 2.35)	1.66 (1.34, 2.07)	2.27 (1.90, 2.70)	2.07 (1.72, 2.50)
<1/month	1.54 (1.23, 1.93)	1.43 (1.12, 1.84)	1.67 (1.37, 2.03)	1.59 (1.29, 1.96)
1-3/month	1.00	1.00	1.00	1.00
1-4/week[a]	0.97 (0.79, 1.19)	1.00 (0.80, 1.25)	--	--
≥5/week[a]	0.89 (0.67, 1.17)	0.96 (0.71, 1.29)	--	--
≥1/week[b]	--	--	0.95 (0.74, 1.21)	1.04 (0.80, 1.36)
Annual drinking volume (g)				
0	1.53 (1.29, 1.81)	1.33 (1.10, 1.60)	1.44 (1.25, 1.66)	1.38 (1.18, 1.60)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	0.72 (0.59, 0.89)	0.76 (0.61, 0.96)	0.71 (0.56, 0.90)	0.75 (0.59, 0.96)
4001-8000[a] /501-1500[b]	0.61 (0.45, 0.81)	0.58 (0.42, 0.79)	0.57 (0.45, 0.73)	0.62 (0.48, 0.80)
>8000[a] />1500[b]	0.75 (0.57, 0.98)	0.78 (0.59, 1.04)	0.63 (0.62, 0.82)	0.74 (0.56, 0.99)
Average drinking quantity/day				
Non-drinker	1.74 (1.48, 2.04)	1.45 (1.22, 1.73)	1.60 (1.40, 1.84)	1.43 (1.23, 1.66)
Light	1.00	1.00	1.00	1.00
Moderate	0.80 (0.58, 1.10)	0.73 (0.52, 1.03)	0.72 (0.60, 0.86)	0.71 (0.59, 0.87)
Heavy	0.96 (0.76, 1.21)	0.84 (0.65, 1.07)	0.98 (0.68, 1.39)	0.80 (0.55, 1.18)
Drinking pattern				
Non-drinker	1.90 (1.56, 2.33)	1.47 (1.18, 1.84)	2.39 (1.84, 3.10)	1.99 (1.51, 2.63)
Irregular light-to-moderate	1.31 (1.07, 1.60)	1.15 (0.93, 1.43)	1.42 (1.09, 1.86)	1.28 (0.97, 1.69)
Regular light-to-moderate	1.00	1.00	1.00	1.00
Irregular heavy	0.81 (0.65, 1.02)	0.68 (0.53, 0.87)	1.41 (1.01, 1.98)	1.34 (0.94, 1.92)
Regular heavy	1.11 (0.71, 1.72)	1.01 (0.63, 1.62)	0.91 (0.58, 1.45)	0.82 (0.51, 1.33)
Problem drinking[c]				
No	1.00	1.00	--	--
Yes	1.10 (0.84, 1.43)	0.98 (0.73, 1.31)	--	--

[a] Among men, [b] Among women, [c] Among drinkers;
[1] Adjusted for age;
[2] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

5.3.2 Past drinking behaviour and physical limitations

The associations between past drinking behaviour and physical limitations in the Russian cohort are presented in Table 5.15. Data on past drinking behaviour were not available in the other two cohorts.

In the fully-adjusted models (model 2), compared with continuing drinkers (i.e., subjects who maintained their alcohol consumption), the highest odds of physical limitations were found in former drinkers who stopped drinking because of health reasons in both Russian men (OR: 2.90, 95% CI: 2.06–4.09) and women (OR: 3.32, 95% CI: 2.49–4.43). In addition, reduced drinkers (i.e., those who cut down their alcohol intake) because of health reasons also had higher odds of physical limitations in men (OR: 2.58, 95% CI: 2.01–3.32) and in women (OR: 2.05, 95% CI: 1.66–3.54) compared to continuing drinkers. In contrast to Russian men, Russian female lifetime abstainers had higher odds of physical limitations than continuing drinkers (OR: 1.36, 95% CI: 1.09–1.71); female reduced drinkers for non-health reasons also had a higher risk of physical limitations (OR: 1.81, 95% CI: 1.35–2.43), compared with continuing drinkers.

Table 5.15. Odds ratios (95% confidence intervals) of physical limitations by past drinking behaviour in the Russian cohort, imputed data

	Model 1[1]	**Model 2**[2]
Men		
Lifetime abstainer	1.53 (0.70, 3.36)	1.31 (0.56, 3.03)
Former drinker, health reasons	4.13 (3.01, 5.66)	2.90 (2.06, 4.09)
Former drinker, non-health reasons	1.30 (0.90, 1.88)	1.22 (0.83, 1.79)
Reduced drinker, health reasons	3.23 (2.56, 4.07)	2.58 (2.01, 3.32)
Reduced drinker, non-health reasons	1.04 (0.82, 1.32)	0.88 (0.68, 1.14)
Continuing drinker	1.00	1.00
Women		
Lifetime abstainer	1.44 (1.16, 1.79)	1.36 (1.09, 1.71)
Former drinker, health reasons	4.03 (3.05, 5.31)	3.32 (2.49, 4.43)
Former drinker, non-health reasons	1.90 (1.43, 2.52)	1.81 (1.35, 2.43)
Reduced drinker, health reasons	2.27 (1.85, 2.78)	2.05 (1.66, 2.54)
Reduced drinker, non-health reasons	0.91 (0.76, 1.09)	0.88 (0.73, 1.07)
Continuing drinker	1.00	1.00

[1] Adjusted for age;
[2] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking

Further categorising continuing drinkers by their drinking pattern, as seen in Table 5.16, essentially did not change the pattern of the association between past drinking behaviour and physical limitations. In Russian men, compared to the results in Table 5.15, the ORs attenuated 20% in both former drinkers who quit drinking due to health reasons and reduced drinkers who cut down on drinking for health reasons. In Russian women, by contrast, the ORs increased by approximately 70% in lifetime abstainers, former drinkers (both due to health reasons and non-health reasons) and reduced drinkers (for health reasons and non-health reasons). This is because the drinking pattern among male continuing drinkers, compared with female continuing drinkers, was more similar between those with physical limitations and those without.

Table 5.16. Odds ratios (95% confidence intervals) of physical limitations by past drinking behaviour combined with drinking pattern in the Russian cohort, imputed data

	Model 1[1]	**Model 2**[2]
Men		
Lifetime abstainer	1.37 (0.60, 3.12)	1.05 (0.44, 2.55)
Former drinker, health reasons	3.67 (2.44, 5.52)	2.32 (1.49, 3.60)
Former drinker, non-health reasons	1.16 (0.74, 1.81)	0.97 (0.60, 1.55)
Reduced drinker, health reasons	2.88 (2.04, 4.06)	2.07 (1.43, 3.00)
Reduced drinker, non-health reasons	0.93 (0.65, 1.32)	0.70 (0.48, 1.02)
Irregular light-to-moderate drinker	1.03 (0.70, 1.53)	0.99 (0.65, 1.51)
Regular light-to-moderate drinker	1.00	1.00
Irregular heavy drinker	0.75 (0.51, 1.10)	0.64 (0.42, 0.96)
Regular heavy drinker	0.85 (0.54, 1.33)	0.69 (0.43, 1.11)
Women		
Lifetime abstainer	2.75 (1.69, 4.49)	2.35 (1.41, 3.90)
Former drinker, health reasons	7.67 (4.57, 12.88)	5.71 (3.34, 9.77)
Former drinker, non-health reasons	3.62 (2.15, 6.11)	3.11 (1.81, 5.34)
Reduced drinker, health reasons	4.32 (2.67, 6.99)	3.50 (2.13, 5.77)
Reduced drinker, non-health reasons	1.73 (1.08, 2.77)	1.51 (0.93, 2.47)
Irregular light-to-moderate drinker	2.11 (1.33, 3.33)	1.90 (1.18, 3.05)
Regular light-to-moderate drinker	1.00	1.00
Irregular heavy drinker	1.27 (0.77, 2.11)	1.09 (0.65, 1.85)
Regular heavy drinker	2.25 (1.32, 3.85)	2.06 (1.18, 3.60)

[1] Adjusted for age;
[2] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking

5.3.3 Sensitivity analyses

Two sensitivity analyses were performed: 1) among participants who were free of CVD and cancer at baseline in the multiply imputed cross-sectional datasets; and 2) complete cases (see Section 4.6.3). The fully-adjusted models were estimated.

The first sensitivity analysis contained 3,152–3,158 Czech men, 3,692–3,696 Czech women, 3,198 Russian men, 3,893 Russian women, 3,815–3,822 Polish men, and 4,051–4,057 Polish women. The variation of subjects in the Czech and Polish cohorts was because of the multiple imputation of missing data on CVD and cancer. The relationships of alcohol consumption and physical limitations among participant without CVD or cancer at baseline are depicted in Table 5.17. Compared to the results from the full samples (Table 5.12–5.14), the pattern of the associations between alcohol consumption and physical limitations was basically unchanged. After exclusion of participants who had CVD or cancer at baseline, non-drinkers still had the highest odds of physical limitations in all cohorts and both sexes (ORs: 1.13–2.35), in comparison with regular and/or light-to-moderate drinkers. The tendency that the odds of physical limitations decreased with more frequent and heavier drinking persisted. Similarly, problem drinking was not associated with physical limitations among male drinkers without CVD and cancer at baseline.

Complete-case analysis included 2,924 Czech men, 3,445 Czech women, 4,207 Russian men, 5,048 Russian women, 4,357 Polish men and 4,587 Polish women. Similar to the first sensitivity analysis, the results on alcohol consumption, past drinking behaviour and physical limitations from the complete-case analysis were essentially the same as in the full samples, although the 95% confidence intervals were, as expected, larger in the complete-case analysis (Appendix I). Only the ORs in Czech male non-drinkers attenuated 15%–20% in the complete-case analysis than in the analysis of imputed datasets (Table 5.12).

Table 5.17. Fully-adjusted alcohol consumption and physical limitations among participants without CVD and cancer at baseline, imputed data

	Czech Republic		Russia		Poland	
	Men (N=3152-3158)	Women (N=3692-3696)	Men (N=3198)	Women (N=3893)	Men (N=3815-3822)	Women (N=4051-4057)
Average drinking frequency						
0	2.35 (1.37, 4.03)	1.91 (1.42, 2.57)	1.71 (1.13, 2.58)	1.39 (1.09, 1.76)	1.69 (1.25, 2.30)	1.76 (1.41, 2.20)
<1/month	1.54 (0.99, 2.41)	1.06 (0.80, 1.21)	1.00 (0.64, 1.58)	1.00 (0.83, 1.20)	1.47 (1.04, 2.08)	1.48 (1.16, 1.90)
1-3/month	1.00	1.00	1.00	1.00	1.00	1.00
1-4/week[a]	1.25 (0.83, 1.86)	--	1.38 (0.99, 1.93)	--	1.01 (0.74, 1.38)	--
≥5/week[a]	0.93 (0.50, 0.99)	--	1.39 (0.85, 2.27)	--	1.04 (0.70, 1.54)	--
≥1/week[b]	--	0.90 (0.67, 1.21)	--	0.88 (0.64, 1.20)	--	0.97 (0.71, 1.32)
Annual drinking volume (g)						
0	1.84 (1.14, 2.96)	1.72 (1.31, 2.26)	1.62 (1.07, 2.45)	1.41 (1.18, 1.69)	1.35 (1.04, 1.76)	1.23 (1.02, 1.49)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	0.95 (0.66, 1.38)	0.89 (0.63, 1.26)	1.16 (0.79, 1.70)	0.67 (0.57, 0.80)	0.73 (0.53, 1.00)	0.78 (0.58, 1.04)
4001-8000[a] /501-1500[b]	0.74 (0.48, 1.13)	0.78 (0.56, 1.08)	1.13 (0.74, 1.73)	0.63 (0.50, 0.78)	0.70 (0.47, 1.05)	0.64 (0.47, 0.87)
>8000[a] />1500[b]	0.84 (0.60, 1.17)	0.86 (0.65, 1.15)	1.28 (0.88, 1.87)	0.88 (0.67, 1.16)	0.85 (0.58, 1.23)	0.68 (0.48, 0.95)
Average drinking quantity/day						
Non-drinker	2.14 (1.36, 3.38)	1.70 (1.30, 2.24)	1.19 (0.78, 1.82)	1.40 (1.08, 1.82)	1.52 (1.18, 1.95)	1.28 (1.07, 1.54)
Light	1.00	1.00	1.00	1.00	1.00	1.00
Moderate	0.85 (0.53, 1.37)	0.76 (0.60, 0.97)	0.78 (0.51, 1.20)	1.02 (0.82, 1.26)	1.06 (0.70, 1.60)	0.72 (0.57, 0.91)
Heavy	1.25 (0.90, 1.74)	1.06 (0.74, 1.53)	0.79 (0.56, 1.10)	0.93 (0.70, 1.23)	0.90 (0.64, 1.26)	0.71 (0.43, 1.16)
Drinking pattern						
Non-drinker	2.14 (1.30, 3.53)	2.41 (1.65, 3.51)	1.13 (0.73, 1.74)	1.93 (1.23, 3.02)	1.46 (1.08, 1.99)	1.75 (1.26, 2.43)
Irregular light-to-moderate	1.29 (0.91, 1.84)	1.40 (0.99, 1.98)	0.63 (0.42, 0.97)	1.47 (0.96, 2.23)	1.11 (0.82, 1.49)	1.26 (0.90, 1.75)
Regular light-to-moderate	1.00	1.00	1.00	1.00	1.00	1.00
Irregular heavy	0.84 (0.59, 1.18)	1.00 (0.66, 1.52)	0.72 (0.50, 1.05)	0.92 (0.58, 1.47)	0.71 (0.51, 0.99)	1.32 (0.87, 2.00)
Regular heavy	1.38 (0.83, 2.31)	1.36 (0.87, 2.14)	0.95 (0.61, 1.46)	1.93 (1.17, 3.17)	0.99 (0.54, 1.84)	0.72 (0.39, 1.30)
Problem drinking[c]						
No	1.00	--	1.00	--	1.00	--
Yes	1.01 (0.65, 1.58)	--	1.25 (0.91, 1.72)	--	1.27 (0.89, 1.83)	--

[a] Among men, [b] Among women, [c] Among drinkers; N: number of participants in the multiply imputed datasets;
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

5.3.4 Summary of cross-sectional results

By analysing data from the baseline survey of the HAPIEE study, after adjustment for age, marital status, SEP, spine/joint problems, BMI and smoking, non-drinkers in all cohorts and both sexes had the highest odds of physical limitations compared with regular and/or light-to-moderate drinkers. Despite some differences across cohorts and sexes, the odds of physical limitations tended to decrease with increasing drinking frequency, annual drinking volume, average drinking quantity per drinking day, and from less to more harmful drinking pattern. Among male drinkers, problem drinking was not associated with physical limitations. The lack of association between problem drinking and physical limitations among male drinkers was consistent with results on heavy drinking (classified by the GF) and physical limitations in this thesis.

In the Russian cohort with data available on past drinking behaviour before baseline, excess odds of physical limitations were found in former drinkers who quit drinking because of health reasons and reduced drinkers who cut down their alcohol intake for health reasons, among both men and women. Compared with drinkers who maintained their drinking, higher odds of physical limitations among lifetime abstainers and reduced drinkers for non-health reasons were only found in Russian women but not men.

After exclusion of participants with CVD or cancer at baseline and those with any missing variable, the pattern of the relationships between alcohol consumption and physical limitations remained largely the same.

5.4 Longitudinal Analyses

This section addresses Objectives 3–4 (i.e., longitudinal changes in the PF-10 score and their relationships with alcohol consumption at baseline). The PF-10 trajectories throughout follow-up of the HAPIEE cohorts were investigated by growth curve modelling via MLM approach in the multiply imputed datasets, separately by cohort and sex (details provided in the Methodology Chapter, see Section 4.6.2.3).

The shape of the PF-10 trajectories over time was determined first by comparing linear and quadratic growth curve models. The quadratic models were also performed in the Czech and Polish cohorts to validate the linear assumption made in the adjustment of the PF-10 score at re-examination. Subsequently, alcohol consumption, age and other covariates measured at baseline were introduced into the growth curve models as time-invariant covariates.

5.4.1 Shape of growth curves

In order to make the comparison of the linear and quadratic growth curve model understandable, the interpretation of growth parameters is introduced below.

5.4.1.1 Interpretation of growth parameters

In a **linear growth curve model**, two growth parameters, intercept and slope, describe the shape of the PF-10 trajectories over time. The **intercept** parameter indicates the initial status of the outcome variable at time zero. Baseline of the HAPIEE study was coded as time zero throughout the longitudinal analyses; the **intercept** growth parameter thus is the estimated PF-10 score at baseline. Statistically significant mean and variance of the intercept growth parameter suggest that the average PF-10 score in the population at baseline is not zero and the PF-10 score at baseline differs between individuals, respectively.

The **slope** parameter describes the rate of change in the outcome variable for each unit increase in time. Individually varying follow-up years in the HAPIEE study was used as the time metric in the longitudinal analyses. Statistically significant mean and variance of the **slope** growth parameter suggest that the average rate of change in the PF-10 score in the population over one year increase of follow-up is not zero, and the rate of change in the PF-10 score differs between individuals.

Another growth parameter, **quadratic slope**, can be included in growth curve models to examine whether the rate of change accelerates, decelerates or levels off over time. If the mean of the quadratic slope growth parameter is not statistically significant, the rate of change does not differ as a function of time; as a result, one can conclude that

a linear growth curve model is efficient enough to fit the data. Statistically significant variance of the quadratic slope suggests that the slope growth parameter accelerates or decelerates differently between individuals.

5.4.1.2 Linear versus quadratic model

Table 5.18 compares the simple linear and quadratic growth curve models with random intercepts, linear and quadratic (if applicable) slopes by freely estimating variances of these growth parameters. According to a robust chi-square difference test based on log-likelihood and scaling correction factor obtained with the MLR estimator,[316] a simple linear growth curve model with random intercept and random slope fitted the data poorer than the model with fixed intercept and slope (Appendix J). However, the chi-square test is very sensitive to sample size and it is usually statistically significant when the sample size is 400 or larger.[317] In fact, as seen in Table 5.18, across cohorts and both sexes, the variances of intercept and slope growth parameters were statistically significant. Linear growth curve models with random intercept and random slope thereby were used to estimate longitudinal changes in the PF-10 score.

The quadratic slope was not statistically significant in Czech women, Polish men and Polish women, which was consistent with the linear assumption made in the adjustment of the PF-10 score at re-examination. The quadratic slope parameter was marginally statistically significant in Czech men ($p=0.04$) but, as shown in Figure 5.2, the population-level PF-10 trajectories estimated in the linear and quadratic growth curve model were visually identical. The same pattern was also seen in Czech women, Polish men and Polish women (Figure 5.2), hence the linear model fitted the longitudinal data of the PF-10 score in the Czech and Polish cohorts efficiently.

In the Russian cohort, the population-level PF-10 trajectories estimated in the linear and quadratic growth curve model in Figure 5.2 were overlapping to a great extent, although the quadratic slope was statistically significant. Since the mode of data collection procedure changed between the first two measurement occasions (baseline and re-examination) and the latter two (PQ2009 and PQ2012) in the Russian cohort,

it is likely that this change influenced the self-reported PF-10 score (see details in Section 6.2.2.4). Participants might over-report their physical functioning at baseline and re-examination with the presence of interviewers, due to the shame or stigma attached to being unhealthy (social desirability bias).[258] In consequence, a linear growth curve model was also used to fit data from the Russian cohort.

In all three cohorts, the mean of the intercept growth parameter–the estimated population-level PF-10 score at baseline–was higher in men than in women (Table 5.18). This gender difference was largest in Russians (9.18 points), followed by Poles (6.24 points), and was smallest in Czechs (3.29 points). At population level, the PF-10 score declined over the 10 years of follow-up across cohorts and sexes, and the rate of decline varied across individuals (Table 5.18). Although direct cross-cohort comparisons should be carried out carefully, the estimates of slopes, to some extent, indicated a slower decline in the PF-10 score per year in Czechs (men: -0.68, standard error [SE]: 0.04; women: -0.59, SE: 0.04) than their Russian (men: -1.85, SE: 0.06; women: -2.10, SE: 0.06) and Polish (men: -1.60, SE: 0.05; women: -1.70, SE: 0.05) counterparts. Only among Russians, the covariance between the intercept and slope was statistically significant and positive, suggesting that Russians who had a higher PF-10 score at baseline experienced a slower decline during follow-up.

Table 5.18. Linear versus quadratic growth curve models by cohort and sex, imputed data

	Czech Republic (S.E.)		Russia (S.E.)		Poland (S.E.)	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Linear						
Intercept						
Mean	85.544 (0.280)***	82.251 (0.283)***	87.859 (0.312)***	78.678 (0.320)***	83.565 (0.272)***	77.326 (0.298)***
Variance	264.450 (14.454)***	304.844 (14.744)***	182.837 (17.868)***	234.270 (15.637)***	292.822 (16.666)***	327.197 (15.880)***
Slope						
Mean	-0.675 (0.039)***	-0.591 (0.036)***	-1.851 (0.062)***	-2.096 (0.056)***	-1.596 (0.052)***	-1.700 (0.051)***
Variance	0.674 (0.220)**	0.509 (0.208)*	1.188 (0.342)**	1.374 (0.350)***	1.512 (0.304)***	1.288 (0.302)***
Covariance						
Intercept & slope	-0.631 (1.415)	-0.399 (1.454)	8.866 (2.056)***	7.241 (1.766)***	-1.771 (1.719)	-2.450 (1.667)
Residual variances of PF-10						
Baseline/re-examination	47.705 (8.524)***	59.887 (9.369)***	169.033 (14.163)***	229.262 (11.946)***	116.781 (11.297)***	150.749 (11.060)***
PQ2009/PQ2012	192.812 (11.834)***	213.119 (11.730)***	387.534 (21.491)***	385.366 (18.482)***	351.414 (15.286)***	398.252 (14.788)***
Residual covariance of PF-10						
Baseline & Re-examination	-43.937 (7.606)***	-45.999 (8.845)***	2.773 (14.121)	-5.167 (11.987)	-49.351 (10.618)***	-52.247 (10.228)***
Re-examination & PQ2009	8.485 (4.542)	10.491 (4.555)*	24.851 (8.080)**	7.932 (7.663)	16.098 (6.559)*	11.710 (7.656)
PQ2009 & PQ2012	92.157 (11.020)***	101.503 (10.940)***	131.081 (21.424)***	121.824 (18.846)***	183.957 (15.651)***	218.462 (15.577)***
Quadratic						
Intercept						
Mean	85.344 (0.294)***	82.116 (0.286)***	87.400 (0.304)***	78.299 (0.318)***	83.710 (0.282)***	77.137 (0.296)***
Variance	280.099 (16.923)***	309.753 (15.405)***	195.467 (20.942)***	240.354 (17.682)***	313.131 (18.495)***	353.668 (16.914)***
Slope						
Mean	-0.463 (0.104)***	-0.482 (0.101)***	-1.210 (0.144)***	-1.639 (0.145)***	-1.741 (0.108)***	-1.505 (0.129)***
Variance	0.989 (2.948)	1.429 (1.907)	8.389 (4.225)*	7.275 (3.594)*	7.829 (2.743)**	9.230 (2.589)***
Quadratic slope						
Mean	-0.026 (0.013)*	-0.013 (0.012)	-0.081 (0.018)***	-0.057 (0.018)**	0.017 (0.013)	-0.022 (0.015)
Variance	0.013 (0.036)	0.014 (0.024)	0.088 (0.051)	0.077 (0.044)	0.044 (0.027)	0.057 (0.023)*
Covariance						
Intercept & slope	-8.415 (3.945)*	-8.396 (3.198)**	11.526 (5.366)*	10.504 (4.543)*	-9.053 (4.271)*	-14.015 (4.243)**
Intercept & quadratic slope	0.970 (0.370)**	1.090 (0.317)**	-0.761 (0.508)	-0.700 (0.445)	0.494 (0.385)	0.929 (0.407)*
Slope & quadratic slope	-0.070 (0.313)	-0.111 (0.204)	-0.762 (0.449)	-0.641 (0.382)	-0.540 (0.263)*	-0.680 (0.236)**
Residual						
Baseline/re-examination	46.522 (11.481)***	66.728 (10.347)***	140.940 (17.555)***	206.695 (14.912)***	96.826 (13.642)***	128.806 (12.943)***
PQ2009/PQ2012	189.947 (13.424)***	203.666 (11.765)***	369.149 (23.460)***	366.205 (19.946)***	351.228 (15.212)***	392.386 (14.086)***

Table 5.18 continued

	Czech Republic (S.E.)		Russia (S.E.)		Poland (S.E.)	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Residual covariance of PF-10						
Baseline & Re-examination	-44.464 (7.568)***	-37.022 (8.459)***	-8.773 (14.180)	-12.881 (12.096)	-49.220 (11.069)***	-48.236 (10.308)***
Re-examination & PQ2009	8.406 (8.550)	11.165 (6.365)	0.729 (12.598)	-14.388 (11.342)	4.257 (9.637)	-2.036 (9.724)
PQ2009 & PQ2012	92.040 (11.107)***	93.898 (10.567)***	125.256 (21.130)***	113.921 (19.057)***	185.007 (14.795)***	214.818 (14.464)***

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error

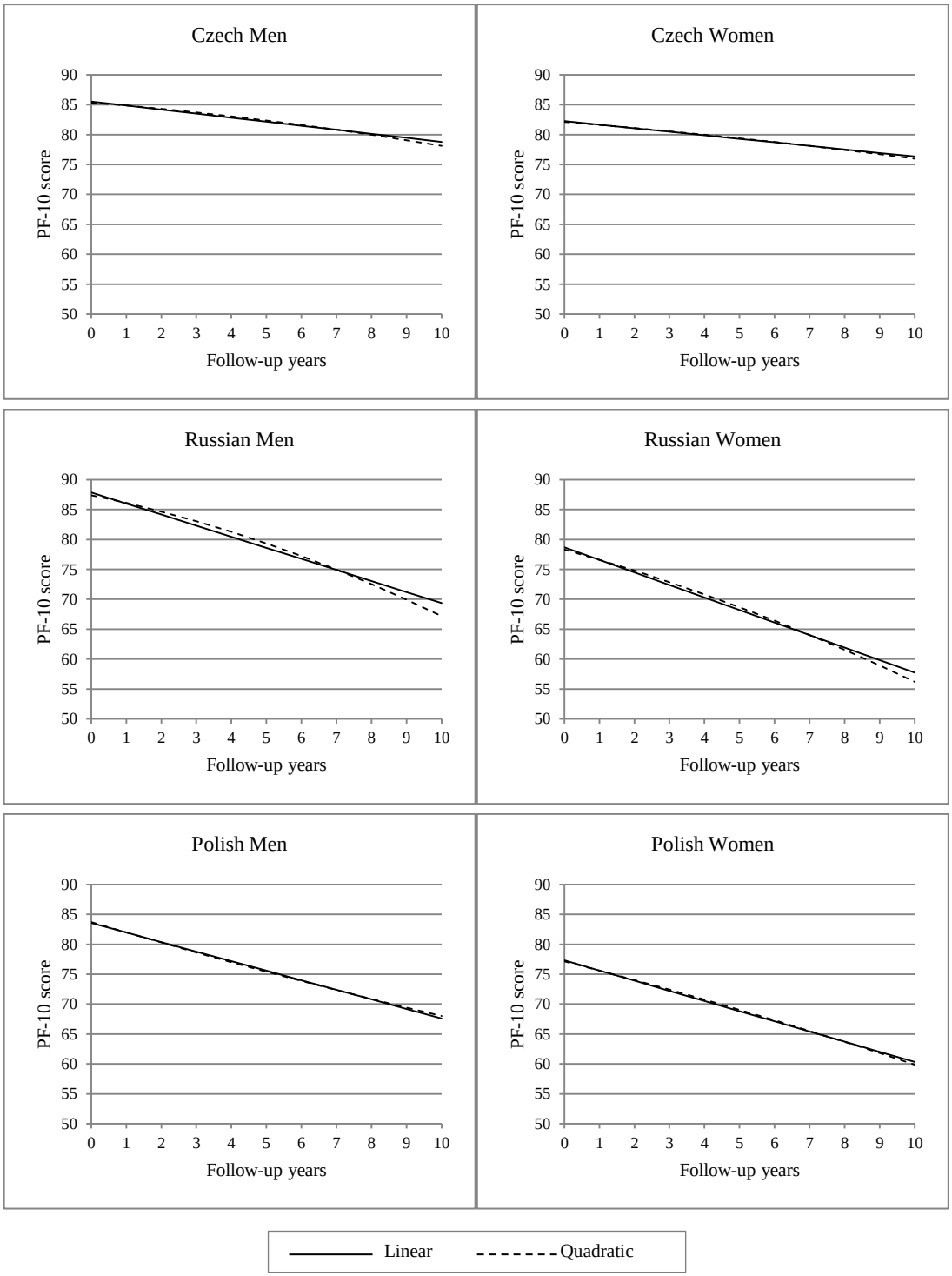


Figure 5.2. Linear vs. quadratic population-level PF-10 trajectories

5.4.2 Alcohol consumption and PF-10 trajectories

Alcohol consumption and covariates measured at baseline were entered into growth curve models as time-invariant covariates. As in cross-sectional analyses, two models were estimated: adjusting for age only (model 1) and fully adjusting for age, marital status, SEP, spine/joint problems, BMI and smoking status (model 2).

The effects of covariates were explored by adding each covariate separately into the age-adjusted growth curve model. All the covariates were statistically significantly associated with the intercept growth parameter; whilst SEP, joint/spine problems, BMI and smoking were commonly associated with the slope growth parameter in the three cohorts and both sexes (results not shown).

5.4.2.1 Average drinking frequency and PF-10 trajectories

Results on average drinking frequency and the PF-10 trajectories are summarised in Table 5.19. After adjusting for age, the variance of the slope reduced by 6.4%, 18.3%, 27.1%, 29.9%, 8.0% and 14.2% in Czech men and women, Russian men and women, and Polish men and women, respectively. After additional adjustment for all covariates, compared to the age-adjusted models, the variance of slope further fell by 7.2%, 15.0%, 16.0%, 23.1%, 13.6% and 18.5%, respectively. When fully adjusted for all covariates, the variance of slope was no longer statistically significant among women. The full results of fully-adjusted model are provided in Appendix K.1.

The association of average drinking frequency with the intercept growth parameter was consistent with the cross-sectional results (shown previously in Table 5.12–5.14). Across cohorts and sexes, after controlling for all covariates and compared with drinkers who consumed alcohol 1–3/month, non-drinkers had a PF-10 score 4.04–7.31 points lower at baseline. The PF-10 score at baseline increased with increasing average drinking frequency. The score was 2.24 points (SE: 0.89) lower in Russian male drinkers who drank <1/month than those drank 1–3/month; likewise a 1.70 point (SE: 0.79) lower PF-10 score was also found in Polish male drinkers who drank <1/month. Czech male frequent drinkers (≥5/week) had a 1.42 point (SE: 0.67) higher PF-10 score at baseline than Czech men who drank 1–3/month. Among Czech

and Polish women, the PF-10 score at baseline was lower in those who drank <1/month than 1–3 times /month.

Average drinking frequency was not associated with the slope growth parameter in any cohort or either sex after full adjustment for all covariates, except in Russian women. Compared with Russian female drinkers who consumed alcohol 1–3/month, those who drank ≥1/week had a faster decline in the PF-10 score during follow-up (slope:-0.39, SE: 0.18, p=0.03). As seen in Figure 5.3, Russian female frequent drinkers (≥1/week) had a PF-10 score 0.77 point higher at baseline than less frequent drinkers (1–3/month). Their PF-10 scores began to be lower than less frequent drinkers at approximately the 2nd year of follow-up. At the 10th year of follow-up, the gap of the PF-10 score between the frequent and less frequent Russian female drinkers increased to 3.16 points.

Table 5.19. Average drinking frequency and PF-10 trajectories, imputed data

Average drinking frequency	Model 1 (mean, S.E.)[a]			Model 2 (mean, S.E.)[b]		
	Czech Republic	**Russia**	**Poland**	**Czech Republic**	**Russia**	**Poland**
Men						
Intercept						
0	-8.902 (1.645)***	-4.984 (1.079)***	-5.985 (0.875)***	-5.953 (1.479)***	-4.036 (0.972)***	-4.338 (0.813)***
<1/month	-0.811 (1.012)	-2.432 (1.006)*	-2.777 (0.848)**	-0.605 (0.879)	-2.239 (0.889)*	-1.702 (0.791)*
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	1.193 (0.794)	1.617 (0.653)*	-0.142 (0.666)	0.515 (0.697)	0.650 (0.605)	-0.364 (0.617)
≥5/week	2.033 (0.760)**	2.072 (0.945)*	0.196 (0.817)	1.419 (0.669)*	0.654 (0.900)	-0.399 (0.765)
Slope						
0	0.152 (0.204)	-0.255 (0.185)	-0.032 (0.148)	0.177 (0.205)	-0.213 (0.183)	0.032 (0.149)
<1/month	0.083 (0.140)	0.125 (0.186)	0.167 (0.140)	0.083 (0.140)	0.070 (0.182)	0.141 (0.140)
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	0.171 (0.111)	-0.023 (0.138)	0.042 (0.122)	0.168 (0.111)	-0.006 (0.138)	0.041 (0.122)
≥5/week	0.124 (0.111)	-0.121 (0.209)	-0.170 (0.157)	0.120 (0.111)	-0.125 (0.209)	-0.133 (0.157)
Women						
Intercept						
0	-8.545 (0.926)***	-9.015 (0.945)***	-6.221 (0.712)***	-4.806 (0.800)***	-7.314 (0.891)***	-4.736 (0.683)***
<1/month	-2.638 (0.672)***	-1.469 (0.615)*	-3.422 (0.727)***	-1.183 (0.592)*	-0.813 (0.580)	-2.496 (0.681)***
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥1/week	0.108 (0.610)	2.016 (0.928)*	0.721 (0.852)	-0.191 (0.553)	0.765 (0.904)	0.099 (0.810)
Slope						
0	-0.055 (0.126)	-0.204 (0.165)	-0.130 (0.121)	-0.037 (0.123)	-0.106 (0.165)	0.053 (0.125)
<1/month	0.037 (0.091)	-0.184 (0.115)	0.039 (0.130)	0.033 (0.090)	-0.124 (0.115)	0.140 (0.130)
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥1/week	0.113 (0.087)	-0.327 (0.186)	0.032 (0.157)	0.081 (0.088)	-0.392 (0.184)*	-0.058 (0.155)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Figure 5.3. Population-level PF-10 trajectories by average drinking frequency, Russian women, fully-adjusted model

5.4.2.2 Annual drinking volume and PF-10 trajectories

Table 5.20 depicts the association of annual drinking volume with the PF-10 trajectories. Similar to the analysis of average drinking frequency, non-drinkers in all cohorts and both sexes had the lowest PF-10 score at baseline. Generally, the higher amount participants drank at baseline, the better PF-10 score at baseline they had. For example, after controlling for all covariates, compared with male drinkers who consumed 1–1500 g of alcohol annually, those who drank 1501–8000 g of alcohol annually were found having a 2.01–3.58 points higher PF-10 score in Russian men and 1.41–1.61 point higher score in Polish men. Likewise, Russian and Polish women who drank 251–1500 g of alcohol annually versus 1–150 g had a PF-10 score 2.83–3.22 points higher at baseline. In addition, a higher PF-10 score was also seen in the heaviest drinkers among Russian men (>8000 g) and Polish women (>1500 g).

After adjusting for age, and compared with drinking 1–1500 g of alcohol annually, a faster decline in the PF-10 score at follow-up was observed in Russian male non-drinkers (slope: -0.37, SE: 0.18, p=0.04) and Polish male drinkers who consumed >8000 g of alcohol annually (slope: -0.38, SE: 0.15, p=0.01). After full adjustment for all covariates, the rate of change in the PF-10 score was no longer statistically significantly different by annual drinking volume groups in Russian and Polish men. The rate of change did not vary by annual drinking volume in Czech men and women, Russian women and Polish women.

The full results of the model 2 on annual drinking volume, covariates and the PF-10 trajectories are presented in Appendix K.2.

Table 5.20. Annual drinking volume and PF-10 trajectories, imputed data

Annual drinking volume	Model 1 (mean, S.E.)[a]			Model 2 (mean, S.E.)[b]		
	Czech Republic	**Russia**	**Poland**	**Czech Republic**	**Russia**	**Poland**
Men						
Intercept						
0	-8.785 (1.585)***	-3.535 (1.088)**	-4.509 (0.817)***	-5.750 (1.430)***	-2.195 (0.981)*	-3.183 (0.755)***
1-1500	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000	1.039 (0.779)	1.703 (0.820)*	2.107 (0.639)**	0.340 (0.688)	2.009 (0.747)**	1.411 (0.605)*
4001-8000	1.912 (0.789)*	4.089 (0.786)***	1.864 (0.836)*	1.290 (0.698)	3.581 (0.748)***	1.605 (0.762)*
>8000	1.388 (0.652)*	3.175 (0.737)***	1.215 (0.821)	1.087 (0.580)	2.670 (0.694)***	0.730 (0.767)
Slope						
0	0.092 (0.189)	-0.372 (0.181)*	-0.157 (0.134)	0.130 (0.190)	-0.242 (0.182)	-0.068 (0.134)
1-1500	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000	0.105 (0.114)	-0.040 (0.154)	-0.123 (0.115)	0.105 (0.114)	0.049 (0.153)	-0.102 (0.114)
4001-8000	0.094 (0.115)	-0.260 (0.167)	-0.214 (0.158)	0.096 (0.115)	-0.121 (0.165)	-0.150 (0.158)
>8000	0.060 (0.099)	-0.234 (0.153)	-0.379 (0.154)*	0.092 (0.099)	-0.081 (0.157)	-0.271 (0.154)
Women						
Intercept						
0	-6.065 (0.956)***	-6.485 (0.962)***	-2.772 (0.696)***	-3.453 (0.819)***	-5.246 (0.898)***	-2.163 (0.655)**
1-250	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
251-500	1.827 (0.846)*	2.940 (0.690)***	3.804 (0.857)***	1.461 (0.753)	2.862 (0.647)***	2.829 (0.798)***
501-1500	2.551 (0.727)***	3.535 (0.837)***	3.963 (0.855)***	1.111 (0.652)	3.220 (0.801)***	2.972 (0.805)***
>1500	2.333 (0.673)**	2.916 (1.017)**	4.271 (0.968)***	1.081 (0.601)	1.775 (1.002)	2.598 (0.915)**
Slope						
0	-0.083 (0.123)	-0.152 (0.161)	-0.203 (0.121)	-0.054 (0.122)	-0.079 (0.160)	-0.091 (0.123)
1-250	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
251-500	0.009 (0.116)	-0.135 (0.127)	-0.060 (0.156)	0.022 (0.116)	-0.127 (0.127)	-0.118 (0.155)
501-1500	-0.012 (0.104)	-0.132 (0.156)	-0.151 (0.162)	-0.006 (0.104)	-0.102 (0.156)	-0.212 (0.161)
>1500	0.043 (0.096)	-0.237 (0.190)	-0.060 (0.174)	0.035 (0.104)	-0.286 (0.194)	-0.224 (0.175)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

5.4.2.3 Average drinking quantity per drinking day and PF-10 trajectories

Table 5.21 describes the relationship between average drinking quantity per drinking day and the PF-10 trajectories. The PF-10 score at baseline was lowest among non-drinkers in all three cohorts and both sexes, and they were higher among moderate and heavy drinkers (except in the Czech cohort). In the fully-adjusted models, non-drinkers had a PF-10 score 1.84–6.31 points lower at baseline than light drinkers. In the Russian cohort, about 3.00 points higher PF-10 score at baseline was found in both male moderate and heavy drinkers than light drinkers; whilst among women, the differences was smaller in moderate (1.56 points) and heavy (2.57 points) drinkers compared with light drinkers. A similar pattern was also observed among Poles that moderate drinkers and heavy drinkers had 2.01–2.24 and 1.65–2.38 points higher PF-10 score than light drinkers, respectively.

Regarding the slope growth parameter, among men, after adjusting for age, a steeper decline in the PF-10 score during follow-up, compared with light drinkers, was found in Czech moderate drinkers (slope: -0.27, SE: 0.13, p=0.04), Russian non-drinkers (slope: -0.53, SE: 0.19, p<0.001), Russian heavy drinkers (slope: -0.43, SE: 0.14, p<0.01), and Polish heavy drinkers (slope: -0.28, SE: 0.13, p=0.04). After controlling for all covariates, the rates of change in the PF-10 score by average drinking quantity per drinking day were slightly attenuated and no longer statistically significant (Russian male non-drinkers: -0.36, SE: 0.19, p=0.06). As shown in Figure 5.4, among Russian men, the PF-10 score at baseline was 1.84 point lower in non-drinkers than in light drinkers; at the 10^{th} year of follow-up, the gap enlarged to 5.45 points.

Among women, in the age-adjusted models, no differential rates of change in the PF-10 score across the categories of average drinking quantity per day were found in Czechs and Russians. A faster decline was found in Polish female non-drinkers (slope: -0.28, SE: 0.11, p=0.01) and moderate drinkers (slope: -0.29, SE: 0.12, p=0.01) in comparison with light drinkers. In the fully-adjusted models, the accelerated decline in Polish female moderate drinkers remained marginally statistically significant (slope: -0.25, SE: 0.12, p=0.03). As displayed in Figure 5.5,

the PF-10 score in Polish female moderate drinkers was 2.24 points higher than in light drinkers at baseline. The score started to become similar between the two drinking groups at approximately the 8.5th year of follow-up. At the 10th year of follow-up, the score in moderate drinkers was 0.25 point lower than in light drinkers.

In Figures 5.4 and 5.5, light drinkers (the reference group) had a slightly slower rate of decline in the PF-10 score during follow-up, compared with other drinking categories of average drinking quantity per drinking day. However, as reported in Table 5.21, the rate of decline in light drinkers was not statistically significantly different from non-, moderate or heavy drinkers in either Russian men or Polish women (except Polish female moderate drinkers). This lack of statistical significance may be due to the relatively short follow-up time. In the only previous longitudinal study which investigated alcohol consumption and rate of change in physical functioning by Wang *et al.*[55], light drinkers were not identified due to the very crude measure of alcohol consumption applied in their study. For this reason, no previous study could be compared with the findings on light drinkers in this thesis. Detailed discussion of longitudinal findings in this thesis in the context of previous longitudinal studies will be presented in Section 6.3.2.

Appendix K.3 provides details of the results of the fully-adjusted models on average drinking quantity per drinking day and the PF-10 trajectories in the three cohorts.

