FRESHER

FORESIGHT AND MODELLING FOR EUROPEAN HEALTH POLICY AND REGULATION

Project Acronym: FRESHER
Project Full Title: Foresight and Modelling for European Health Policy and regulation
Grant Agreement: 643576
Project Duration: 36 months (January 2013 - December 2015)
Coordinator: AMU - Jean Paul Moatti

D 2.4 Report on heterogeneity

Title: Report on heterogeneity
WP: WP2 Mapping social, behavioural, and biomedical determinants of chronic diseases
Authors: Lalla Attaiaa, Carla Blazquez, David Cantarero, Sebastien Cortaredona, Aurore Fayosse, Mika Gissler, Rafał Halik, Taavi Lai, Benedetta Mattioli, Audrey Michel-Lepage, Markku Peltonen, Maria Giovanna Quaranta, Archana Singh-Manoux, Maria Elena Tosti, Liina Üksik, Stefano Vella, Bruno Ventelou, Joanna Zembala-John.
Organisations: INSERM
Dissemination: Public
Date of publication: 28/06/2016

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

TABLE OF CONTENTS

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1 SOCIOECONOMIC STATUS & CHRONIC DISEASES

1.1 Introduction

Social determinants of health are broadly defined by the World Health Organization (WHO) as the conditions in which persons are born, grow, live, work, and age; conditions that are shaped by the distribution of power, income and resources. The inverse association between socioeconomic status (SES) and both mental and physical health is a consistent finding in population studies.[1] Multiple markers from across the lifecourse are used to assess SES: parental social class, education, occupational position, income, and various area level indicators. There is consistent evidence of socioeconomic differences in general morbidity and mortality all over Europe.[2-4] Chronic diseases such as heart disease, cerebrovascular disease, chronic obstructive lung disease, and lung cancer are some of the illnesses that contribute the most to social inequality and the burden of disease in Europe.[5-9] Although some of the social differences are due to treatment and survival being unevenly distributed across social groups, differences in incidence rates for the underlying conditions seem to play a major role.[10-12]

The aim of this chapter is to examine the evidence for social inequalities in the seven chronic diseases listed below. In this umbrella review we only analyse existing meta-analysis and systematic reviews. However, the initial search terms are not restrictive and not recovered papers can be found in the accompanying excel document. We first describe the methodology which is common to all seven outcomes and then we describe the results for each outcome separately.

a. Cardiovascular disease
b. Diabetes
c. Cancer
d. Chronic lung disease
e. Musculoskeletal disorders
f. Depression
g. Neurologic disorders

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1.2 Methods

The following six steps were used to identify papers relevant to our analysis.

Step