Table 5.21. Average drinking quantity per drinking day and PF-10 trajectories, imputed data

Average drinking quantity per day	Model 1 (mean, S.E.)[a]			Model 2 (mean, S.E.)[b]		
	Czech Republic	**Russia**	**Poland**	**Czech Republic**	**Russia**	**Poland**
Men						
Intercept						
Non-drinker	-9.886 (1.559)***	-3.692 (1.110)**	-5.099 (0.786)***	-6.305 (1.396)***	-1.843 (1.005)	-3.350 (0.726)***
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	0.389 (0.813)	3.595 (0.785)***	1.726 (0.878)*	0.909 (0.737)	2.967 (0.730)***	2.007 (0.800)*
Heavy	-0.743 (0.710)	2.092 (0.705)**	0.726 (0.749)	0.052 (0.651)	2.996 (0.657)***	1.650 (0.715)*
Slope						
Non-drinker	-0.007 (0.184)	-0.534 (0.188)**	-0.122 (0.126)	0.039 (0.185)	-0.361 (0.190)	-0.037 (0.128)
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	-0.265 (0.131)*	-0.298 (0.160)	-0.267 (0.168)	-0.213 (0.130)	-0.220 (0.160)	-0.185 (0.165)
Heavy	-0.117 (0.099)	-0.427 (0.137)**	-0.275 (0.134)*	-0.051 (0.100)	-0.203 (0.140)	-0.167 (0.134)
Women						
Intercept						
Non-drinker	-7.510 (0.925)***	-7.219 (1.032)***	-3.879 (0.662)***	-4.108 (0.810)***	-5.539 (0.975)***	-2.623 (0.635)***
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	0.137 (0.565)	1.374 (0.739)	2.524 (0.679)***	0.311 (0.505)	1.561 (0.694)*	2.236 (0.635)***
Heavy	-0.334 (0.830)	1.755 (0.948)	1.055 (1.256)	0.046 (0.755)	2.570 (0.914)**	2.382 (1.118)*
Slope						
Non-drinker	-0.112 (0.115)	-0.214 (0.177)	-0.284 (0.113)*	-0.062 (0.115)	-0.081 (0.177)	-0.110 (0.117)
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	-0.020 (0.078)	-0.186 (0.134)	-0.289 (0.117)*	0.005 (0.078)	-0.121 (0.135)	-0.249 (0.116)*
Heavy	-0.106 (0.134)	-0.247 (0.181)	-0.428 (0.239)	-0.017 (0.134)	-0.063 (0.188)	-0.293 (0.236)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

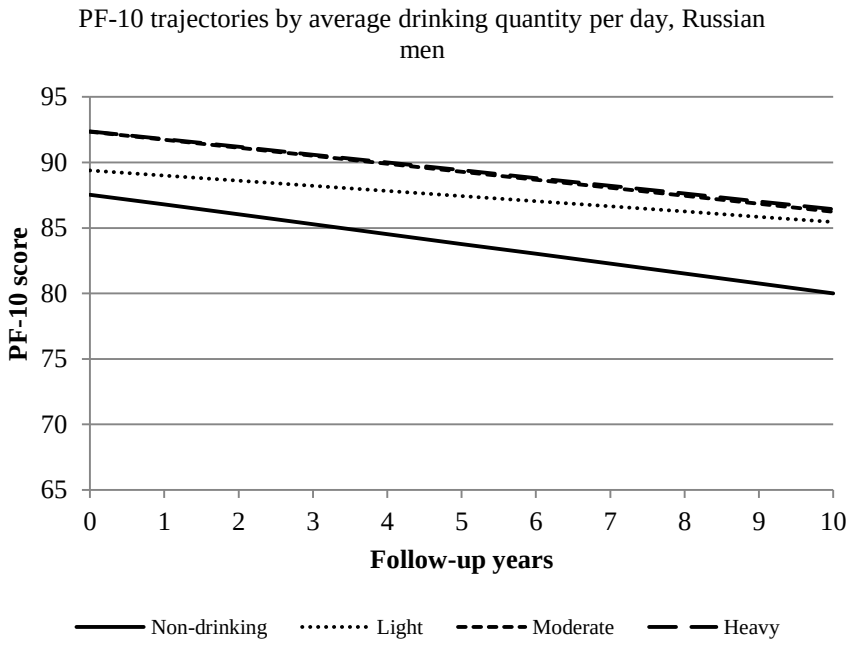
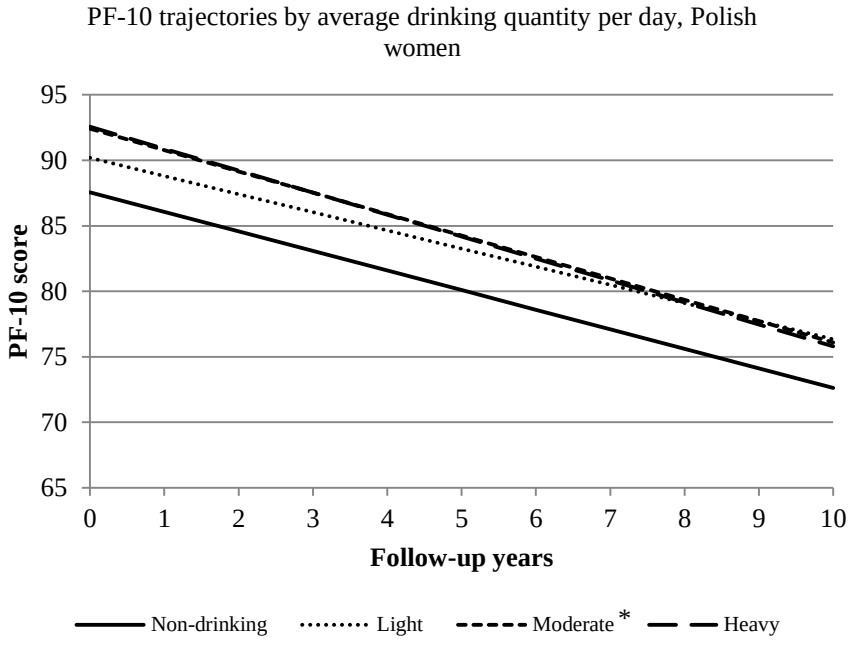


Figure 5.4. Population-level PF-10 trajectories by average drinking quantity per day, Russian men, fully-adjusted model



* p<0.05

Figure 5.5. Population-level PF-10 trajectories by average drinking quantity per day, Polish women, fully-adjusted model

5.4.2.4 Drinking pattern and PF-10 trajectories

Table 5.22 contains the results of analyses of the association of drinking pattern with the PF-10 trajectories. Similar to other drinking indices derived from the GF, the results of drinking pattern on the intercept growth parameter (the PF-10 score at baseline) were consistent with the cross-sectional findings. In the fully-adjusted models, the PF-10 score at baseline, again, was lowest in non-drinkers (3.24–8.67 points lower than regular light-to-moderate drinkers). Lower PF-10 scores were also found in irregular light-to-moderate drinkers in Russian men (-2.74), Russian women (-2.32) and Polish women (-2.19). The scores were not statistically significantly different between regular light-to-moderate drinkers and heavy drinkers, both irregular and regular, except in Polish men that irregular heavy drinkers had a 2.24 points higher PF-10 score than regular light-to-moderate drinkers.

The rate of change in the PF-10 score at follow-up did not vary significantly by drinking pattern among women. Among men, after adjustment for age, a faster decline in the PF-10 score at follow-up was seen in Czech regular heavy drinkers (slope: -0.40, SE: 0.18, p=0.02), Polish irregular heavy drinkers (slope: -0.29, SE: 0.14, p=0.04) and Polish regular heavy drinkers (slope: -0.82, SE: 0.28, p<0.01). After controlling for all covariates, the steeper decline remained statistically significant in Polish male regular heavy drinkers (slope: -0.64, SE: 0.28, p=0.02) and it was marginally statistically significant in Czech male regular heavy drinkers (slope: -0.32, SE: 0.18, p=0.08).

Figure 5.6 and Figure 5.7 show the PF-10 trajectories by drinking pattern in Czech men and Polish men, respectively. From Figure 5.6, it can be seen that, among Czech men, regular heavy and regular light-to-moderate drinkers had a similar PF-10 score at baseline. The gap of the PF-10 score between the two drinking groups expanded with increasing years of follow-up. At the 10^{th} year of follow-up, the PF-10 score in Czech male regular heavy drinkers was 3.30 points lower than in regular light-to-moderate drinkers.

Among Polish men, the PF-10 score at baseline in regular heavy drinkers was around 4.23 points higher than in non-drinkers. After approximately 7.5 years of follow-up, however, the PF-10 score among Polish regular heavy drinkers started to become the lowest among the drinking pattern groups (even lower than non-drinkers as displayed in Figure 5.7). At the 10^{th} year of follow-up, the PF-10 score in regular heavy drinkers was 1.30 point lower than in non-drinkers.

The detailed results of drinking pattern and all the covariates on the PF-10 trajectories are set out in Appendix K.4.

Table 5.22. Drinking pattern and PF-10 trajectories, imputed data

Drinking pattern	Model 1 (mean, S.E.)[a]			Model 2 (mean, S.E.)[b]		
	Czech Republic	**Russia**	**Poland**	**Czech Republic**	**Russia**	**Poland**
Men						
Intercept						
Non-drinker	-9.961 (1.596)***	-6.411 (1.112)***	-5.564 (0.879)***	-6.427 (1.415)***	-4.310 (1.014)***	-3.235 (0.810)***
Irregular light-to-moderate	-1.850 (0.770)*	-3.454 (0.872)***	-1.446 (0.716)*	-1.106 (0.669)	-2.737 (0.805)**	-0.314 (0.662)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	0.838 (0.634)	0.258 (0.732)	1.265 (0.679)	0.821 (0.579)	1.030 (0.693)	2.242 (0.629)***
Regular heavy	-0.251 (1.042)	-0.213 (0.854)	0.102 (1.390)	-0.120 (0.970)	0.506 (0.827)	0.998 (1.323)
Slope						
Non-drinker	-0.102 (0.194)	-0.264 (0.211)	-0.181 (0.147)	-0.048 (0.195)	-0.168 (0.212)	-0.086 (0.149)
Irregular light-to-moderate	-0.213 (0.115)	0.184 (0.176)	-0.017 (0.131)	-0.196 (0.115)	0.139 (0.175)	-0.007 (0.131)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	-0.145 (0.095)	-0.068 (0.170)	-0.294 (0.139)*	-0.097 (0.095)	0.042 (0.171)	-0.218 (0.139)
Regular heavy	-0.403 (0.179)*	-0.233 (0.209)	-0.821 (0.283)**	-0.318 (0.180)	-0.075 (0.210)	-0.639 (0.281)*
Women						
Intercept						
Non-drinker	-8.285 (1.065)***	-11.796 (1.372)***	-7.181 (0.984)***	-4.455 (0.931)***	-8.667 (1.341)***	-5.298 (0.954)***
Irregular light-to-moderate	-1.800 (0.800)*	-4.092 (1.155)***	-3.035 (0.955)**	-0.796 (0.707)	-2.323 (1.135)*	-2.185 (0.917)*
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	1.273 (0.830)	-1.738 (1.286)	-2.054 (1.173)	1.197 (0.754)	0.372 (1.252)	-1.736 (1.104)
Regular heavy	0.016 (0.948)	-2.966 (1.460)*	0.134 (1.469)	0.167 (0.848)	-1.741 (1.435)	0.542 (1.386)
Slope						
Non-drinker	-0.252 (0.143)	0.185 (0.258)	-0.202 (0.183)	-0.194 (0.143)	0.419 (0.257)	0.056 (0.186)
Irregular light-to-moderate	-0.176 (0.109)	0.292 (0.232)	-0.015 (0.177)	-0.143 (0.109)	0.446 (0.229)	0.107 (0.175)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	-0.161 (0.119)	0.209 (0.251)	-0.182 (0.213)	-0.133 (0.119)	0.458 (0.248)	-0.058 (0.211)
Regular heavy	-0.248 (0.146)	0.016 (0.298)	-0.260 (0.289)	-0.177 (0.147)	0.241 (0.298)	-0.187 (0.290)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

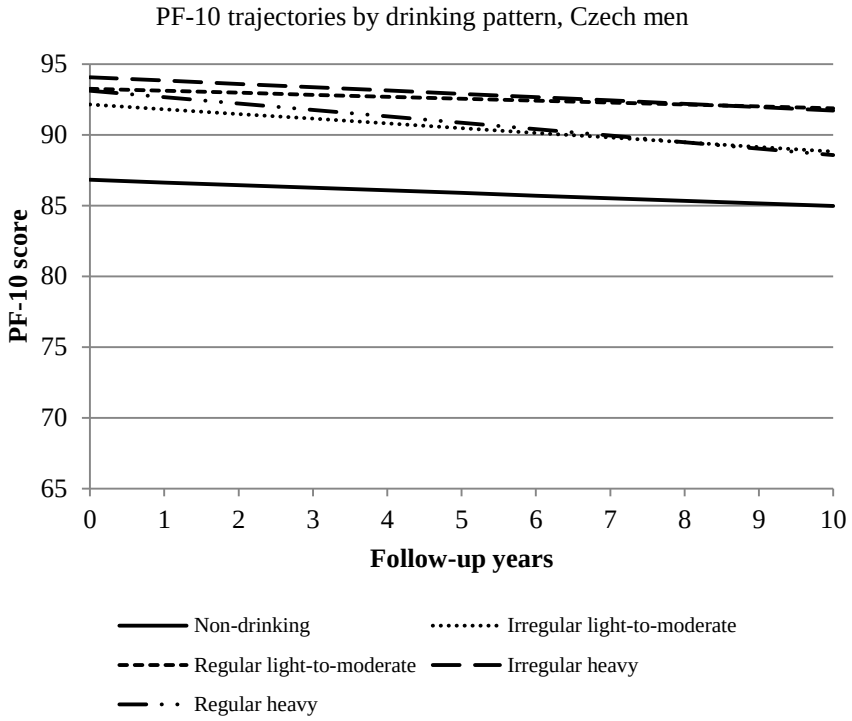
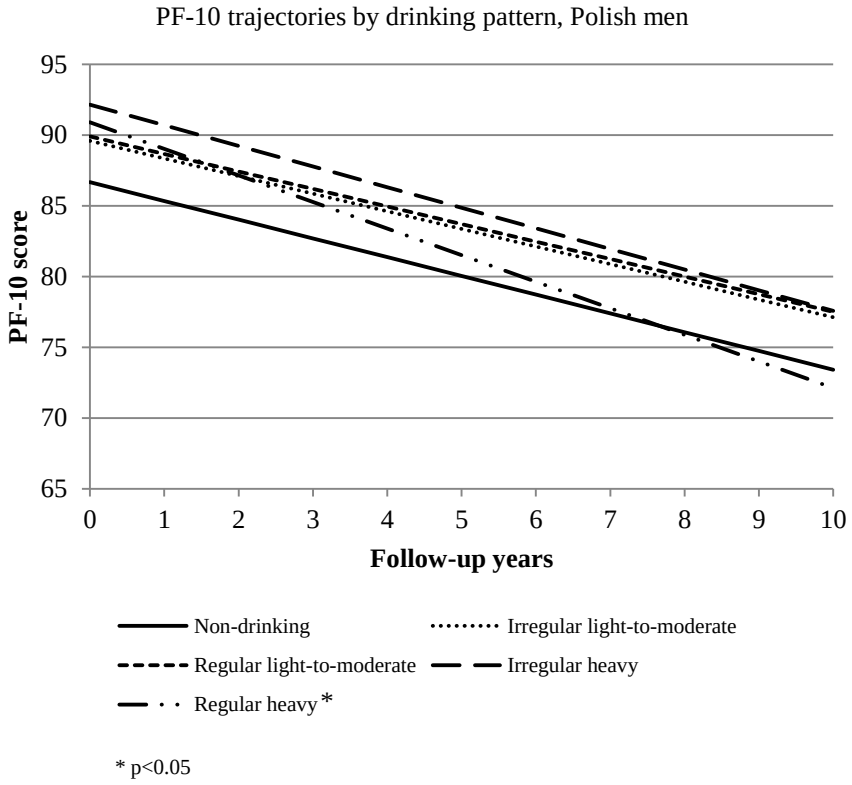


Figure 5.6. Population-level PF-10 trajectories by drinking pattern, Czech men, fully-adjusted model



* p<0.05

Figure 5.7. Population-level PF-10 trajectories by drinking pattern, Polish men, fully-adjusted model

5.4.2.5 Problem drinking and PF-10 trajectories

The relationship between problem drinking and the PF-10 trajectories was only investigated among male drinkers in the three cohorts due to the small number of female problem drinkers identified by the CAGE questionnaire. In the 70 imputed longitudinal datasets, 366–383 Czech men, 813–814 Russian men and 464–479 Polish men were identified as problem drinkers, whilst 3,796–3,808 Czech men, 3,667–3,668 Russian men and 4,067–4,079 Polish men were drinkers. The variations in the number of observations were due to the multiple imputation of missing data on the GF and CAGE.

As shown in Table 5.23, problem drinking was not associated with the rate of change in the PF-10 score during follow-up in any cohorts, in both age-adjusted and fully-adjusted models. The full results of fully-adjusted models are presented in Appendix K.5.

Table 5.23. Problem drinking and PF-10 trajectories among male drinkers, imputed data

Problem drinking	Model 1 (mean, S.E.)[a]			Model 2 (mean, S.E.)[b]		
	Czech Republic	**Russia**	**Poland**	**Czech Republic**	**Russia**	**Poland**
Intercept						
Problem drinking						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	-1.662 (0.921)	0.462 (0.631)	-1.949 (0.924)*	-0.664 (0.857)	1.270 (0.602)*	-0.937 (0.863)
Slope						
Problem drinking						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	-0.123 (0.135)	-0.157 (0.154)	-0.299 (0.203)	-0.105 (0.135)	-0.052 (0.156)	-0.170 (0.199)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

5.4.2.6 Past drinking behaviour and PF-10 trajectories

The role of past drinking behaviour prior to baseline on the PF-10 trajectories was examined in the Russian cohort (Table 5.24 and Table 5.25). Information on past drinking was not available in the Czech and Polish cohorts.

In Table 5.24, after controlling for all covariates, among both men and women, the PF-10 score at baseline was substantially lower in former drinkers who quit drinking for health reasons (men: -11.45 points, SE: 1.53; women: -12.80 points, SE: 1.51) and in reduced drinkers who cut down drinking for health reasons (men: -7.84 points, SE: 0.83; women: -5.61 points, SE: 0.94), compared with those who maintained their drinking. In addition, among Russian women, a lower PF-10 score at baseline was also found in lifetime abstainers (-4.74 points, SE: 1.13) and reduced drinkers who cut down their alcohol intake for non-health reasons (-6.20 points, SE: 1.51); but this was not observed in Russian men. The pattern was the same as in cross-sectional results (Table 5.15).

Regarding the slope growth parameter, among Russian women, after adjusting for age and compared with continuing drinkers, those who reduced their drinking for health reasons had a slower decline in the PF-10 score during follow-up (slope: 0.38, SE: 0.18, p=0.04). In the fully-adjusted models, however, the rates of change in the PF-10 score did not differ by past drinking behaviour in either Russian men or women. This was consistent with the majority of findings on drinking indices derived from the GF and the PF-10 trajectories described above (Table 5.19–5.23).

Likewise, further dividing current drinkers according to their drinking pattern, as shown in Table 5.25, did not change the pattern of the association between past drinking behaviour and the PF-10 trajectories. After controlling for age, compared with regular light-to-moderate drinkers, the rate of decline in the PF-10 score during follow-up was slower in male reduced drinkers for non-health reasons (slope: 0.44, SE: 0.21, p=0.04) and in female reduced drinkers for health reasons (slope: 0.59, SE: 0.28, p=0.04). The statistical significance disappeared after controlling for all covariates.

The results of fully-adjusted models of the PF-10 trajectories with past drinking behaviour and with past drinking behaviour combined with drinking pattern are provided in more detail in Appendix K.6 and Appendix K.7, respectively.

Table 5.24. Past drinking behaviour and PF-10 trajectories in the Russian cohort, imputed data

	Mode 1 (mean, S.E.)[a]		**Model 2 (mean, S.E.)[b]**	
	Men	**Women**	**Men**	**Women**
Intercept				
Lifetime abstainer	-6.139 (3.413)	-5.859 (1.204)***	-4.554 (2.845)	-4.735 (1.130)***
Former drinker, health reasons	-15.261 (1.760)***	-16.008 (1.569)***	-11.452 (1.534)***	-12.802 (1.508)***
Former drinker, non-health reasons	-1.375 (0.993)	-7.230 (1.605)***	-0.652 (0.949)	-6.198 (1.511)***
Reduced drinker, health reasons	-10.342 (0.930)***	-7.258 (0.982)***	-7.840 (0.834)***	-5.610 (0.937)***
Reduced drinker, non-health reasons	-0.501 (0.602)	0.885 (0.720)	0.386 (0.577)	1.083 (0.685)
Continuing drinker	Ref.	Ref.	Ref.	Ref.
Slope				
Lifetime abstainer	0.172 (0.575)	-0.076 (0.208)	0.012 (0.538)	-0.020 (0.206)
Former drinker, health reasons	-0.014 (0.278)	0.046 (0.247)	-0.005 (0.275)	0.110 (0.248)
Former drinker, non-health reasons	-0.381 (0.216)	0.170 (0.258)	-0.285 (0.215)	0.175 (0.257)
Reduced drinker, health reasons	0.183 (0.179)	0.378 (0.180)*	0.171 (0.177)	0.322 (0.178)
Reduced drinker, non-health reasons	0.138 (0.125)	0.193 (0.129)	0.121 (0.125)	0.126 (0.128)
Continuing drinker	Ref.	Ref.	Ref.	Ref.

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Table 5.25. Past drinking behaviour combined with drinking pattern and PF-10 trajectories in the Russian cohort, imputed data

	Model 1 (mean, S.E.)[a]		Model 2 (mean, S.E.)[b]	
	Men	**Women**	**Men**	**Women**
Intercept				
Lifetime abstainer	-6.120 (3.436)	-6.074 (1.601)***	-5.294 (2.922)	-4.738 (1.531)**
Former drinker, health reasons	-15.240 (1.846)***	-16.210 (1.879)***	-12.120 (1.665)***	-12.797 (1.815)***
Former drinker, non-health reasons	-1.343 (1.164)	-7.444 (1.911)***	-1.271 (1.133)	-6.182 (1.813)**
Reduced drinker, health reasons	-10.328 (1.108)***	-7.433 (1.422)***	-8.515 (1.052)***	-5.546 (1.366)***
Reduced drinker, non-health reasons	-0.480 (0.861)	0.709 (1.263)	-0.281 (0.869)	1.142 (1.222)
Irregular light-to-moderate drinker	-1.130 (1.067)	-0.990 (1.173)	-2.182 (1.045)*	-0.663 (1.145)
Regular light-to-moderate drinker	Ref.	Ref.	Ref.	Ref.
Irregular heavy drinker	0.608 (1.006)	4.071 (1.615)*	-0.786 (1.009)	2.611 (1.610)
Regular heavy drinker	0.436 (0.867)	1.813(1.331)	0.012 (0.878)	2.265 (1.282)
Slope				
Lifetime abstainer	0.474 (0.596)	0.134 (0.304)	0.206 (0.563)	0.139 (0.306)
Former drinker, health reasons	0.287 (0.331)	0.254 (0.325)	0.182 (0.329)	0.268 (0.329)
Former drinker, non-health reasons	-0.084 (0.270)	0.380 (0.339)	-0.103 (0.265)	0.332 (0.341)
Reduced drinker, health reasons	0.485 (0.245)	0.585 (0.278)*	0.359 (0.243)	0.475 (0.278)
Reduced drinker, non-health reasons	0.438 (0.214)*	0.400 (0.252)	0.308 (0.213)	0.280 (0.253)
Irregular light-to-moderate drinker	0.535 (0.231)*	0.250 (0.234)	0.290 (0.235)	0.191 (0.237)
Regular light-to-moderate drinker	Ref.	Ref.	Ref.	Ref.
Irregular heavy drinker	0.410 (0.245)*	0.096 (0.346)	0.242 (0.246)	-0.114 (0.345)
Regular heavy drinker	0.242 (0.221)	0.157 (0.272)	0.189 (0.219)	0.167 (0.273)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

[a] Adjusted for age;

[b] Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

5.4.3 Sensitivity analyses

As in the cross-sectional analyses, sensitivity analyses were conducted restricting the samples to be: 1) free of CVD and cancer at baseline in the multiply imputed longitudinal datasets, and 2) complete cases. All covariates were controlled for in the sensitivity analyses.

The results of the first sensitivity analysis are summarised in Table 5.26 and Table 5.27. This analysis included 3,154–3,158 Czech men, 3,691–3,696 Czech women, 3,198 Russian men, 3,893 Russian women, 3,815–3,822 Polish men, and 4,050–4,057 Polish women. The relationships between alcohol consumption and the PF-10 trajectories based on the subsamples without CVD and cancer at baseline, as shown in Table 5.26, were very similar to the results from the full samples (Table 5.19–5.23). The gap of the PF-10 score at baseline between non-drinkers and regular and/or light-to-moderate drinkers was, as expected, smaller in the subsamples (1.12–3.03 points) than in the full cohorts (1.84–8.67 points), because the subsamples were healthier.

Unlike in the main analyses, the accelerated decline in the PF-10 score during follow-up among Czech male regular heavy drinkers versus regular light-to-moderate drinkers became statistically significant (Table 5.26, slope: -0.38, SE: 0.18, p=0.04), after full adjustment of all covariates. Figure 5.8 presents the predicted PF-10 trajectories by drinking pattern among Czech men who were free of CVD and cancer at baseline. Similar to Figure 5.6 based on the full sample, the gap in the PF-10 score between Czech male regular heavy drinkers and regular light-to-moderate drinkers widened during follow-up. The regular heavy drinkers had 0.88 point lower PF-10 score at baseline than regular light-to-moderate drinkers. At the 10^{th} year of follow-up, the difference between the two drinking groups increased to 4.66 points.

Similar to the analyses in the full cohorts, no association was found between past drinking behaviour and the rate of change in the PF-10 score over time, restricting the analysis to subjects without CVD and cancer at baseline (Table 5.27). However, further categorising continuing drinkers by their drinking pattern, Russian male

drinkers who cut down drinking because of health reasons had a slower decline in the PF-10 score during follow-up (slope: 0.54, SE: 0.27, p=0.04) in comparison with regular light-to-moderate drinkers.

The complete-case analysis of the longitudinal data was based on 1,269 Czech men, 1,679 Czech women, 1,426 Russian men, 2,219 Russian women, 1,334 Polish men and 1,485 Polish women. Among complete cases, alcohol consumption was not associated with the rate of change in the PF-10 score at follow-up across cohorts and in both sexes with a few exceptions (e.g. average drinking quantity per day in Czech men, drinking pattern in Czech and Polish men, and past drinking behaviour combined with drinking pattern in Russian women). Again, the pattern of results for alcohol consumption and the PF-10 trajectories did not vary substantially between those from complete cases and those from imputed datasets, although the standard errors were wider in the complete-case analysis (Appendix L).

Table 5.26. Alcohol consumption and PF-10 trajectories among participants without CVD and cancer at baseline, imputed data

	Fully-adjusted model (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Drinking frequency			
Men			
Intercept			
0	-2.707 (1.398)	-2.215 (0.922)*	-2.472 (0.823)**
<1/month	-0.853 (0.918)	-1.069 (0.859)	-1.075 (0.818)
1-3/month	Ref.	Ref.	Ref.
1-4/week	0.076 (0.696)	-0.311 (0.563)	-0.338 (0.600)
≥5/week	0.834 (0.664)	-0.777 (0.874)	-0.871 (0.748)
Slope			
0	0.070 (0.216)	-0.205 (0.201)	-0.063 (0.161)
<1/month	-0.039 (0.146)	0.148 (0.197)	0.178 (0.156)
1-3/month	Ref.	Ref.	Ref.
1-4/week	0.102 (0.115)	0.139 (0.146)	0.075 (0.127)
≥5/week	0.088 (0.114)	-0.152 (0.220)	-0.067 (0.168)
Women			
Intercept			
0	-4.265 (0.851)***	-4.638 (1.013)***	-2.937 (0.708)***
<1/month	-0.609 (0.597)	-0.310 (0.614)*	-2.052 (0.708)**
1-3/month	Ref.	Ref.	Ref.
≥1/week	0.085 (0.551)	1.181 (0.946)*	0.503 (0.812)
Slope			
0	-0.043 (0.133)	-0.276 (0.192)	0.059 (0.135)
<1/month	0.004 (0.095)	-0.199 (0.126)	0.205 (0.140)
1-3/month	Ref.	Ref.	Ref.
≥1/week	0.059 (0.093)	-0.460 (0.195)*	-0.093 (0.164)
Annual drinking volume			
Men			
Intercept			
0	-2.490 (1.309)	-1.472 (0.937)	-1.628 (0.780)*
1-1500	Ref.	Ref.	Ref.
1501-4000	0.106 (0.696)	0.247 (0.702)	1.107 (0.599)
4001-8000	0.940 (0.692)	1.299 (0.718)	0.881 (0.753)
>8000	0.354 (0.592)	0.173 (0.683)	-0.008 (0.776)
Slope			
0	0.108 (0.198)	-0.250 (0.204)	-0.193 (0.149)
1-1500	Ref.	Ref.	Ref.
1501-4000	0.155 (0.113)	0.093 (0.168)	-0.123 (0.123)
4001-8000	0.147 (0.119)	0.003 (0.173)	-0.150 (0.166)
>8000	0.137 (0.102)	0.003 (0.171)	-0.254 (0.170)
Women			
Intercept			
0	-3.369 (0.860)***	-3.293 (1.031)**	-0.851 (0.699)
1-250	Ref.	Ref.	Ref.
251-500	1.236 (0.769)	1.971 (0.700)**	2.161 (0.833)**
501-1500	1.030 (0.628)	2.505 (0.823)**	2.265 (0.855)**
>1500	0.832 (0.596)	1.296 (1.054)	3.084 (0.887)**
Slope			
0	-0.050 (0.135)	-0.149 (0.189)	-0.141 (0.133)
1-250	Ref.	Ref.	Ref.
251-500	-0.008 (0.125)	-0.016 (0.137)	-0.159 (0.163)
501-1500	-0.026 (0.107)	-0.050 (0.164)	-0.294 (0.172)
>1500	0.031 (0.103)	-0.183 (0.204)	-0.322 (0.186)
Average drinking quantity per day			
Men			
Intercept			

Table 5.26 continued

	Fully-adjusted model (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Non-drinker	-2.843 (1.285)*	-1.121 (0.956)	-1.753 (0.745)*
Light	Ref.	Ref.	Ref.
Moderate	0.372 (0.720)	1.041 (0.690)	0.251 (0.861)
Heavy	-0.365 (0.659)	0.897 (0.638)	1.361 (0.705)
Slope			
Non-drinker	-0.024 (0.192)	-0.361 (0.215)	-0.157 (0.146)
Light	Ref.	Ref.	Ref.
Moderate	-0.211 (0.133)	-0.107 (0.172)	-0.092 (0.181)
Heavy	-0.066 (0.104)	-0.118 (0.154)	-0.222 (0.150)
Women			
Intercept			
Non-drinker	-3.945 (0.851)***	-3.965 (1.102)***	-1.337 (0.671)*
Light	Ref.	Ref.	Ref.
Moderate	0.288 (0.501)	0.681 (0.730)	1.716 (0.654)**
Heavy	-0.229 (0.764)	1.031 (0.946)	2.784 (1.146)*
Slope			
Non-drinker	-0.062 (0.129)	-0.084 (0.203)	-0.131 (0.128)
Light	Ref.	Ref.	Ref.
Moderate	-0.015 (0.081)	0.037 (0.146)	-0.284 (0.124)*
Heavy	-0.013 (0.129)	0.070 (0.194)	-0.251 (0.259)
Drinking pattern			
Men			
Intercept			
Non-drinker	-3.034 (1.316)*	-1.839 (1.272)	-1.360 (0.828)
Irregular light-to-moderate	-1.058 (0.689)	-0.209 (4.493)	0.119 (0.666)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	0.206 (0.569)	0.403 (1.104)	1.857 (0.615)**
Regular heavy	-0.879 (0.954)	-0.603 (1.069)	0.911 (1.306)
Slope			
Non-drinker	-0.126 (0.207)	-0.273 (0.354)	-0.206 (0.171)
Irregular light-to-moderate	-0.224 (0.121)	0.003 (1.286)	-0.022 (0.140)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	-0.129 (0.100)	0.024 (0.335)	-0.189 (0.140)
Regular heavy	-0.378 (0.183)*	-0.061 (0.251)	-0.629 (0.289)*
Women			
Intercept			
Non-drinker	-4.360 (0.949)***	-6.417 (1.438)***	-3.343 (1.013)**
Irregular light-to-moderate	-0.861 (0.680)	-2.239 (1.166)	-1.709 (0.959)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	0.748 (0.721)	-0.517 (1.282)	-1.121 (1.159)
Regular heavy	-0.055 (0.824)	-2.336 (1.483)	1.812 (1.304)
Slope			
Non-drinker	-0.188 (0.156)	0.316 (0.280)	0.098 (0.200)
Irregular light-to-moderate	-0.142 (0.114)	0.467 (0.245)	0.174 (0.189)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	-0.155 (0.124)	0.447 (0.263)	-0.025 (0.228)
Regular heavy	-0.181 (0.153)	0.352 (0.313)	-0.089 (0.298)
Problem drinking[a]			
Men			
Intercept			
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.177 (0.836)	-0.412 (0.606)	-1.805 (0.875)*
Slope			
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.254 (0.134)	0.056 (0.160)	-0.226 (0.213)

* p<0.05, ** p<0.01, *** p<0.001; [a] among drinkers only; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Table 5.27. Past drinking behaviour and PF-10 trajectories among participants without CVD or cancer at baseline in the Russian cohort, imputed data

	Fully-adjusted model (mean, S.E.)	
	Men	**Women**
Past drinking behaviour		
Intercept		
Lifetime abstainer	-4.412 (2.745)	-3.433 (1.294)**
Former drinker, health reasons	-7.044 (1.781)***	-8.863 (1.868)***
Former drinker, non-health reasons	0.185 (0.892)	-3.410 (1.753)
Reduced drinker, health reasons	-6.146 (0.978)***	-4.081 (1.027)***
Reduced drinker, non-health reasons	0.370 (0.536)	0.916 (0.717)
Continuing drinker	Ref.	Ref.
Slope		
Lifetime abstainer	0.214 (0.573)	-0.067 (0.244)
Former drinker, health reasons	-0.156 (0.348)	-0.139 (0.338)
Former drinker, non-health reasons	-0.274 (0.221)	0.013 (0.305)
Reduced drinker, health reasons	0.380 (0.216)	0.386 (0.210)
Reduced drinker, non-health reasons	0.134 (0.133)	0.091 (0.135)
Continuing drinker	Ref.	Ref.
Past drinking behaviour combined with drinking pattern		
Intercept		
Lifetime abstainer	-4.133 (2.812)	-3.049 (1.689)
Former drinker, health reasons	-6.745 (1.879)***	-8.501 (2.160)***
Former drinker, non-health reasons	0.494 (1.072)	-3.026 (2.054)
Reduced drinker, health reasons	-5.850 (1.147)***	-3.652 (1.470)*
Reduced drinker, non-health reasons	0.668 (0.817)	1.322 (1.281)
Infrequent light-to-moderate drinker	-0.175 (1.014)	-0.089 (1.205)
Frequent light-to-moderate drinker	Ref.	Ref.
Infrequent heavy drinker	0.412 (0.924)	2.417 (1.689)
Frequent heavy drinker	0.646 (0.816)	1.838 (1.339)
Slope		
Lifetime abstainers	0.382 (0.595)	0.052 (0.341)
Former drinker, health reasons	0.004 (0.390)	-0.014 (0.403)
Former drinkers, non-health reasons	-0.118 (0.268)	0.132 (0.375)
Reduced drinkers, health reasons	0.541 (0.266)*	0.498 (0.307)
Reduced drinkers, non-health reasons	0.295 (0.221)	0.209 (0.263)
Infrequent light-to-moderate drinker	0.276 (0.247)	0.146 (0.250)
Frequent light-to-moderate drinker	Ref.	Ref.
Infrequent heavy drinker	0.203 (0.253)	-0.178 (0.361)
Frequent heavy drinker	0.159 (0.222)	0.162 (0.288)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

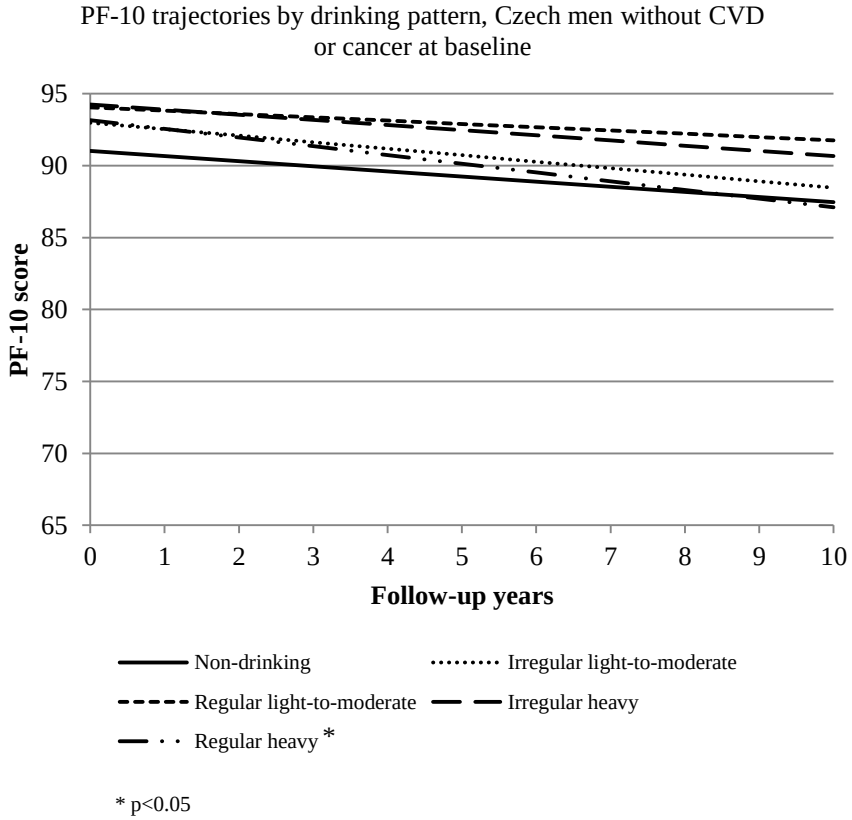


Figure 5.8. Population-level PF-10 trajectories by drinking pattern, Czech men without CVD or cancer at baseline, fully-adjusted model

5.4.4 Summary of longitudinal results

The PF-10 score declined linearly over the 10 years of follow-up in all three cohorts and both men and women in the HAPIEE study. The relationships between alcohol consumption at baseline and the intercept growth parameter, interpreted as the initial status of the PF-10 score at baseline, were essentially the same as in the cross-sectional analyses. Non-drinkers in all cohorts and both men and women consistently had the lowest PF-10 score at baseline, and the score increased with increasing level of alcohol consumption in terms of average drinking frequency, annual drinking amount, average drinking quantity and drinking pattern.

A summary of longitudinal results on alcohol consumption and the rate of decline in the PF-10 score is presented in Table 5.28. In most study groups, alcohol consumption, problem drinking and past drinking behaviour were not found to be associated with the rate of decline in the PF-10 score during follow-up. The few exceptions included an accelerated decline in the PF-10 score over time found in Russian female regular drinkers (≥1/week), in Polish female moderate drinkers (20.0–39.9g/drinking day), and in Polish male regular heavy drinkers (>4 drinks during one day, ≥1/week). As shown in Figure 5.3, Russian female frequent drinkers (≥1/week) had a faster decline in the PF-10 score during follow-up than those who drank 1-3/month; whereas the PF-10 trajectories in other drinking categories of average drinking frequency were parallel. In Figures 5.5 and 5.7, besides the accelerated decline in Polish female moderate drinkers and Polish male regular heavy drinkers, the PF-10 score seemed to decrease more slowly in Polish female light drinkers (Figure 5.5) and in Polish male irregular and regular light-to-moderate drinkers (Figure 5.7). However, these apparent decelerations in declines were not statistically significant. This may reflect random variation but it is also possible that a longer follow-up time may be needed to detect statistical differences in rates of decline in the PF-10 score among these drinking groups.

Table 5.28. Summary of longitudinal findings on alcohol consumption and rate of decline in physical functioning during follow-up

	Czech Republic		**Russia**		**Poland**	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Average drinking frequency	N.S.	N.S.	N.S.	Frequent drinkers (≥1/week) had 0.392 unit per year faster decline in the PF-10 score than those who drank 1-3/month	N.S.	N.S.
Annual drinking volume	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Average drinking quantity/day	N.S.	N.S.	Non-drinkers had 0.361 unit per year faster decline in the PF-10 score than light drinkers, but it was marginally significant (p=0.06)	N.S.	N.S.	Moderate drinkers had 0.249 unit per year faster decline in the PF-10 score than light drinkers
Drinking pattern	Regular heavy drinkers had 0.318 unit per year faster decline in the PF-10 score than regular light-to-moderate drinkers, but it was marginally significant (p=0.08)	N.S.	N.S.	N.S.	Regular heavy drinkers had 0.639 unit per year faster decline in the PF-10 score than regular light-to-moderate drinkers	N.S.
Problem drinking	N.S.	N/A	N.S.	N/A	N.S.	N/A
Past drinking behaviour	N/A	N/A	N.S.	N.S.	N/A	N/A

N.S.: not significant; N/A: not applicable

Consistently with previous cross-sectional studies, higher odds of physical limitations were found in non-drinkers in all three HAPIEE cohorts, compared with regular and/or light-to-moderate drinkers. Previous cross-sectional studies have reported either no difference in physical functioning or poorer physical functioning in heavy drinkers than in light-to-moderate drinkers. In contrast, in this thesis, the odds of physical limitations tended to decrease with increasing level of alcohol consumption. An important improvement on previous studies is the availability of data on past drinking behaviour in this thesis. The cross-sectional associations between alcohol consumption and physical limitations were found to be biased by past drinking behaviour. The excess odds of physical limitations in non-drinkers were largely explained by 'sick quitters' who stopped drinking because of health reasons. The apparently protective effect of alcohol consumption on physical limitations may be due to former heavier drinkers reducing their alcohol intake because of their poor health (and thus moving to lower drinking categories).

By contrast, in the longitudinal analyses, no clear associations between alcohol consumption and the rate of decline in physical functioning during follow-up were seen in most study groups (but there were some exceptions). The lack of longitudinal associations was consistent with about a third of previous longitudinal studies; however, the comparability with previous studies was limited, as only one previous longitudinal study investigated alcohol consumption and rate of change in physical functioning over time. A more detailed comparison of the findings in this thesis with the literature is presented in Section 6.3.

CHAPTER 6 DISCUSSION

This chapter summarises the cross-sectional and longitudinal findings presented in this thesis, discusses the key methodological issues including strengths and limitations, and interprets the findings in the context of existing literature.

6.1 Summary of the Main Findings

The cross-sectional associations between alcohol consumption and physical limitations (PF-10 score <75) were consistent across the Czech, Russian and Polish cohorts and between men and women (Objective 1). Non-drinking was associated with higher odds of physical limitations in comparison with regular and/or light-to-moderate drinking. The odds of physical limitations tended to decrease with increasing drinking frequency and quantity, and from less to more hazardous drinking pattern. Problem drinking was not associated with physical limitations among male drinkers across these cohorts.

The 'sick quitter' hypothesis was directly addressed by examining past drinking behaviour and physical limitations in the Russian cohort (Objective 2). Former drinkers who quit drinking due to health reasons and drinkers who reduced their alcohol consumption due to health reasons had considerably increased odds of physical limitations, compared with continuing drinkers who maintained their alcohol intake. Higher odds of physical limitations in lifetime abstainers and reduced drinkers due to non-health reasons than continuing drinkers were only found in Russian women but not in Russian men.

At the population level, physical functioning declined over the 10 years of follow-up in all three cohorts and both sexes (Objective 3). The rate of decline in physical functioning did not differ substantially or consistently between non-drinkers and regular and/or light-to-moderate drinkers (Objective 4). There was weak evidence only in Russian men that non-drinkers' physical functioning declined faster over time than light drinkers (classified by average drinking quantity per drinking day). This finding was not replicated in Russian women or in the other two cohorts.

Compared with regular and/or light-to-moderate drinkers, a more rapid decline in physical functioning was found among more frequent and heavier drinkers in some subgroups; for example, among Russian female regular drinkers (≥1/week), Polish female moderate drinkers (20.0–39.9g/drinking day), and Polish male regular heavy drinkers (>4 drinks during one day, ≥1/week). There was a suggestion that physical functioning in Czech male regular heavy drinkers declined more steeply than regular light-to-moderate drinkers. However, the results were not consistent across cohorts and sexes. Despite the lack of statistical significance, the rate of decline in physical functioning in light drinkers among Russian men and Polish women seemed to be slower than in other drinking categories of average drinking quantity per drinking day. If there are genuine differences in the trajectories of physical functioning, a longer follow-up time may be needed to detect statistically significant differences in the rate of decline across drinking categories. In addition, no difference in the rate of decline in physical functioning was found between male non-problem and problem drinkers. Regarding former drinking, the rate of decline in physical functioning was not found to differ by past drinking behaviour among either Russian men or Russian women (Objective 4).

6.2 Methodological Issues

Methodological issues important for the interpretation of findings described in this thesis will be discussed below, including strengths, limitations, and specific methodological concerns regarding my cross-sectional and longitudinal findings.

6.2.1 Strengths

This thesis has several important strengths. First and foremost, to my knowledge, this is the first study examining alcohol consumption and physical functioning in ageing cohorts from CEE, a region characterised by high alcohol consumption, hazardous drinking patterns, and high alcohol-attributable health burden. The design of the multi-centre HAPIEE study, with uniform methodology across cohorts, optimises the cross-cohort comparability of the results.

Second, the Czech, Russian and Polish cohorts were randomly selected from population registers and electoral lists of non-institutionalised individuals to be representative of their urban populations. The large sample sizes of the three cohorts ensure the statistical power to detect meaningful associations between alcohol consumption indices and physical functioning (see Section 4.6.5).

Third, physical functioning was measured repeatedly by the same instrument, the PF-10 subscale of the widely used SF-36 questionnaire. The SF-36 questionnaire has been validated in various countries, including Czech Republic, Russia and Poland.[144,265] This study, to my knowledge, is the first one investigating alcohol consumption and individual trajectories of physical functioning over time among middle-aged and older adults.

Fourth, several dimensions of alcohol consumption were examined in this study. As urged by researchers in the field of alcohol epidemiology,[180,182,231,247] especially in CEE,[318] this project focused on drinking pattern and its relation to physical functioning, which has not been assessed in the vast majority of previous studies.

Finally, data on past drinking behaviour, although only available in the Russian cohort, are invaluable for assessing participants' drinking behaviour and separating former drinkers from lifetime abstainers. Additional data on the reasons why participants had cut down on drinking prior to baseline facilitates testing of the 'sick quitters' hypothesis in relation to physical functioning directly. These data have not been previously applied to investigate alcohol consumption and physical functioning in CEE, and former drinking alongside the reasons has not been assessed in most studies in other regions.

6.2.2 Limitations

Several important limitations of this study should be considered when interpreting the findings and their implications.

6.2.2.1 Non-response to initial recruitment of cohorts

Non-response is a major methodological concern in population-based studies. Systematic differences in exposures and outcomes may exist between respondents and non-respondents, bringing into question the representativeness of the study sample for the target population and thereby limiting the generalizability of findings (non-response bias).[319-321]

Non-response to initial recruitment is often studied in cross-sectional settings. Previous studies have indicated that, compared to respondents, non-respondents are more likely to be younger,[322-327] male,[323,324,326,327] with poorer health (e.g., respiratory symptoms, CVD, hypertension, hypercholesterolemia and psychiatric illness),[322,323,327-335] use medications,[325,335,336] with poorer SEP (e.g., lower educational attainment,[322,324,326,327,330-332,334,335] lower income,[322,324,326,334] and not in paid employment or with an unskilled job[323,325,333,334,337]), be unmarried,[323,324,329-331,337] smoke,[322,323,328-330,336] drink less alcohol,[323] be less physically active,[323] and have higher BMI[335].

Non-response may be related to both drinking behaviour and physical functioning. Studies have shown a lower proportion of respondents than non-respondents who reported having limitations in ADLs, IADLs and mobility.[330,331,333,334] Soggard *et al.*[324] also found a higher proportion of non-respondents than respondents receiving disability benefits. Heavy drinkers are less likely to take part in studies, therefore heavy episodic drinking is likely to be substantially less prevalent among respondents compared to the general population.[201,338] Lahaut *et al.*[339] reported that drinking alcohol to two extremes, abstinence and frequent heavy drinking, were more prevalent among non-respondents than respondents. In a survey of Dutch adults aged 20–50 years, a higher proportion of non-respondents versus respondents were current drinkers and with poor physical functioning.[323]

The response rate of the baseline survey of the HAPIEE study was 55% in the Czech towns and 61% in both Novosibirsk and Krakow.[259] Taking into account non-respondents who had moved away or died prior to the baseline survey, the response

rate was actually higher (>60% in the Czech towns, >71% in Novosibirsk and >68% in Krakow).[259] This is moderately high but most contemporary studies suffer from the same problem.[321,325,340,341] It is increasingly difficult to achieve higher response rates in population studies in Europe and North America.[321,325,340,341] A high response rate is generally preferable in research, however, Grove and colleagues[342,343] showed in simulation studies that a high response rate did not necessarily result in a diminished non-response bias or improved statistical estimates.

In the HAPIEE study, the respondents in the baseline survey were more likely to be female, of older age, with higher education, report good health, and smoke less than non-respondents, which are consistent with previous studies.[259] It seems likely that the non-response to initial recruitment of the HAPIEE cohorts was associated with physical functioning at baseline, but might not be related to alcohol consumption. The non-response may result in an underestimation of the prevalence of physical limitations across drinking categories at baseline, compared to the target population. It is less clear whether the non-response also biases the association between alcohol consumption and physical limitations, depending on whether the underestimated prevalence of physical limitations is differential or non-differential across drinking categories.

6.2.2.2 Non-response to follow-up

In prospective studies, non-response can occur during initial recruitment of participants (at baseline) and at follow-up. Non-response to follow-up is a crucial concern pertaining to my longitudinal findings. Non-response to follow-up can be caused by death, refusal, or difficulties in contacting participants, leading to doubts of how well respondents who stay in studies at follow-up represent the initial study sample and the target population. The key issue is whether non-response to follow-up is missing at random or not, and whether it affects the effect estimates.[319]

The response rate in all HAPIEE cohorts decreased considerably at re-examination, and it further dropped at PQ2012 in the Russian and Polish cohorts. Less healthy participants were more likely to be lost to follow-up (see Appendix D).

Chatfiled *et al.*[344] reported in a systematic review that older age, ill health, frailty and cognitive impairment are associated with dropout from prospective studies of older adults. Other studies have documented that non-response to follow-up (not due to death) is more likely to occur among males,[345] people of older age,[345-349] those who are retired,[350] with lower SEP (lower educational attainment,[346-348,351-356] lower occupational status,[345,351,354,356] less income,[348,354,357] and not a home owner[345,356]), living alone,[347] unmarried,[349,354,356] with poorer health (poorer self-rated health,[346,352,353,355,357] comorbidity,[348,357] long standing illness,[345] poorer cognitive functioning,[351,352] and functional impairments or disability[347,350,357]), and those who do not drink alcohol or drink heavily,[354] smoke,[353-356] are obese or with high BMI,[354,356] and are physically inactive.[354,355]

Rehm *et al.*[179] argued that health-conscious middle-class people who have relatively favourable patterns of drinking tend to be over-represented in prospective studies of alcohol consumption and CHD. By following a middle-aged cohort for 10 years, Goldberg *et al.*[337] showed that non-participation was associated with diseases, especially those related to alcohol consumption. Goldberg and colleagues also found that, among men, diseases caused by alcohol or smoking attributed largely to the differences in health observed between respondents and non-respondents.

To address these issues in this thesis, several auxiliary variables from the baseline survey of the HAPIEE study were incorporated in the process of multiple imputation (see Section 4.5.4). This was to take into account differences (in those auxiliary variables at baseline) between respondents and non-respondents at follow-up. Some other characteristics listed above or some unmeasured characteristics, nevertheless, may be associated with non-response to follow-up in the HAPIEE study, which were not specified as part of the MICE model. This implies that there may still be systematic differences between non-respondents and respondents that were not taken account of, and some of these differences could bias my findings.

During follow-up, by the end of 2012, a total of 542 Czech men (13.9%), 309 Czech women (6.9%), 708 Russian men (16.7%), 288 Russian women (5.7%), 541 Polish men (11.1%), and 287 Polish women (5.6%) died. These participants were not

excluded from the longitudinal analyses. The PF-10 scores in later measurement occasions after participants died were treated as missing data and were replaced by imputed values. From a technical standpoint, modelling individual trajectories using MLM does not differentiate loss to follow-up due to death and due to dropout, assuming the trajectories continue beyond death ('immortal cohort' approach).[358] I used the 'immortal cohort' approach based on the concern that deceased participants might have had experienced a substantial decline in physical functioning before they died (e.g., certain cancer with relatively long survival time). Excluding them from the longitudinal analyses may underestimate the rate of decline in physical functioning. However, the results from a sensitivity analysis excluding the deceased participants were largely similar to the results from the full cohorts (Appendix M), probably due to the relatively small number of deceased participants. Incorporating time-to-event information to account for selective attrition due to death alongside longitudinal measures of physical functioning would be welcomed, but it is beyond the scope of this thesis.

The fundamental issue caused by non-response to follow-up is related to missing data mechanisms: whether missingness is MAR or MNAR (see Section 4.5.2). MICE was used to handle missing data in the HAPIEE study under the assumption of MAR. Under MAR, multiple imputation outperforms traditional methods such as complete-case analysis to handle missing data, yields unbiased estimates, and is more powerful without loss of statistical power.[261,264,282] As pointed out by Graham[261], the three missing data mechanisms (i.e., MCAR, MAR and MNAR) are not mutually exclusive, and missing data should be viewed as a continuum between MAR and MNAR rather than purely MAR or MNAR.

In this thesis, the possibility of MAR is supported by incorporating several auxiliary variables in MICE. Sensitivity analysis assuming MNAR may increase confidence of the longitudinal findings under MAR. Statistical techniques assuming MNAR (e.g., pattern-mixture models and selection models), however, are not immune from drawbacks, since these techniques have their own assumptions when modelling individual trajectories.[359,360] For instance, selection models assume a multivariate distribution of individual intercepts and slopes of the repeatedly measured outcome

variable.[359] Additionally, after controlling for the individual intercepts and slopes, selection models assume no residual correlation between the outcome variable at time *i* and missing indicator of it at time *i*.[359] The accuracy of estimates relies on both of these assumptions–which are not testable.[359] Pattern-mixture models assume normality of the outcome variable conditional on missing patterns, and need specific constrains on parameters across missing patterns, which can lead to very different estimates.[359,360]

If some participants, at each measurement occasion of follow-up, did not take part in the study because of their poor physical functioning, then part of the missingness of the PF-10 scores at follow-up is MNAR. The imputed PF-10 scores in these participants might be higher than their true scores, because, using MICE, their missing scores were replaced based on observed values from participants who attended the study and shared similar background with them. In consequence, the rate of decline in physical functioning in the populations, and the differences in the rate of decline between drinking groups, might be underestimated in the imputed datasets. In other words, the effect of alcohol consumption on the trajectories of physical functioning might be underestimated, in this case of MNAR.

Overall, I tried to deal with missing data as well as I could, but I acknowledge that residual bias may still affect my findings.

6.2.2.3 Measurement error in alcohol consumption

It has been reported repeatedly that survey estimates of alcohol consumption usually cover only about 50% of sales data.[192,198] Self-reported alcohol consumption as the usual method employed in population surveys is prone to recall error and therefore introduces the possibility of underestimating 'true' intake.[182,233,239,245,247] As pointed out by Sobell and Sobell[201], the underestimation of alcohol consumption in population surveys compared to sales data may because: 1) heavy drinkers may be less covered in surveys; 2) under-reporting may raise with increasing level of alcohol consumption; and 3) measurement methods used in surveys may be prone to bias, and the estimated alcohol consumption is affected by questionnaire construction and

length of reference period. Social stigma attached to drinking may also attribute to the underestimation.[228] Boniface and Shelton[361] found that, in a hypothetical scenario that alcohol consumption were equally under-reported in population, the odds of binge drinking, compared with before revision, no longer differed between men and women, and the odds of binge drinking increased with increasing income and deprivation. One consequence of the underestimation is a dilution of the size and strength of the attributed effect of alcohol consumption on health outcomes.[247,361]

Therefore, there is a common belief that the higher drinking volume a measure of alcohol consumption yields, the better the measure.[194,196] Rehm[194], however, argued that this belief is not always true because marginalised groups (e.g., homeless) who drink more alcohol may not be included in population studies, and respondents sometimes over-report their drinking (e.g., due to double counting). Gmel *et al.*[362] showed in their comparison of different measures that the higher drinking volume yielded did not necessarily performed better in estimating the associations of alcohol consumption with alcohol use disorder, alcohol dependence, and alcohol-related social and health consequences.

The GF questionnaire, a 'customary drinking habits' measure, was used to assess participants' alcohol consumption in the last 12 months at the baseline survey of the HAPIEE study. In general, 'customary drinking habits' measures (e.g., QF and GF) yield lower drinking volume than 'recent drinking occasions' measures (e.g., dairy and timeline follow-back).[194] The 'recent drinking occasions' measures, nevertheless, tend to overestimate drinking frequency,[191] and are more useful to describe alcohol consumption rather than examining associations between alcohol use and its consequences.[196]

Regarding the 'customary drinking habits' measures, it has been well recognised that the more detailed questions are asked, the higher drinking volume is yielded.[194,197,203,204] Compared with the QF, the GF generally generates higher mean drinking volume, more heavy drinking and less light drinking.[194,197,200,205] In theory, the GF is less biased than the QF because respondents do not have to average their

drinking quantities over many different occasions,[191] and it is believed to outperform the QF.[194]

Despite many advantages, the GF may be too complex to be administrated correctly.[203] Gmel *et al.*[203] argued that, the beverage-combined QF and GF may cause a considerable measurement error under the circumstances of no dominant preference of beverage or largely varied drink sizes across beverages. Respondents may not intent or be able to convert their actual size of drink into standard drink.[363] Reviews have indicated that, when respondents were asked to pour a standard drink, they tended to pour more; the drinking volume thus was probably underestimated.[364,365] A study conducted by Boniface *et al.*[366], however, did not find a systematic underestimation comparing the actual alcohol of a 'usual glass' of wine or spirits poured by participants and the estimated alcohol reported by participants. In addition, if the biases of drinking frequency and quantity are interrelated (e.g., frequent drinkers disproportionately underestimate their quantities compared to less frequent drinkers), the GF may lead to a differential misclassification of drinkers to defined drinking categories, and in the extreme case could distort the rank order stability between the 'true' and estimated drinking volume.[191] Finally, since the GF requires respondents to remember all of their drinking occasions correctly and distribute total drinking days correctly over different levels of drinking quantity,[191,203,204] the GF is more cognitively demanding and persons with insufficient cognitive skills (e.g., with cognitive impairment or with low education) may be less able to respond correctly.[367]

The reference period of the GF used in the HAPIEE study was last 12 months. A long reference period may result in a larger recall error than a short period; on the other hand, it allows more accurate drinking patterns, especially for highly infrequent drinkers (e.g., drink on festivals), to be obtained.[193,206] Respondents may perceive the reference period subjectively; for example, the past 12 months could be interpreted as the last calendar year, and either include the current month or not.[196]

The possibility that participants' alcohol consumption might be under-reported in the HAPIEE study cannot be eliminated. Gmel *et al.*[203] claimed that some respondents

tend to report drinking frequency to only one level of drinking quantity in the GF. This, however, was not the case in this thesis. In the three HAPIEE cohorts, 4%–5% Czechs and Poles answered to only one level, whilst 94% of Czechs and Poles and all Russians responded to at least five levels of drinking quantity in the GF.

11% of Czechs, 1% of Russians and 4% of Poles reported their total drinking days exceeding 365 days in the previous 12 months prior to the baseline survey. This may be because participants had difficulties in averaging their drinking occasions over the six levels of drinking quantity, or they had difficulties in understanding that these drinking quantity levels are mutually exclusive (double counting). This was not corrected by capping,[191,206] considering that: 1) I used average drinking frequency instead of total drinking days, and drinking more than 365 days annually was transformed into drinking at least 5 days a week, and one could argue the capping is artificial; and 2) it is unknown whether the correction will diminish or even exaggerate the misclassification of drinking categories. Greenfield *et al.*[368] pointed out that alcohol consumption derived by capping and without capping might not differ considerably when the number of respondents reporting drinking days over 365 is not large.

In the HAPIEE study, there is one problem specific to the Polish cohort. Polish participants were asked, before the GF, whether they had drunk any alcohol in the past year (a filter question). If this response was 'no', they did not complete the GF questionnaire. Consequently, classification of non-drinkers was largely based on both the filter question and the GF. This may introduce a misclassification error and likely is the reason why the prevalence of non-drinkers was higher among Poles than Czechs and Russians. As shown in Table 6.1, 3,639 Poles answered 'no' to the filter question. Among them, 1,949 Poles skipped the GF questionnaire, and they might have drunk alcohol in the past year. Among the 1,690 Poles who answered 'no' to the filter question and responded to the GF, 19 actually reported drinking in the past year. 7,063 Poles reported 'yes' to the filter question, and 53 of them did not answer the GF who might actually be non-drinkers. 54 Poles answered 'yes' to the filter question but reported no alcohol consumption in the GF. As a result, the misclassification could occur in these 2,075 (19%) Poles.

Table 6.1. Responding to questions on alcohol consumption in the Polish cohort

Responded item to the GF	Drinking in the past year					
	No		Total	Yes		Total
	Men	Women		Men	Women	
0	583 (51.68%)	1366 (54.40%)	1949	31 (0.76%)	22 (0.74%)	53
≥1	545 (48.32%)	1145 (45.60%)	1690	4058 (99.24%)	2952 (99.26%)	7010
Total	1128	2511	3639	4089	2974	7063

Even though, the GF still has great advantages as it captures the within-individual variability of drinking,[191,203,206] and assesses drinking patterns directly.[202,206]

Another measure of alcohol consumption used in the HAPIEE study was the CAGE questionnaire to capture problem drinking. Concerns have been raised about the appropriateness of using the CAGE in older populations. According to the review conducted by Maisto *et al.*[369], the CAGE outperforms the MAST among the elderly. Chan *et al.*[370] found that the CAGE was applicable in both primary care outpatients and general population samples, having acceptable sensitivity and specificity values. In contrast, some studies have reported a low sensitivity of the CAGE in the general population,[371] in women,[268,372] and in psychiatric older populations.[222]

A widely used cut-off value for problem drinking is ≥2 positive responses to the CAGE, but some researchers advocate the use of ≥1 positive responses.[221,268,373] Aertgeerts *et al.*[221] showed in their meta-analysis of 10 studies that, using the cut-off of ≥2, the pooled sensitivity was low in primary care patients (0.71) and ambulatory patients (0.60), although the pooled specificity was over 0.90 in both groups. Smart *et al.*[374] found that the cut-off of ≥2 was able to identify heavy drinkers consuming 4 drinks per day in a general population. Dhalla and Kopec[268] recommended to use a cut-off of ≥2 given that it provides the best combination of sensitivity, specificity and positive predictive values.

In the HAPIEE study, both GF-based drinking indices and problem drinking at baseline were strongly associated with separately taken measures of alcohol consumption (i.e., weekly drinking recall and FFQ assessing consumption in the last 3 months) and with serum gamma-glutamyl transferase (GGT) measured at baseline (Appendix N). This is evidence in favour of the validity of the GF-based drinking indices and problem drinking used in this thesis.

6.2.2.4 Measurement error in the PF-10 subscale

The PF-10 subscale of the SF-36 questionnaire was employed to measure physical functioning repeatedly throughout the HAPIEE study. The SF-36 questionnaire has been shown of good validity and reliability.[144,265,375-377] McHorney *et al.*[376] reported good internal-consistency reliability and item-discriminant validity in all eight subscales of the SF-36 questionnaire, across subgroups with different socio-demographic characteristics, disease diagnoses and disease severity. Of the PF-10 subscale, all item-scale correlations were over 0.70 except vigorous activities (0.62) and bathing or dressing (0.49), which may be because the limitation in bathing or dressing reflects relatively severe disability.[115,376]

The PF-10 subscale captures both functional limitations and disability, and it is correlated with other measures of physical functioning.[378-382] In older populations, fair-to-strong correlations have been shown between the PF-10 and performance-based test of lower extremity function (0.74),[380] ADL scales (0.56–0.79)[378-381] and IADL scales (0.61–0.78).[378,379] Although the PF-10 attempts to capture a wide spectrum of physical functioning, Anderson *et al.*[383] argued that it centres on gross physical activities and fails to include coordinated activities (e.g., cooking, cleaning and shopping).

A moderate ceiling effect of the PF-10 (i.e., proportion of respondents with an optimal score of 100) was found ranging from 16% to 28% in different studies,[376,384,385] but a greater ceiling effect of 43% was reported in a study of 7,862 adults in New Zealand.[377] The ceiling effect was observed in all three HAPIEE

cohorts that 16% of Czechs, 21% of Russians and 22% of Poles were classified having the optimal PF-10 score of 100 at baseline.

At re-examination, additional physical performances (i.e., grip strength and 5 chair stands capturing upper- and lower-extremity function, respectively) were measured. The PF-10 score at re-examination was related to grip strength and chair stands in the expected direction in all three cohorts (Appendix O). This further confirms the validity of the PF-10 subscale.

Another important issue relates to the change in the mode of administration in the HAPIEE study, which affects non-response and data quality (see Section 4.1). With the presence of interviewers, social desirability bias is likely to occur, and participants tend to take social norms into account.[258] For this reason, participants may over-report favourable health status and under-report socially undesirable behaviours.[258]

Several studies have compared health ratings of the SF-36 questionnaire administered by mail and by interview, and reported a 1.3–3.8 points lower PF-10 score by mail compared to by interview.[386-390] McHorney *et al.*[386] and Perkins and Sanson-Fisher[387] found that older people were more likely to respond to the SF-36 by mail than by interview, which may be because older people believe mails tend to have better anonymity. Perkins and Sanson-Fisher[387] argued that the SF-36 is reliable under both modes of administration with Cronbach's alpha coefficients over 0.70.

These published data are consistent with the discrepancy of the PF-10 scores observed at baseline and re-examination in the Czech and Polish cohorts. This is why I adjusted the PF-10 score at re-examination in these two cohorts. One may argue that the adjustment appears to be data driven. However, the increase of the PF-10 score at re-examination was observed across all ages and in both sexes, making it more likely to have been caused by the change of the mode of administration than a genuine increase.

In the Russian cohort, the data were collected by interview at baseline and re-examination and by mail at PQ2009 and PQ2012. The difference in the PF-10 scores due to the change of the mode of administration was not adjusted, considering that, if adjusted, the adjustment had to be done at both baseline and re-examination based on the change between PQ2009 and PQ2012, which may introduce a substantial bias. Instead, it was taken into account by constraining the residual variances of the PF-10 score the same between baseline and re-examination and between PQ2009 and PQ2012 in the longitudinal analyses. Nevertheless, it is possible that the relatively sharp drop of the PF-10 score between re-examination and PQ2009 observed in the Russian cohort may be exaggerated owing to the change of the mode of administration.

6.2.2.5 Measurement error in covariates

In this thesis, several potential major confounders were controlled for in both cross-sectional and longitudinal analyses, including socio-demographic characteristics (age and marital status), SEP (highest educational attainment, current economic activity and household amenities), spine/joint problems, BMI and smoking. These variables are subject to measurement error as in alcohol consumption and physical functioning. For example, spine/joint problems and smoking were both self-reported and thereby may also be subject to the social desirability bias. BMI, which was derived from objectively measured height and weight, can suffer an error in measurements by nurses, or difference in the measurement tools used in different research centres.[391,392]

The way how measurement error in covariates affects the association between alcohol consumption and physical functioning can be complex. Measurement error in a variable (misclassification in categorical variables) is non-differential if the error is not related to other variables; otherwise it is differential.[391-395] Measurement error in two variables can be independent (i.e., the error in one variable is uncorrelated with error in the other variable) or dependent (i.e., the errors of these two variables are correlated).[393,395,396] According to these definitions, measurement error can be

classified into four categories: 1) independent and non-differential; 2) dependent and non-differential; 3) independent and differential; and 4) dependent and differential.

In the simplest case that the measurement error/misclassification in an explanatory variable and an outcome is independent and non-differential, estimation of the effect of the explanatory variable is biased, usually 'towards the null'.[393,394,397] When the explanatory variable refers to the exposure variable, the effect of the exposure is underestimated; when the explanatory variable refers to the confounder, the confounding effect is underestimated, resulting in an incomplete removal of confounding (residual confounding due to measurement error).[393-395]

Apart from the failure to remove confounding entirely, measurement error in covariates may distort the association between the exposure and the outcome, possibly 'towards to the null' or 'away from the null'.[398] When measurement error in exposure or confounders is differential and/or dependent, this issue is much more complex and unpredictable.[393,398,399] Rothman *et al.*[395] pointed out that 'the problem then becomes not only one of residual confounding [due to measurement error], but of additional distortion produced by differential selection of subjects into different analysis strata' (p.145). In addition, compared to single-level data, biases caused by measurement error in exposure, outcome and confounders in multilevel data (e.g., longitudinal data with repeated measurements) are even more complex and much less well-understood.[400,401] Several measurement error models have been developed to account for measurement error, on the basis of assumptions on the distribution, correlation and function (additive or multiplicative) of measurement error.[397,398,402]

Given the complicity of this issue, it is possible that there is bias due to measurement error in this thesis. It is unknown that whether the measurement error in alcohol consumption, physical functioning and covariates are non-differential or differential, or whether they are independent or dependent. In the simplest situation of independent and non-differential measurement error, the measurement error in alcohol consumption may affect the estimation of its relationship with physical functioning 'towards the null'. Measurement error in covariates then may result in residual confounding, and this incomplete removal of confounding may lead to an

overestimation of the association between alcohol consumption and physical functioning. If the measurement error is dependent and/or non-differential, the relationship between alcohol consumption and physical functioning can be either underestimated or overestimated. Nevertheless, how measurement error behaves in the HAPIEE study is beyond the scope of this thesis.

6.2.2.6 Residual confounding due to under-adjustment

Since both alcohol consumption and physical functioning are associated with so many factors, confounding is unlikely to be entirely controlled for.[182,247,250,251] Residual confounding is recognised as one serious methodological drawback in epidemiology.[182,183,251,338] As described previously (see Section 2.4.4.2), abstainers tend to have poorer health and less favourable risk profile, such as lower SEP, poorer lifestyle and health behaviours, poorer social networks, and depression.[248,403] Bondy and Rehm[404] showed that not drinking to excess, higher SEP, favourable health behaviours, and better health status tended to cluster in population; whilst high-volume drinking occasions, poorer health status, and high levels of risk factors for chronic diseases also tended to cluster. It is difficult to control for all of these relevant factors, especially if these factors are not fully known.[182,183]

The quality of studies was found to modify the dose-response relationship between alcohol consumption and CHD in the meta-analysis performed by Corrao *et al.*[226]. Studies with high quality (i.e., adjusted for the main confounders, separated former drinkers, and excluded subjects with pre-existing diseases at baseline) were more likely to report less protective effect of alcohol consumption on CHD than studies that did not meet these high quality criteria. Fekjær[183] argued that the low protective dose of alcohol consumption (2–5 g/day) against CHD found in observational studies may be an indicator of the clustered favourable lifestyle and fewer risk factors of diseases, the effects of which are failed to be fully controlled for, rather than the cause. These questions are relevant to studies of alcohol consumption and physical functioning as well.

I did not adjust for self-rated health status, specific chronic conditions (e.g., CVD, diabetes and arthritis), comorbidity (e.g., number of chronic conditions), or physical activity in the cross-sectional and longitudinal analyses as confounders. It is because, to a greater or less extent, these factors are related to physical functioning, controlling of which may lead to an over-adjustment.[405,406] Some variables may be on the pathway between alcohol consumption and physical functioning (e.g., CVD), and controlling for them may bias the estimation of the relationship between alcohol consumption and physical functioning.[405] Other variables, such as self-rated health and comorbidity, are closely related to physical functioning, adjustment of which may reduce the precision of the estimates.[405] The cross-sectional and longitudinal associations between alcohol consumption and physical functioning remained largely similar after the exclusion of participants with CVD and cancer at baseline (see Section 5.3.3 and 5.4.3). It is possible that there is still residual confounding due to the failure to take all confounders into account, including those confounders which were not measured in the HAPIEE study.

6.2.2.7 Reference group

Non-drinkers, as a diverse group consisting of never and former drinkers, are not a suitable reference group to compare with when estimating the association between alcohol consumption and health outcomes.[249,251,255] Despite this, one third of previous studies included in the literature review in the Background Chapter used non-drinkers as the reference group (Appendix B–C), which may overestimate the protective effect of alcohol consumption on physical functioning.

Using lifetime abstainers as the reference group is also problematic due to the measurement error in self-reported abstention and the small number of lifetime abstainers in some populations, especially in Western societies.[245,249,255] A large proportion of self-reported lifetime abstainers identified at one time point have been shown to have reported drinking previously.[182,255,407] Rehm *et al.*[255] claimed that the ideal control group would be those who are lifetime abstainers and irregular light drinkers based on multiple assessments across time.

Regular and/or light-to-moderate drinkers were used as the reference group in this thesis, considering that this group may be less heterogeneous than non-drinkers or abstainers. This may help to reduce confounding. Since drinking categories in this thesis are based on alcohol consumption measured at baseline, a misclassification may also occur among light-to-moderate drinkers. If the misclassification is related to physical functioning or other possibly uncontrolled confounders, estimates of the association between alcohol consumption and physical functioning may be biased.

6.2.3 Reverse causation

Reverse causation is the major methodological concern of cross-sectional studies, including studies on alcohol consumption and physical functioning.

A number of meta-analyses have reported a J-shaped relationship between alcohol consumption and CVD.[38,226,229,238-240] CVD has been documented to be associated with poor physical functioning and disability.[160,162,164] Among the elderly, CVD and osteoarthritis are the top two diseases causing physical disability.[164] As above mentioned in Section 4.6.3, non-drinkers and heavy drinkers might have had developed CVD before baseline and reported poor physical functioning at baseline. Owing to the poor health status, heavy drinkers might have had reduced their alcohol intake prior to the baseline survey. In consequence, at baseline, those former heavy drinkers with poor health and/or poor physical functioning may be classified as non-drinkers or less heavier drinkers. This possible reverse causation may mask the real relationship between alcohol consumption and physical functioning by not taking into account the possible confounding, modifying or mediating role of health status.

An important question is whether there is evidence that people change their drinking behaviour due to health reasons. The literature on this topic is somewhat mixed. Zins *et al.*[408] reported that middle-aged men who rated their health as bad were more likely to abstain from drinking 2 years later. Pringle *et al.*[409] found that older adults with poor-to-fair health at baseline and those who experienced a decline in health over 2 years of follow-up were more likely to quit drinking. Similarly, Shaw *et al.*[410] showed that adults who reported poor health or functional limitations over a study

period of 16 years were more likely to stop drinking at the same time. Newsom *et al.*[411] analysed the HRS cohort and found some short-term (2 years) decline in heavy episodic drinking after newly diagnosed cancer, diabetes, lung disease and stroke, but no long-term change. In the study of Brennan *et al.*[412], poor health at baseline predicted the decline in drinking frequency but not in drinking quantity over 10-year follow-up of a cohort of older adults.

Another question is whether health status modifies the association between alcohol consumption and physical functioning. Here the evidence is sparse. Kalamangla *et al.*[257] found a lower risk of incident disability at follow-up, compared with occasional drinkers, only among female light-to-moderate drinkers in the strata of women with good or better self-rated health at baseline; no association was found either among women with fair or worse health or among men.

In this thesis, past drinking behaviour and its relation to physical limitations in the Russian cohort suggested that abstinence and reduction of drinking due to health reasons partly explained the excess risk of physical limitations in non-drinkers and the apparently protective effect of heavier drinking. Furthermore, I performed a sensitivity analysis on the cross-sectional association between alcohol consumption and physical limitations in subsamples of participants with CVD free and fair-to-good self-rated health (Appendix P). The results in this sensitivity analysis were similar as those from the full cohorts, but no excess odds of physical limitations in non-drinkers were found among Russian women and Polish men and no association was observed in Russian men. These findings may suggest potential modification by health status in some groups in this thesis.

6.2.4 Change in alcohol consumption over time

Alcohol consumption is dynamic and time-varying. Moderate and heavy drinkers tend to drift towards light drinking or abstinence with increasing age,[88,182,245,249-252] and this drift is often due to accumulated ill health and medication use.[250,251] Liu *et al.*[413] showed that, compared with older adults with less severe limitations in

mobility, those with more severe limitations were less likely to drink alcohol regularly.

The majority of observational studies have relied heavily on alcohol consumption measured at one time point, usually drinking volume at baseline.[175,245] The use of baseline alcohol consumption assumes individuals' drinking behaviour is stable and time invariant, which introduces errors in prospective studies.[232] It is possible that the bias caused by the misclassification of drinking categories based on one measurement may increase over increasing follow-up time.[240] Not taking into account the changes in alcohol consumption over time may bias the estimation of the association of light-to-moderate drinking with CVD and all-cause mortality.[250] The same bias may operate between alcohol consumption and physical functioning and may apply to this thesis. It is preferable to measure alcohol consumption at multiple time points in alcohol epidemiology.[245,251,255]

Lin *et al.*[61] studied how the change in alcohol consumption over 2 years was associated with incident functional limitations and disability 2 years later, using data from the HRS. That study reported a lower risk of developing functional limitations or disability among consistent low-risk drinkers (defined as ≤14 drinks/week for men aged <65 years, ≤7 drinks/week for women and men aged ≥65, and no binge drinking) than consistent non-drinkers. No difference in risk was found among consistent high-risk drinkers, those who had quit drinking, and those with other patterns.

I used data on alcohol consumption measured at baseline. Past drinking behaviour in the Russian cohort helped to clarify how changes in alcohol consumption prior to the baseline survey were related to the trajectories of physical functioning during follow-up. Given the similarity of longitudinal findings across cohorts, and if the data on past drinking behaviour were available in the Czech and Polish cohorts, it is very likely that I would find similar associations between past drinking behaviour and the PF-10 trajectories in these two cohorts as in the Russian cohort. In addition, since alcohol consumption was not measured repeatedly at every measurement occasion of

the HAPIEE study, it is not possible to investigate how changes in alcohol consumption are associated with changes in physical functioning simultaneously.

Alcohol consumption, however, was evaluated at two occasions in the HAPIEE study: baseline and re-examination. During the mean 3.6 years follow-up between baseline and re-examination, among participants with alcohol consumption data available at both occasions, 41%–56% remained in the same drinking categories, 5%–12% quit drinking, and 11%–24% moved to lower drinking categories (Appendix Q). At the same time, a sizeable proportion of participants reported increased drinking to light-to-moderate quantity (10%–13% in Czechs, 3%-7% in Russians and 17%–27% in Poles), as well as to heavy quantity (10%–15% in Czechs, 14%–19% in Russians, and 12%–22% in Poles). It should be noted that the number of levels of drinking quantity asked in the GF questionnaire at baseline (≥10, 7–9, 5–6, 3–4, 1–2 and 0.5 drink) and re-examination (≥5, 3–4 and 0.5–2 drinks) were different (see Section 4.4.2 and 4.4.3.3). Since more levels of drinking quantity were asked at baseline, it is likely that, if the same GF was employed at re-examination as at baseline, the alcohol consumption reported by participants at re-examination would be higher. The changes in alcohol consumption between baseline and re-examination therefore may consist of genuine changes and changes due to the discrepancy in methodology of data collection. For this reason, I did not include alcohol consumption at re-examination in my main data analyses in this thesis.

6.2.5 Multiple imputation of missing data

The purpose of multiple imputation is to augment the dataset and to preserve relations and characteristics in observed data (e.g., non-linearity, interactions and missing patterns).[261,414] MICE has been criticised by some researchers for the lacking theoretical justification, and the fully specified conditional distributions may be incompatible (i.e., there is no joint distribution allowing the different conditional distributions specified for variables with varied nature in imputation models to be yielded).[263,284,285,287,415] One consequence of potential incompatibility is that the distribution of imputed values may depend on the order of imputations and the last variable imputed.[263,414] In a simulation study, van Buuren *et al.*[415] showed that MICE

performed reasonably well in the circumstance of strong incomparable models with limited harms to the estimates. van Buuren[414] argued that incompatibility may play a small role; conserving the characteristics in datasets may be more crucial than the joint distribution.

Another issue pertaining to multiple imputation of longitudinal data is that MICE in Stata requires the datasets to be in a wide format (i.e., one row for each participant and repeated measures are separate variables within each participant). Wide format reduces the multilevel datasets (i.e., repeated measures are naturally nested within individuals) to be single-level datasets.[270,416] van Buuren[416] claimed that ignoring data structure in multiple imputation of longitudinal data (flat-file imputation) leads to underestimated standard errors and narrower confidence intervals. Multiple imputation for multilevel data has been developed in some software, such as REALCOM-IMPUTE[417] and the *mice* package implemented in R[418]. However, the applicability of these tools in large datasets with a number of auxiliary variables is limited.[417,418] Further studies are needed to make recommendations of flat-file imputation in use of multilevel data.[270,416]

Both the incompatibility and ignorance of data structure are beyond the scope of this thesis. Despite these potential limitations, as pointed out by Graham[261], multiple imputation performs well, and often much better than traditional methods (e.g., compared with complete-case analysis). In this thesis, the point estimates of the association between drinking indices and trajectories of physical functioning in the imputed datasets were similar as those based on complete cases, but the standard errors were much smaller (Appendix L). In other words, the application of MICE in this thesis does not influence the direction or magnitude of the estimates and avoids the loss of statistical power in comparison with the complete-case analysis.

6.3 Interpretation of Findings

The widely used Bradford Hill criteria for causal inference in epidemiology (i.e., strength, consistency, specificity, temporality, plausibility, coherence, experimental evidence and analogy)[419] have been criticised for being neither sufficient nor

necessary conditions of causation.[420,421] Nevertheless, these criteria continue to be widely used and remain useful for interpretation of epidemiological studies.[421] In particular, consistency of findings in different studies is an important consideration. Several issues, however, complicate the comparability of my findings with previous studies.

First and foremost, human physical functioning is a hierarchical concept, from basic physical components, specific physical movements to task or goal-oriented function (see Section 2.3.2.2). The instruments used to measure physical functioning varied markedly in previous cross-sectional and longitudinal studies on alcohol consumption and physical functioning (see Appendix B–C). For instance, few studies measured grip strength, poor performance of which reflects impairments in the Nagi model (see Section 2.3.1.1). The majority of the remaining studies measured functional limitations, disability or both via performance tests or questionnaires, such as walking, climbing stairs, ADLs or IADLs. Consequently, the specific concept captured in previous studies, referring to the Nagi model, varies from impairments, functional limitations, disability, to the combination of them.

The PF-10 subscale of the SF-36 questionnaire captures both functional limitations and disability, challenging the direct comparability of my findings with previous studies that employed other instruments to measure physical functioning. Although the three stages of the disablement process are conceptually related to each other, there is no causal pathway between stages in both the Nagi model and ICF.[101,106] Evidence on alcohol consumption and any stage of the disablement process may be viewed as suggestive on other stages, but does not provide direct evidence on all stages of disability.

Almost all previous longitudinal studies examined alcohol consumption and risk of (incident) functional limitations and/or disability. By contrast, I investigated individual trajectories of the PF-10 score over time and how alcohol consumption was associated with these trajectories. It is a different approach. Most previous studies have focused on the (negative) extreme of physical functioning by defining the outcome as at least one limitation in mobility, ADLs or IADLs. As a result, it is

unknown how alcohol consumption is associated with less severe functional limitations (e.g., limited in walking a long distance) or with increasing severity of disability (e.g., limited in several ADLs or IADLs). I studied physical functioning from a positive prospective by defining physical functioning as a continuum. This approach allows me to assess the effect of alcohol consumption on a wider spectrum of physical functioning. While this has benefits, one drawback is that it makes drawing comparisons between my findings and those from other studies difficult.

6.3.1 Comparison with previous cross-sectional studies

Findings from previous cross-sectional studies are fairly consistent, reporting an L-shaped[25,28,33,34,36] or J-shaped[26,27,29-32,35] relationship between alcohol consumption and physical functioning. My cross-sectional findings published in *Age and Ageing*,[422] overall, suggested a somewhat more linear inverse relationship between alcohol consumption and physical limitations. This linear inverse association found in the cross-sectional analyses in this thesis was partly explained by past drinking behaviour. In other words, former heavier drinkers reduced their alcohol intake because of health reasons and moved to lower drinking categories. The use of past drinking behaviour distinguished this thesis from other studies. A detailed interpretation of my cross-sectional findings is provided in Section 6.3.3.

Several cross-sectional studies have employed the PF-10 subscale.[26-28,30,35] The study conducted by Green *et al.*[30] is worth of a special focus, as several drinking indices (including drinking frequency, drinking quantity per occasion, drinking volume per month and drinking pattern) were examined in relation to the PF-10 score. After adjustment for age, ethnicity, marital status, body water index and smoking, in both men and women, non-drinkers constantly had the lowest PF-10 score across drinking categories. The highest PF-10 score was observed in drinkers who consumed alcohol 2–3/week, 1–2 drinks/occasion, 15–29 drinks/month, and drinkers who engaged in regular light-to-moderate drinking (1–2 drinks/occasion, ≥2/week). This study was based on a population with very wide age range (25–100 years, mean age 58 years). Young adults, compared with older ones, generally drink more alcohol and have

better health and physical functioning. Inclusion of young adults thereby may over-estimate the protective effect of alcohol consumption on physical functioning.

Previously, Volk *et al.*[26] looked at the association between drinking pattern and the PF-10 score and found that, compared with non-drinkers and occasional drinkers (defined as drinking ≤12 drinks in a given year), only regular low-quantity drinkers (defined as drinking >5 days in the preceding 30 days and 1–4 drinks/occasion) had a higher PF-10 score. Their study was based on a population aged 18–86 years (mean age 43). Volk and colleagues[26] applied the same cut-off in men and women to categorise drinking pattern, although other studies have shown that women tend to drink less frequently and less heavily than men.[79,81,195,423] For example, a gender ratio (men versus women) of 2–3 in drinking frequency, drinking quantity and heavy episodic drinking was found across European countries.[424] Therefore, part of female frequent low-quantity drinkers in Volk and colleagues' study might actually be high-risk drinkers, and if so, the protective effect of regular low-quantity drinking might be underestimated among women.

Two cross-sectional studies showed that problem drinking was associated with a lower PF-10 score and limitations in mobility and IADLs.[26,32] In contrast, no association between problem drinking and physical limitations among male drinkers was found in this thesis. In the HAPIEE cohorts, results on problem drinking are consistent with the results on drinking indices derived from the GF that heavier drinking was not found to be associated with excess odds of physical limitations.

Less favourable physical functioning in former drinkers was also revealed in previous cross-sectional studies. Green *et al.*[28] showed a lower PF-10 score in former drinkers than in drinkers who consumed 1–60 drinks per month. Likewise, Canavan *et al.*[36] found a higher risk of limitations in ADLs and IADLs among former drinkers than abstainers. Nelson *et al.*[25] reported that, compared with light-to-moderate drinkers, former drinkers had poorer physical functioning (measured by self-reported mobility, ADLs, IADLs and physical performances); but among former drinkers, lifetime alcohol consumption was not associated with physical functioning.

My findings of past drinking behaviour in the Russian cohort suggested that the excess odds of physical limitations found in non-drinkers were at least partly driven by 'sick quitters' who had quit drinking due to health reasons. In addition, the apparently protective effect of more frequent and heavier drinking was partly due to less healthy former heavy drinkers who had cut down their alcohol intake and moved to lower drinking categories. Since my findings rely on past drinking behaviour in the Russian cohort, one may argue that generalisation of the findings to the Czech and Polish cohorts may not be appropriate. However, the pattern of findings for drinking indices and physical limitations are similar across the three cohorts. It is reasonable to speculate that, if data on past drinking behaviour were available in the other two cohorts, similar associations would be observed.

I am aware of one cross-sectional study of alcohol consumption on physical health (captured by physical component summary score of the SF-12) in Russia conducted by Dissing *et al.*[425]. Although this study is not strictly comparable to my work, Dissing and colleagues found that, among Russian men aged 25–60 years, drinking 10–19 litres of alcohol in the past year was associated with better physical health compared with non-drinking.

6.3.2 Comparison with previous longitudinal studies

My longitudinal findings showed a faster decline in physical functioning among more frequent and heavier drinkers in some subgroups. Weak evidence of a steeper decline among non-drinkers was found only in Russian men. No association was found between most drinking indices including problem drinking and the rate of change in physical functioning over 10 years of follow-up of the three cohorts.

Two published prospective studies used the PF-10 subscale to measure physical functioning.[40,57] Stafford *et al.*[40] found no association between alcohol consumption at baseline and the PF-10 score five years later among middle-aged adults (35–55 years old at baseline). In their study, alcohol consumption was measured by drinking volume in the past week, and physical functioning was evaluated only once at follow-up but not at baseline. With the absence of the PF-10 score at baseline, the

change of the score over time was not available, yet the effect of alcohol consumption on the change.

Another study, conducted by Byles *et al.*[57], investigated drinking pattern and the PF-10 score over time in a sample of Australian older women aged 70–75 years at baseline. Over 6 years of follow-up, Byles and colleagues showed that the PF-10 scores were consistently lower among rare drinkers (<1/week) and lowest among non-drinkers compared with frequent light-to-moderate drinkers (1–2 drinks/day and 3–6 days/week). Throughout the follow-up of the HAPIEE study, among women, the PF-10 scores were the lowest in non-drinkers, which is consistent with Byles and colleagues' findings, even though the HAPIEE cohorts are younger. Nevertheless, Byles and colleagues did not assess in detail whether the rate of decline in the PF-10 scores differed by drinking categories. Visually from the figure presented by Byles *et al.*[57] without formal tests, it seems that the slopes of decline were similar across the three drinking groups.

In the literature review in Section 2.4.5, 12 prospective studies have reported no association between alcohol consumption at baseline and physical functioning at follow-up.[39,41-51] All of these studies used data from only two time points (baseline and one follow-up 2–22 years later), except the study by Artaud *et al.*[46] in which mobility, ADLs and IADLs were repeatedly measured at six time points. As mentioned earlier, most of these studies examined the risk of developing at least one limitation in mobility, ADLs and/or IADLs, reflecting functional limitations (i.e., limitations in mobility) and disability. Seeman *et al.*[39], Tabbarah *et al.*[42] and Stenholm *et al.*[51] investigated changes in physical performances (e.g., grip strength, gait speed, chair rise and balance). However, these studies did not shed light on how alcohol consumption is associated with less severe functional limitations or disability. The misclassification of alcohol consumption based on one measurement may be more problematic for some of these studies with a long time interval between baseline and the follow-up assessment.

Three papers using longitudinal data of two time points have found an association between heavy drinking and physical functioning.[53,56,172] Two of them were based on

the British Regional Heart Study (BRHS) and reported that drinking more than 6 units of alcohol per day was related to an increased risk of limitations in mobility.[56,172] Perreira *et al.*[53], using data from the HRS, showed that, compared with light drinkers (1–2 drinks/day), the risk of developing at least one limitation in ADLs 6 years later was two-fold higher among non-drinkers and four-fold higher among heavy drinkers (≥5 drinks/day). In contrast, Ostbye *et al.*[54] found that drinking more than 2 drinks a day was associated with a lower risk of having at least one limitation in IADLs compared with no drinking, using data from the AHEAD cohort. Ostbye and colleagues reduced their longitudinal data into single level as cross-sectional study, and failed to take account of missing data, both of which may lead to biased results.

Lang *et al.*[59] and Liao *et al.*[60] reported an increased risk of disability only among non-drinkers. Lang and colleagues compared the HRS/AHEAD and ELSA cohorts. In their sensitivity analysis among subjects from the HRS/AHEAD cohort who were free of ADL limitations at baseline, no association between alcohol consumption and development of limitations in ADLs was found. This finding may be due to the possibility that without controlling for ADLs at baseline, the elevated risk of disability at one follow-up occasion in non-drinkers may be subject to 'sick quitters' bias. Alternatively, it also could be because the disablement process is long-drawn, and by 'removing' disabled subjects, the follow-up time is not long enough to allow major differences to occur. The same sensitivity analysis was not possible among the ELSA subjects. Exclusion of 'sick quitters' and former drinkers at baseline from the ELSA subjects did not change the result. Similarly, due to the nature of the data, Lang and colleagues did not assess the effect of alcohol consumption on the transition from disability free to disabled. The other study by Liao and colleagues measured alcohol consumption (weekly drinking frequency) and physical functioning (only two items of walking and bathing) crudely, and this may have contributed to the negative findings.

Wang *et al.*[55] were the only team who investigated alcohol consumption and its relation to the rate of change in physical functioning in a cohort of older adults aged 65 years and over at baseline. They constructed separate scores for ADLs, IADLs

and performance-based physical function (PPF: 10-foot timed walk, 5 chair stands, standing balance and grip strength). They found that, compared with consuming less than 5 drinks in the past year, drinking at least 5 drinks with no problem drinking was associated with a slower decline in the scores of ADLs, IADLs and PPF. One major drawback is that Wang and colleagues assessed alcohol consumption very crudely by asking only one question–whether participants had more than 5 drinks in the past year. As a result, the reference group (<5 drinks in the past year) used in the study consisted of both non-drinkers and very irregular light drinkers. The very irregular light drinkers were also likely to be categorised into the drinking group (≥5 drinks in the past year) alongside heavy drinkers. In addition, the study failed to further categorise drinkers according to their level of alcohol intake. It is possible that the slower decline in physical functioning may be driven by one specific drinking category (e.g., regular light-to-moderate drinkers) and a faster decline may occur in more frequent and heavier drinkers. Or more extremely, the (large) measurement error in alcohol consumption in their study may cause an overestimation of the protective effect of drinking on physical functioning, even if there is no effect. The inconsistency between Wang and colleagues' and my longitudinal findings may also because their cohort is older than the three HAPIEE cohorts.

Two studies examined problem drinking using data from the HRS/AHEAD cohorts, but the findings were not consistent.[53,54] Similar to my findings, Perreira *et al.*[53] showed no association between problem drinking and the development of at least two limitations in ADLs at follow-up in the HRS cohort. In contrast, Ostbye *et al.*[54] found that, in the HRS cohort (51–61 years old), problem drinking was positively associated with the risk of limitations in ADLs and mobility; but in the AHEAD cohort (≥70 years old), problem drinking was only positively associated with the risk of limitations in climbing stairs. As mentioned above, the limitations in the study by Ostbye and colleagues may have led to biased estimates.

Four studies[46,64,256,257] separated former drinkers from never drinkers; among which two reported no association between former drinking and disability at follow-up.[46,257] Maraldi *et al.*[256] found an increased risk of incident limitations in mobility among

male former drinkers but not among female former drinkers in comparison with never and occasional drinkers (<1 drink/week); whilst Abbott *et al.*[64] reported a higher risk of developing limitations in ADLs among former drinkers than in abstainers. I did not find evidence of differential rates of change in physical functioning over time by past drinking behaviour in the Russian cohort.

I am not aware of any previous studies in CEE using longitudinal data to study the relationships of alcohol consumption and past drinking behaviour with physical functioning. There was some suggestion in this thesis that a longer follow-up time may be required to detect statistically significant differences in the rates of decline in physical functioning among drinking categories. By applying the estimated rates of decline across drinking categories found in this thesis, it is not possible to predict how many extra years of follow-up would be needed to reliably detect heterogeneity in the (linear) decline rates. To detect statistically significant differences in the decline rates across drinking categories in the HAPIEE study, large sample size and longer follow-up time would help. Since the decline in physical functioning is closely related to age, it is reasonable to presume that younger participants (e.g., aged 45–49 years at baseline) may maintain their physical functioning or undergo only a slight decline over a relatively long time (e.g., 20 year, until the age of, say, 64–69 years). In contrast, those who were older at baseline (e.g., 60–69 years) may experience a decline in their physical functioning to a greater extent, or the rate of decline may be non-linear; it may rather accelerate with time. With such additional data, it would be possible to estimate different shapes of the trajectories of physical functioning over time (as well as differential rates of decline across drinking categories) more precisely and more reliably.

6.3.3 Possible explanations

The previous cross-sectional findings were fairly consistent. Although reverse causation plays a role in the cross-sectional association between alcohol consumption and physical limitations, it is not clear whether it would entirely explain the association. The discrepancy between the cross-sectional and longitudinal associations of alcohol consumption with physical functioning found in this thesis

may be explained by the bi-directional relationship and the population heterogeneity in the trajectories of physical functioning.

6.3.3.1 Possible biological mechanisms

One possible biological mechanism linking alcohol consumption and physical functioning is inflammation and its markers. Studies have documented a J-shaped relationship between alcohol consumption and C-reactive protein (CRP) that non-drinkers and heavy drinkers have a higher level of CRP than moderate drinkers.[426-432] Raum *et al.*[430] reported a J-shaped relationship between average drinking volume in the past year and the CRP level, with a nadir of drinking less than 16 g of alcohol per day. In a sample of Russian adult drinkers, Averina *et al.*[433] found a linear relationship between weekly alcohol intake and CRP level. Chronic alcohol use has been revealed to be associated with an elevated level of circulating interleukin (IL)-6.[434,435] Lu *et al.*[436] observed a J-shaped relationship between alcohol consumption and IL-6 level and the lowest IL-6 level was seen at alcohol intake of 10 g per day. Volpato *et al.*[437] found a J-shaped relationship between alcohol consumption and both IL-6 and CRP that drinkers consuming no more than 7 drinks a week had the lowest levels of both. Pai *et al.*[428] showed that drinking 1–2 drinks per day was related to 26% and 36% lower CRP and IL-6 levels respectively in men, and a stronger association was observed in women at a lower level (0.5 drink/day).

Singh and Newman[438] reported in their review that, among elderly adults, an elevated level of inflammatory markers, including tumor necrosis factor-alpha (TNF-α), CRP and especially IL-6, are strongly associated with limitations in mobility and disability. An increased level of CRP and IL-6 has been shown to be positively associated with poor physical performances (e.g., grip strengths, chair rise and walking speed)[439-442] and limitations in ADLs[443]. In addition, findings from prospective studies have also demonstrated that high levels of CRP and/or IL-6 are related to loss of muscle strength,[444-446] decline in gait speed and mobility,[447-449] as well as onset of disability[447].

Another potential mechanism is high-density lipoprotein cholesterol (HDL-C). Previous reviews have shown that light-to-moderate drinking is associated with an elevated level of HDL-C.[241,450] In the meta-analysis of experimental studies on alcohol consumption and changes in biomarkers by Rimm *et al.*[242], 30 g of ethanol a day was found to be related to an increase of HDL-C level by 3.99 mg/dl. In another meta-analysis of experimental studies, Brien *et al.*[243] showed that, compared with during no drinking, during drinking, HDL-C level increased by 0.09 mmol/L. However, a recent Mendelian randomisation meta-analysis of 56 epidemiologic studies by Holmes *et al.*[451] suggested a causal association between alcohol consumption and IL-6 level, but not between alcohol consumption and HDL-C level.

Several studies have investigated the level of HDL-C and physical functioning.[36,452-456] HDL-C level has been reported to be positively associated with knee extension torque,[454] gait speed,[452-454] and a performance score of 4-m walking, balance and chair-stand[453]. In a population of the oldest of old aged 85 years, Formiga *et al.*[455] found that normal level of HDL-C was associated with the ability to perform ADLs. Similarly, in a large cross-sectional study of Irish people aged 50 years and over, Canavan *et al.*[36] showed an inverse relationship between HDL-C level and limitations in both ADLs and IADL. Cesari *et al.*[456] reported that, among older adults aged 75 years and over with a low level of HDL-C, elevated IL-6 and CRP levels were related to poor gait speed and limitations in IADLs; an elevated level of IL-6 was positively associated with limitations in ADLs.

Based on the evidence from previous studies, CRP, IL-6 and HDL-C may play a role as possible biological mechanisms linking alcohol consumption and physical functioning, as seen in Figure 6.1. Non-drinking and heavy drinking may lead to elevated levels of CRP and IL-6 and a lowered level of HDL-C, which in turn, possibly via vascular damages, may result in impairments, functional limitations and disability. However, the evidence is indirect, and further research is needed to investigate the role of CRP, IL-6, HDL-C or other possible biomarkers on the pathway.

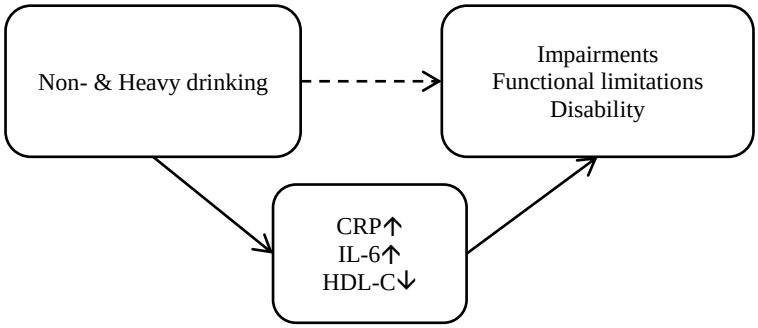


Figure 6.1. Possible biological mechanisms linking alcohol consumption and physical functioning

Furthermore, Urbano-Marquez and Fernandez-Sola[174] reported in their review that high alcohol intake is associated with acute alcoholic myopathy (mainly among men with heavy episodic drinking) and chronic alcoholic myopathy (among both men and women with long-term high alcohol intake). The damages of muscle fibres caused by heavy drinking may be another pathway, besides inflammation and HDL-C, linking heavy drinking to poor physical functioning.

Despite the presence of potential biological mechanisms, it should be noted that this is not a strong criterion of causality. The methodological weaknesses of cross-sectional studies are more important than the presence of such mechanisms.

6.3.3.2 Bi-directionality between alcohol consumption and physical functioning

My longitudinal findings are not entirely consistent across the three HAPIEE cohorts. Generally, little evidence was found for differential declines in physical functioning over time by drinking categories. In some subgroups, more frequent and heavier drinkers seemed to have a faster decline; however, the evidence is rather weak. The puzzling questions are why non-drinkers and former drinkers had poorer physical functioning at baseline with no faster decline at follow-up; and why, in contrast, heavy drinkers had better physical functioning at baseline with an accelerated decline.

One possibility is that, as briefly mentioned in Section 6.2.3 on reverse causation, non-drinkers and former drinkers identified at baseline might have been heavier

drinkers prior to baseline, and they might have cut down their alcohol intake because of their poor health. Heavier drinkers with good health prior to the baseline survey might have maintained their high level of alcohol intake. This may explain the cross-sectional findings of an apparently protective effect of alcohol consumption on physical limitations at baseline. In fact, both drinking behaviour and health status change over time. During follow-up of the HAPIEE study, heavy drinkers at baseline might have cut down their drinking once their health conditions deteriorate (Figure 6.2). This dynamic between drinking behaviour and health status might continuously take place over time. In other words, from a long-term prospective, individuals' drinking behaviour may be driven by their health conditions. This is supported by findings by Ng Fat and colleagues[457,458] that long-standing illness at early adulthood was associated with abstinence at young and middle age; and findings by Bell and Britton[459] that poor mental health drove an increase in alcohol consumption in middle-aged adults and kept them drinking heavily. This may explain the faster decline in physical functioning among heavy drinkers identified at baseline in some subgroups.

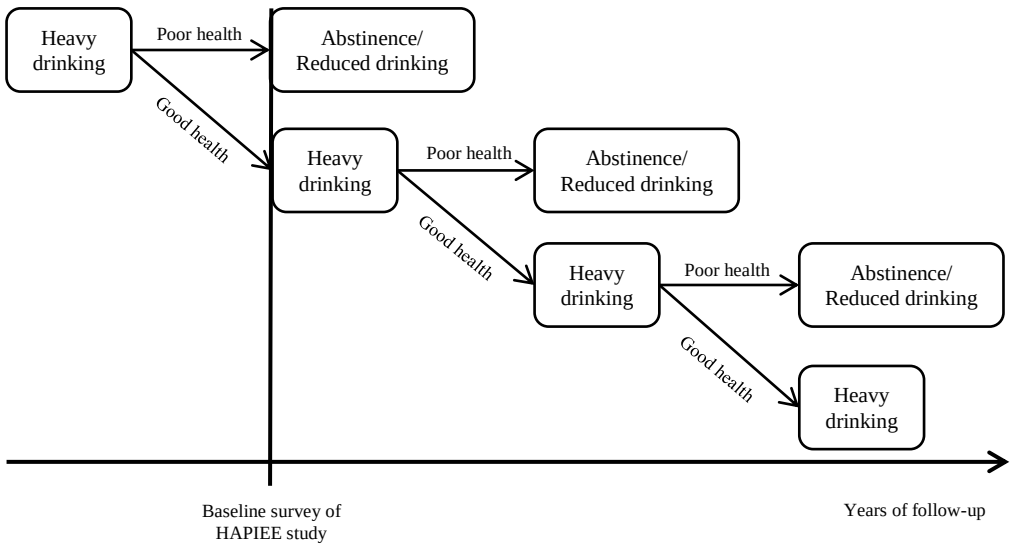


Figure 6.2. Dynamic between alcohol consumption and health status over time

I explored the possibly bi-directional relationship between drinking pattern and physical functioning using data from baseline and re-examination (Appendix R).[460,461] Drinking pattern at baseline was found to be predictive of the PF-10 score at re-examination only among Russians, with more frequent and heavier drinkers at baseline having a higher PF-10 score at re-examination (Appendix R). In all three cohorts, the PF-10 score at baseline was predictive of drinking pattern at re-examination: participants with a higher PF-10 score at baseline tended to drink more frequently and heavily at re-examination (Appendix R). These findings suggested a bi-directional relationship between alcohol consumption and physical functioning in the Russian cohort; whereas in the Czech and Polish cohorts, it seems more likely that participants' drinking behaviour was driven by their good physical functioning rather than vice versa.

Nevertheless, data on both alcohol consumption and physical functioning were available at only two time points over an average of 3.6 years, which may not be adequate to obtain reliable estimates. Further research with more repeated measurement occasions over a longer period is needed to bring further evidence on bi-directionality of the association between alcohol consumption and physical functioning.

6.3.3.3 Population heterogeneity in trajectories of physical functioning

Another potential explanation for the puzzling findings of this thesis is related to the bi-directional disablement process. In theory, the disablement process can be reversed (see the enabling process in the IOM model of disability in Section 2.3.1.1).[96] Accommodation, defined as 'actions that people take in response to their limitations, such as changing their behaviour, using assistive or mainstream technology, or relying on personal care', can moderate or modify disability in late-life (see the late-life disablement process in Section 2.3.1.4).[97] In the HAPIEE study, physical functioning was evaluated by subjective self-report, although, as previously discussed, the self-reported physical functioning has a good validity as it was highly correlated with objective physical performance tests. It is possible that participants who reported poor physical functioning at baseline might have sought medication,

rehabilitation, or help from others, to carry out certain daily activities at follow-up. They might have either recovered from their physical dysfunction, or stopped doing some specific daily activities by themselves anymore (e.g., if they moved to a more suitable flat). As a result, they might no longer feel as limited as before and report an improvement in their physical functioning over time. This may explain the poorer physical functioning in non-drinkers and former drinkers at baseline but no notable difference in the rate of decline during follow-up.

The longitudinal analyses of physical functioning trajectories in this thesis assume that within each population (i.e., each cohort by men and women separately), all participants are drawn from a single population with common population parameters (e.g., intercepts, slopes, and variances) and the heterogeneity in the population is captured by random effects (e.g., intercept and slope variances).[300,462] It is still possible that, within each population, there are clusters with distinct and varied trajectories of the PF-10 score over time. For instance, as mentioned above, participants with a low PF-10 score at baseline might have reported an increase in their PF-10 scores at follow-up, due to medication, rehabilitation or accommodation. It is also likely that, among participants with a fair-to-good PF-10 score at baseline, some might have reported a dramatic drop in their PF-10 scores, while some others might have reported a slight decrease.

As presented in the Results Chapter (see the Spaghetti plots in Figure 5.1), and also shown in Figure 6.3, some participants reported their physical functioning improved over time (Figure 6.3, above the horizontal line). The degree of decline in physical functioning (Figure 6.3, below the horizontal line) varied across individuals and the PF-10 scores at baseline. It is possible there is population heterogeneity (clusters) in the physical functioning trajectories. For example, Terrera *et al.*[463] found three distinct clusters of decline in cognitive functioning in an ageing cohort: 1) high cognitive function at age 81 and a relatively slow decline over 10 years of follow-up; 2) low cognitive function at age 81 and a linearly faster decline; 2) low cognitive function at age 81 and an accelerated non-linear decline. Likewise, Peeters *et al.*[75] showed a faster decline in physical functioning among women who had a lower initial PF-10 score than those with a higher score. In the three HAPIEE cohorts,

similarly, there may also be some clusters that participants might have experienced a slow decline, a fast decline, or an increase in physical functioning over time, according to their different levels of physical functioning at baseline.

In the case that clusters of physical functioning trajectories are involved, several questions remain, for instance, whether alcohol consumption is associated with the probability of participants allocated in which specific cluster; and furthermore, within each cluster, whether the rate of change in physical functioning differs across the level of alcohol consumption. However, these interesting questions about clusters of the trajectories are beyond the scope of this thesis.

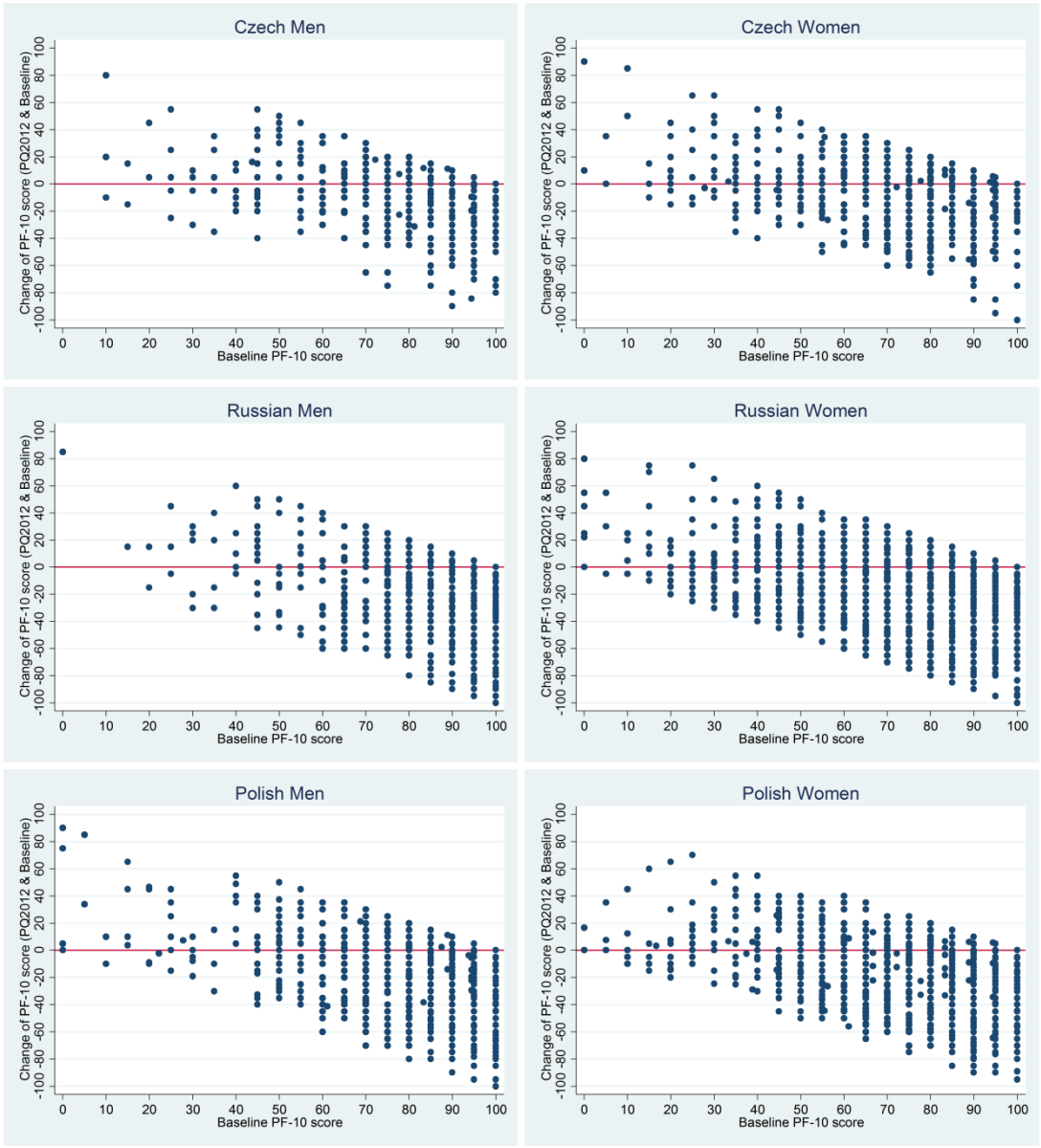


Figure 6.3. Scatter plot of change in PF-10 score (baseline–PQ2012) by baseline PF-10 score

This thesis did not find consistent longitudinal associations between alcohol consumption and rate of decline in physical functioning in most drinking groups. There were three exceptions of more frequent and heavier drinkers who had a faster decline in physical functioning than regular and/or light-to-moderate drinkers. These exceptions may be caused by noise but they may also be genuine.

The absence of similar findings in the Czech cohort may reflect a better health status of middle-aged and older adults in the Czech Republic than in Russia and Poland. This was found in the HAPEIE cohorts (health-related auxiliary variables at baseline in Appendix H), and is consistent with the literature which shows that the Czech Republic has the highest life expectancy, following by Poland, and Russia has the lowest.[6,8,10] There may be some other factors mitigating the adverse effect of alcohol consumption on health in the Czech Republic, such as health care and social care system. It also could be that Czechs might have experienced less dramatic decline in their living standards after the fall of communism than Poles and Russians. This may be linked with fewer negative influences on population health in the Czech Republic. One consequence of this may be that Czechs are more likely to maintain good health and good physical functioning than Poles and Russians.

On the other hand, health status in Russia is generally poorer than in the Czech Republic and Poland. If alcohol consumption has genuine effects on physical functioning, it might have happened at earlier adulthood of Russians and it may no longer exert such effects in mid- or later life. Russian female frequent drinkers (≥1/week) were found to have a faster decline in physical functioning than in less frequent drinkers (1–3/month). This was not replicated in either Czech or Polish women. Russian women, compared with Czech and Polish women, reported fewer drinking days in the past 12 months prior to baseline. Considering the strong stigma attached to drinking in Russian women, Russian female frequent drinkers may be different in terms of some underlying characteristics associated with physical functioning from Czech and Polish female frequent drinkers.

One may also speculate that the drinking cultures differ. Czech men are regular or frequent drinkers, and are mainly beer drinkers; while Russian men are mostly vodka

drinkers, and the predominant pattern is irregular consumption of large quantities. These differences may be associated with differential measurement error of alcohol consumption and this could lead to different estimates of the decline rates in physical functioning among drinking categories.

Given the difference in health, drinking culture and many other variables across the three countries, as well as the considerable gender difference in drinking behaviour, it may not be appropriate to pool the three cohorts or to pool men and women together in the data analyses. This is the reason why the thesis presented results separately by sex and country.

In spite of all the issues discussed above, given that no longitudinal associations between alcohol consumption and physical functioning were found in most study groups, an alternative explanation should be acknowledged. It is possible that alcohol consumption may genuinely have no effect on physical functioning, or if any, it is too small and difficult to be detected by the relatively crude instruments used in this thesis.

CHAPTER 7 RECOMMENDATIONS AND CONCLUSIONS

7.1 Recommendations

Findings in this thesis may have some implications for future research and policy.

7.1.1 Implications for future research

Regarding future research on alcohol consumption, physical functioning and other ageing outcomes, there are several methodological lessons learned from this thesis.

Previous studies have applied crude measures of alcohol consumption most of which do not capture drinking pattern. Drinking pattern was capture by the GF in this thesis. In addition, for specific research purposes, some other measurements besides the GF may be applied in future research to capture drinking pattern, such as frequency of drunkenness, maximum drinking quantity on one single occasion and its frequency, and whether drinking occurs more daily-basis or more on social occasions. However, all measures of alcohol consumption, including the GF, are still subjective to significant measurement error. In consequence, measures of alcohol consumption which are more reliable, less prone to bias and are able to capture drinking pattern are of crucial importance for observational population studies. In addition to biomarkers of alcohol consumption (e.g., liver enzymes, abnormalities of blood cell, and transdermal alcohol sensor/recorder), genetic information on certain alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) alleles,[464] which are associated with an individual's level of alcohol consumption, could be collected and used in epidemiologic studies. The genetic information will facilitates the Mendelian randomisation studies on alcohol consumption and ageing outcomes, helping to address the methodological concerns of confounding and reverse causation in observational studies.[451,464-466]

Self-reported physical functioning was used in this thesis. As shown in Section 2.3.2.2 (building blocks of physical functioning), in order to improve the understanding of physical functioning and its determinants, it may be useful to

measure the full spectrum of physical functioning in future research. This may include measuring objective physical parameters (e.g., muscle strength, balance, flexibility and walking speed), assessing functional limitations (e.g., walking several blocks, climbing stairs, lifting or carrying heavy objects), and measuring physical disability (e.g., ADLs). However, it should be kept in mind that: 1) objective measures of physical parameters are not necessarily superior to self-reported measures of functional limitations or disability;[131] and 2) self-reported measures may be equally important as objective measures of physical parameters. This is because self-reported measures reflect an individual's perception on his/her ability to perform physical activities in real environment ('perform' in the ICF in Section 2.3.1.3); while objective measures of physical parameters assess an individual's highest probable level of functioning independently from his/her real-life context ('capability' in the ICF Section 2.3.1.3).

Another direction of future work is the application of statistical methods to handle missing data in prospective studies with repeated measures. For instance, given the great flexibility of MICE, further efforts from researchers are needed in term of making recommendations for the best practice of MICE in longitudinal data with multilevel structure, and developing statistical software capable of handling large datasets with a number of variables. Missing data in real-life research is a mixture of MAR and MNAR, which is untestable.[261] Findings in this thesis were based on an assumption of MAR, but the possibility of some MNAR cannot be ruled out. The MNAR models (pattern-mixture models and selection models) do not necessarily yield more accurate estimates. More research on what and how factors are related to missingness in prospective studies of ageing populations, and on how to incorporate these factors in statistical models, especially in MNAR models, will be welcomed.

In this thesis, using cross-sectional data, the relationship between alcohol consumption and physical functioning appeared to be masked by 'sick quitters' and reverse causation. Some evidence of a bi-directional relationship between alcohol consumption and physical functioning was also found in this thesis. For these reasons, prospective studies with clear temporality and continuously repeated measurements of alcohol consumption in ageing populations are urgently needed. No such studies

exist in the CEE region where is a good place to study alcohol and ageing, considering its rapidly ageing population, high level of alcohol consumption and high level of health burden attributable to alcohol. The HAPIEE cohorts represent urban populations in the Czech Republic, Russia and Poland. Further waves of data collection in the HAPIEE study would greatly enhance its potential to address important questions regarding determinants of ageing-related outcomes.

In the framework of late-life disablement process,[97] factors at early, middle and late stage of life, including biological factors, medical care, SEP, health behaviours and environmental factors, directly or indirectly influence the disablement process in late-life via forming a chain of risk. How exactly these factors act together is still not fully understood. For example, as previously mentioned, little is known about the role of CVD, inflammation and lipids on the pathway linking alcohol consumption to physical functioning. Although my results on the bi-directionality between alcohol consumption and physical functioning suggested that alcohol consumption was not associated with physical functioning but vice versa in the Czech and Polish cohorts, these results were based on data from only two time points, which is not adequate to obtain trustworthy estimates. Therefore, longitudinal data with repeated measures of alcohol consumption, physical functioning, CVD, inflammation and lipids will further facilitate better understanding of the pathway between alcohol consumption and physical functioning.

Finally, while studying the negative extreme of physical functioning is beneficial in terms of preventing the development of functional limitations and disability, studying physical functioning from a positive prospective of it being on a continuum is advantageous in understanding the dynamic loss of physical functioning in ageing populations, and what factors and how they influence the acceleration of decline in physical functioning and those which contribute to maintain adequate functioning. Knowing which factors contribute to the early decline in physical functioning, prior to the onset of major functional limitations and/or disability, will be advantageous for planning prevention strategies and tailoring interventions to reverse the disablement process and restore physical functioning. More work will need to be done to determine these factors.

7.1.2 Implications for policy

Populations in CEE region is ageing rapidly, and this process challenges the social care systems and health services in this region.[2,3] As a result, it is imperative to maintain and optimise older adults' physical functioning–a central component of health and quality of life. Owing to ageing-related physiological changes, older adults are more sensitive to harmful effect of alcohol consumption than younger adults.[21,22,80,82-85] Although I found alcohol consumption was not associated with the rate of decline in physical functioning in most of the groups in the Czech, Russian and Polish HAPIEE cohorts, it does not imply that alcohol consumption does not have negative effect on physical functioning. In fact, in some subgroups in these HAPIEE cohorts, there was some suggestion that more frequent and heavier drinking was associated with an accelerated decline in physical functioning, although the evidence was rather weak and inconsistent. It is not appropriate to draw the conclusion that alcohol consumption does not cause poor physical functioning. It also would be inappropriate to use my findings as evidence for policy of advocating alcohol use on the basis of the inappropriate conclusion that alcohol consumption does not cause poor physical functioning, even in moderation.

Alcohol causes organotoxicity, carcinogenicity, teratogenicity, hepatotoxicity, neurotoxicity, and exerts adverse effects on genes and immunological system, through ethanol, its metabolites, and reactions with constituents of the body.[177,225] There is ample evidence that alcohol is associated with numerous diseases and conditions,[177-181] most of which show a linear dose-response relationship that the risk of disease increases with increasing dose of alcohol.[175,177-179,181,226-230] Even the apparently protective effect of alcohol consumption in moderation on mortality and CVD is currently being debated, because interpretation of observational studies is affected by important methodological issues, such as 'sick quitter' bias, measurement error and misclassification of self-reported alcohol consumption, confounding and divergent characteristics in drinking groups especially in abstainers.[182,183,467] Taking into account the harmful effect of alcohol on a number of medical conditions, it is sensible to support the WHO position that abstaining from drinking is the optimal situation for ageing populations.[468]

7.2 Conclusions

This thesis investigated the role of alcohol consumption in physical functioning in three large cohorts of middle-aged and older adults from the Czech Republic, Russia and Poland, using both cross-sectional and longitudinal data from the HAPIEE study.

In the cross-sectional analyses, an inverse association was found between alcohol consumption and physical limitations in the Czech, Russian and Polish cohorts. No association was found between problem drinking and physical limitations. Using data on past drinking suggested that the excess risk of physical limitations in non-drinkers was partly explained by 'sick quitters' who quit drinking because of health reasons, and that the apparently protective effect of heavier drinking was partly due to less healthy former heavy drinkers who moved to lower drinking categories.

In the prospective data, using 10-year follow-up, physical functioning declined in all three cohorts, albeit at different pace across cohorts. The main finding is that, overall, alcohol consumption at baseline was not associated with the rate of decline in physical functioning over time, although in some subgroups, more frequent and heavier drinkers were found to have a faster decline. Problem drinking and past drinking behaviour were not associated with the rate of decline in physical functioning over time. The interpretation of this lack of associations is not entirely clear–it may reflect the enabling process of disablement (physical functioning can be improved via medication, rehabilitation and accommodation) or the dynamic relationship between alcohol consumption and physical functioning (heavy drinkers tend to reduce or abstain from drinking once their physical functioning deteriorates).

However, it is also possible that there is genuinely no association between alcohol and physical functioning or that, if it exists, it is too weak to be detected by the relatively crude instruments used in this study.

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APPENDICES

Appendix A. Literature search on alcohol consumption and physical functioning

1. Activities of Daily Living.mp. or "Activities of Daily Living"/
2. Geriatric Assessment/
3. Quality of Life.mp. or "Quality of Life"/
4. Health Status.mp. or exp Health Status/
5. Health Surveys/
6. exp Disabled Persons/
7. exp Walking/
8. Hand Strength/
9. (physical adj function*).mp.
10. (physical adj performance).mp.
11. (physical adj limit*).mp.
12. (physical adj disabl*).mp.
13. (physical adj impair*).mp.
14. (functional adj status).mp.
15. (functional adj ability).mp.
16. (functional adj capacity).mp.
17. (functional adj limit*).mp.
18. (functional adj impair*).mp.
19. (functional adj disab*).mp.
20. ((grip or hand) adj strength).mp.
21. mobility.mp.
22. disabl*.mp.
23. or/1-22
24. exp Alcohol Drinking/
25. Alcoholism.mp. or Alcoholism/
26. alcohol.mp. or alcohols/ or ethanol/
27. (alcohol adj3 beverage).mp.
28. (alcohol adj3 consum*).mp.
29. (alcohol adj3 drink*).mp.
30. (alcohol adj3 use*).mp.
31. (binge adj drinking).mp.
32. (heav* adj2 drink*).mp.
33. ((risky or irregular or hazardous or problem) adj drinking).mp.
34. (drink* adj3 pattern*).mp.
35. (alcohol* adj3 (dependen* or abuse or misuse)).mp.
36. or/24-35
37. aged/
38. middle aged/
39. "aged, 80 and over"/
40. middle aged.mp.
41. (old* or elder*).mp.
42. (aged or ag?ing).mp.
43. or/37-42

44. Epidemiologic studies/
45. exp case control studies/
46. exp cohort studies/
47. Case control.tw.
48. (cohort adj (study or studies)).tw.
49. Cohort analy$.tw.
50. (Follow up adj (study or studies)).tw.
51. (observational adj (study or studies)).tw.
52. Longitudinal.tw.
53. Retrospective.tw.
54. Retrospective study/
55. Prospective study/
56. Cross sectional.tw.
57. Cross-sectional studies/
58. or/44-57
59. 23 and 36 and 43 and 58

Appendix B. Previous cross-sectional findings on the association between alcohol consumption and physical functioning

First author	Year	Study	Sample	Sample size	Age	Measure of PF	Measure of alcohol consumption	Result	Reference group	Adjustment
Nelson[25]*§	1994	The Study of Osteoporotic Fractures (US)	Community-dwelling older women	9,704	65-85	Self-reported mobility, ADLs, IADLs, performance tasks	Number of drinks per week in the past 30 days	Non-drinkers had poorer physical functioning on all measures except tandem walk; No consistent differences found in heavy drinkers; No association between lifetime intake and physical functioning in former drinkers	Light-to-moderate drinking: >0 to <14 drinks/week	Age, history of stroke, BMI, clinic site, physical activity and smoking
Volk[26]*	1997	US	Primary care patients, probability sample	1,333	18-86 (mean: 43)	SF-36	Usual QF in the last 12 months & AUDADIS	Only frequent low-quantity drinkers (>5/month & 1-4 drinks/occasion) had a higher PF-10 score; Subjects with alcohol dependence had a lower PF-10 than those with alcohol abuse, but no difference for those with no alcohol use disorder	Non-drinking	Age, sex, race/ethnicity and smoking
Michael[27]	1999	The Nurse's Health Study (US)	Female nurses without CHD, cancer or stroke	56,436	55-72	SF-36	Food frequency questionnaire by specific beverages	PF-10 score were highest in light-to-moderate drinkers (1-150g/week) and higher in heavy drinkers (>150g/week)	Non-drinking	Age & comorbidity (hypertension, diabetes mellitus, osteo- and rheumatoid arthritis), BMI, physical activity, smoking
Green[28]*§	2001	US	Members of a health maintenance organization	3,803	18-102 (mean: 52)	SF-36	Quantity & frequency in the past year (from AUDIT); past drinking behaviour among non-drinkers	Former drinkers and lifetime abstainers had lower PF-10 scores; No difference for heavy drinkers (>60 drinks/month)	Light-to-moderate drinking: 1-60 drinks/month	Age, sex, marital status, education, income, household size, employment status and smoking
Moore[29]*	2003	US	Primary care patients with at least one drink in the last 3 months	161	≥60	IADLs	Timeline calendar of drinking in last 30 days; binge drinking in last 12 months	Heavy drinkers (8-14 & >14 drinks/week) and binge drinkers were at a higher risk of IADL limitations	Light-to-moderate drinking: ≤7 drinks/week; No binge drinking	Age, sex, education, cognitive impairment, number of medications and psychiatric condition
Green[30]*	2004	US (same as Green *et al.* 2001)	Members of a health maintenance organization	5,669	25-100 (mean: 58)	SF-36	Usual QF in last 12 months	Highest PF-10 scores were in drinkers who drank 2-3/week, 1-2/occasion, 15-29 drinks/month, and regular light-to-moderate drinking; and lowest score in non-drinkers	N/A	Age, ethnicity, marital status, body water index and smoking; Stratified by sex
Sulander[31]	2005	Finland (three cross-sectional surveys at 1985-1989, 1993-1995 and 1997-2001)	Community-dwelling older adults	11,793	65-79	ADLs	Number of beers, alcopops, wine and spirits in the past week	Drinking <8 units/week was associated with a lower risk of ADL limitations in both sexes; Drinking 8-14 units/week was associated with the lowest risk in men; No difference for heavy drinking (>14 unit/week)	Non-drinking	Age, smoking, diet, physical activity, BMI, time period, occupation, marital status, CVD, musculoskeletal diseases, chronic bronchitis/emphysema; Stratified by sex

Cawthon[32]*	2007	The Osteoporotic Fractures in Men (MrOS) study (US)	Community-dwelling older men without hip replacements or assistance/aide to walk	5,962	≥65	Performance tasks, IADLs and self-reported mobility	Food frequency questionnaire (last 12 months); History of sustained excessive drinking (≥5 drinks almost every day in lifetime); CAGE	Light and low-moderate drinkers (1-14 drinks/week) performed better in physical tasks, and drinkers (≥1 drink/week) were at a lower risk of IADL and mobility limitations (lowest among drinking 7-14 drinks/week); Problem drinkers performed worse in gait speed and walk speed, and were at a higher risk of IADL and mobility limitations; Men with history of sustained excessive drinking performed worse in all tasks but not for IADL and mobility limitations	Non- & very light-drinking: <12 drinks/year; No history of problem drinking; No history of sustained excessive drinking	Age, education, self-rated health, weight, number of medical conditions, physical activity, race and smoking
Santos[33]	2008	The SABE study (Brazil)	Community-dwelling older adults	1,479	>60	IADLs	Had any alcoholic beverage in the previous 3 months	Drinkers were at a lower risk of IADL limitations	Non-drinking in the previous 3 months	Age, sex, ethnicity, education, income, physical activity, depression, number of diseases
Klijs[34]	2011	The Dutch Permanent Survey of the Living Situation (POLS) (Netherland)	Community-dwelling late-middle aged and older adults	6,446	≥55	Self-reported mobility & ADLs	Number of drinks in the week and weekends	Non-drinkers were at a higher risk of ADL and mobility limitations; no difference for heavy drinkers (>14 alcohol consumptions/week)	Light-to-moderate drinking: 1-14 alcohol consumptions/week (No definition of one alcohol consumption)	Age, sex and marital status
Lima[35]	2011	The Multi-Center Health Survey (Brazil)	Community-dwelling older adults	1,958	≥60	SF-36	Beverage-specific QF in a typical week	The PF-10 score was highest in frequent drinkers (≥1/week), and higher in infrequent drinkers (<1/week)	Non-drinking	Age, sex, education, income, work status, place of residence, and number of chronic diseases
Canavan[36]§	2014	The Cardiovascular Multimorbidity in Primary Care (CLARITY) (Irland)	Community-dwelling middle-aged and older adults	3.499	≥50	ADLs & IADLs	Drinking 5+ units in a day, ≥1/week in last month; Categorise drinking into never, former, and current	Current drinkers had a lower risk of functional impairments (defined as ≥1 limitation in ADLs & IADLs); Former drinkers had a higher risk	Non-drinking	Age, sex, education, smoking, hypertension, diabetes, HDL, LDL, atrial fibrillation, CVD, chronic kidney disease

Note: * alcohol consumption as primary research aim; § separated former drinkers from non –drinkers

Appendix C. Previous longitudinal findings on the association between alcohol consumption and physical functioning

First author	Year	Study	Sample	Sample size	Age at baseline	Measure of PF	Measure of alcohol consumption	Result	Reference group	Adjustment	Follow-up (year)
LaCroix[168]	1993	The Established Populations for Epidemiologic Study of the Elderly (EPESE) (US)	Community-dwelling older adults without mobility limitations at baseline	6,981	≥65	Self-reported mobility (climb up & down stairs, walk 0.5 mile) at baseline and 4 follow-ups	Beverage-specific QF in the last month at baseline	Non-drinkers had a higher risk of loss of mobility only in subjects with ≥1 chronic conditions at baseline; No association among subjects without chronic conditions at baseline	Light-to-moderate drinking: ≤1 ounce/day	Age, smoking, physical activity and BMI; Stratified by sex and chronic conditions	4
Seeman[39]	1995	The MacArthur Research Network on Successful Aging Community Study (US)	Community-dwelling older adults with high functioning	1,015	70-79	Performance tasks at baseline and one follow-up	Beverage-specified QF in last month at baseline	No association between baseline alcohol consumption and either decline or improve in physical performance	Non-drinking	Age, sex, race, education, income, baseline physical and cognitive functioning, peak flow, BMI and comorbidity (hypertension, diabetes, cancer)	2.5
Stafford[40]	1998	The Whitehall II study (UK)	Middle-aged civil servants	8,349	35-55	SF-36 at one follow-up	Number of drinking units in last 7 days at baseline	No association between baseline alcohol consumption and PF-10 at follow-up in either men and women; No change after excluded subjects with chronic diseases at baseline or follow-up	Moderate drinking: ≤21 units/week	Age, employment grade, chronic disease, smoking, physical activity, eating habits, BMI, biomedical factors and heart rate; Stratified by sex	5.3 (3.7-7.6)
Penninx[52]	1999	The EPESE study (US)	Community-dwelling older adults without ADL and mobility limitations at baseline	6,247	≥65	ADLs & self-reported mobility at 4 follow-ups	Usual QF of drinking in last month at baseline	Light-to-moderate drinkers (≤3 glasses/day) were at a lower risk of developing ADL and mobility limitations at follow-up, no difference for heavy drinkers (>3 glasses/day)	Non-drinking	Age, sex, education, income, depression, baseline cognitive impairment, smoking, physical activity, BMI, marital status, having no children, social network, baseline and incident medical conditions	6
Ebrahim[172]	2000	The British Regional Heart Study (BRHS) (UK)	Community-dwelling middle-aged men	5,717	40-59	ADLs & self-reported mobility at one follow-up	Weekly number of drinks at baseline	Heavy drinking at baseline was associated with locomotor disability at follow-up consistently among subjects without disease, with CVD, or with other diseases at baseline	Non-drinking and less than heavy drinking: ≤6 units/day	Age, social class, smoking, BMI, physical activity	12-14
Lantz[41]	2001	The Americans' Changing Lives (ACL) study (US)	Non-institutionalised adults	3,617	≥25(48% ≥45, 20% ≥65)	Index of functional status (transfer, mobility, heavy work inside or outside home) at one follow-up	Number of drinks in the last month at baseline	No association between baseline alcohol consumption and low or moderate/severe limitations at follow-up	Light-to-moderate drinking: 1-89 drinks in the past month	Age, sex, race, education, income, smoking, physical activity, BMI and baseline functional status	7.5

Perreira[53]*	2002	The Health and Retirement Study (HRS) (wave 1 & wave 4) (US)	Community-dwelling middle-aged and older men	3,931	51-61	ADLs at wave 4	Usual number of drinks per day & CAGE at wave 1	Non-drinkers without problem drinking were at a higher risk of developing ≥2 ADL limitations; heavy drinkers (≥5 drinks/day) were at the highest risk; No difference for drinking <1 and 3-4 drinks/day, and non-drinkers with problem drinking; No association for problem drinking	Light drinking: 1-2 drinks/day; Non-problem drinking	Age, race, education, smoking, BMI, medical conditions, health status and religiosity	6
Ostbye[54]	2002	The HRS study (wave 1-4) & Aging and Health Dynamics Among the Oldest Old (AHEAD) study (wave 1-3) (US)	Community-dwelling middle-aged and older adults	12,652 in HRS; 8,124 in AHEAD	51-61 in HRS; ≥70 in AHEAD	ADLs and self-reported mobility in HRS and AHEAD; plus IADLs in AHEAD at all follow-ups	Usual number of drinks per day & CAGE at wave 1	HRS: light drinkers (≤2 drinks/day) were at a lower risk of ADL and mobility limitations at follow-up; problem drinkers had a higher risk; not for heavy drinkers (>2 drinks/day); AHEAD: light drinkers were at a lower risk of ADL, IADL and mobility limitations at follow-up, heavy drinkers had a lower risk of only ADL limitations, and problem drinkers had a higher risk in climbing stairs only	Non-drinking	HRS: age, sex, race, education, marital status, smoking, physical activity and BMI; AHEAD: age, sex, race, education, marital status, smoking and BMI	6 for HRS, 5 for AHEAD
Tabbarah[42]	2002	The MacArthur Research network on Successful Aging Community Study (US)	Community-dwelling older adults with high functioning	488	70-79	Performance tasks at baseline and one follow-up	Beverage-specified QF of drinking in the last month at baseline	No association between alcohol consumption at baseline and change on physical performance tasks, except non-drinkers in the past year had a decline in tandem stand with eye open	Occasional drinking: <1 g/month	Age, sex, education, comorbidity, BMI, smoking, depression, peak expiratory flow rate, cognitive performance	7
Wang[55]	2002	The Adult Changes in Thought (ACT) study (US)	Members of a health maintenance organization, cognitively intact	2,578	≥65	ADLs, IADLs, and PPF at baseline and two follow-ups	Whether drank ≥5 drinks in last year and problem drinking at baseline	Drinkers who drank ≥5 drinks/year without problem drinking at baseline had a decreased age-adjusted rate of decline in ADLs, IADLs and PPF	Occasional drinking: <5 drinks/year	Age, smoking, exercise, baseline functional status, depression, and medical conditions (diabetes, arthritis, hypertension, CHD, CVD, cancer, etc)	3.4 (0-7)
Wannamethee[56]	2005	The BRHS (UK)	Community-dwelling middle-aged and older men without mobility limitation	4,430	52-73	Mobility at baseline and one follow-up	Weekly number of drinks at baseline	Heavy drinkers (>42 units/week; >6 units/day) were at a higher risk of onset of mobility limitation; No associated with recovery from mobility limitation	Occasional drinkers: <1 unit/week	Age, BMI, physical activities, smoking, social class, number of chronic diseases, breathlessness, calf pain on walking	4
Byles[57]*	2006	The Australian Longitudinal Study on Women's Health (ALSWH) study (Australia)	Community-dwelling older women	11,878	70-75	SF-36 at baseline and two follow-ups	Usual QF of drinking not specified reference time at baseline	Rare drinkers (<1 time/week) at baseline had a lower PF-10 score in all baseline and tow follow-ups, and non-drinkers had the lowest score	Frequent light-to-moderate drinking: 1-2 drinks, 3-6 days/week	Residence area, smoking, BMI, education, medical conditions, survey time point	6
Turvey[58]*	2006	The AHEAD study (wave 1&2) (US)	Community-dwelling older adults	6,222	≥70	ADLs and IADLs at wave 2	Usual QF in the last three months at baseline	Drinking at wave 1 had a lower risk of ADL & IADL limitations at wave 2	Non-drinking	Age, sex, education, baseline ADLs and IADLs	2

Koster[169]§	2007	The Health, Aging and Body Composition (Health ABC) study (US)	Community-dwelling older adults without mobility and ADL limitation	2,694	70-79	Self-reported mobility (walking ¼ mile and climbing 10 steps) at 13 semiannual follow-ups	Number of drinks in a typical week in last 12 months & whether drank more than typical drinking in last 12 months at baseline	Only former non-obese drinkers had a higher risk of early onset of mobility limitation (within first 2 years of follow-up); no association among obese subjects; No association between alcohol consumption and late onset of mobility limitation (2-6.5 years of follow-up)	Moderate drinking: 1-7 drinks/week for women, 1-14 drinks/week for men	Age, sex, race, research site, marital status, education, baseline functional performance, medical conditions, depression and cognitive impairment; Stratified by obesity	6.5
Lang[59]*§	2007	The AHEAD/HRS study (US) & English Longitudinal Study of Aging (ELSA) study (UK)	Community-dwelling older adults	10,710 in HRS/AHEAD; 2,623 in ELSA	≥65	ADLs and IADLs at one follow-up	AHEAD/HRS: usual QF in last 3 months ELSA: usual QF in last 12 months; at baseline	Only non-drinkers at baseline had a higher risk of ADL and IADL limitations 4 years later in both studies; Exclusion of sick quitters and all former drinkers in ELSA didn't change the association between alcohol consumption and ADL/IADL limitations	Light drinking: >0 to <1 drink/day	Age, sex, education, income, material, BMI, smoking, exercise, medical conditions and depression	4
Tas[43]	2007	The Rotterdam Study (Netherlands)	Community-dwelling middle-aged and older women, disability-free at baseline	5,024	≥55	The Stanford Health Assessment Questionnaire (HAQ) at baseline and one follow-up	Food frequency questionnaire at baseline	No association between alcohol consumption at baseline and incident disability 6 years later	Non-drinking	Age, partner, cognitive impairment, self-rated health, smoking, BMI, depression, medical conditions, medication use	6
Maraldi[256]*§	2009	The Health ABC study (US)	Community-dwelling older adults without mobility and ADL limitation	3,061	70-79	Self-reported mobility (walking ¼ mile and climbing 10 steps) at 13 semiannual follow-ups	Number of drinks in a typical week in last 12 months & whether drank more than that in the past 12 months at baseline	Only former and light drinkers (1-7 drinks/week) at baseline had a higher risk of developing mobility limitation in men; no association in women; No association between alcohol consumption at baseline and severe mobility disability in either men or women	Non-& occasional drinking: <1 drink/week	Age, race, research site, education, family income, smoking, physical activity, BMI, medical conditions and cognitive impairment; Stratified by sex	6.5
Karlamangla[257]*§	2009	The National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS) (US)	Non-institutionalized late-middle-aged and older adults, disability free at baseline	4,276	≥50	Stanford Health Assessment Questionnaire (HAQ) Disability Index at baseline and 2 follow-ups	Usual QF of drinking in last 12 months at baseline and 2 follow-ups	Only female light (≤7 drinks/week & <4 drinks/drinking day) and moderate (≥7 to <15 drinks/week & <4 drinks/drinking day) drinkers had a lower risk of incident disability 5 years later in the strata with good or better health status; No association in women with fair or worse health No association in men; No association between former drinking and incident disability	Non-& occasional drinking: <12 drinks/year	Age, race, education, marital status, income, employment, smoking, exercise, medical condition, time period, years of follow-up and interactions; Stratified by sex and self-rated health	10

Balzi[50]	2010	The InCHIANTI study (Italy)	Community-dwelling older adults	897	≥65	ADLs & IADLs at baseline and one follow-up	Food frequency questionnaire at baseline	Baseline alcohol consumption did not predict worsening ADLs and IADLs, development of new ADLs; drinking 10-20 g/day was protective over development of IADL limitations	Non-& light drinking: <10 g/day	Age, physical performance score, physical activity, energy intake	3
Abbott[64]§	2011	The Honolulu-Asia Aging Study (HAAS) (US) & NIPPON DATA (Japan)	Community-dwelling Japanese-American and Japanese older men	1,893 in HAAS; 543 in NIPPON DATA	70-98 in 1995-1999	ADLs at 1995-1999	Whether is non-drinkers, ex-drinkers, occasional drinkers or everyday drinkers at 1991-1993	Former drinkers at baseline had a higher risk of developing ADL limitation in both Hawaii and Japan cohorts, Current drinkers had a lower risk only in the Hawaii cohort	Non-drinking	Age, smoking, BMI, hypertension, diabetes, history of CVD and total cholesterol	6 in HAA; 5 in NIPPON DATA
Liao[60]	2011	The Taiwan Longitudinal Study in Aging (TLSA) (Taiwan)	Community-dwelling older adults	3,187	≥60	taking a bath & walking 200-300 m at baseline and 4 follow-ups	Frequency of drinking per week at baseline	Only non-drinkers had a higher hazard ratio of onset of functional disability	Frequent drinkers: <1/week to every other day	Sex, marital status, education, stroke, diabetes, heart diseases, number of diseases, smoking, sleep, physical activity	14
Lin[61]*§	2011	The HRS (wave 4-8) (US)	Community dwelling middle-aged and older adults without functional limitations	5,594	≥50	IADLs and self-reported upper- and lower-extremity function at 2000, 2002, 2004, 2006	Usual QF in last 3 months & binge drinking (≥4 drinks/occasion) in last 3 months at 1998, 2000, 2002, 2004	Consistent low risk drinkers (≤14 drinks/week for men, ≤7 drinks/week for women, 1998-2000, and 2002-2004) had a lower risk of developing IADL and functional limitation, but not for consistent high risk drinkers, recent quitters and drinkers with other patterns	Consistent non-drinking	Age, sex, marital status, race, education, employment status, income, self-rated health, smoking and chronic conditions	8
Tsubota-Utsugi[44]	2011	The Ohasama Study (Japan)	Community-dwelling older adults	1,050	≥60	IADLs at baseline and one follow-up	Lifetime abstainers, former or current drinkers at baseline	No association between baseline alcohol consumption and onset of IADL limitations	Non-drinking	Age, education, history of hypertension, hypercholesterolemia, cataract, osteoporosis, BMI	7
Wolinsky[62]	2011	The AHEAD study (wave 1-7) (US)	Community-dwelling older adults	5,871	≥70	ADLs, IADLs and self-reported upper- and lower-extremity function at baseline and 6 follow-ups	Usual QF in last 3 months at baseline	Drinkers with ≥1 drink/day had a lower risk of decline in mobility during follow-up, but not in ADLs or IADLs	Non- & light drinking: <1 drink/day	Age, sex, race, marital status, education, income, number of diseases, baseline function, follow-up years and continuity of care	14
Stenholm[51]	2012	Mini-Finland Health Examination Survey (Finland)	Community-dwelling adults	963	30-73	Grip strength at baseline and one follow-up	Weekly alcohol consumption in last one month at baseline and one follow-up	No association between alcohol consumption at baseline or change of alcohol consumption and rate of change in grip strength	Non-heavy drinkers (men<280 g/week, women<140 g/week); Persistent non-drinkers and non-heavy drinkers	Age, sex, education, BMI, physical activity and smoking	22

Tas[45]	2012	The Rotterdam Study (Netherlands)	Community-dwelling middle-aged and older adults with mild disability	1,166	≥55	Health Assessment Questionnaire (HAQ) at baseline and one follow-up	Food frequency questionnaire at baseline	No association between alcohol consumption and recovery from or worsen disability	Continuous	Age, sex, income, smoking, cognition, self-rated health	6
Artaud[46]§	2013	Three-City Dijion cohort study (France)	Community-dwelling older adults, disability free	4,931	≥65	Combined mobility, IADLs and ADLs at baseline and 5 follow-ups	Weekly number of drinks at baseline	No association between alcohol consumption at baseline and development of disability at follow-up; Female former drinkers had a higher risk of limitations in IADLs or ADLs, but not among men	Light-to-moderate drinking: men: 1-21 drinks/wk, women:1-14 drinks/wk	Sex, marital status, education, physical activity, consumption of fruits and vegetables, smoking	12
Kim[47]	2013	The British Women's Heart and Health Study (UK)	Community-dwelling older women, locomotor disability free	2,430	60-79	ADLs and falls at baseline and one follow-up	Usual frequency of drinking at baseline	No association between baseline alcohol consumption and incident of locomotor disability	Socially drinking: weekend only OR 1-2/month OR special occasions	Age, SES, BMI, smoking, physical activity, fruit intake	7
Lee[48]	2013	The Korean Longitudinal Study of Aging (KLoSA) (South Korea)	Community-dwelling older adults	3,511	≥65	ADLs & IADLs at baseline and one follow-up	AUDIT-K at baseline and one follow-up	No association between transition of heavy drinking at follow-up and transition of disability at follow-up	Heavy drinking at follow-up but not at baseline	Age, sex, marital status, education, self-rated health, comorbidity, depressive symptoms, cognitive function, baseline and change of smoking, physical activity, and unhealthy weight	2
Leng[63]	2013	The TLSA (Taiwan)	Community-dwelling middle-aged and older adults	5,464	≥50	Upper- & lower-extremity function at baseline and 3 follow-ups	Frequency of drinking per week at baseline	Drinking ≥1/week was associated a higher risk of with incident mobility limitation; no difference among drinking <1/week	Non-drinking	Age, sex, education, living in nursing home, employment, physical conditions, CESD, cognitive function, duration of exercise, leisure time activity, social connection	11
Rodriguez Lopez [49]	2014	The Survey of Health, Ageing and Retirement in Europe (SHARE), Spanish cohort (Spain)	Community-dwelling older adults	699	≥65	ADLs & IADLs at baseline and one follow-up	Frequency of drinking in the last 6 month & frequency of >2 drinks at a time at baseline	No association between baseline alcohol consumption and functional decline at follow-up	Non-drinking & non-heavy drinking: ≤2 glasses of alcohol 5-6 days/week	Age, living arrangement, education, self-rated health, No. of chronic diseases, No. of symptoms, BMI, cognitive functioning, physical activity, smoking	2

Note: * alcohol consumption as primary research aim; § separated former drinkers from non –drinkers

Appendix D. Baseline self-rated health by main missing patterns of the PF-10 score throughout follow-up of the HAPIEE study

Self-rated health	Czech Republic		Russia		Poland	
	Men	Women	Men	Women	Men	Women
Completers						
Good/very good	704 (47.12%)	934 (47.39%)	258 (18.00%)	131 (5.89%)	681 (47.39%)	633 (39.29%)
Average	681 (45.58%)	883 (44.80%)	1001 (69.85%)	1577 (70.94%)	619 (43.08%)	794 (49.29%)
Poor/very poor	109 (7.30%)	154 (7.81%)	174 (12.14%)	515 (23.17%)	137 (9.53%)	184 (11.42%)
N	1494	1971	1433	2223	1437	1611
Missing PF-10 score at Re-examination, PQ2009 & PQ2012						
Good/very good	390 (33.16%)	398 (32.95%)	118 (12.37%)	52 (6.03%)	428 (33.36%)	331 (27.51%)
Average	580 (49.32%)	628 (51.99%)	584 (61.22%)	520 (60.32%)	596 (46.45%)	611 (50.79%)
Poor/very poor	206 (17.52%)	182 (15.07%)	252 (26.42%)	290 (33.64%)	259 (20.19%)	261 (21.70%)
N	1176	1208	954	862	1283	1203
Missing PF-10 score at PQ2012 only						
Good/very good	113 (36.10%)	126 (37.72%)	131 (15.78%)	46 (5.35%)	494 (39.55%)	407 (30.69%)
Average	151 (48.24%)	180 (53.89%)	575 (69.28%)	568 (66.05%)	582 (46.60%)	725 (54.68%)
Poor/very poor	49 (15.65%)	28 (8.38%)	124 (14.94%)	246 (28.60%)	173 (13.85%)	194 (14.63%)
N	313	334	830	860	1249	1326
Missing PF-10 score at PQ2009 & PQ2012						
Good/very good	134 (35.92%)	119 (33.06%)	58 (15.30%)	10 (3.48%)	141 (33.10%)	89 (23.86%)
Average	196 (52.55%)	191 (53.06%)	247 (65.17%)	175 (60.98%)	203 (47.65%)	214 (57.37%)
Poor/very poor	43 (11.53%)	50 (13.89%)	74 (19.53%)	102 (35.54%)	82 (19.25%)	70 (18.77%)
N	373	360	379	287	426	373
Missing PF-10 score at Re-examination & PQ2012						
Good/very good	61 (41.50%)	50 (34.01%)	37 (14.80%)	13 (4.94%)	210 (41.92%)	155 (26.09%)
Average	75 (51.02%)	76 (51.70%)	175 (70.00%)	182 (69.20%)	243 (48.50%)	323 (54.38%)
Poor/very poor	11 (7.48%)	21 (14.29%)	38 (15.20%)	68 (25.86%)	48 (9.58%)	116 (19.53%)
N	147	147	250	263	501	594
Missing PF-10 score at Re-examination only						
Good/very good	127 (39.56%)	177 (45.85%)	33 (14.67%)	26 (7.22%)	89 (45.88%)	83 (35.32%)
Average	164 (51.09%)	175 (45.34%)	164 (72.89%)	238 (66.11%)	94 (48.45%)	120 (51.06%)
Poor/very poor	30 (9.35%)	34 (8.81%)	28 (12.44%)	96 (26.67%)	11 (5.67%)	32 (13.62%)
N	321	386	225	360	194	235

Appendix E. Traditional statistical techniques of handling missing data

Allison[277] reviewed several traditional methods to deal with missing data: 1) complete-case analysis (also known as listwise deletion); 2) available-case analysis (also known as pairwise deletion); and 3) replacing missing value by a specific value (i.e., missing data is a specific category) and/or modelling the missing indicator simultaneously. The last one is commonly used in epidemiology,[469] however, it generally yields biased estimates even under MCAR.[277,469]

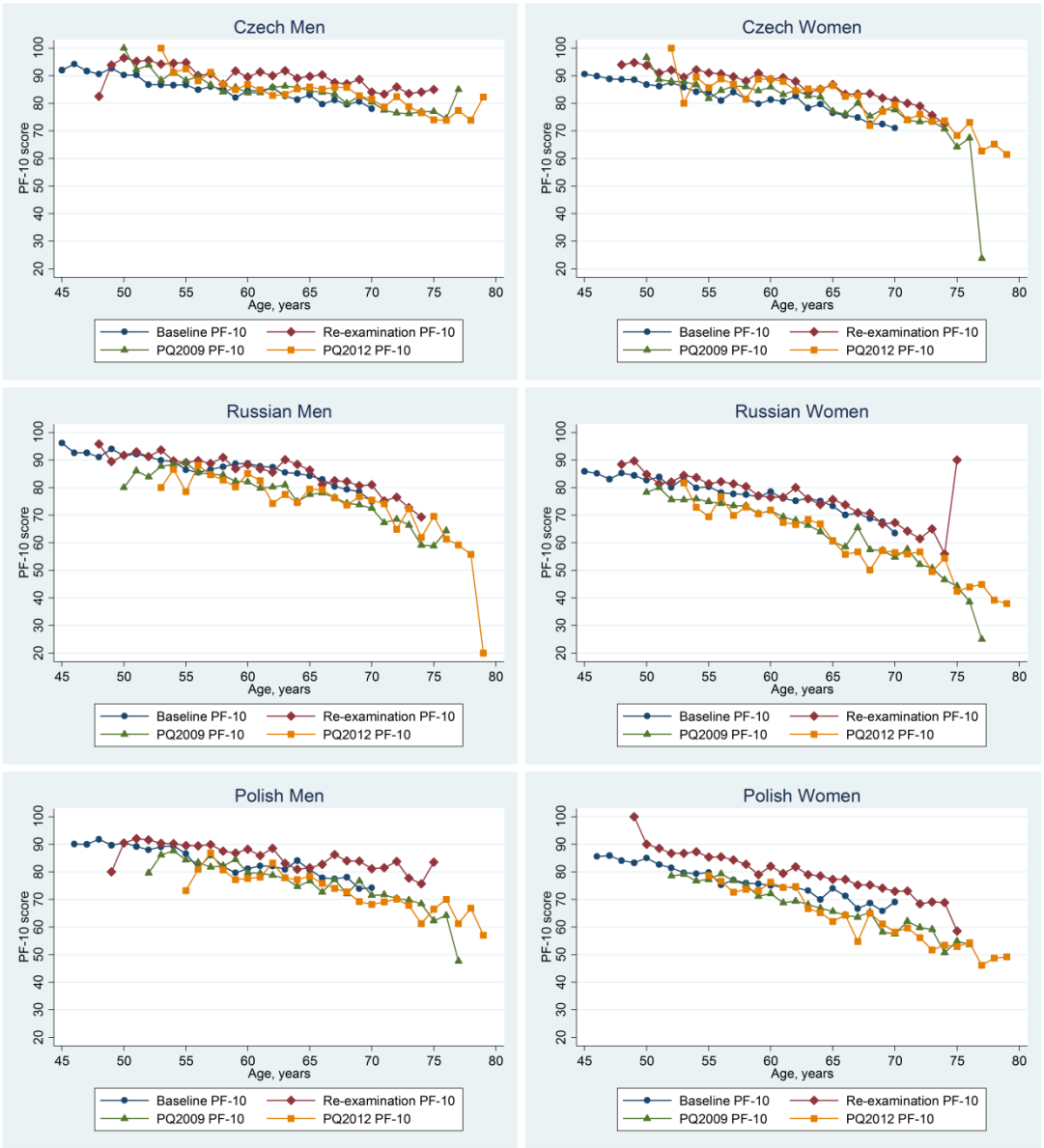
Complete-case analysis yields unbiased estimates of parameters and confidence intervals under MCAR as completers are a random sample of the target population, in spite of larger standard errors and loss of statistical power.[272,277,279-281] In the case that missingness is not MCAR, complete-case analysis leads to a selection bias.[272,470] Graham[261] states that complete-case analysis is appropriate when the proportion of incomplete cases is small (e.g. <5%).

Pairwise deletion, involving the estimation of a correlation or covariance matrix, uses all possible information based on the cases with data on both variables.[261,281] It is unbiased in a large sample under MCAR.[277] However, since the estimation of parameters is based on different sets of cases, it is difficult to compute standard errors and carry out significance tests.[261,272,277] Correlation or covariance matrices may be non-positive definite which hampers the ability to perform most multivariate analyses.[261,277]

Single imputation replaces missing values by the mean (mean imputation), predicted values from regression equation (regression imputation), values from another case with similar background characteristics (hot deck imputation), or last observation carried forward.[281,282] Single imputation results in biased standard errors and significance tests, and underestimates the uncertainty of imputed values.[264,281] Alison[277] pointed out that the regression imputation, in general, yields unbiased estimates in a large sample under MCAR.

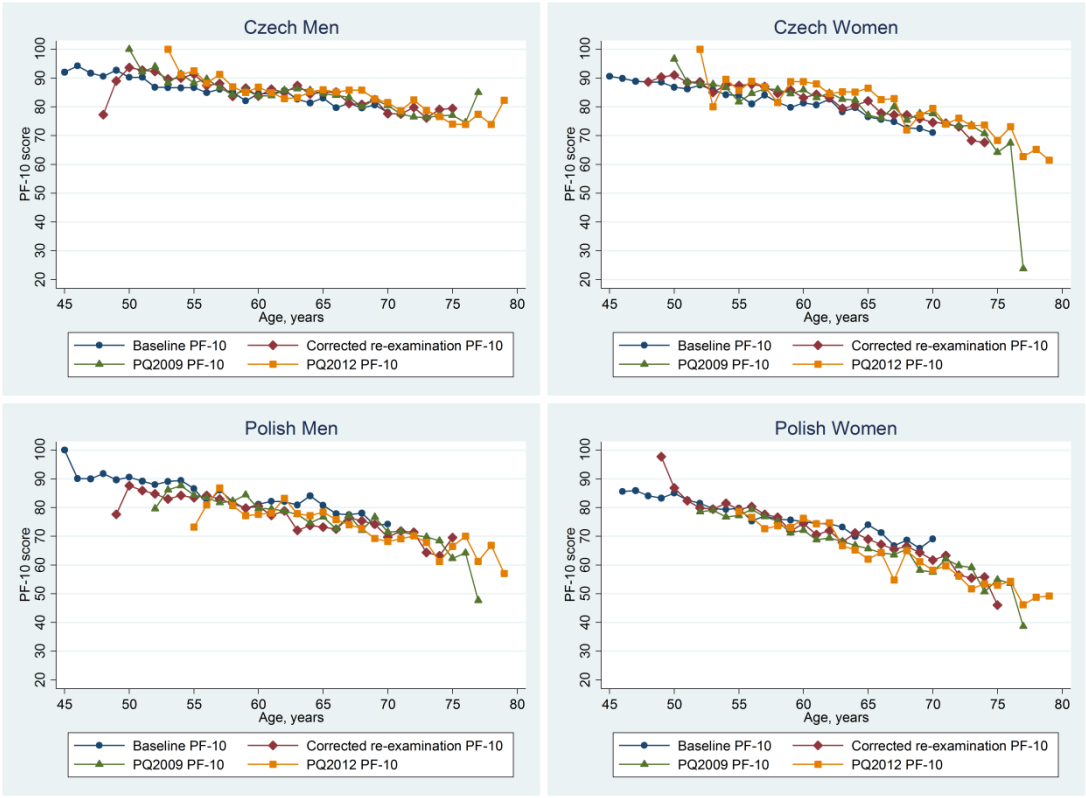
Appendix F. Adjustment of PF-10 score at re-examination

Appendix F.1 displays the mean age-specific PF-10 scores throughout follow-up of the HAPIEE study by sex and cohort, among completers (i.e., with non-missing PF-10 scores at all the four measurement occasions). Compared with baseline, Czechs' and Poles' mean PF-10 scores at re-examination were higher at all ages and in both sexes. The samples were restricted to completers as the increase in the PF-10 score between baseline and re-examination may simply because participants with good health were more likely to stay in the study.



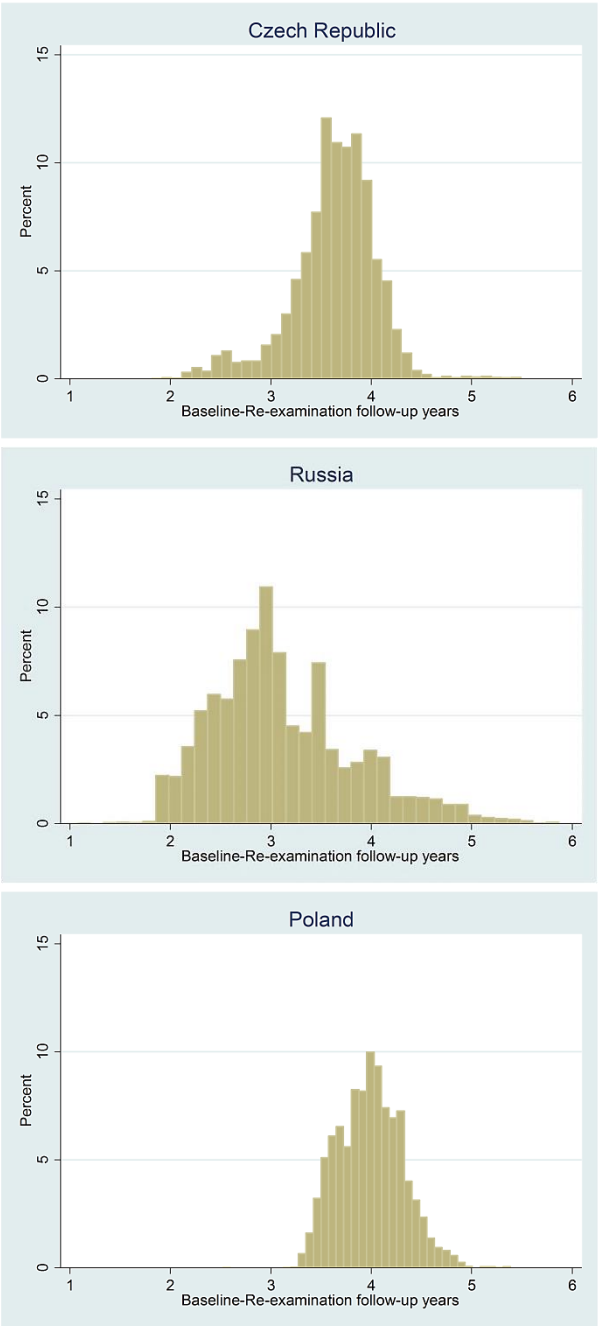
Appendix E.1. Mean age-specific PF-10 scores throughout follow-up of the HAPIEE study among completers

The adjusted PF-10 score at re-examination along with the PF-10 scores measured at other occasions in the Czech and Polish cohorts among participants with non-missing PF-10 scores at any measurement occasions is shown in Appendix F.2.

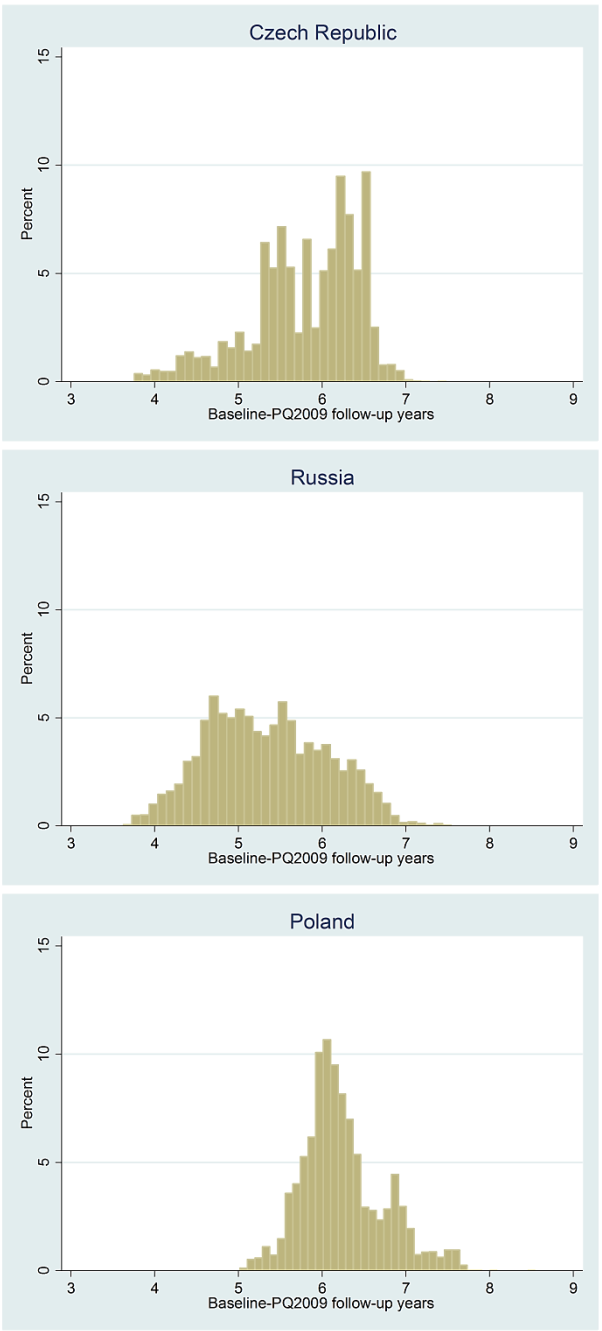


Appendix E.2. Mean age-specific PF-10 scores throughout follow-up in the Czech and Polish cohorts, with adjusted PF-10 score at re-examination

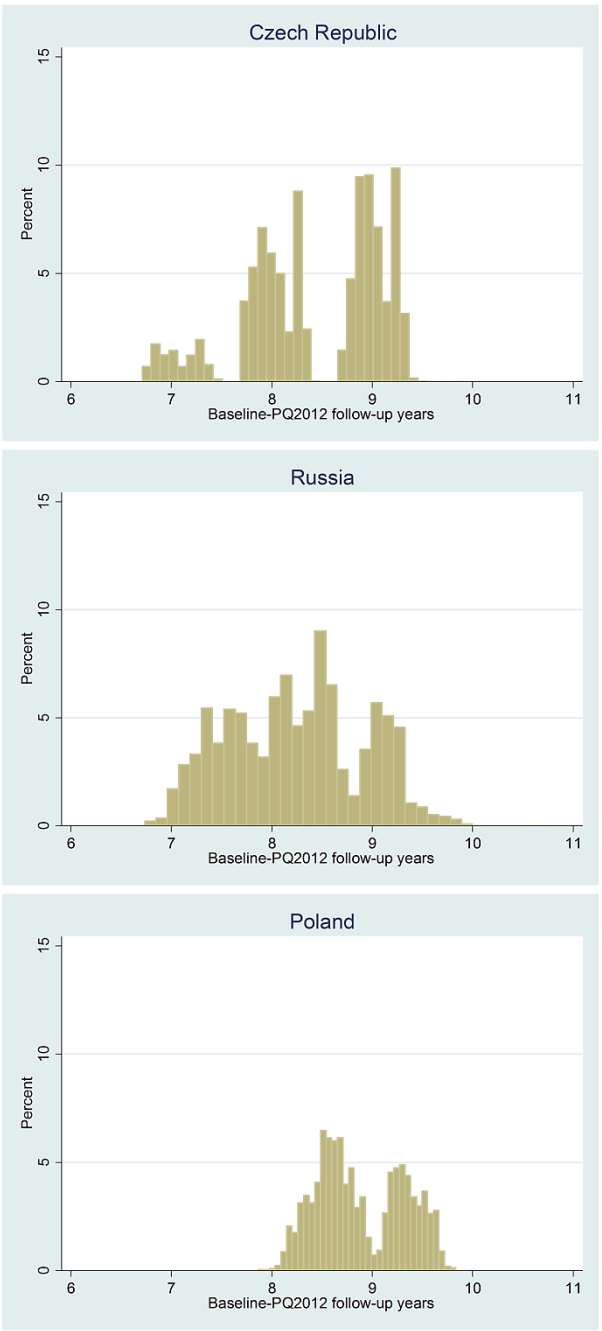
Appendix G. Distribution of follow-up years in the HAPIEE study



Appendix G.1. Distribution of follow-up years between baseline and re-examination



Appendix G.2. Distribution of follow-up years between baseline and PQ2009



Appendix G.3. Distribution of follow-up years between baseline and PQ2012

Appendix H. Sample characteristics of auxiliary variables

	Czech Republic		Russia		Poland	
	Men	Women	Men	Women	Men	Women
Household amenities in childhood						
Mean (S.D.)	4.15 (1.44)	4.24 (1.38)	2.22 (1.75)	2.24 (1.69)	3.33 (1.91)	3.49 (1.90)
Missing	200 (4.91%)	293 (6.23%)	35 (0.83%)	23 (0.45%)	157 (3.01%)	173 (3.15%)
Self-rated health						
Very good	136 (3.34%)	160 (3.40%)	10 (0.24%)	10 (0.20%)	246 (4.71%)	160 (2.91%)
Good	1467 (36.04%)	1740 (37.00%)	658 (15.52%)	284 (5.61%)	1842 (35.29%)	1578 (28.74%)
Average	1965 (48.28%)	2262 (48.10%)	2854 (67.33%)	3401 (67.19%)	2399 (45.97%)	2866 (52.20%)
Poor	442 (10.86%)	471 (10.01%)	673 (15.88%)	1260 (24.89%)	658 (12.61%)	783 (14.26%)
Very poor	39 (0.96%)	37 (0.79%)	44 (1.04%)	107 (2.11%)	66 (1.26%)	92 (1.68%)
Missing	21 (0.52%)	33 (0.70%)	0	0	8 (0.15%)	11 (0.20%)
Long-term health problem						
No	1747 (42.29%)	1755 (37.32%)	3761 (65.13%)	2624 (51.84%)	2394 (45.87%)	2009 (36.59%)
Yes	2269 (55.75%)	2885 (61.34%)	1478 (34.87%)	2438 (48.16%)	2790 (53.46%)	3450 (62.84%)
Missing	54 (1.33%)	63 (1.34%)	0	0	35 (0.67%)	31 (0.56%)
Injury						
No	3544 (87.08%)	4207 (89.45%)	3845 (90.71%)	4565 (90.18%)	4842 (92.78%)	5051 (92.00%)
Yes	494 (12.14%)	462 (9.82%)	394 (9.29%)	497 (9.82%)	271 (5.19%)	348 (6.34%)
Missing	32 (0.79%)	34 (0.72%)	0	0	106 (2.03%)	91 (1.66%)
CVD						
No	3268 (80.29%)	3974 (84.50%)	3237 (76.36%)	4046 (79.93%)	3928 (75.26%)	4277 (77.91%)
Yes, never hospitalisation	164 (4.03%)	207 (4.40%)	304 (7.17%)	525 (10.37%)	478 (9.16%)	718 (13.08%)
Yes, hospitalisation	505 (12.41%)	263 (5.59%)	698 (16.47%)	491 (9.70%)	764 (14.64%)	446 (8.12%)
Missing	133 (3.27%)	259 (5.51%)	0	0	49 (0.94%)	49 (0.89%)
Hypertension						
No	892 (21.92%)	1625 (34.55%)	1553 (36.64%)	1684 (33.27%)	1516 (29.05%)	2104 (38.32%)
Yes	2379 (58.45%)	2284 (48.56%)	2679 (63.20%)	3375 (66.67%)	2974 (56.98%)	2634 (47.98%)
Missing	799 (19.63%)	794 (16.88%)	7 (0.17%)	3 (0.06%)	729 (16.97%)	752 (13.70%)
Cancer						
No	3737 (91.28%)	4074 (86.63%)	4182 (98.66%)	4861 (96.03%)	4999 (95.78%)	5111 (93.10%)
Yes	160 (3.93%)	364 (7.74%)	57 (1.34%)	201 (3.97%)	169 (3.24%)	334 (6.08%)
Missing	173 (4.25%)	265 (5.63%)	0	0	51 (0.98%)	45 (0.82%)
Physical activity (hours/week)						
Mean (S.D.)	15.49 (13.02)	19.59 (15.09)	17.61 (13.53)	21.85 (13.73)	16.68 (12.62)	20.33 (13.30)
Missing	142 (3.49%)	234 (4.98%)	6 (0.14%)	11 (0.22%)	316 (6.05%)	315 (5.74%)
CES-D score						
<16	3268 (80.29%)	3326 (70.72%)	2620 (61.81%)	2513 (49.64%)	4063 (77.85%)	3605 (65.66%)
≥16	537 (13.19%)	1057 (22.48%)	462 (10.90%)	1271 (25.11%)	1043 (19.98%)	1768 (32.20%)
Missing	265 (6.51%)	320 (6.80%)	1157 (27.29%)	1278 (25.25%)	113 (2.17%)	117 (2.13%)
Social networks						
<1/month	320 (7.86%)	156 (3.32%)	855 (20.17%)	816 (16.12%)	1009 (19.33%)	871 (15.87%)
1/month	468 (11.50%)	321 (6.83%)	617 (14.56%)	616 (12.17%)	1082 (20.73%)	926 (16.87%)
2-3/month	776 (19.07%)	690 (14.67%)	389 (9.18%)	435 (8.59%)	1100 (21.08%)	1103 (20.09%)
1/week	1171 (28.77%)	1351 (28.73%)	1176 (27.74%)	1385 (27.36%)	1219 (23.36%)	1430 (26.05%)
>1/week	1310 (32.19%)	2154 (45.80%)	1201 (28.33%)	1810 (35.76%)	800 (15.33%)	1149 (20.93%)
Missing	25 (0.61%)	31 (0.66%)	1 (0.02%)	0	9 (0.17%)	11 (0.20%)

S.D.: standard deviation

Appendix I. Fully-adjusted alcohol consumption and physical limitations among complete cases

Appendix I.1. Odds ratios (95% confidence intervals) of physical limitations by alcohol consumption, complete cases

	Czech Republic		Russia		Poland	
	Men (N=2924)	Women (N=3445)	Men (N=4207)	Women (N=5048)	Men (N=4357)	Women (N=4587)
Average drinking frequency						
0	1.58 (0.99, 2.51)	1.50 (1.12, 1.99)	1.68 (1.26, 2.23)	1.78 (1.47, 2.16)	1.62 (1.28, 2.06)	2.04 (1.66, 2.50)
<1/month	1.17 (0.80, 1.73)	1.20 (0.92, 1.55)	1.34 (1.00, 1.79)	1.05 (0.89, 1.23)	1.37 (1.05, 1.79)	1.55 (1.24, 1.95)
1-3/month	1.00	1.00	1.00	1.00	1.00	1.00
1-4/week[a]	0.84 (0.59, 1.18)	--	1.04 (0.81, 1.33)	--	0.99 (0.77, 1.26)	--
≥5/week[a]	0.71 (0.50, 0.99)	--	0.97 (0.65, 1.44)	--	0.78 (0.55, 1.10)	--
≥1/week[b]	--	0.90 (0.68, 1.20)	--	0.91 (0.69, 1.20)	--	1.01 (0.76, 1.34)
Annual drinking volume (g)						
0	1.44 (0.94, 2.20)	1.25 (0.96, 1.63)	1.29 (0.98, 1.70)	1.41 (1.18, 1.69)	1.34 (1.09, 1.64)	1.37 (1.16, 1.62)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	0.76 (0.54, 1.08)	0.90 (0.66, 1.24)	0.78 (0.59, 1.01)	0.67 (0.57, 0.80)	0.79 (0.61, 1.01)	0.76 (0.58, 0.99)
4001-8000[a] /501-1500[b]	0.61 (0.41, 0.89)	0.74 (0.55, 1.01)	0.67 (0.49, 0.92)	0.63 (0.50, 0.78)	0.52 (0.37, 0.75)	0.58 (0.44, 0.77)
>8000[a] />1500[b]	0.68 (0.50, 0.91)	0.76 (0.58, 1.00)	0.74 (0.56, 0.97)	0.88 (0.67, 1.16)	0.71 (0.51, 0.99)	0.76 (0.56, 1.04)
Average drinking quantity/day						
Non-drinker	1.76 (1.17, 2.64)	1.35 (1.04, 1.75)	1.06 (0.80, 1.41)	1.58 (1.29, 1.94)	1.48 (1.21, 1.80)	1.43 (1.22, 1.69)
Light	1.00	1.00	1.00	1.00	1.00	1.00
Moderate	0.66 (0.42, 1.05)	0.88 (0.70, 1.10)	0.55 (0.41, 0.75)	0.91 (0.76, 1.08)	0.67 (0.46, 0.98)	0.72 (0.58, 0.89)
Heavy	1.05 (0.77, 1.44)	1.05 (0.73, 1.52)	0.58 (0.46, 0.73)	0.76 (0.60, 0.97)	0.88 (0.67, 1.16)	0.83 (0.55, 1.26)
Drinking pattern						
Non-drinker	1.83 (1.18, 2.82)	1.71 (1.20, 2.42)	1.41 (1.03, 1.93)	2.34 (1.59, 3.46)	1.54 (1.20, 1.97)	1.97 (1.47, 2.65)
Irregular light-to-moderate	1.32 (0.97, 1.79)	1.37 (1.00, 1.87)	1.16 (0.87, 1.55)	1.45 (1.01, 2.10)	1.21 (0.95, 1.54)	1.26 (0.93, 1.70)
Regular light-to-moderate	1.00	1.00	1.00	1.00	1.00	1.00
Irregular heavy	0.78 (0.57, 1.07)	0.92 (0.63, 1.35)	0.72 (0.54, 0.96)	0.87 (0.58, 1.32)	0.71 (0.54, 0.93)	1.39 (0.95, 2.03)
Regular heavy	0.98 (0.59, 1.61)	1.12 (0.72, 1.74)	0.75 (0.52, 1.07)	1.63 (1.04, 2.56)	0.93 (0.53, 1.64)	0.74 (0.43, 1.28)
Problem drinking[c]						
No	1.00	--	1.00	--	1.00	--
Yes	0.95 (0.63, 1.42)	--	0.84 (0.65, 1.09)	--	0.98 (0.70, 1.36)	--

[a] Among men, [b] Among women, [c] Among drinkers;
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix I.2. Odds ratios (95% confidence intervals) of physical limitations by past drinking behaviour in the Russian cohort, complete cases

	OR	
	Men (N=4207)	Women (N=5048)
Past drinking behaviour		
Lifetime abstainer	1.37 (0.59, 3.19)	1.35 (1.07, 1.69)
Former drinker, health reasons	2.95 (2.09, 4.16)	3.35 (2.51, 4.47)
Former drinker, non-health reasons	1.24 (0.84, 1.82)	1.80 (1.34, 2.42)
Reduced drinker, health reasons	2.65 (2.06, 3.41)	2.05 (1.65, 2.53)
Reduced drinker, non-health reasons	0.90 (0.69, 1.16)	0.88 (0.73, 1.07)
Continuing drinker	1.00	1.00
Past drinking behaviour combined with drinking pattern		
Lifetime abstainer	1.10 (0.45, 2.69)	2.33 (1.40, 3.87)
Former drinker, health reasons	2.36 (1.51, 3.66)	5.77 (3.37, 9.87)
Former drinker, non-health reasons	0.98 (0.61, 1.58)	3.10 (1.81, 5.33)
Reduced drinker, health reasons	2.12 (1.46, 3.08)	3.50 (2.12, 5.77)
Reduced drinker, non-health reasons	0.72 (0.49, 1.04)	1.52 (0.93, 2.47)
Irregular light-to-moderate drinker	0.97 (0.63, 1.49)	1.90 (1.19, 3.06)
Regular light-to-moderate drinker	1.00	1.00
Irregular heavy drinker	0.63 (0.42, 0.96)	1.09 (0.65, 1.85)
Regular heavy drinker	0.71 (0.44, 1.14)	2.08 (1.19, 3.62)

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problem, BMI and smoking.

Appendix J. Model fit of simple linear growth curve model with fixed and random effects, estimated by FIML

	Czech Republic		Russia		Poland	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Total	4047	4661	4239	5062	5204	5477
Excluded from model	23	42	0	0	15	13
Fixed intercept and slope (H0)						
Log-likelihood	-44744.34	-54850.10	-50809.64	-67572.13	-59721.10	-65334.36
Scaling correction factor	2.73	2.30	2.05	1.36	2.09	1.40
Number of free parameters	7	7	7	7	7	7
Random intercept and slope (H1)						
Log-likelihood	-43697.66	-53581.90	-50322.69	-66832.03	-58943.46	-64553.34
Scaling correction factor	2.72	2.25	1.97[a]	1.27	1.93	1.32
Number of free parameters	10	10	10	10	10	10
Robust chi-square difference test						
H1-H0	775.127***	1187.445***	1516.984***	1405.696***	1003.186***	1370.209***

*** p<0.001

Footnote: Robust chi-square difference test was performed based on log-likelihood and scaling correction factor obtained with MLR estimator. FIML was used to deal with missing data in the PF-10 score over time because *Mplus* does not give information on scaling correction factor when analysing multiply imputed datasets with MLR estimator.

Appendix K. Fully-adjusted alcohol consumption and PF-10 trajectories, imputed data

The full results of drinking indices, problem drinking and past drinking behaviour and their relations to the PF-10 trajectories in the imputed datasets are presented below, after full adjustment for age, marital status, SEP (education, current economic activity, and household amenities), spine/joint problems, BMI and smoking.

Appendix K.1. Fully-adjusted average drinking frequency and PF-10 trajectories, imputed data

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	92.669 (1.233)***	90.330 (1.218)***	91.642 (1.340)***	89.145 (1.284)***	91.026 (1.297)***	92.424 (1.401)***
Variance	174.269 (12.327)***	167.766 (11.245)***	98.921 (14.223)***	135.735 (14.048)***	170.697 (14.217)***	194.456 (14.010)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.119 (0.611)**	-0.336 (0.572)	-0.636 (0.689)	-0.386 (0.738)	-0.212 (0.593)	-0.379 (0.682)
55-59	-3.039 (0.668)***	1.440 (0.810)	-2.139 (0.729)**	2.303 (1.246)	-3.244 (0.724)***	-0.907 (0.858)
60-64	1.478 (0.953)	4.250 (1.080)***	3.466 (1.133)**	2.410 (1.388)	-0.509 (0.862)	-1.160 (1.011)
≥65	0.347 (1.117)	0.477 (1.183)	0.461 (1.207)	-1.918 (1.427)	-3.405 (1.046)**	-5.035 (1.113)***
Average drinking frequency						
0	-5.953 (1.479)***	-4.806 (0.800)***	-4.036 (0.972)***	-7.314 (0.891)***	-4.338 (0.813)***	-4.736 (0.683)***
<1/month	-0.605 (0.879)	-1.183 (0.592)*	-2.239 (0.889)*	-0.813 (0.580)	-1.702 (0.791)*	-2.496 (0.681)***
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	0.515 (0.697)	-0.191 (0.553)	0.650 (0.605)	0.765 (0.904)	-0.364 (0.617)	0.099 (0.810)
≥5/week	1.419 (0.669)*	--	0.654 (0.900)	--	-0.399 (0.765)	--
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.761 (0.562)	1.743 (0.519)**	0.331 (0.636)	-1.139 (0.636)	0.660 (0.643)	-0.506 (0.686)
University	-0.165 (0.639)	2.453 (0.701)***	1.343 (0.630)*	0.493 (0.635)	0.080 (0.647)	0.482 (0.757)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-2.617 (0.969)**	-2.703 (1.065)*	-3.070 (0.863)***	-2.826 (1.183)*	-4.625 (0.948)***	-4.521 (1.173)***
Pensioner, unemployed	-10.996 (0.971)***	-9.176 (0.897)***	-14.653 (1.038)***	-9.983 (1.168)***	-9.152 (0.740)***	-8.194 (0.777)***
Unemployed	-4.391 (1.609)**	-2.237 (1.439)	-3.855 (1.084)***	-4.691 (1.646)**	-1.620 (0.994)	-2.386 (1.246)
Household amenities	0.731 (0.124)***	0.709 (0.127)***	1.047 (0.133)***	0.814 (0.140)***	1.080 (0.137)***	0.577 (0.141)***
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.563 (0.729)	0.479 (0.578)	-0.522 (0.860)	-0.055 (0.588)	0.595 (0.791)	0.706 (0.601)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-5.933 (0.510)***	-6.697 (0.445)***	-3.352 (0.504)***	-5.086 (0.557)***	-5.144 (0.511)***	-8.644 (0.548)***
Yes, hospitalised	-13.465 (0.950)***	-18.758 (0.973)***	-9.623 (1.083)***	-14.656 (1.082)***	-16.848 (1.130)***	-22.234 (1.259)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.703 (0.587)	-1.979 (0.502)***	0.150 (0.564)	-0.700 (0.695)	-0.501 (0.649)	-0.189 (0.663)
≥30	-6.122 (0.735)***	-7.709 (0.671)***	-3.716 (0.725)***	-7.004 (0.717)***	-3.160 (0.808)***	-4.033 (0.759)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-2.030 (0.551)***	-1.565 (0.611)*	-2.033 (0.700)**	-3.864 (1.380)**	-2.538 (0.610)***	-1.341 (0.689)
Current smoking	-2.026 (0.586)**	0.221 (0.526)	-1.660 (0.634)**	0.465 (0.860)	-3.153 (0.629)***	-1.759 (0.628)**
Slope						
Constant	-0.372 (0.209)	-0.325 (0.205)	-0.532 (0.275)	-1.335 (0.276)***	-1.372 (0.249)***	-1.560 (0.274)***
Variance	0.581 (0.216)**	0.345 (0.205)	0.715 (0.330)*	0.701 (0.361)	1.199 (0.302)***	0.887 (0.307)**
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-0.066 (0.111)	0.115 (0.099)	-0.465 (0.150)**	-0.144 (0.149)	-0.202 (0.129)	-0.118 (0.128)
55-59	0.028 (0.113)	-0.116 (0.130)	-0.785 (0.160)***	-0.745 (0.249)**	-0.197 (0.140)	-0.323 (0.157)*
60-64	-0.296 (0.151)	-0.602 (0.165)***	-1.598 (0.229)***	-1.379 (0.281)***	-0.667 (0.164)***	-0.652 (0.178)***
≥65	-0.567 (0.170)**	-0.775 (0.179)***	-2.107 (0.238)***	-1.526 (0.289)***	-0.833 (0.185)***	-0.802 (0.207)***
Average drinking frequency						
0	0.177 (0.205)	-0.037 (0.123)	-0.213 (0.183)	-0.106 (0.165)	0.032 (0.149)	0.053 (0.125)
<1/month	0.083 (0.140)	0.033 (0.090)	0.070 (0.182)	-0.124 (0.115)	0.141 (0.140)	0.140 (0.130)
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	0.168 (0.111)	0.081 (0.088)	-0.006 (0.138)	-0.392 (0.184)*	0.041 (0.122)	-0.058 (0.155)
≥5/week	0.120 (0.111)	--	-0.125 (0.209)	--	-0.133 (0.157)	--
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.182 (0.089)*	0.161 (0.083)	-0.026 (0.136)	0.063 (0.123)	0.239 (0.125)	0.345 (0.116)**
University	0.304 (0.103)**	0.124 (0.115)	0.272 (0.136)*	0.507 (0.128)***	0.496 (0.131)***	0.601 (0.133)***
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.084 (0.166)	0.248 (0.171)	0.111 (0.186)	0.13 (0.246)	-0.300 (0.190)	-0.107 (0.220)
Pensioner, unemployed	0.060 (0.140)	0.174 (0.143)	0.223 (0.203)	0.018 (0.245)	-0.022 (0.142)	-0.167 (0.134)
Unemployed	0.178 (0.273)	0.211 (0.237)	0.031 (0.244)	0.309 (0.314)	-0.007 (0.225)	0.099 (0.247)
Household amenities	-0.009 (0.020)	-0.001 (0.021)	0.052 (0.029)	0.083 (0.028)**	0.058 (0.025)*	0.059 (0.025)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.046 (0.113)	-0.025 (0.087)	-0.116 (0.179)	-0.105 (0.111)	-0.190 (0.143)	-0.079 (0.114)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.003 (0.086)	0.043 (0.079)	-0.253 (0.115)*	-0.285 (0.115)*	-0.019 (0.098)	0.058 (0.104)
Yes, hospitalised	0.102 (0.133)	0.462 (0.137)**	0.081 (0.222)	0.194 (0.199)	0.368 (0.190)	0.657 (0.200)**
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.122 (0.092)	-0.177 (0.083)*	-0.359 (0.123)**	-0.217 (0.133)	-0.265 (0.119)*	-0.366 (0.116)**
≥30	-0.392 (0.118)**	-0.473 (0.100)***	-0.617 (0.156)***	-0.464 (0.136)**	-0.660 (0.155)***	-0.715 (0.141)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.133 (0.092)	0.041 (0.092)	0.131 (0.151)	0.821 (0.245)**	0.019 (0.109)	-0.138 (0.122)
Current smoking	-0.246 (0.099)*	-0.182 (0.098)	-0.699 (0.142)***	-0.383 (0.188)*	-0.363 (0.119)**	-0.221 (0.118)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.2. Fully-adjusted annual drinking volume and PF-10 trajectories, imputed data

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	92.565 (1.165)***	89.002 (1.207)***	89.897 (1.326)***	87.027 (1.283)***	89.886 (1.247)***	89.797 (1.398)***
Variance	174.781 (12.400)***	168.143 (11.257)***	98.458 (14.396)***	132.445 (13.944)***	170.381 (14.191)***	194.524 (14.011)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.105 (0.610)**	-0.328 (0.579)	-0.582 (0.696)	-0.315 (0.742)	-0.247 (0.594)	-0.326 (0.683)
55-59	-3.032 (0.670)***	1.454 (0.814)	-2.026 (0.735)**	2.410 (1.243)	-3.247 (0.724)***	-0.872 (0.860)
60-64	1.501 (0.955)	4.294 (1.080)***	3.569 (1.132)**	2.547 (1.383)	-0.452 (0.862)	-1.128 (1.012)
≥65	0.395 (1.122)	0.494 (1.184)	0.669 (1.208)	-1.690 (1.421)	-3.354 (1.046)**	-4.955 (1.114)***
Annual drinking volume (g)						
0	-5.750 (1.430)***	-3.453 (0.819)***	-2.195 (0.981)*	-5.246 (0.898)***	-3.183 (0.755)***	-2.163 (0.655)**
1-150[a] /1-250[b]	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000[a] /251-500[b]	0.340 (0.688)	1.461 (0.753)	2.009 (0.747)**	2.862 (0.647)***	1.411 (0.605)*	2.829 (0.798)***
4001-8000[a] /501-1500[b]	1.290 (0.698)	1.111 (0.652)	3.581 (0.748)***	3.220 (0.801)***	1.605 (0.762)*	2.972 (0.805)***
>8000[a] />1500[b]	1.087 (0.580)	1.081 (0.601)	2.670 (0.694)***	1.775 (1.002)	0.730 (0.767)	2.598 (0.915)**
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.778 (0.561)	1.800 (0.519)**	0.371 (0.634)	-1.095 (0.634)	0.668 (0.644)	-0.475 (0.686)
University	-0.131 (0.642)	2.529 (0.706)***	1.503 (0.630)*	0.570 (0.636)	0.094 (0.647)	0.552 (0.757)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-2.650 (0.969)**	-2.713 (1.065)*	-3.103 (0.866)***	-2.783 (1.180)*	-4.655 (0.951)***	-4.513 (1.171)***
Pensioner, unemployed	-11.011 (0.972)***	-9.172 (0.896)***	-14.615 (1.032)***	-9.900 (1.162)***	-9.163 (0.739)***	-8.213 (0.777)***
Unemployed	-4.365 (1.612)**	-2.149 (1.443)	-3.957 (1.086)***	-4.712 (1.646)**	-1.695 (0.994)	-2.413 (1.246)
Household amenities	0.737 (0.125)***	0.714 (0.127)***	1.036 (0.133)***	0.811 (0.140)***	1.080 (0.137)***	0.578 (0.141)***
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.558 (0.730)	0.466 (0.578)	-0.602 (0.857)	-0.040 (0.586)	0.570 (0.791)	0.681 (0.601)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-5.932 (0.510)***	-6.685 (0.448)***	-3.371 (0.505)***	-5.171 (0.559)***	-5.120 (0.511)***	-8.591 (0.547)***
Yes, hospitalised	-13.475 (0.951)***	-18.788 (0.972)***	-9.595 (1.076)***	-14.630 (1.077)***	-16.866 (1.130)***	-22.158 (1.260)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.710 (0.588)	-1.977 (0.507)***	0.131 (0.563)	-0.804 (0.697)	-0.484 (0.648)	-0.203 (0.662)
≥30	-6.162 (0.736)***	-7.737 (0.671)***	-3.835 (0.723)***	-7.182 (0.720)***	-3.146 (0.808)***	-4.056 (0.759)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-2.020 (0.552)***	-1.583 (0.612)*	-2.127 (0.701)**	-3.914 (1.374)**	-2.579 (0.614)***	-1.336 (0.690)
Current smoking	-2.053 (0.589)***	0.206 (0.528)	-1.884 (0.642)**	0.242 (0.876)	-3.210 (0.635)***	-1.822 (0.630)**
Slope						
Constant	-0.325 (0.199)	-0.306 (0.208)	-0.504 (0.275)	-1.352 (0.263)***	-1.273 (0.245)***	-1.416 (0.267)***
Variance	0.582 (0.216)**	0.346 (0.205)	0.717 (0.329)*	0.697 (0.360)	1.195 (0.302)***	0.886 (0.307)**
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-0.069 (0.111)	0.115 (0.100)	-0.466 (0.151)**	-0.146 (0.150)	-0.202 (0.129)	-0.121 (0.128)
55-59	0.028 (0.112)	-0.118 (0.131)	-0.790 (0.161)***	-0.748 (0.250)**	-0.201 (0.140)	-0.325 (0.157)*
60-64	-0.296 (0.151)*	-0.605 (0.166)***	-1.602 (0.229)***	-1.389 (0.281)***	-0.676 (0.165)***	-0.655 (0.178)***
≥65	-0.568 (0.169)**	-0.778 (0.179)***	-2.113 (0.239)***	-1.548 (0.289)***	-0.844 (0.185)***	-0.807 (0.207)***
Annual drinking volume (g)						
0	0.130 (0.190)	-0.054 (0.122)	-0.242 (0.182)	-0.079 (0.160)	-0.068 (0.134)	-0.091 (0.123)
1-150[a] /1-250[b]	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000[a] /251-500[b]	0.105 (0.114)	0.022 (0.116)	0.049 (0.153)	-0.127 (0.127)	-0.102 (0.114)	-0.118 (0.155)
4001-8000[a] /501-1500[b]	0.096 (0.115)	-0.006 (0.104)	-0.121 (0.165)	-0.102 (0.156)	-0.150 (0.158)	-0.212 (0.161)
>8000[a] />1500[b]	0.092 (0.099)	0.035 (0.097)	-0.081 (0.157)	-0.286 (0.194)	-0.271 (0.154)	-0.224 (0.175)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.183 (0.089)*	0.165 (0.082)*	-0.027 (0.136)	0.062 (0.123)	0.238 (0.125)	0.344 (0.117)**
University	0.307 (0.103)**	0.127 (0.115)	0.266 (0.136)	0.506 (0.128)***	0.494 (0.131)***	0.598 (0.132)***
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.082 (0.166)	0.251 (0.171)	0.111 (0.186)	0.119 (0.247)	-0.298 (0.190)	-0.110 (0.220)
Pensioner, unemployed	0.061 (0.140)	0.176 (0.143)	0.220 (0.202)	0.005 (0.245)	-0.020 (0.142)	-0.167 (0.134)
Unemployed	0.176 (0.273)	0.212 (0.238)	0.035 (0.244)	0.313 (0.315)	0.005 (0.226)	0.099 (0.247)
Household amenities	-0.008 (0.020)	0 (0.021)	0.052 (0.029)	0.083 (0.028)**	0.058 (0.025)*	0.060 (0.025)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.045 (0.112)	-0.026 (0.087)	-0.114 (0.179)	-0.108 (0.111)	-0.185 (0.143)	-0.078 (0.114)
Spine/joint problems						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes, not hospitalised	0 (0.086)	0.043 (0.080)	-0.253 (0.115)*	-0.279 (0.115)*	-0.021 (0.097)	0.056 (0.104)
Yes, hospitalised	0.102 (0.133)	0.463 (0.136)**	0.081 (0.221)	0.202 (0.199)	0.366 (0.189)	0.652 (0.200)**
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.125 (0.092)	-0.178 (0.083)*	-0.353 (0.123)**	-0.211 (0.134)	-0.266 (0.119)*	-0.364 (0.116)**
≥30	-0.395 (0.118)**	-0.475 (0.101)***	-0.609 (0.156)***	-0.457 (0.137)**	-0.658 (0.155)***	-0.714 (0.141)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.136 (0.093)	0.042 (0.092)	0.130 (0.151)	0.830 (0.247)**	0.027 (0.109)	-0.136 (0.122)
Current smoking	-0.249 (0.099)*	-0.181 (0.098)	-0.694 (0.145)***	-0.359 (0.190)	-0.350 (0.121)**	-0.215 (0.118)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.3. Fully-adjusted drinking quantity per drinking day and PF-10 trajectories, imputed data

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	93.036 (1.151)***	89.643 (1.203)***	89.384 (1.367)***	87.276 (1.362)***	90.024 (1.240)***	90.182 (1.385)***
Variance	175.031 (12.399)***	168.153 (11.196)***	98.257 (14.217)***	134.918 (14.015)***	170.875 (14.194)***	195.315 (14.014)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.111 (0.615)**	-0.405 (0.573)	-0.694 (0.702)	-0.333 (0.739)	-0.224 (0.593)	-0.370 (0.682)
55-59	-3.069 (0.669)***	1.365 (0.810)	-2.177 (0.737)**	2.417 (1.244)	-3.194 (0.725)***	-0.808 (0.862)
60-64	1.440 (0.956)	4.215 (1.080)***	3.418 (1.134)**	2.483 (1.386)	-0.413 (0.862)	-1.054 (1.013)
≥65	0.320 (1.121)	0.372 (1.180)	0.404 (1.201)	-1.890 (1.423)	-3.332 (1.045)**	-4.899 (1.117)***
Average drinking quantity/day						
Non-drinker	-6.305 (1.396)***	-4.108 (0.810)***	-1.843 (1.005)	-5.539 (0.975)***	-3.350 (0.726)***	-2.623 (0.635)***
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	0.909 (0.737)	0.311 (0.505)	2.967 (0.730)***	1.561 (0.694)*	2.007 (0.800)*	2.236 (0.635)***
Heavy	0.052 (0.651)	0.046 (0.755)	2.996 (0.657)***	2.570 (0.914)**	1.650 (0.715)*	2.382 (1.118)*
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.777 (0.564)	1.792 (0.518)**	0.357 (0.634)	-1.169 (0.635)	0.661 (0.643)	-0.431 (0.687)
University	-0.141 (0.642)	2.564 (0.700)***	1.558 (0.632)*	0.587 (0.635)	0.149 (0.648)	0.723 (0.757)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-2.588 (0.970)**	-2.748 (1.066)*	-3.081 (0.867)***	-2.805 (1.183)*	-4.669 (0.949)***	-4.585 (1.167)***
Pensioner, unemployed	-11.020 (0.973)***	-9.217 (0.899)***	-14.623 (1.032)***	-9.946 (1.166)***	-9.210 (0.738)***	-8.304 (0.779)***
Unemployed	-4.288 (1.610)**	-2.204 (1.438)	-3.782 (1.085)***	-4.803 (1.649)**	-1.714 (0.995)	-2.466 (1.251)*
Household amenities	0.744 (0.124)***	0.723 (0.127)***	1.089 (0.133)***	0.847 (0.139)***	1.091 (0.137)***	0.602 (0.141)***
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.579 (0.730)	0.479 (0.579)	-0.468 (0.857)	-0.145 (0.588)	0.553 (0.791)	0.694 (0.602)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-5.949 (0.510)***	-6.676 (0.444)***	-3.418 (0.506)***	-5.123 (0.556)***	-5.128 (0.512)***	-8.641 (0.548)***
Yes, hospitalised	-13.466 (0.954)***	-18.798 (0.976)***	-9.676 (1.074)***	-14.593 (1.081)***	-16.917 (1.128)***	-22.150 (1.265)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.727 (0.588)	-1.976 (0.505)***	0.017 (0.564)	-0.736 (0.694)	-0.507 (0.647)	-0.331 (0.663)
≥30	-6.223 (0.741)***	-7.767 (0.670)***	-3.994 (0.728)***	-7.149 (0.720)***	-3.174 (0.805)***	-4.184 (0.756)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-1.939 (0.551)***	-1.547 (0.613)*	-2.011 (0.696)**	-3.904 (1.376)**	-2.601 (0.611)***	-1.227 (0.690)
Current smoking	-1.975 (0.589)**	0.247 (0.528)	-1.807 (0.633)**	0.286 (0.870)	-3.233 (0.629)***	-1.775 (0.630)**
Slope						
Constant	-0.237 (0.196)	-0.294 (0.208)	-0.392 (0.281)	-1.347 (0.277)***	-1.299 (0.246)***	-1.384 (0.264)***
Variance	0.580 (0.215)**	0.349 (0.204)	0.719 (0.325)*	0.713 (0.360)*	1.204 (0.302)***	0.887 (0.307)**
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-0.073 (0.111)	0.112 (0.099)	-0.459 (0.151)**	-0.146 (0.149)	-0.199 (0.128)	-0.123 (0.128)
55-59	0.016 (0.113)	-0.122 (0.130)	-0.785 (0.161)***	-0.750 (0.249)**	-0.199 (0.140)	-0.338 (0.157)*
60-64	-0.308 (0.151)*	-0.609 (0.165)***	-1.589 (0.230)***	-1.385 (0.280)***	-0.672 (0.164)***	-0.669 (0.178)***
≥65	-0.591 (0.170)***	-0.783 (0.179)***	-2.106 (0.237)***	-1.539 (0.288)***	-0.837 (0.184)***	-0.821 (0.207)***
Average drinking quantity/day						
Non-drinker	0.039 (0.185)	-0.062 (0.115)	-0.361 (0.190)	-0.081 (0.177)	-0.037 (0.128)	-0.110 (0.117)
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	-0.213 (0.130)	0.005 (0.078)	-0.220 (0.160)	-0.121 (0.135)	-0.185 (0.165)	-0.249 (0.116)*
Heavy	-0.051 (0.100)	-0.017 (0.134)	-0.203 (0.140)	-0.063 (0.188)	-0.167 (0.134)	-0.293 (0.236)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.179 (0.089)*	0.164 (0.083)*	-0.026 (0.136)	0.063 (0.123)	0.239 (0.125)	0.339 (0.117)**
University	0.299 (0.103)**	0.128 (0.115)	0.258 (0.137)	0.506 (0.128)***	0.491 (0.132)***	0.581 (0.132)***
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.090 (0.166)	0.251 (0.171)	0.106 (0.187)	0.130 (0.247)	-0.295 (0.190)	-0.097 (0.220)
Pensioner, unemployed	0.057 (0.141)	0.176 (0.143)	0.212 (0.203)	0.015 (0.246)	-0.015 (0.142)	-0.158 (0.134)
Unemployed	0.179 (0.273)	0.213 (0.238)	0.026 (0.244)	0.303 (0.315)	-0.009 (0.226)	0.106 (0.247)
Household amenities	-0.007 (0.020)	0 (0.021)	0.050 (0.029)	0.080 (0.028)**	0.057 (0.025)*	0.058 (0.025)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.050 (0.112)	-0.026 (0.087)	-0.121 (0.179)	-0.107 (0.111)	-0.188 (0.143)	-0.079 (0.114)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.004 (0.086)	0.043 (0.079)	-0.248 (0.115)*	-0.276 (0.115)*	-0.016 (0.098)	0.058 (0.104)
Yes, hospitalised	0.097 (0.133)	0.463 (0.137)**	0.086 (0.221)	0.205 (0.198)	0.381 (0.190)*	0.647 (0.199)**
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.118 (0.092)	-0.178 (0.083)*	-0.347 (0.123)**	-0.216 (0.133)	-0.267 (0.119)*	-0.354 (0.115)**
≥30	-0.387 (0.118)**	-0.475 (0.101)***	-0.591 (0.157)***	-0.461 (0.137)**	-0.660 (0.156)***	-0.704 (0.141)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.131 (0.092)	0.045 (0.092)	0.137 (0.149)	0.803 (0.245)**	0.021 (0.108)	-0.145 (0.121)
Current smoking	-0.229 (0.100)*	-0.178 (0.097)	-0.681 (0.142)***	-0.396 (0.193)*	-0.363 (0.119)**	-0.213 (0.118)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.4. Fully-adjusted drinking pattern and PF-10 trajectories, imputed data

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	93.238 (1.219)***	89.858 (1.338)***	91.885 (1.383)***	90.477 (1.660)***	89.898 (1.302)***	93.061 (1.580)***
Variance	174.176 (12.388)***	167.875 (11.221)***	98.298 (14.328)***	133.702 (14.045)***	169.025 (14.214)***	195.239 (14.035)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.076 (0.614)**	-0.245 (0.575)	-0.581 (0.695)	-0.280 (0.738)	-0.200 (0.594)	-0.457 (0.683)
55-59	-2.956 (0.669)***	1.534 (0.814)	-2.020 (0.735)**	2.398 (1.250)	-3.128 (0.724)***	-0.953 (0.860)
60-64	1.576 (0.959)	4.411 (1.083)***	3.514 (1.132)**	2.487 (1.390)	-0.316 (0.862)	-1.235 (1.015)
≥65	0.574 (1.125)	0.663 (1.187)	0.649 (1.203)	-1.788 (1.428)	-3.149 (1.049)**	-5.075 (1.117)***
Drinking pattern						
Non-drinker	-6.427 (1.415)***	-4.455 (0.931)***	-4.310 (1.014)***	-8.667 (1.341)***	-3.235 (0.810)***	-5.298 (0.954)***
Irregular light-to-moderate	-1.106 (0.669)	-0.796 (0.707)	-2.737 (0.805)**	-2.323 (1.135)*	-0.314 (0.662)	-2.185 (0.917)*
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	0.821 (0.579)	1.197 (0.754)	1.030 (0.693)	0.372 (1.252)	2.242 (0.629)***	-1.736 (1.104)
Regular heavy	-0.120 (0.970)	0.167 (0.848)	0.506 (0.827)	-1.741 (1.435)	0.998 (1.323)	0.542 (1.386)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.759 (0.562)	1.741 (0.517)**	0.388 (0.634)	-1.132 (0.635)	0.721 (0.643)	-0.499 (0.686)
University	-0.185 (0.641)	2.479 (0.698)***	1.565 (0.630)*	0.590 (0.635)	0.229 (0.648)	0.564 (0.756)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-2.545 (0.967)**	-2.640 (1.063)*	-3.080 (0.865)***	-2.826 (1.188)*	-4.631 (0.947)***	-4.453 (1.172)***
Pensioner, unemployed	-10.936 (0.970)***	-9.076 (0.897)***	-14.586 (1.034)***	-10.008 (1.172)***	-9.156 (0.738)***	-8.255 (0.778)***
Unemployed	-4.357 (1.608)**	-2.126 (1.434)	-3.925 (1.082)***	-4.692 (1.644)**	-1.780 (0.992)	-2.405 (1.248)
Household amenities	0.723 (0.125)***	0.705 (0.126)***	1.054 (0.133)***	0.823 (0.140)***	1.072 (0.137)***	0.588 (0.141)***
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.586 (0.730)	0.446 (0.576)	-0.540 (0.855)	-0.147 (0.588)	0.593 (0.791)	0.674 (0.602)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-5.962 (0.510)***	-6.672 (0.444)***	-3.318 (0.504)***	-5.072 (0.557)***	-5.078 (0.511)***	-8.672 (0.548)***
Yes, hospitalised	-13.448 (0.950)***	-18.809 (0.974)***	-9.587 (1.080)***	-14.538 (1.080)***	-16.912 (1.128)***	-22.228 (1.261)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.769 (0.588)	-1.997 (0.502)***	0.166 (0.563)	-0.776 (0.694)	-0.518 (0.647)	-0.230 (0.663)
≥30	-6.242 (0.739)***	-7.748 (0.670)***	-3.923 (0.725)***	-7.143 (0.718)***	-3.209 (0.806)***	-4.103 (0.757)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-2.057 (0.551)***	-1.623 (0.611)**	-2.146 (0.699)**	-4.038 (1.375)**	-2.703 (0.613)***	-1.266 (0.689)
Current smoking	-2.079 (0.591)***	0.160 (0.529)	-1.942 (0.645)**	0.283 (0.880)	-3.337 (0.632)***	-1.789 (0.632)**
Slope						
Constant	-0.137 (0.208)	-0.161 (0.225)	-0.589 (0.296)*	-1.859 (0.342)***	-1.239 (0.268)***	-1.559 (0.303)***
Variance	0.580 (0.215)**	0.345 (0.205)	0.710 (0.334)*	0.695 (0.362)	1.183 (0.303)***	0.886 (0.306)**
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-0.070 (0.111)	0.110 (0.100)	-0.460 (0.150)**	-0.145 (0.149)	-0.205 (0.128)	-0.119 (0.128)
55-59	0.014 (0.112)	-0.128 (0.130)	-0.787 (0.160)***	-0.741 (0.249)**	-0.213 (0.140)	-0.326 (0.158)*
60-64	-0.311 (0.151)*	-0.615 (0.166)***	-1.589 (0.228)***	-1.382 (0.281)***	-0.692 (0.165)***	-0.657 (0.179)***
≥65	-0.586 (0.170)**	-0.789 (0.180)***	-2.108 (0.236)***	-1.540 (0.288)***	-0.868 (0.186)***	-0.808 (0.208)***
Drinking pattern						
Non-drinker	-0.048 (0.195)	-0.194 (0.143)	-0.168 (0.212)	0.419 (0.257)	-0.086 (0.149)	0.056 (0.186)
Irregular light-to-moderate	-0.196 (0.115)	-0.143 (0.109)	0.139 (0.175)	0.446 (0.229)	-0.007 (0.131)	0.107 (0.175)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	-0.097 (0.095)	-0.133 (0.119)	0.042 (0.171)	0.458 (0.248)	-0.218 (0.139)	-0.058 (0.211)
Regular heavy	-0.318 (0.180)	-0.177 (0.147)	-0.075 (0.210)	0.241 (0.298)	-0.639 (0.281)*	-0.187 (0.290)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.180 (0.089)*	0.161 (0.083)	-0.025 (0.137)	0.064 (0.123)	0.237 (0.125)	0.344 (0.117)**
University	0.297 (0.103)**	0.126 (0.115)	0.265 (0.136)	0.510 (0.128)***	0.485 (0.131)***	0.592 (0.132)***
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.087 (0.166)	0.244 (0.171)	0.104 (0.186)	0.126 (0.247)	-0.307 (0.190)	-0.112 (0.220)
Pensioner, unemployed	0.050 (0.141)	0.174 (0.143)	0.215 (0.203)	0.010 (0.246)	-0.019 (0.142)	-0.166 (0.134)
Unemployed	0.169 (0.273)	0.215 (0.237)	0.042 (0.244)	0.309 (0.315)	0.005 (0.224)	0.095 (0.247)
Household amenities	-0.010 (0.020)	0 (0.021)	0.053 (0.029)	0.085 (0.028)**	0.057 (0.025)*	0.058 (0.025)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.055 (0.112)	-0.024 (0.087)	-0.116 (0.179)	-0.110 (0.111)	-0.185 (0.143)	-0.079 (0.114)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.005 (0.086)	0.042 (0.079)	-0.253 (0.115)*	-0.283 (0.115)**	-0.028 (0.097)	0.058 (0.104)
Yes, hospitalised	0.096 (0.133)	0.463 (0.137)***	0.084 (0.221)	0.196 (0.198)	0.367 (0.189)	0.655 (0.200)**
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-0.119 (0.091)	-0.176 (0.083)*	-0.358 (0.123)**	-0.217 (0.133)	-0.262 (0.119)*	-0.360 (0.115)**
≥30	-0.385 (0.118)**	-0.471 (0.101)***	-0.607 (0.157)***	-0.464 (0.136)**	-0.652 (0.155)***	-0.709 (0.141)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.127 (0.092)	0.044 (0.092)	0.138 (0.151)	0.830 (0.246)**	0.036 (0.108)	-0.139 (0.122)
Current smoking	-0.232 (0.099)*	-0.173 (0.098)	-0.684 (0.145)***	-0.372 (0.193)	-0.334 (0.120)**	-0.211 (0.118)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.5. Fully-adjusted problem drinking and PF-10 trajectories, imputed data

	Czech (mean, S.E.)	Russia (mean, S.E.)	Poland (mean, S.E.)
	Men	Men	Men
Intercept			
Constant	93.024 (1.134)***	91.072 (1.325)***	91.545 (1.279)***
Variance	161.715 (12.044)***	91.474 (14.634)***	129.336 (14.725)***
Age			
45-49	Ref.	Ref.	Ref.
50-54	-2.151 (0.609)***	-0.544 (0.723)	-0.508 (0.605)
55-59	-3.375 (0.672)***	-1.348 (0.745)	-3.589 (0.736)***
60-64	1.437 (0.946)	3.395 (1.143)**	-1.225 (0.896)
≥65	0.441 (1.131)	0.204 (1.220)	-2.846 (1.094)**
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.664 (0.857)	1.270 (0.602)*	-0.937 (0.863)
Education			
<secondary	Ref	Ref	Ref
Secondary	1.049 (0.563)	0.254 (0.656)	0.902 (0.665)
University	0.526 (0.609)	1.421 (0.643)*	-0.207 (0.682)
Current economic activity			
Working	Ref.	Ref.	Ref.
Pensioner, employed	-2.640 (0.955)**	-3.015 (0.877)**	-5.134 (1.032)***
Pensioner, unemployed	-10.798 (1.000)***	-13.181 (1.047)***	-9.002 (0.803)***
Unemployed	-4.538 (1.625)**	-3.577 (1.132)**	-1.565 (1.039)
Household amenities	0.676 (0.126)***	1.051 (0.138)***	0.922 (0.142)***
Marital status			
Married/cohabiting	Ref.	Ref.	Ref.
Single/divorced/widowed	0.775 (0.731)	-0.791 (0.905)	0.526 (0.841)
Spine/joint problems			
No	Ref.	Ref.	Ref.
Yes, not hospitalised	-5.466 (0.496)***	-3.473 (0.515)***	-5.104 (0.516)***
Yes, hospitalised	-12.839 (0.977)***	-9.668 (1.114)***	-15.118 (1.218)***
BMI			
<25	Ref.	Ref.	Ref.
25.0-29.9	-0.643 (0.579)	0.152 (0.578)	-0.704 (0.665)
≥30	-5.755 (0.735)***	-3.761 (0.751)***	-3.364 (0.833)***
Smoking			
Never	Ref.	Ref.	Ref.
Former smoking	-2.159 (0.545)***	-2.044 (0.696)**	-1.731 (0.618)**
Current smoking	-1.827 (0.570)**	-1.979 (0.623)**	-3.029 (0.645)***
Slope			
Constant	-0.276 (0.203)	-0.512 (0.283)	-1.459 (0.259)***
Variance	0.631 (0.215)**	0.697 (0.333)*	0.958 (0.313)**
Age			
45-49	Ref.	Ref.	Ref.
50-54	-0.076 (0.113)	-0.494 (0.163)**	-0.137 (0.136)
55-59	0.024 (0.115)	-0.873 (0.170)***	-0.141 (0.145)
60-64	-0.301 (0.152)*	-1.604 (0.238)***	-0.663 (0.173)***
≥65	-0.595 (0.172)**	-2.127 (0.250)***	-0.954 (0.199)***
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.105 (0.135)	-0.052 (0.156)	-0.170 (0.199)
Education			
<secondary	Ref	Ref	Ref
Secondary	0.168 (0.089)	0.012 (0.145)	0.179 (0.137)
University	0.287 (0.104)**	0.344 (0.141)*	0.518 (0.139)***
Current economic activity			
Working	Ref.	Ref.	Ref.
Pensioner, employed	-0.084 (0.171)	0.121 (0.195)	-0.193 (0.206)
Pensioner, unemployed	0.054 (0.149)	0.185 (0.214)	0.023 (0.155)
Unemployed	0.171 (0.275)	0.023 (0.265)	0.042 (0.236)
Household amenities	-0.005 (0.021)	0.042 (0.030)	0.072 (0.027)**
Marital status			
Married/cohabiting	Ref.	Ref.	Ref.
Single/divorced/widowed	0.047 (0.113)	-0.146 (0.192)	-0.222 (0.159)
Spine/joint problems			
No	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.030 (0.085)	-0.209 (0.121)	0 (0.103)
Yes, hospitalised	0.089 (0.139)	0.063 (0.234)	0.237 (0.210)
BMI			
<25	Ref.	Ref.	Ref.
25.0-29.9	-0.128 (0.093)	-0.296 (0.132)*	-0.237 (0.127)
≥30	-0.394 (0.120)**	-0.588 (0.165)***	-0.688 (0.161)***
Smoking			
Never	Ref.	Ref.	Ref.
Former smoking	-0.085 (0.093)	0.099 (0.156)	-0.001 (0.117)
Current smoking	-0.208 (0.099)*	-0.665 (0.147)***	-0.326 (0.127)*

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.6. Fully-adjusted past drinking behaviour and PF-10 trajectories in the Russian cohort, imputed data

	Russia	
	Men (mean, S.E.)	Women (mean, S.E.)
Intercept		
Constant	92.131 (1.293)***	88.589 (1.235)***
Variance	87.267 (13.341)***	128.727 (13.847)***
Age		
45-49	Ref.	Ref.
50-54	-0.353 (0.724)	-0.410 (0.735)
55-59	-2.034 (0.747)**	2.244 (1.239)
60-64	2.912 (1.117)**	2.230 (1.379)
≥65	-0.037 (1.172)	-2.334 (1.415)
Former drinking		
Lifetime abstainer	-4.554 (2.845)	-4.735 (1.130)***
Former drinker, health reasons	-11.452 (1.534)***	-12.802 (1.508)***
Former drinker, non-health reasons	-0.652 (0.949)	-6.198 (1.511)***
Reduced drinker, health reasons	-7.840 (0.834)***	-5.610 (0.937)***
Reduced drinker, non-health reasons	0.386 (0.577)	1.083 (0.685)
Continuing drinker	Ref.	Ref.
Education		
<secondary	Ref.	Ref.
Secondary	0.317 (0.619)	-1.045 (0.631)
University	1.296 (0.621)*	0.399 (0.631)
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	-2.436 (0.870)**	-2.577 (1.175)*
Pensioner, unemployed	-13.251 (1.009)***	-9.668 (1.161)***
Unemployed	-3.639 (1.082)**	-4.820 (1.640)**
Household amenities	1.022 (0.130)***	0.873 (0.140)***
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.750 (0.835)	-0.194 (0.583)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-3.203 (0.503)***	-5.077 (0.552)***
Yes, hospitalised	-9.689 (1.045)***	-13.996 (1.082)***
BMI		
<25	Ref.	Ref.
25.0-29.9	0.171 (0.553)	-0.639 (0.686)
≥30	-3.476 (0.710)***	-6.793 (0.710)***
Smoking		
Never	Ref.	Ref.
Former smoking	-1.329 (0.687)	-3.151 (1.382)*
Current smoking	-1.563 (0.614)*	0.856 (0.847)
Slope		
Constant	-0.569 (0.271)*	-1.447 (0.260)***
Variance	0.713 (0.320)*	0.690 (0.354)
Age		
45-49	Ref.	Ref.
50-54	-0.470 (0.156)**	-0.147 (0.149)
55-59	-0.787 (0.164)***	-0.749 (0.250)**
60-64	-1.586 (0.231)***	-1.385 (0.281)***
≥65	-2.100 (0.237)***	-1.536 (0.289)***
Former drinking		
Lifetime abstainer	0.012 (0.538)	-0.020 (0.206)
Former drinker, health reasons	-0.005 (0.275)	0.110 (0.248)
Former drinker, non-health reasons	-0.285 (0.215)	0.175 (0.257)
Reduced drinker, health reasons	0.171 (0.177)	0.322 (0.178)
Reduced drinker, non-health reasons	0.121 (0.125)	0.126 (0.128)
Continuing drinker	Ref.	Ref.
Education		
<secondary	Ref.	Ref.
Secondary	-0.033 (0.135)	0.054 (0.123)
University	0.267 (0.136)	0.507 (0.128)***
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	0.093 (0.187)	0.113 (0.248)
Pensioner, unemployed	0.188 (0.204)	-0.004 (0.247)
Unemployed	0.021 (0.246)	0.298 (0.314)
Household amenities	0.051 (0.028)	0.077 (0.028)**
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.119 (0.177)	-0.112 (0.111)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-0.253 (0.115)*	-0.272 (0.115)*
Yes, hospitalised	0.082 (0.218)	0.186 (0.199)
BMI		
<25	Ref	Ref
25.0-29.9	-0.355 (0.122)**	-0.218 (0.133)
≥30	-0.613 (0.155)***	-0.473 (0.136)**
Smoking		
Never	Ref	Ref
Former smoking	0.110 (0.150)	0.745 (0.245)**
Current smoking	-0.705 (0.141)***	-0.414 (0.187)*

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix K.7. Fully-adjusted past drinking behaviour combined with drinking pattern and PF-10 trajectories in the Russian cohort, imputed data

	Russia	
	Men (mean, S.E.)	Women (mean, S.E.)
Intercept		
Constant	92.910 (1.463)***	88.561 (1.612)***
Variance	87.152 (13.219)***	126.330 (13.861)***
Age		
45-49	Ref.	Ref.
50-54	-0.333 (0.721)	-0.306 (0.740)
55-59	-1.929 (0.744)*	2.268 (1.241)
60-64	2.993 (1.113)**	2.253 (1.379)
≥65	0.125 (1.171)	-2.206 (1.415)
Former drinking		
Lifetime abstainer	-5.294 (2.922)	-4.738 (1.531)**
Former drinker, health reasons	-12.120 (1.665)***	-12.797 (1.815)***
Former drinker, non-health reasons	-1.271 (1.133)	-6.182 (1.813)**
Reduced drinker, health reasons	-8.515 (1.052)***	-5.546 (1.366)***
Reduced drinker, non-health reasons	-0.281 (0.869)	1.142 (1.222)
Irregular light-to-moderate drinker	-2.182 (1.045)*	-0.663 (1.145)
Regular light-to-moderate drinker	Ref.	Ref.
Irregular heavy drinker	-0.786 (1.009)	2.611 (1.610)
Regular heavy drinker	0.012 (0.878)	2.265 (1.282)
Education		
<secondary	Ref.	Ref.
Secondary	0.320 (0.620)	-1.015 (0.630)
University	1.381 (0.622)*	0.455 (0.632)
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	-2.428 (0.868)**	-2.499 (1.178)*
Pensioner, unemployed	-13.224 (1.007)***	-9.567 (1.161)***
Unemployed	-3.681 (1.080)**	-4.781 (1.642)**
Household amenities	1.016 (0.130)***	0.853 (0.140)***
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.793 (0.832)	-0.264 (0.583)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-3.180 (0.503)***	-5.029 (0.553)***
Yes, hospitalised	-9.625 (1.042)***	-13.914 (1.076)***
BMI		
<25	Ref.	Ref.
25.0-29.9	0.155 (0.552)	-0.674 (0.687)
≥30	-3.574 (0.712)***	-6.868 (0.711)***
Smoking		
Never	Ref.	Ref.
Former smoking	-1.534 (0.692)*	-3.389 (1.380)*
Current smoking	-1.825 (0.627)**	0.665 (0.870)
Slope		
Constant	-0.770 (0.326)*	-1.609 (0.343)***
Variance	0.714 (0.316)*	0.680 (0.356)
Age		
45-49	Ref.	Ref.
50-54	-0.470 (0.155)**	-0.150 (0.150)
55-59	-0.792 (0.163)***	-0.747 (0.250)**
60-64	-1.590 (0.230)***	-1.386 (0.281)***
≥65	-2.110 (0.238)***	-1.540 (0.289)***
Former drinking		
Lifetime abstainer	0.206 (0.563)	0.139 (0.306)
Former drinker, health reasons	0.182 (0.329)	0.268 (0.329)
Former drinker, non-health reasons	-0.103 (0.265)	0.332 (0.341)
Reduced drinker, health reasons	0.359 (0.243)	0.475 (0.278)
Reduced drinker, non-health reasons	0.308 (0.213)	0.280 (0.253)
Irregular light-to-moderate drinker	0.290 (0.235)	0.191 (0.237)
Regular light-to-moderate drinker	Ref.	Ref.
Irregular heavy drinker	0.242 (0.246)	-0.114 (0.345)
Regular heavy drinker	0.189 (0.219)	0.167 (0.273)
Education		
<secondary	Ref.	Ref.
Secondary	-0.029 (0.136)	0.056 (0.123)
University	0.262 (0.136)	0.508 (0.128)***
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	0.092 (0.187)	0.106 (0.248)
Pensioner, unemployed	0.186 (0.205)	-0.011 (0.247)
Unemployed	0.034 (0.244)	0.307 (0.315)
Household amenities	0.051 (0.028)	0.079 (0.028)**
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.115 (0.177)	-0.110 (0.111)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-0.256 (0.116)*	-0.277 (0.115)*
Yes, hospitalised	0.077 (0.218)	0.182 (0.199)
BMI		
<25	Ref.	Ref.
25.0-29.9	-0.354 (0.122)**	-0.218 (0.133)
≥30	-0.605 (0.157)***	-0.472 (0.136)**
Smoking		
Never	Ref	Ref
Former smoking	0.129 (0.151)	0.762 (0.246)**
Current smoking	-0.680 (0.144)***	-0.395 (0.191)*

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L. Fully-adjusted alcohol consumption and PF-10 trajectories among complete cases

The full results of drinking indices, problem drinking and past drinking behaviour and their relations to the PF-10 trajectories among complete cases are provided below, after full adjustment for age, marital status, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.1. Fully-adjusted average drinking frequency and PF-10 trajectories, complete cases

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	94.726 (1.585)***	91.011 (1.661)***	93.535 (1.802)***	88.362 (1.733)***	93.847 (1.989)***	93.746 (2.418)***
Variance	104.696 (17.866)***	133.261 (14.316)***	63.640 (18.226)***	145.209 (17.416)***	133.986 (19.714)***	177.718 (20.441)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.886 (0.920)**	-0.288 (0.863)	-0.592 (0.978)	0.042 (0.989)	-0.516 (0.959)	-0.136 (1.181)
55-59	-2.519 (0.840)**	2.061 (1.243)	-0.534 (0.965)	2.477 (1.867)	-3.379 (1.129)**	-1.138 (1.428)
60-64	-0.020 (1.250)	3.851 (1.626)*	2.585 (1.408)	3.288 (2.065)	0.688 (1.198)	-1.810 (1.639)
≥65	-1.316 (1.519)	3.134 (1.742)	0.589 (1.531)	-1.169 (2.148)	-0.847 (1.508)	-5.001 (1.936)*
Average drinking frequency						
0	-1.872 (2.221)	-3.723 (1.345)**	-3.195 (1.401)*	-6.064 (1.271)***	-2.558 (1.296)*	-5.463 (1.097)***
<1/month	-1.302 (1.293)	-0.117 (0.803)	0.055 (1.033)	-1.152 (0.770)	-1.127 (1.221)	-3.257 (1.131)**
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	0.179 (0.968)	-0.149 (0.762)	-0.736 (0.823)	0.292 (1.252)	-1.591 (0.940)	-0.160 (1.134)
≥5/week	1.045 (0.921)	--	0.723 (1.084)	--	0.011 (1.124)	--
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	1.931 (0.766)*	1.221 (0.767)	-0.297 (0.902)	-0.702 (0.901)	-0.985 (1.095)	-0.887 (1.337)
University	1.825 (0.826)*	2.857 (0.883)**	0.385 (0.836)	0.785 (0.848)	-1.521 (1.067)	0.708 (1.355)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-1.639 (1.288)	-2.820 (1.460)	-1.904 (1.038)	-2.048 (1.773)	-5.992 (1.475)***	-3.105 (1.743)
Pensioner, unemployed	-6.646 (1.340)***	-8.777 (1.336)***	-9.549 (1.372)***	-7.805 (1.804)***	-7.532 (1.151)***	-3.782 (1.289)**
Unemployed	-4.082 (2.208)	-4.089 (2.586)	-2.660 (1.985)	-0.894 (2.270)	-4.846 (2.739)	-4.147 (2.929)
Household amenities	0.274 (0.162)	0.488 (0.171)**	0.787 (0.178)***	0.763 (0.193)***	0.894 (0.201)***	0.429 (0.232)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	1.200 (0.926)	1.222 (0.815)	-0.460 (1.297)	-0.070 (0.803)	0.371 (1.487)	-0.205 (0.999)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-4.932 (0.639)***	-6.445 (0.602)***	-3.014 (0.625)***	-4.933 (0.763)***	-5.776 (0.752)***	-8.446 (0.840)***
Yes, hospitalised	-10.135 (1.275)***	-15.976 (1.421)***	-7.514 (1.574)***	-15.229 (1.461)***	-14.534 (1.689)***	-20.751 (2.283)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-1.261 (0.707)	-1.432 (0.670)*	-0.580 (0.735)	0.325 (0.939)	-0.893 (0.863)	-0.389 (0.947)
≥30	-4.966 (1.005)***	-6.785 (0.923)***	-3.390 (1.013)**	-6.807 (0.978)***	-3.682 (1.131)**	-4.168 (1.160)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-1.537 (0.756)*	-1.576 (0.865)	-2.004 (0.925)*	0.420 (1.813)	-0.877 (0.889)	-1.348 (1.099)
Current smoking	-0.016 (0.744)	0.848 (0.721)	0.098 (0.787)	1.095 (1.340)	-1.123 (1.050)	-2.052 (1.086)
Slope						
Constant	-0.304 (0.278)	-0.380 (0.224)	-0.307 (0.354)	-1.516 (0.306)***	-1.616 (0.357)***	-1.827 (0.368)***
Variance	0.739 (0.275)**	0.191 (0.257)	1.259 (0.428)**	0.743 (0.387)	1.221 (0.355)**	0.285 (0.326)
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	0.052 (0.155)	0.235 (0.114)*	-0.333 (0.195)	-0.020 (0.177)	-0.187 (0.189)	0.145 (0.182)
55-59	0.070 (0.147)	0.125 (0.171)	-0.666 (0.200)**	-0.546 (0.327)	0.155 (0.194)	-0.404 (0.215)
60-64	-0.134 (0.198)	-0.299 (0.218)	-1.275 (0.278)***	-1.077 (0.360)**	-0.708 (0.226)**	-0.547 (0.248)*
≥65	-0.482 (0.223)*	-0.708 (0.242)**	-1.949 (0.294)***	-1.345 (0.364)***	-0.897 (0.261)**	-0.663 (0.282)*
Average drinking frequency						
0	-0.051 (0.328)	0.034 (0.180)	-0.359 (0.258)	0.009 (0.208)	0.030 (0.223)	0.200 (0.175)
<1/month	-0.019 (0.182)	-0.019 (0.116)	-0.158 (0.239)	-0.056 (0.139)	-0.025 (0.210)	0.158 (0.182)
1-3/month	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1-4/week	0.053 (0.156)	0.164 (0.107)	0.050 (0.174)	-0.117 (0.219)	0.195 (0.171)	0.128 (0.185)
≥5/week	0.031 (0.152)	--	0.103 (0.260)	--	-0.119 (0.240)	--
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.027 (0.127)	0.067 (0.105)	0.069 (0.191)	0.102 (0.153)	0.183 (0.195)	0.488 (0.198)*
University	0.204 (0.140)	0.039 (0.135)	0.370 (0.181)*	0.629 (0.150)***	0.621 (0.201)**	0.735 (0.212)**
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.027 (0.208)	0.081 (0.251)	0.066 (0.215)	0.207 (0.319)	-0.009 (0.265)	0.287 (0.239)
Pensioner, unemployed	0.013 (0.173)	0.014 (0.196)	0.212 (0.259)	-0.021 (0.314)	0.054 (0.191)	-0.427 (0.185)*
Unemployed	-0.116 (0.515)	0.320 (0.300)	0.118 (0.323)	0.062 (0.401)	0.057 (0.498)	0.398 (0.414)
Household amenities	0.003 (0.026)	0.022 (0.025)	0.034 (0.038)	0.071 (0.033)*	0.075 (0.037)*	0.037 (0.034)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.162 (0.152)	-0.093 (0.112)	0.089 (0.273)	-0.174 (0.137)	-0.144 (0.221)	-0.008 (0.147)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.076 (0.107)	-0.051 (0.090)	-0.422 (0.144)**	-0.341 (0.137)*	-0.014 (0.135)	0.120 (0.147)
Yes, hospitalised	-0.175 (0.217)	0.550 (0.162)**	-0.557 (0.281)*	0.141 (0.230)	0.101 (0.285)	0.588 (0.297)*
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	0.049 (0.123)	-0.245 (0.098)*	-0.309 (0.155)*	-0.206 (0.169)	-0.318 (0.163)	-0.352 (0.148)*
≥30	-0.338 (0.162)*	-0.519 (0.132)***	-0.787 (0.215)***	-0.465 (0.168)**	-0.826 (0.206)***	-0.775 (0.172)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.197 (0.125)	0.175 (0.113)	-0.047 (0.187)	0.852 (0.321)**	0.084 (0.146)	-0.128 (0.157)
Current smoking	-0.317 (0.124)*	-0.214 (0.120)	-0.814 (0.177)***	-0.340 (0.236)	-0.463 (0.179)**	-0.118 (0.158)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.2. Fully-adjusted annual drinking volume and PF-10 trajectories, complete cases

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	94.346 (1.451)***	90.646 (1.605)***	93.342 (1.714)***	86.038 (1.754)***	93.010 (1.849)***	90.126 (2.551)***
Variance	104.815 (17.921)***	133.138 (14.318)***	65.856 (18.429)***	142.040 (17.309)***	133.203 (19.704)***	178.677 (20.377)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.877 (0.922)**	-0.288 (0.863)	-0.651 (0.972)	0.212 (0.991)	-0.602 (0.961)	-0.072 (1.179)
55-59	-2.518 (0.844)**	2.109 (1.239)	-0.483 (0.965)	2.650 (1.857)	-3.335 (1.127)**	-1.289 (1.425)
60-64	-0.027 (1.247)	3.849 (1.624)*	2.498 (1.398)	3.517 (2.054)	0.671 (1.197)	-1.984 (1.631)
≥65	-1.364 (1.527)	3.191 (1.741)	0.626 (1.536)	-0.858 (2.135)	-0.789 (1.505)	-4.998 (1.924)**
Annual drinking volume (g)						
0	-1.619 (2.157)	-3.284 (1.336)*	-2.786 (1.376)*	-3.791 (1.318)**	-1.643 (1.234)	-1.937 (1.163)
1-150[a] /1-250[b]	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000[a] /251-500[b]	0.300 (0.952)	0.998 (1.005)	-0.435 (0.963)	2.415 (0.874)**	0.106 (0.915)	4.558 (1.176)***
4001-8000[a] /501-1500[b]	1.211 (0.859)	0.112 (0.922)	0.670 (1.005)	3.361 (1.047)**	0.597 (1.235)	3.969 (1.228)**
>8000[a] />1500[b]	0.826 (0.800)	0.722 (0.828)	0.441 (0.871)	2.324 (1.415)	0.069 (1.342)	2.970 (1.441)*
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	1.960 (0.768)*	1.191 (0.766)	-0.259 (0.899)	-0.581 (0.903)	-0.995 (1.101)	-0.959 (1.335)
University	1.875 (0.831)*	2.775 (0.878)**	0.485 (0.832)	0.875 (0.847)	-1.515 (1.069)	0.651 (1.351)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-1.612 (1.290)	-2.763 (1.463)	-1.812 (1.034)	-2.002 (1.761)	-5.967 (1.478)***	-3.034 (1.745)
Pensioner, unemployed	-6.558 (1.345)***	-8.765 (1.332)***	-9.426 (1.364)***	-7.809 (1.788)***	-7.526 (1.148)***	-3.714 (1.289)**
Unemployed	-4.039 (2.224)	-4.033 (2.597)	-2.563 (1.983)	-0.978 (2.281)	-4.831 (2.723)	-4.334 (2.914)
Household amenities	0.281 (0.162)	0.476 (0.171)**	0.762 (0.178)***	0.756 (0.193)***	0.881 (0.198)***	0.451 (0.233)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	1.255 (0.933)	1.199 (0.819)	-0.480 (1.297)	-0.044 (0.803)	0.338 (1.482)	-0.250 (0.996)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-4.960 (0.641)***	-6.447 (0.602)***	-2.991 (0.631)***	-5.087 (0.762)***	-5.796 (0.753)***	-8.315 (0.842)***
Yes, hospitalised	-10.150 (1.280)***	-15.982 (1.423)***	-7.411 (1.555)***	-15.199 (1.455)***	-14.540 (1.674)***	-20.564 (2.295)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-1.220 (0.704)	-1.434 (0.671)*	-0.644 (0.739)	0.212 (0.936)	-0.923 (0.861)	-0.355 (0.944)
≥30	-4.960 (1.004)***	-6.785 (0.924)***	-3.506 (1.012)**	-6.944 (0.975)***	-3.697 (1.132)**	-4.223 (1.160)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-1.478 (0.759)	-1.629 (0.869)	-2.083 (0.926)*	0.187 (1.826)	-0.793 (0.898)	-1.423 (1.098)
Current smoking	-0.046 (0.755)	0.810 (0.724)	-0.065 (0.807)	0.799 (1.363)	-1.091 (1.063)	-2.210 (1.088)*
Slope						
Constant	-0.311 (0.255)	-0.400 (0.228)	-0.365 (0.340)	-1.538 (0.307)***	-1.558 (0.348)***	-1.700 (0.376)***
Variance	0.742 (0.274)**	0.190 (0.258)	1.297 (0.430)**	0.724 (0.386)	1.210 (0.354)**	0.289 (0.326)
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	0.045 (0.156)	0.240 (0.114)*	-0.338 (0.194)	-0.027 (0.177)	-0.183 (0.189)	0.149 (0.183)
55-59	0.060 (0.147)	0.116 (0.172)	-0.673 (0.201)**	-0.555 (0.328)	0.145 (0.194)	-0.393 (0.214)
60-64	-0.146 (0.198)	-0.310 (0.218)	-1.278 (0.277)***	-1.097 (0.362)**	-0.711 (0.227)**	-0.532 (0.246)*
≥65	-0.490 (0.223)*	-0.714 (0.242)**	-1.967 (0.292)***	-1.373 (0.365)***	-0.913 (0.262)***	-0.658 (0.281)*
Annual drinking volume (g)						
0	-0.020 (0.313)	0.051 (0.181)	-0.320 (0.263)	0.030 (0.212)	-0.050 (0.207)	0.075 (0.168)
1-150[a] /1-250[b]	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1501-4000[a] /251-500[b]	0.172 (0.148)	0.094 (0.148)	0.119 (0.202)	0.026 (0.155)	-0.071 (0.166)	-0.142 (0.209)
4001-8000[a] /501-1500[b]	0.060 (0.151)	0.109 (0.123)	0.062 (0.231)	-0.084 (0.190)	0.061 (0.222)	-0.070 (0.196)
>8000[a] />1500[b]	0.039 (0.128)	0.105 (0.120)	0.040 (0.203)	-0.206 (0.243)	-0.193 (0.252)	0.084 (0.203)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.027 (0.127)	0.074 (0.105)	0.071 (0.190)	0.105 (0.153)	0.185 (0.195)	0.489 (0.198)*
University	0.205 (0.140)	0.057 (0.133)	0.375 (0.181)*	0.628 (0.150)***	0.619 (0.200)**	0.730 (0.212)**
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.026 (0.208)	0.093 (0.251)	0.064 (0.214)	0.205 (0.319)	-0.011 (0.263)	0.286 (0.238)
Pensioner, unemployed	0.015 (0.173)	0.026 (0.196)	0.203 (0.257)	-0.020 (0.314)	0.042 (0.189)	-0.427 (0.185)*
Unemployed	-0.139 (0.516)	0.328 (0.302)	0.117 (0.323)	0.055 (0.401)	0.061 (0.501)	0.412 (0.413)
Household amenities	0.002 (0.026)	0.023 (0.025)	0.037 (0.038)	0.073 (0.033)*	0.079 (0.037)*	0.035 (0.034)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.158 (0.151)	-0.098 (0.113)	0.093 (0.273)	-0.166 (0.137)	-0.130 (0.221)	-0.005 (0.147)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.078 (0.107)	-0.056 (0.090)	-0.427 (0.144)**	-0.340 (0.137)*	-0.019 (0.135)	0.121 (0.147)
Yes, hospitalised	-0.168 (0.217)	0.554 (0.162)**	-0.576 (0.281)*	0.139 (0.230)	0.083 (0.286)	0.591 (0.297)*
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	0.045 (0.123)	-0.251 (0.097)*	-0.311 (0.154)*	-0.204 (0.169)	-0.310 (0.163)	-0.355 (0.147)*
≥30	-0.342 (0.163)*	-0.525 (0.132)***	-0.785 (0.214)***	-0.461 (0.168)**	-0.809 (0.207)***	-0.770 (0.172)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.198 (0.126)	0.177 (0.114)	-0.034 (0.187)	0.878 (0.321)**	0.085 (0.147)	-0.131 (0.157)
Current smoking	-0.314 (0.124)*	-0.213 (0.120)	-0.799 (0.180)***	-0.305 (0.239)	-0.444 (0.178)*	-0.121 (0.157)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.3. Fully-adjusted drinking quantity per drinking day and PF-10 trajectories, complete cases

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	94.769 (1.398)***	91.013 (1.636)***	92.534 (1.784)***	85.509 (1.843)***	93.002 (1.856)***	91.056 (2.501)***
Variance	104.867 (17.941)***	133.529 (14.331)***	63.464 (18.216)***	143.010 (17.380)***	133.326 (19.659)***	178.575 (20.518)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.921 (0.923)**	-0.287 (0.864)	-0.691 (0.980)	0.119 (0.989)	-0.602 (0.963)	-0.135 (1.181)
55-59	-2.544 (0.844)**	2.056 (1.240)	-0.510 (0.957)	2.587 (1.858)	-3.330 (1.131)**	-1.197 (1.429)
60-64	-0.064 (1.251)	3.846 (1.620)	2.424 (1.402)	3.352 (2.055)	0.591 (1.213)	-1.795 (1.645)
≥65	-1.419 (1.530)	3.111 (1.735)	0.616 (1.528)	-1.121 (2.136)	-0.890 (1.515)	-4.904 (1.933)*
Average drinking quantity/day						
Non-drinker	-2.091 (2.081)	-3.702 (1.309)**	-2.007 (1.391)	-3.344 (1.420)*	-1.613 (1.181)	-2.758 (1.089)*
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	1.368 (1.045)	-0.217 (0.682)	0.774 (0.897)	2.401 (0.960)*	1.947 (1.073)	2.992 (0.955)**
Heavy	-0.531 (0.974)	0.377 (1.134)	1.477 (0.798)	3.907 (1.231)**	-0.296 (1.295)	2.456 (1.991)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	1.924 (0.767)*	1.228 (0.764)	-0.292 (0.897)	-0.682 (0.899)	-1.015 (1.101)	-0.844 (1.340)
University	1.854 (0.831)*	2.837 (0.860)**	0.595 (0.835)	0.941 (0.844)	-1.514 (1.075)	0.939 (1.355)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-1.597 (1.290)	-2.795 (1.449)	-1.742 (1.029)	-1.992 (1.766)	-5.908 (1.485)***	-3.270 (1.721)
Pensioner, unemployed	-6.620 (1.354)***	-8.764 (1.326)***	-9.464 (1.367)***	-7.723 (1.796)***	-7.418 (1.148)***	-3.955 (1.293)**
Unemployed	-4.021 (2.230)	-4.081 (2.587)	-2.562 (1.975)	-1.254 (2.273)	-4.905 (2.741)	-4.298 (2.921)
Household amenities	0.290 (0.162)	0.485 (0.171)**	0.783 (0.177)***	0.805 (0.193)***	0.880 (0.197)***	0.458 (0.233)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	1.373 (0.932)	1.236 (0.814)	-0.368 (1.301)	-0.146 (0.803)	0.348 (1.478)	-0.263 (1.001)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-4.990 (0.641)***	-6.451 (0.602)***	-2.996 (0.629)***	-5.038 (0.761)***	-5.813 (0.757)***	-8.471 (0.837)***
Yes, hospitalised	-10.194 (1.289)***	-15.990 (1.423)***	-7.440 (1.573)***	-15.158 (1.456)***	-14.562 (1.664)***	-20.784 (2.322)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-1.230 (0.705)	-1.442 (0.669)*	-0.664 (0.739)	0.225 (0.940)	-0.925 (0.858)	-0.537 (0.954)
≥30	-5.027 (1.018)***	-6.788 (0.920)***	-3.623 (1.019)***	-7.030 (0.983)***	-3.728 (1.129)**	-4.412 (1.160)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-1.314 (0.752)	-1.597 (0.866)	-2.135 (0.908)*	0.288 (1.803)	-0.790 (0.894)	-1.180 (1.102)
Current smoking	0.060 (0.762)	0.838 (0.727)	-0.161 (0.776)	0.771 (1.350)	-1.109 (1.041)	-2.070 (1.098)
Slope						
Constant	-0.252 (0.249)	-0.335 (0.232)	-0.183 (0.359)	-1.375 (0.319)***	-1.528 (0.346)***	-1.726 (0.367)***
Variance	0.730 (0.273)**	0.193 (0.258)	1.258 (0.427)**	0.685 (0.385)	1.216 (0.355)**	0.287 (0.326)
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	0.044 (0.155)	0.238 (0.114)*	-0.337 (0.194)	-0.028 (0.177)	-0.181 (0.187)	0.150 (0.182)
55-59	0.042 (0.146)	0.110 (0.170)	-0.677 (0.200)**	-0.560 (0.326)	0.142 (0.194)	-0.398 (0.214)
60-64	-0.154 (0.198)	-0.308 (0.217)	-1.264 (0.277)***	-1.096 (0.359)**	-0.714 (0.226)**	-0.533 (0.248)*
≥65	-0.528 (0.223)*	-0.719 (0.241)**	-1.983 (0.292)***	-1.375 (0.361)***	-0.917 (0.262)***	-0.654 (0.282)*
Average drinking quantity/day						
Non-drinker	-0.113 (0.305)	-0.022 (0.177)	-0.536 (0.263)*	-0.123 (0.233)	-0.072 (0.197)	0.090 (0.157)
Light	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	-0.372 (0.212)	-0.011 (0.093)	-0.208 (0.210)	-0.188 (0.171)	-0.253 (0.231)	-0.057 (0.155)
Heavy	-0.038 (0.136)	-0.106 (0.190)	-0.234 (0.177)	-0.393 (0.220)	-0.199 (0.228)	0.115 (0.333)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.027 (0.126)	0.080 (0.104)	0.073 (0.191)	0.099 (0.153)	0.181 (0.195)	0.491 (0.198)*
University	0.207 (0.140)	0.070 (0.130)	0.351 (0.184)	0.615 (0.150)***	0.608 (0.200)**	0.733 (0.211)**
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.031 (0.208)	0.067 (0.248)	0.052 (0.214)	0.202 (0.318)	-0.008 (0.263)	0.284 (0.239)
Pensioner, unemployed	0.030 (0.174)	0.009 (0.193)	0.202 (0.257)	-0.028 (0.313)	0.045 (0.190)	-0.424 (0.185)*
Unemployed	-0.111 (0.515)	0.318 (0.300)	0.114 (0.321)	0.083 (0.399)	0.058 (0.500)	0.409 (0.414)
Household amenities	0.005 (0.026)	0.024 (0.025)	0.037 (0.037)	0.070 (0.033)*	0.077 (0.037)*	0.037 (0.034)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.166 (0.150)	-0.093 (0.113)	0.082 (0.274)	-0.164 (0.137)	-0.129 (0.221)	-0.005 (0.147)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.070 (0.108)	-0.054 (0.090)	-0.420 (0.144)**	-0.329 (0.137)*	-0.018 (0.136)	0.125 (0.147)
Yes, hospitalised	-0.178 (0.216)	0.550 (0.163)**	-0.580 (0.281)*	0.137 (0.229)	0.092 (0.284)	0.591 (0.297)*
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	0.055 (0.123)	-0.244 (0.097)*	-0.302 (0.155)	-0.194 (0.169)	-0.306 (0.162)	-0.358 (0.147)*
≥30	-0.314 (0.164)	-0.520 (0.131)***	-0.760 (0.215)***	-0.445 (0.169)**	-0.800 (0.207)***	-0.778 (0.171)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.200 (0.124)	0.191 (0.112)	-0.002 (0.181)	0.878 (0.317)**	0.086 (0.147)	-0.135 (0.157)
Current smoking	-0.295 (0.124)*	-0.198 (0.119)	-0.758 (0.172)***	-0.282 (0.238)	-0.439 (0.177)*	-0.125 (0.158)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.4. Fully-adjusted drinking pattern and PF-10 trajectories, complete cases

	Czech (mean, S.E.)		Russia (mean, S.E.)		Poland (mean, S.E.)	
	Men	Women	Men	Women	Men	Women
Intercept						
Constant	95.353 (1.443)***	90.384 (1.886)***	93.326 (1.905)***	89.276 (2.223)***	92.093 (1.998)***	94.532 (2.676)***
Variance	104.503 (17.978)***	133.421 (14.317)***	63.639 (18.234)***	142.496 (17.368)***	133.296 (19.724)***	179.095 (20.539)***
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	-2.885 (0.918)**	-0.169 (0.862)	-0.643 (0.974)	0.199 (0.991)	-0.634 (0.960)	-0.269 (1.182)
55-59	-2.529 (0.841)**	2.197 (1.246)	-0.494 (0.962)	2.593 (1.870)	-3.390 (1.132)**	-1.284 (1.437)
60-64	-0.038 (1.252)	3.942 (1.622)*	2.561 (1.401)	3.417 (2.066)	0.642 (1.211)	-2.018 (1.646)
≥65	-1.402 (1.524)	3.297 (1.748)	0.644 (1.531)	-1.061 (2.143)	-0.837 (1.515)	-5.136 (1.945)**
Drinking pattern						
Non-drinker	-2.614 (2.105)	-3.270 (1.481)*	-2.830 (1.456)	-7.094 (1.870)***	-0.789 (1.318)	-6.060 (1.427)***
Irregular light-to-moderate	-1.349 (0.904)	0.018 (0.961)	-0.196 (0.981)	-2.251 (1.543)	1.247 (0.996)	-2.499 (1.299)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	-0.422 (0.723)	1.287 (1.051)	0.430 (0.924)	0.358 (1.696)	1.688 (0.991)	-2.747 (1.654)
Regular heavy	-0.264 (1.342)	1.107 (1.160)	-0.169 (1.194)	-1.296 (2.000)	-0.436 (2.411)	0.629 (1.886)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	1.934 (0.768)*	1.143 (0.761)	-0.239 (0.900)	-0.708 (0.900)	-1.023 (1.099)	-0.930 (1.341)
University	1.877 (0.834)*	2.714 (0.869)**	0.501 (0.843)	0.880 (0.846)	-1.463 (1.070)	0.777 (1.356)
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-1.600 (1.285)	-2.570 (1.454)	-1.849 (1.033)	-1.953 (1.777)	-5.968 (1.474)***	-3.211 (1.744)
Pensioner, unemployed	-6.628 (1.344)***	-8.560 (1.333)***	-9.492 (1.369)***	-7.796 (1.805)***	-7.491 (1.148)***	-3.940 (1.289)**
Unemployed	-4.178 (2.206)	-3.923 (2.582)	-2.526 (1.989)	-1.039 (2.260)	-4.977 (2.726)	-4.317 (2.918)
Household amenities	0.284 (0.161)	0.488 (0.172)**	0.772 (0.178)***	0.779 (0.193)***	0.898 (0.200)***	0.457 (0.233)*
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	1.321 (0.932)	1.188 (0.815)	-0.484 (1.300)	-0.157 (0.805)	0.378 (1.493)	-0.266 (1.003)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-4.954 (0.643)***	-6.436 (0.602)***	-3.033 (0.629)***	-4.968 (0.764)***	-5.835 (0.745)***	-8.524 (0.841)***
Yes, hospitalised	-10.140 (1.283)***	-15.994 (1.424)***	-7.487 (1.577)***	-15.113 (1.458)***	-14.670 (1.661)***	-20.943 (2.306)***
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	-1.244 (0.706)	-1.483 (0.670)*	-0.630 (0.741)	0.277 (0.941)	-0.892 (0.861)	-0.384 (0.952)
≥30	-4.963 (1.011)***	-6.831 (0.923)***	-3.560 (1.023)**	-6.924 (0.980)***	-3.657 (1.127)**	-4.281 (1.162)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-1.453 (0.751)	-1.659 (0.865)	-2.075 (0.915)*	0.250 (1.806)	-0.853 (0.895)	-1.173 (1.095)
Current smoking	0.017 (0.771)	0.759 (0.725)	-0.016 (0.798)	0.917 (1.372)	-1.125 (1.037)	-2.113 (1.097)
Slope						
Constant	-0.204 (0.258)	-0.156 (0.255)	-0.422 (0.404)	-1.772 (0.396)***	-1.359 (0.356)***	-1.866 (0.401)***
Variance	0.738 (0.273)**	0.189 (0.257)	1.260 (0.428)**	0.713 (0.387)	1.183 (0.353)**	0.279 (0.326)
Age						
45-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-54	0.040 (0.153)	0.229 (0.116)*	-0.340 (0.194)	-0.018 (0.178)	-0.179 (0.187)	0.168 (0.183)
55-59	0.041 (0.144)	0.112 (0.172)	-0.673 (0.203)**	-0.540 (0.328)	0.139 (0.194)	-0.382 (0.214)
60-64	-0.162 (0.195)	-0.308 (0.218)	-1.274 (0.275)***	-1.082 (0.360)**	-0.735 (0.227)**	-0.507 (0.248)*
≥65	-0.512 (0.220)*	-0.722 (0.244)**	-1.985 (0.293)***	-1.357 (0.363)***	-0.940 (0.263)***	-0.627 (0.283)*
Drinking pattern						
Non-drinker	-0.131 (0.313)	-0.175 (0.198)	-0.310 (0.287)	0.254 (0.302)	-0.224 (0.216)	0.211 (0.212)
Irregular light-to-moderate	-0.070 (0.141)	-0.223 (0.134)	0.160 (0.231)	0.235 (0.254)	-0.179 (0.170)	0.083 (0.198)
Regular light-to-moderate	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Irregular heavy	-0.009 (0.122)	-0.174 (0.144)	0.088 (0.222)	0.248 (0.286)	-0.419 (0.174)*	0.199 (0.258)
Regular heavy	-0.520 (0.250)*	-0.109 (0.166)	-0.092 (0.276)	-0.171 (0.339)	-0.568 (0.540)	0.466 (0.313)
Education						
<secondary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secondary	0.018 (0.127)	0.076 (0.103)	0.078 (0.191)	0.108 (0.153)	0.190 (0.195)	0.486 (0.198)*
University	0.193 (0.140)	0.059 (0.131)	0.370 (0.183)*	0.630 (0.150)***	0.604 (0.200)**	0.725 (0.212)**
Current economic activity						
Working	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pensioner, employed	-0.010 (0.209)	0.077 (0.250)	0.058 (0.214)	0.202 (0.320)	-0.005 (0.263)	0.293 (0.239)
Pensioner, unemployed	0.018 (0.174)	0.014 (0.195)	0.205 (0.257)	-0.032 (0.314)	0.046 (0.189)	-0.421 (0.184)*
Unemployed	-0.130 (0.507)	0.318 (0.301)	0.133 (0.322)	0.047 (0.397)	0.077 (0.496)	0.414 (0.413)
Household amenities	0.001 (0.026)	0.021 (0.025)	0.040 (0.037)	0.074 (0.033)*	0.075 (0.037)*	0.037 (0.034)
Marital status						
Married/cohabiting	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Single/divorced/widowed	0.179 (0.152)	-0.094 (0.113)	0.086 (0.274)	-0.172 (0.137)	-0.130 (0.220)	-0.003 (0.147)
Spine/joint problems						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.092 (0.107)	-0.051 (0.091)	-0.421 (0.144)**	-0.342 (0.137)*	-0.025 (0.134)	0.132 (0.147)
Yes, hospitalised	-0.201 (0.216)	0.555 (0.163)**	-0.580 (0.281)*	0.136 (0.230)	0.087 (0.283)	0.603 (0.297)*
BMI						
<25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
25.0-29.9	0.062 (0.123)	-0.251 (0.097)*	-0.309 (0.155)*	-0.200 (0.169)	-0.306 (0.162)	-0.361 (0.147)*
≥30	-0.326 (0.163)*	-0.524 (0.132)***	-0.779 (0.217)***	-0.458 (0.168)**	-0.804 (0.207)***	-0.781 (0.172)***
Smoking						
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former smoking	-0.182 (0.124)	0.176 (0.113)	-0.005 (0.185)	0.875 (0.321)**	0.104 (0.147)	-0.136 (0.157)
Current smoking	-0.282 (0.121)*	-0.216 (0.120)	-0.763 (0.175)***	-0.281 (0.239)	-0.413 (0.177)*	-0.139 (0.158)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.5. Fully-adjusted problem drinking and PF-10 trajectories, complete cases

	Czech (mean, S.E.)	Russia (mean, S.E.)	Poland (mean, S.E.)
	Men	Men	Men
Intercept			
Constant	95.091 (1.436)***	93.411 (1.718)***	93.482 (2.037)***
Variance	104.681 (18.725)***	23.223 (14.683)	36.555 (6.872)***
Age			
45-49	Ref.	Ref.	Ref.
50-54	-2.987 (0.922)**	-0.405 (1.001)	-0.888 (1.053)
55-59	-2.872 (0.864)**	-0.524 (0.956)	-3.853 (1.221)**
60-64	0.184 (1.282)	2.347 (1.334)	0.470 (1.309)
≥65	-0.751 (1.575)	0.097 (1.463)	0.747 (1.609)
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.305 (1.194)	-0.244 (0.829)	-1.950 (1.640)
Education			
<secondary	Ref.	Ref.	Ref.
Secondary	1.804 (0.800)*	-0.115 (0.943)	0.956 (1.244)
University	1.851 (0.850)*	0.796 (0.852)	-0.291 (1.219)
Current economic activity			
Working	Ref.	Ref.	Ref.
Pensioner, employed	-2.057 (1.330)	-1.186 (1.033)	-7.247 (1.661)***
Pensioner, unemployed	-7.220 (1.397)***	-8.080 (1.334)***	-8.880 (1.280)***
Unemployed	-4.133 (2.327)	-2.181 (1.998)	-6.706 (3.308)*
Household amenities	0.257 (0.165)	0.701 (0.180)***	0.791 (0.220)***
Marital status			
Married/cohabiting	Ref.	Ref.	Ref.
Single/divorced/widowed	1.088 (0.966)	-0.763 (1.358)	1.359 (1.547)
Spine/joint problems			
No	Ref.	Ref.	Ref.
Yes, not hospitalised	-4.838 (0.650)***	-3.304 (0.629)***	-6.104 (0.797)***
Yes, hospitalised	-9.584 (1.284)***	-7.757 (1.681)***	-14.705 (1.932)***
BMI			
<25	Ref.	Ref.	Ref.
25.0-29.9	-1.137 (0.715)	-1.031 (0.735)	-0.961 (0.947)
≥30	-4.737 (1.030)***	-3.768 (1.046)***	-4.330 (1.277)**
Smoking			
Never	Ref.	Ref.	Ref.
Former smoking	-1.307 (0.770)	-1.638 (0.931)	-0.287 (0.961)
Current smoking	-0.303 (0.762)	-0.183 (0.795)	-0.764 (1.138)
Slope			
Constant	-0.350 (0.259)	-0.374 (0.367)	-1.839 (0.382)***
Variance	0.804 (0.283)**	3.378 (0.592)***	1.690 (0.269)***
Age			
45-49	Ref	Ref	Ref
50-54	0.046 (0.157)	-0.392 (0.204)	-0.175 (0.211)
55-59	0.072 (0.147)	-0.817 (0.206)***	0.330 (0.207)
60-64	-0.186 (0.201)	-1.334 (0.291)***	-0.664 (0.246)**
≥65	-0.514 (0.228)*	-2.046 (0.306)***	-0.860 (0.285)**
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.108 (0.170)	-0.036 (0.192)	0.120 (0.294)
Education			
<secondary	Ref.	Ref.	Ref.
Secondary	0.040 (0.131)	0.055 (0.208)	0.150 (0.218)
University	0.207 (0.142)	0.471 (0.193)*	0.675 (0.221)**
Current economic activity			
Working	Ref.	Ref.	Ref.
Pensioner, employed	-0.031 (0.216)	0.017 (0.222)	0.011 (0.279)
Pensioner, unemployed	0.043 (0.180)	0.193 (0.272)	0.003 (0.216)
Unemployed	-0.193 (0.528)	0.284 (0.328)	-0.015 (0.514)
Household amenities	0.008 (0.027)	0.021 (0.040)	0.109 (0.041)**
Marital status			
Married/cohabiting	Ref.	Ref.	Ref.
Single/divorced/widowed	0.163 (0.159)	0.036 (0.301)	-0.214 (0.248)
Spine/joint problems			
No	Ref.	Ref.	Ref.
Yes, not hospitalised	-0.046 (0.108)	-0.340 (0.154)*	0.023 (0.148)
Yes, hospitalised	-0.155 (0.223)	-0.591 (0.290)*	-0.137 (0.306)
BMI			
<25	Ref.	Ref.	Ref.
25.0-29.9	0.035 (0.127)	-0.183 (0.165)	-0.324 (0.176)
≥30	-0.297 (0.167)	-0.597 (0.227)**	-0.891 (0.223)***
Smoking			
Never	Ref.	Ref.	Ref.
Former smoking	-0.136 (0.128)	-0.176 (0.194)	0.112 (0.157)
Current smoking	-0.236 (0.121)	-0.840 (0.184)***	-0.442 (0.195)*

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.6. Fully-adjusted past drinking and PF-10 trajectories in the Russian cohort, complete cases

	Russia	
	Men (mean, S.E.)	Women (mean, S.E.)
Intercept		
Constant	93.649 (1.731)***	87.537 (1.685)***
Variance	60.911 (18.169)**	138.439 (17.255)***
Age		
45-49	Ref.	Ref.
50-54	-0.777 (0.971)	-0.118 (0.977)
55-59	-0.674 (0.946)	2.256 (1.828)
60-64	1.870 (1.381)	3.070 (2.029)
≥65	0.078 (1.485)	-1.617 (2.105)
Former drinking		
Lifetime abstainer	-4.360 (3.414)	-2.731 (1.678)
Former drinker, health reasons	-8.631 (2.510)**	-11.765 (2.275)***
Former drinker, non-health reasons	-0.946 (1.519)	-5.056 (2.147)
Reduced drinker, health reasons	-5.190 (1.034)***	-5.604 (1.357)***
Reduced drinker, non-health reasons	0.691 (0.731)	1.675 (0.838)*
Continuing drinker	Ref.	Ref.
Education		
<secondary	Ref.	Ref.
Secondary	-0.143 (0.888)	-0.636 (0.891)
University	0.661 (0.819)	0.679 (0.841)
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	-1.375 (1.008)	-1.973 (1.745)
Pensioner, unemployed	-8.468 (1.340)***	-7.700 (1.765)***
Unemployed	-2.633 (1.956)	-1.128 (2.233)
Household amenities	0.766 (0.174)***	0.819 (0.192)***
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.440 (1.257)	-0.093 (0.792)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-2.878 (0.620)***	-4.777 (0.760)***
Yes, hospitalised	-7.645 (1.550)***	-14.463 (1.453)***
BMI		
<25	Ref.	Ref.
25.0-29.9	-0.604 (0.725)	0.400 (0.924)
≥30	-3.212 (0.992)**	-6.563 (0.965)***
Smoking		
Never	Ref.	Ref.
Former smoking	-1.685 (0.884)	0.917 (1.817)
Current smoking	-0.030 (0.761)	1.470 (1.283)
Slope		
Constant	-0.354 (0.344)	-1.565 (0.295)***
Variance	1.250 (0.427)**	0.655 (0.385)
Age		
45-49	Ref.	Ref.
50-54	-0.356 (0.194)	-0.009 (0.176)
55-59	-0.686 (0.201)**	-0.545 (0.325)
60-64	-1.325 (0.276)***	-1.094 (0.358)**
≥65	-2.035 (0.291)***	-1.354 (0.361)***
Former drinking		
Lifetime abstainer	-0.199 (1.074)	-0.028 (0.274)
Former drinker, health reasons	-0.711 (0.426)	-0.094 (0.328)
Former drinker, non-health reasons	-0.158 (0.277)	0.482 (0.366)
Reduced drinker, health reasons	-0.179 (0.237)	0.389 (0.209)
Reduced drinker, non-health reasons	0.241 (0.162)	-0.027 (0.157)
Continuing drinker	Ref.	Ref.
Education		
<secondary	Ref.	Ref.
Secondary	0.064 (0.190)	0.101 (0.153)
University	0.378 (0.181)*	0.636 (0.149)***
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	0.089 (0.214)	0.198 (0.319)
Pensioner, unemployed	0.261 (0.258)	-0.026 (0.314)
Unemployed	0.102 (0.321)	0.090 (0.401)
Household amenities	0.036 (0.037)	0.068 (0.033)*
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	0.086 (0.274)	-0.169 (0.136)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-0.401 (0.144)**	-0.337 (0.137)*
Yes, hospitalised	-0.584 (0.279)*	0.123 (0.230)
BMI		
<25	Ref.	Ref.
25.0-29.9	-0.309 (0.154)*	-0.196 (0.168)
≥30	-0.773 (0.213)***	-0.472 (0.167)**
Smoking		
Never	Ref.	Ref.
Former smoking	-0.015 (0.181)	0.792 (0.318)*
Current smoking	-0.800 (0.172)***	-0.353 (0.233)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix L.7. Fully-adjusted past drinking behaviour combined with drinking pattern and PF-10 trajectories in the Russian cohort, complete cases

	Russia	
	Men (mean, S.E.)	Women (mean, S.E.)
Intercept		
Constant	93.073 (2.022)***	87.262 (2.261)***
Variance	60.492 (18.110)**	134.432 (17.100)***
Age		
45-49	Ref.	Ref.
50-54	-0.747 (0.967)	0.140 (0.983)
55-59	-0.557 (0.947)	2.363 (1.829)
60-64	1.970 (1.387)	3.230 (2.026)
≥65	0.186 (1.493)	-1.354 (2.101)
Former drinking		
Lifetime abstainer	-3.822 (3.546)	-2.615 (2.210)
Former drinker, health reasons	-8.040 (2.676)**	-11.645 (2.697)***
Former drinker, non-health reasons	-0.361 (1.804)	-4.938 (2.576)
Reduced drinker, health reasons	-4.619 (1.410)**	-5.446 (1.973)**
Reduced drinker, non-health reasons	1.260 (1.193)	1.827 (1.663)
Irregular light-to-moderate drinker	0.265 (1.424)	-0.653 (1.606)
Regular light-to-moderate drinker	Ref.	Ref.
Irregular heavy drinker	0.124 (1.424)	3.206 (2.212)
Regular heavy drinker	1.215 (1.239)	2.489 (1.793)
Education		
<secondary	Ref.	Ref.
Secondary	-0.102 (0.888)	-0.612 (0.889)
University	0.712 (0.826)	0.719 (0.839)
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	-1.394 (1.008)	-1.868 (1.751)
Pensioner, unemployed	-8.483 (1.345)***	-7.593 (1.767)***
Unemployed	-2.563 (1.975)	-1.159 (2.238)
Household amenities	0.762 (0.175)***	0.805 (0.192)***
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	-0.476 (1.259)	-0.201 (0.793)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-2.880 (0.622)***	-4.833 (0.759)***
Yes, hospitalised	-7.670 (1.548)***	-14.489 (1.450)***
BMI		
<25	Ref.	Ref.
25.0-29.9	-0.628 (0.727)	0.421 (0.926)
≥30	-3.298 (0.998)**	-6.545 (0.966)***
Smoking		
Never	Ref.	Ref.
Former smoking	-1.736 (0.897)	0.549 (1.819)
Current smoking	-0.082 (0.796)	1.304 (1.310)
Slope		
Constant	-0.607 (0.431)	-1.994 (0.400)***
Variance	1.252 (0.426)**	0.635 (0.384)
Age		
45-49	Ref.	Ref.
50-54	-0.358 (0.194)	-0.005 (0.177)
55-59	-0.701 (0.203)**	-0.540 (0.326)
60-64	-1.341 (0.276)***	-1.098 (0.358)**
≥65	-2.060 (0.291)***	-1.356 (0.360)***
Former drinking		
Lifetime abstainer	0.044 (1.098)	0.400 (0.382)
Former drinker, health reasons	-0.489 (0.482)	0.331 (0.421)
Former drinker, non-health reasons	0.063 (0.356)	0.909 (0.449)*
Reduced drinker, health reasons	0.053 (0.328)	0.813 (0.335)*
Reduced drinker, non-health reasons	0.471 (0.274)	0.397 (0.306)
Irregular light-to-moderate drinker	0.420 (0.312)	0.466 (0.293)
Regular light-to-moderate drinker	Ref.	Ref.
Irregular heavy drinker	0.282 (0.345)	0.303 (0.385)
Regular heavy drinker	0.201 (0.289)	0.484 (0.335)
Education		
<secondary	Ref.	Ref.
Secondary	0.070 (0.190)	0.109 (0.153)
University	0.364 (0.182)*	0.641 (0.150)***
Current economic activity		
Working	Ref.	Ref.
Pensioner, employed	0.085 (0.213)	0.187 (0.320)
Pensioner, unemployed	0.268 (0.258)	-0.038 (0.315)
Unemployed	0.113 (0.321)	0.079 (0.397)
Household amenities	0.037 (0.037)	0.068 (0.033)*
Marital status		
Married/cohabiting	Ref.	Ref.
Single/divorced/widowed	0.083 (0.274)	-0.167 (0.137)
Spine/joint problems		
No	Ref.	Ref.
Yes, not hospitalised	-0.409 (0.144)**	-0.341 (0.137)*
Yes, hospitalised	-0.585 (0.279)*	0.123 (0.230)
BMI		
<25	Ref.	Ref.
25.0-29.9	-0.309 (0.154)*	-0.192 (0.168)
≥30	-0.760 (0.214)***	-0.465 (0.168)**
Smoking		
Never	Ref.	Ref.
Former smoking	0.018 (0.185)	0.815 (0.319)*
Current smoking	-0.756 (0.176)***	-0.313 (0.236)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category

Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M. Fully-adjusted alcohol consumption and PF-10 trajectories among survivors

This sensitivity analysis included 3,366 Czech men, 4,181 Czech women, 3,527 Russian men, 4,767 Russian women, 4,321 Polish men, and 4,846 Polish women who are alive until end of 2012.

Appendix M.1. Fully-adjusted average drinking frequency and PF-10 trajectories among survivors

Drinking frequency	Fully-adjusted model (mean, S.E.)		
	Czech Republic	Russia	Poland
Men			
Intercept			
0	-3.902 (1.555)*	-3.838 (0.984)***	-2.850 (0.820)**
<1/month	-0.818 (0.895)	-1.997 (0.899)**	-1.130 (0.809)
1-3/month	Ref.	Ref.	Ref.
1-4/week	0.522 (0.697)	0.086 (0.592)	-0.215 (0.618)
≥5/week	1.242 (0.677)	0.284 (0.890)	0.036 (0.764)
Slope			
0	0.174 (0.211)	-0.301 (0.187)	-0.035 (0.153)
<1/month	0.067 (0.146)	0.063 (0.189)	0.130 (0.147)
1-3/month	Ref.	Ref.	Ref.
1-4/week	0.129 (0.114)	-0.035 (0.136)	0.023 (0.125)
≥5/week	0.102 (0.115)	-0.126 (0.212)	-0.170 (0.155)
Women			
Intercept			
0	-3.840 (0.828)***	-6.668 (0.909)***	-4.193 (0.690)***
<1/month	-1.168 (0.609)	-0.819 (0.582)	-2.279 (0.687)**
1-3/month	Ref.	Ref.	Ref.
≥1/week	-0.016 (0.562)	0.929 (0.898)	0.078 (0.817)
Slope			
0	-0.026 (0.126)	-0.150 (0.171)	0.009 (0.130)
<1/month	0.026 (0.093)	-0.126 (0.116)	0.101 (0.130)
1-3/month	Ref.	Ref.	Ref.
≥1/week	0.097 (0.089)	-0.451 (0.186)*	-0.089 (0.152)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.2. Fully-adjusted annual drinking volume and PF-10 trajectories among survivors

Annual drinking volume	Fully-adjusted (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Men			
Intercept			
0	-3.724 (1.509)*	-2.237 (0.986)*	-2.297 (1.061)*
1-1500	Ref.	Ref.	Ref.
1501-4000	0.048 (0.687)	1.420 (0.736)	-1.964 (0.768)*
4001-8000	1.260 (0.673)	2.946 (0.743)***	1.176 (0.628)
>8000	0.965 (0.581)	1.740 (0.695)*	1.582 (0.749)*
Slope			
0	0.148 (0.199)	-0.322 (0.189)	-0.122 (0.140)
1-1500	Ref.	Ref.	Ref.
1501-4000	0.123 (0.111)	0.044 (0.279)	-0.085 (0.120)
4001-8000	0.078 (0.114)	-0.158 (0.169)	-0.143 (0.151)
>8000	0.091 (0.100)	-0.072 (0.158)	-0.324 (0.157)*
Women			
Intercept			
0	-2.453 (0.844)**	-4.632 (0.925)***	-1.784 (0.672)**
1-250	Ref.	Ref.	Ref.
251-500	1.754 (0.769)*	2.809 (0.651)***	2.681 (0.801)**
501-1500	1.066 (0.672)	3.128 (0.804)***	2.890 (0.813)***
>1500	1.344 (0.604)*	1.724 (0.998)	2.333 (0.925)*
Slope			
0	-0.042 (0.126)	-0.116 (0.167)	-0.100 (0.127)
1-250	Ref.	Ref.	Ref.
251-500	0.018 (0.118)	-0.119 (0.128)	-0.082 (0.158)
501-1500	-0.009 (0.105)	-0.090 (0.156)	-0.202 (0.164)
>1500	0.060 (0.099)	-0.322 (0.195)	-0.202 (0.177)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.3. Fully-adjusted average drinking quantity per drinking day and PF-10 trajectories among survivors

Average drinking quantity per day	Fully-adjusted model (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Men			
Intercept			
Non-drinker	-4.334 (1.464)**	-1.766 (1.013)	-2.095 (0.736)**
Light	Ref.	Ref.	Ref.
Moderate	0.649 (0.745)	2.735 (0.708)***	2.580 (0.773)**
Heavy	-0.350 (0.646)	2.411 (0.652)***	1.430 (0.715)*
Slope			
Non-drinker	0.073 (0.194)	-0.409 (0.195)*	-0.095 (0.135)
Light	Ref.	Ref.	Ref.
Moderate	-0.175 (0.134)	-0.225 (0.163)	-0.199 (0.164)
Heavy	0.025 (0.102)	-0.153 (0.140)	-0.183 (0.142)
Women			
Intercept			
Non-drinker	-3.196 (0.823)***	-4.807 (1.002)***	-2.224 (0.646)**
Light	Ref.	Ref.	Ref.
Moderate	0.268 (0.518)	1.655 (0.702)*	2.138 (0.642)**
Heavy	0.078 (0.769)	2.846 (0.922)**	2.359 (1.105)*
Slope			
Non-drinker	-0.050 (0.118)	-0.114 (0.184)	-0.128 (0.120)
Light	Ref.	Ref.	Ref.
Moderate	0.010 (0.080)	-0.111 (0.135)	-0.253 (0.118)*
Heavy	0.014 (0.139)	-0.072 (0.187)	-0.264 (0.236)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.4. Fully-adjusted drinking pattern and PF-10 trajectories among survivors

Drinking pattern	Fully-adjusted model (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Men			
Intercept			
Non-drinker	-4.636 (1.500)**	-3.761 (1.014)***	-1.982 (0.823)*
Irregular light-to-moderate	-1.506 (0.668)*	-2.027 (0.794)*	-0.353 (0.680)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	0.247 (0.561)	0.913 (0.656)	2.297 (0.623)***
Regular heavy	-0.309 (0.930)	0.121 (0.814)	0.936 (1.285)
Slope			
Non-drinker	-0.004 (0.207)	-0.196 (0.215)	-0.131 (0.156)
Irregular light-to-moderate	-0.157 (0.119)	0.211 (0.179)	0.013 (0.133)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	-0.063 (0.096)	0.078 (0.168)	-0.214 (0.138)
Regular heavy	-0.261 (0.179)	0.013 (0.209)	-0.665 (0.294)*
Women			
Intercept			
Non-drinker	-3.571 (0.939)***	-7.978 (1.347)***	-4.446 (1.005)***
Irregular light-to-moderate	-0.865 (0.712)	-2.269 (1.125)*	-1.723 (0.961)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	1.191 (0.754)	0.370 (1.248)	-1.200 (1.134)
Regular heavy	0.349 (0.852)	-1.582 (1.428)	1.330 (1.364)
Slope			
Non-drinker	-0.170 (0.144)	0.417 (0.262)	0.037 (0.189)
Irregular light-to-moderate	-0.133 (0.109)	0.484 (0.231)*	0.102 (0.179)
Regular light-to-moderate	Ref.	Ref.	Ref.
Irregular heavy	-0.121 (0.120)	0.505 (0.252)*	-0.039 (0.215)
Regular heavy	-0.122 (0.149)	0.253 (0.297)	-0.179 (0.294)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.5. Fully-adjusted problem drinking and PF-10 trajectories among survivors, male drinkers only

Problem drinking	Fully-adjusted model (mean, S.E.)		
	Czech Republic	**Russia**	**Poland**
Intercept			
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.795 (0.807)	1.563 (0.593)	-1.009 (0.900)
Slope			
Problem drinking			
No	Ref.	Ref.	Ref.
Yes	-0.080 (0.133)	-0.098 (0.153)	-0.157 (0.193)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.6. Fully-adjusted past drinking behaviour and PF-10 trajectories among survivors in the Russian cohort

	Fully-adjusted model (mean, S.E.)	
	Men	**Women**
Intercept		
Lifetime abstainer	-2.862 (2.657)	-4.534 (1.166)***
Former drinker, health reasons	-9.496 (1.653)***	-11.312 (1.560)***
Former drinker, non-health reasons	-1.301 (1.008)	-5.621 (1.571)***
Reduced drinker, health reasons	-7.110 (0.904)***	-5.569 (0.955)***
Reduced drinker, non-health reasons	0.601 (0.541)	1.234 (0.684)
Continuing drinker	Ref.	Ref.
Slope		
Lifetime abstainer	-0.119 (0.567)	-0.017 (0.209)
Former drinker, health reasons	-0.290 (0.300)	-0.054 (0.255)
Former drinker, non-health reasons	-0.221 (0.211)	0.173 (0.267)
Reduced drinker, health reasons	0.100 (0.194)	0.306 (0.183)
Reduced drinker, non-health reasons	0.113 (0.125)	0.118 (0.129)
Continuing drinker	Ref.	Ref.

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix M.7. Fully-adjusted past drinking behaviour combined with drinking pattern and PF-10 trajectories among survivors in the Russian cohort

	Model 2 (mean, S.E.)	
	Men	**Women**
Intercept		
Lifetime abstainer	-3.000 (2.732)	-4.759 (1.546)**
Former drinker, health reasons	-9.592 (1.790)***	-11.527 (1.860)***
Former drinker, non-health reasons	-1.371 (1.172)	-5.825 (1.863)**
Reduced drinker, health reasons	-7.217 (1.141)***	-5.725 (1.372)*
Reduced drinker, non-health reasons	0.498 (0.827)	1.070 (1.210)
Infrequent light-to-moderate drinker	-0.978 (1.013)	-0.907 (1.136)
Frequent light-to-moderate drinker	Ref.	Ref.
Infrequent heavy drinker	-0.310 (0.958)	2.286 (1.586)
Frequent heavy drinker	0.511 (0.837)	2.029 (1.276)
Slope		
Lifetime abstainers	0.059 (0.588)	0.161 (0.305)
Former drinker, health reasons	-0.120 (0.355)	0.123 (0.333)
Former drinkers, non-health reasons	-0.055 (0.259)	0.349 (0.347)
Reduced drinkers, health reasons	0.271 (0.267)	0.478 (0.282)
Reduced drinkers, non-health reasons	0.284 (0.209)	0.290 (0.251)
Infrequent light-to-moderate drinker	0.310 (0.232)	0.212 (0.238)
Frequent light-to-moderate drinker	Ref.	Ref.
Infrequent heavy drinker	0.211 (0.244)	-0.127 (0.343)
Frequent heavy drinker	0.151 (0.214)	0.196 (0.275)

* p<0.05, ** p<0.01, *** p<0.001; S.E.: standard error; Ref: reference category
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

Appendix N. Comparison of GF-based alcohol indices, problem drinking and other alcohol measures at baseline

Appendix N.1. Comparison of GF-based alcohol indices, problem drinking and other alcohol measures at baseline in the Czech cohort

Czech Republic	Men							Women						
	Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]			Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]		
	Median	N	Median	N	Mean	SD	N	Median	N	Median	N	Mean	SD	N
Average drinking frequency														
Never	0	248	0	230	28.82	40.94	107	0	794	0	714	32.84	85.12	172
<1/month	5.71	549	1.40	491	28.97	49.74	218	0	1217	0	1132	21.58	36.76	229
1-3/month	8.57	670	2.66	597	33.13	48.94	264	2.86	1110	1.30	1058	18.04	47.63	183
1-4/week	17.14	1201	7.80	1082	38.86	63.59	421	7.14	923	4.30	844	38.38	102.69	157
≥5/week	38.29	1258	25.00	1153	53.93	95.53	488	17.14	322	10.65	298	69.40	168.16	42
Annual drinking volume (g)														
0	0	248	0	230	28.82	40.94	107	0	794	0	714	32.84	85.12	172
1-1500[a] /1-250[b]	5.71	1243	2.05	1122	28.89	43.09	499	0	1260	0	1182	21.48	45.71	250
1501-4000[a] /251-500[b]	14.29	699	7.21	634	39.53	72.42	258	1.43	526	1.30	492	14.05	20.83	100
4001-8000[a] /501-1500[b]	23.71	583	10.59	519	37.92	70.77	211	3.14	716	2.05	680	20.27	41.42	105
>8000[a] />1500[b]	40.86	1153	25.00	1048	58.41	96.10	423	11.43	1070	5.54	978	53.08	133.58	156
Average drinking quantity per day														
Non-drinker	0	248	0	230	28.82	40.94	107	0	794	0	714	32.84	85.12	172
Light	17.14	2618	8.45	2377	37.41	69.96	1028	2.86	1470	1.40	1386	23.23	62.58	279
Moderate	28.57	374	10.00	344	49.95	60.56	120	2.86	1671	1.40	1551	27.96	78.10	275
Heavy	27.43	686	9.75	602	54.70	88.81	243	4.29	431	1.40	395	52.85	122.51	57
Drinking patterns														
Non-drinker	0	248	0	230	28.82	40.94	107	0	794	0	714	32.84	85.12	172
Irregular light-to-moderate	5.14	505	1.30	453	29.45	53.87	211	0	1148	0	1075	20.71	33.46	230
Regular light-to-moderate	17.14	1492	8.60	1342	36.99	61.72	638	5.71	1113	2.05	1036	24.55	72.88	206
Irregular heavy	22.86	982	10.00	897	38.96	72.18	323	5.71	879	2.41	828	28.85	80.67	109
Regular heavy	37.14	699	13.83	631	70.06	107.14	219	11.43	432	4.30	393	63.88	151.61	66
Problem drinking														
No	16.57	3525	6.71	3197	35.34	55.80	1359	1.43	4194	10.34	3898	27.89	73.93	753
Yes	41.71	359	17.92	326	97.10	154.54	118	20.00	91	0	81	111.89	217.14	15

[a] Among men; [b] Among women; [c] Separate questions on beverage-specific alcohol intake during one week; [d] FFQ: food frequency questionnaire (separate questionnaire); [e] GGT: gamma-glutamyl transferase; please note that the GGT in Russia was analysed in a different laboratory from the GGT in Czech Republic and Poland.

Appendix N.2. Comparison of GF-based alcohol indices, problem drinking and other alcohol measures at baseline in the Russian cohort

Russia	Men							Women						
	Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]			Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]		
	Median	N	Median	N	Mean	SD	N	Median	N	Median	N	Mean	SD	N
Average drinking frequency														
Never	0	571	0	552	30.07	35.02	569	0	901	0	878	27.32	21.31	892
<1/month	0	587	1.24	570	32.34	27.22	585	0	2327	0.65	2281	29.29	30.42	2313
1-3/month	0	1090	3.87	1068	37.49	47.36	1086	0	1411	1.24	1380	28.90	23.29	1407
1-4/week	12.86	1630	9.00	1589	43.08	46.98	1621	4.14	399	2.60	395	33.01	32.91	397
≥5/week	38.29	360	26.26	345	55.13	83.58	359	16.00	24	4.09	24	33.00	22.83	24
Annual drinking volume (g)														
0	0	571	0	552	30.07	35.02	569	0	901	0	878	27.32	21.31	892
1-1500[a] /1-250[b]	0	1194	1.89	1162	33.02	31.88	1188	0	1567	0.59	1533	28.13	25.48	1559
1501-4000[a] /251-500[b]	4.29	823	5.92	805	39.94	52.05	820	0	1425	0.59	1397	29.21	30.71	1417
4001-8000[a] /501-1500[b]	11.00	688	9.00	678	42.55	46.19	683	0	761	1.26	747	30.46	26.10	759
>8000[a] />1500[b]	26.14	962	16.80	927	50.21	64.89	960	5.14	408	3.31	403	34.32	34.13	406
Average drinking quantity per day														
Non-drinker	0	571	0	552	30.07	35.02	569	0	901	0	878	27.32	21.31	892
Light	2.86	1016	3.87	988	36.46	42.84	1011	0	962	0.65	949	28.15	22.85	958
Moderate	5.71	769	8.17	752	40.77	53.47	765	0	2500	0.65	2445	28.86	26.12	2486
Heavy	8.57	1882	8.17	1832	43.31	51.70	1875	0	699	1.26	686	33.86	40.42	697
Drinking patterns														
Non-drinker	0	571	0	552	30.07	35.02	569	0	901	0	878	27.32	21.31	892
Irregular light-to-moderate	0	547	1.24	533	31.37	25.63	546	0	2380	0.65	2332	28.57	25.96	2366
Regular light-to-moderate	5.71	1203	5.82	1175	40.23	50.60	1195	0	809	1.30	795	28.29	23.09	806
Irregular heavy	5.14	649	6.21	636	36.48	27.97	645	0	663	1.26	651	31.97	37.90	660
Regular heavy	16.29	1268	10.40	1228	47.84	63.12	1265	2.29	309	1.91	302	34.95	34.32	309
Problem drinking														
No	0	3425	3.87	3344	36.69	39.75	3409	0	4990	0.65	4888	28.89	26.52	4963
Yes	17.54	813	11.32	780	50.93	72.98	811	2.21	72	1.26	70	46.96	59.56	70

[a] Among men; [b] Among women; [c] Separate questions on beverage-specific alcohol intake during one week; [d] FFQ: food frequency questionnaire (separate questionnaire); [e] GGT: gamma-glutamyl transferase; please note that the GGT in Russia was analysed in a different laboratory from the GGT in Czech Republic and Poland.

Appendix N.3. Comparison of GF-based alcohol indices, problem drinking and other alcohol measures at baseline in the Polish cohort

Poland	Men							Women						
	Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]			Weekly alcohol intake (g/day)[c]		Alcohol intake from FFQ (g/day)[d]		GGT[e]		
	Median	N	Median	N	Mean	SD	N	Median	N	Median	N	Mean	SD	N
Average drinking frequency														
Never	0	1139	0	1011	32.46	70.92	364	0	2532	0	2241	20.37	30.76	360
<1/month	2.86	727	0	642	28.63	47.51	234	0	1205	0	1101	25.83	54.37	148
1-3/month	11.43	1196	1.24	1103	37.03	63.21	333	0	1016	0.65	950	20.17	34.92	125
1-4/week	28.57	1476	4.30	1315	46.08	85.30	388	5.71	554	2.64	516	20.97	26.21	46
≥5/week	25.71	591	11.24	532	73.06	115.23	131	17.1	95	10.00	88	37.90	53.71	7
Annual drinking volume (g)														
0	0	1139	0	1011	32.46	70.92	364	0	2532	0	2241	20.37	30.76	360
1-1500[a] /1-250[b]	0	1993	0.65	1781	34.49	66.42	600	0	1319	0	1206	24.31	51.10	169
1501-4000[a] /251-500[b]	8.57	961	4.30	881	45.71	79.41	240	0	555	0.65	523	26.67	46.66	61
4001-8000[a] /501-1500[b]	16.00	496	5.54	451	44.44	61.63	124	2.86	555	1.40	520	16.40	22.97	62
>8000[a] />1500[b]	34.29	540	10.59	479	76.24	121.28	122	8.57	441	4.30	406	24.16	31.41	34
Average drinking quantity per day														
Non-drinker	0	1139	0	1011	32.46	70.92	364	0	2532	0	2241	20.37	30.76	360
Light	5.71	2996	2.64	2696	41.10	79.53	836	0	1589	0.59	1447	23.12	50.35	176
Moderate	11.09	354	2.55	330	43.03	57.50	89	0	1095	0.65	1040	23.77	37.75	127
Heavy	11.43	640	1.99	566	51.47	78.63	161	0	186	0.59	168	21.10	25.84	23
Drinking patterns														
Non-drinker	0	1139	0	1011	32.46	70.92	364	0	2532	0	2241	20.37	30.76	360
Irregular light-to-moderate	0	749	0	674	28.37	47.11	241	0	1260	0	1160	26.31	53.60	154
Regular light-to-moderate	8.57	1821	4.08	1622	45.51	81.95	512	2.86	1006	1.40	938	21.14	38.63	105
Irregular heavy	8.57	941	3.19	876	41.82	82.08	229	0	453	1.24	423	17.75	24.12	52
Regular heavy	28.57	479	5.56	420	65.02	97.10	104	10.00	151	2.65	134	25.24	26.76	15
Problem drinking														
No	3.57	4027	1.40	3615	39.05	75.80	1144	14.86	3894	0	3579	22.67	41.16	477
Yes	28.57	450	5.56	409	71.67	108.01	112	0	50	5.54	46	26.94	31.44	5

[a] Among men; [b] Among women; [c] Separate questions on beverage-specific alcohol intake during one week; [d] FFQ: food frequency questionnaire (separate questionnaire); [e] GGT: gamma-glutamyl transferase; please note that the GGT in Russia was analysed in a different laboratory from the GGT in Czech Republic and Poland.

Appendix O. Comparison of PF-10 score and objective physical performances at re-examination

	Grip strength			5 chair stands (seconds)		
	Mean	SD	N	Mean	SD	N
Observed re-examination PF-10 quartiles*						
Czech Republic						
1st	29.12	10.50	1522	12.20	4.39	1269
2nd	32.80	10.06	1921	9.93	4.06	1896
≥3rd§	37.00	10.62	1635	8.63	2.63	1622
Russia						
1st	27.63	9.35	1604	13.28	4.08	1240
2nd	32.63	9.84	1985	11.48	3.21	1899
3rd	37.47	10.40	1005	10.55	2.77	994
4th	39.93	10.73	1402	10.24	2.84	1385
Poland						
1st	27.41	10.35	1799	13.12	5.08	1491
2nd	31.53	10.12	1701	10.80	3.45	1642
≥3rd§	35.98	10.39	2888	9.78	3.01	2838
Corrected re-examination PF-10 quartiles*						
Czech Republic						
1st	28.77	10.59	1251	12.54	4.57	1005
2nd	31.94	9.93	1266	10.37	4.45	1247
3rd	34.05	10.09	1280	9.44	3.12	1265
4th	37.33	10.87	1281	8.53	2.59	1270
Poland						
1st	26.93	10.24	1564	13.46	5.24	1265
2nd	30.90	9.95	1611	11.03	3.55	1550
3rd	34.84	10.10	1613	10.10	3.04	1579
4th	36.72	10.73	1600	9.51	2.89	1577

* Country-specific baseline PF-10 quartiles; § unable to distinguish the 3rd and 4th quartile due to the ceiling effect

Appendix P. Fully-adjusted odds ratios (95% confidence intervals) of physical limitations by alcohol consumption among participants with CVD free and fair-to-good self-rated health, imputed data

	Czech Republic		Russia		Poland	
	Men (N=3067-3090)	Women (N=3819-3833)	Men (N=2863)	Women (N=3167)	Men (N=3583-3593)	Women (N=3818-3829)
Average drinking frequency						
0	2.38 (1.20, 4.76)	1.72 (1.25, 2.36)	1.01 (0.54, 1.88)	1.14 (0.83, 1.57)	1.41 (0.96, 2.05)	1.53 (1.20, 1.95)
<1/month	1.83 (1.04, 3.22)	1.10 (0.81, 1.47)	0.69 (0.35, 1.36)	0.99 (0.78, 1.24)	1.84 (1.24, 2.72)	1.42 (1.10, 1.85)
1-3/month	1.00	1.00	1.00	1.00	1.00	1.00
1-4/week[a]	1.52 (0.92, 2.53)	--	1.36 (0.89, 2.10)	--	1.08 (0.75, 1.56)	--
≥5/week[a]	1.22 (0.73, 2.04)	--	1.29 (0.67, 2.45)	--	1.16 (0.73, 1.83)	--
≥1/week[b]	--	0.95 (0.69, 1.31)	--	0.88 (0.60, 1.29)	--	0.94 (0.67, 1.31)
Annual drinking volume (g)						
0	1.81 (0.98, 3.31)	1.55 (1.16, 2.06)	1.07 (0.57, 2.04)	0.97 (0.71, 1.32)	1.06 (0.77, 1.46)	1.09 (0.89, 1.33)
1-1500[a] /1-250[b]	1.00	1.00	1.00	1.00	1.00	1.00
1501-4000[a] /251-500[b]	1.32 (0.84, 2.05)	0.98 (0.68, 1.41)	1.28 (0.76, 2.15)	0.73 (0.57, 0.94)	0.75 (0.52, 1.08)	0.76 (0.55, 1.03)
4001-8000[a] /501-1500[b]	0.75 (0.43, 1.32)	0.80 (0.56, 1.15)	1.21 (0.69, 2.12)	0.66 (0.48, 0.89)	0.86 (0.56, 1.34)	0.62 (0.45, 0.86)
>8000[a] />1500[b]	1.10 (0.74, 1.63)	0.89 (0.65, 1.21)	1.38 (0.83, 2.29)	0.94 (0.65, 1.38)	0.89 (0.57, 1.38)	0.70 (0.48, 1.01)
Average drinking quantity/day						
Non-drinker	1.86 (1.06, 3.28)	1.44 (1.08, 1.92)	0.71 (0.38, 1.35)	1.13 (0.80, 1.59)	1.19 (0.87, 1.62)	1.14 (0.93, 1.39)
Light	1.00	1.00	1.00	1.00	1.00	1.00
Moderate	0.68 (0.36, 1.28)	0.73 (0.57, 0.95)	0.79 (0.45, 1.36)	0.97 (0.75, 1.26)	0.99 (0.60, 1.63)	0.71 (0.55, 0.91)
Heavy	1.48 (1.01, 2.17)	0.87 (0.58, 1.31)	0.75 (0.48, 1.17)	0.92 (0.65, 1.29)	1.17 (0.81, 1.69)	0.73 (0.43, 1.23)
Drinking pattern						
Non-drinker	1.62 (0.88, 2.98)	1.82 (1.22, 2.70)	0.68 (0.36, 1.29)	1.64 (0.93, 2.91)	1.15 (0.79, 1.66)	1.65 (1.14, 2.38)
Irregular light-to-moderate	1.07 (0.70, 1.62)	1.21 (0.84, 1.74)	0.57 (0.32, 1.01)	1.49 (0.89, 2.51)	1.09 (0.77, 1.54)	1.33 (0.92, 1.93)
Regular light-to-moderate	1.00	1.00	1.00	1.00	1.00	1.00
Irregular heavy	0.71 (0.47, 1.08)	0.81 (0.52, 1.27)	0.67 (0.41, 1.09)	1.00 (0.56, 1.78)	0.81 (0.56, 1.17)	1.34 (0.85, 2.12)
Regular heavy	1.34 (0.73, 2.45)	1.05 (0.64, 1.73)	1.03 (0.59, 1.78)	1.92 (1.04, 3.54)	1.42 (0.70, 2.88)	0.88 (0.47, 1.64)
Problem drinking[c]						
No	1.00	--	1.00	--	1.00	--
Yes	0.80 (0.44, 1.44)	--	1.28 (0.85, 1.95)	--	1.21 (0.78, 1.87)	--

[a] Among men, [b] Among women, [c] Among drinkers; Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.

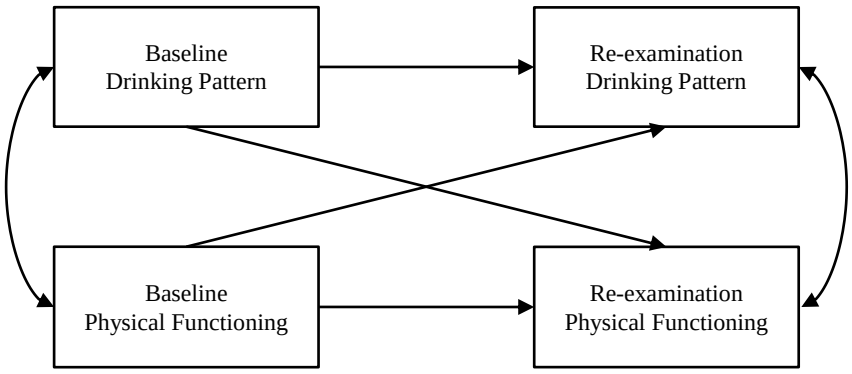
Appendix Q. Transition of drinking pattern between baseline and re-examination

	Czech Republic		Russia		Poland	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Constant non-drinkers	64 (2.82%)	219 (8.04%)	226 (8.37%)	311 (9.02%)	192 (6.05%)	585 (17.22%)
Constant irregular light-to-moderate	190 (8.37%)	594 (21.81%)	333 (12.34%)	1455 (42.20%)	384 (12.09%)	723 (6.45%)
Constant regular light-to-moderate	353 (15.56%)	136 (4.99%)	102 (3.78%)	12 (0.35%)	277 (8.72%)	69 (2.03%)
Constant irregular heavy	406 (17.89%)	149 (5.47%)	447 (16.56%)	92 (2.67%)	408 (12.85%)	65 (1.91%)
Constant regular heavy	44 (1.94%)	77 (2.83%)	130 (4.82%)	67 (1.94%)	33 (1.04%)	25 (0.74%)
Recent quitters	121 (5.33%)	331 (12.15%)	156 (5.78%)	320 (9.28%)	131 (5.01%)	219 (6.45%)
Decreased to irregular light-to-moderate	189 (8.33%)	344 (12.63%)	318 (11.78%)	416 (12.06%)	322 (10.14%)	281 (8.27%)
Decreased to regular light-to-moderate	297 (13.09%)	173 (6.35%)	121 (4.48%)	15 (0.44%)	164 (5.16%)	67 (1.97%)
Decreased to irregular heavy	54 (2.38%)	60 (2.20%)	167 (6.19%)	28 (0.81%)	39 (1.23%)	30 (0.88%)
Increased to irregular light-to-moderate	26 (1.15%)	134 (4.92%)	63 (2.33%)	216 (6.26%)	252 (7.93%)	699 (20.58%)
Increased to regular light-to-moderate	190 (8.37%)	213 (7.82%)	50 (1.85%)	28 (0.81%)	288 (9.07%)	234 (6.89%)
Increased to irregular heavy	248 (10.93%)	160 (5.87%)	405 (15.01%)	238 (6.90%)	587 (18.48%)	255 (7.51%)
Increased to regular heavy	87 (3.83%)	134 (4.92%)	87 (3.83%)	250 (7.25%)	99 (3.12%)	145 (4.27%)
Total	2269	2724	2699	3448	3176	3397

Appendix R. Bi-directional relationship between drinking pattern and physical functioning at baseline and re-examination, imputed data

The bi-directional relationship between drinking pattern and physical functioning in the three HAPIEE cohorts were explored by cross-lagged models.[460,461] For two repeat measures (*X* and *Y*), cross-lagged models estimate how *X* predict *Y* given the history of *Y* and how *Y* predict *X* given the history of *X* in one step.

Alcohol consumption and physical functioning were both measured at baseline and at re-examination in the HAPIEE study. Using data from these two measurement occasions, I constructed the cross-lagged models as shown in Appendix R.1, where arrows denote regression and double arrows denote correlation. Since drinking pattern is an index that combined both drinking frequency and quantity, drinking pattern was selected and entered into the models as an ordinal variable.



Appendx R.1. Diagram of cross-lagged model of alcohol consumption and physical functioning

Drinking pattern was entered into the models as an ordinal variable coded as: 1: no drinking; 2: irregular light-to-moderate drinking; 3: regular light-to-moderate drinking; 4: irregular heavy drinking; and 5: regular heavy drinking.

Appendix R.2. Cross-lagged model of drinking pattern and physical functioning at baseline and re-examination

	Fully-adjusted model (S.E.)		
	Czech Republic	**Russia**	**Poland**
Men			
Re-examination PF-10[a]			
Baseline PF-10	0.585 (0.017)***	0.511 (0.021)***	0.482 (0.018)***
Baseline drinking pattern	0.345 (0.227)	1.068 (0.235)***	0.052 (0.241)
Re-examination drinking pattern[b]			
Baseline PF-10			
Log odds	0.004 (0.001)**	0.004 (0.001)**	0.005 (0.001)***
Odds ratio	1.004	1.004	1.005
Baseline drinking pattern			
Log odds	0.499 (0.020)***	0.477 (0.017)***	0.376 (0.016)***
Odds ratio	1.647	1.611	1.456
Women			
Re-examination PF-10[a]			
Baseline PF-10	0.586 (0.016)***	0.446 (0.015)***	0.436 (0.014)***
Baseline drinking pattern	0.213 (0.221)	1.187 (0.301)***	0.176 (0.297)
Re-examination drinking pattern[b]			
Baseline PF-10			
Log odds	0.004 (0.001)***	0.006 (0.001)***	0.005 (0.001)***
Odds ratio	1.004	1.006	1.005
Baseline drinking pattern			
Log odds	0.419 (0.016)**	0.423 (0.018)***	0.334 (0.018)***
Odds ratio	1.520	1.527	1.397

[a] Linear regression; [b] Ordinal logistic regression; S.E.: standard error
Estimator: weighted least squares means and variance (WLSMV).
Adjusted for age, SEP (education, current economic activity, and household amenities), marital status, spine/joint problems, BMI and smoking.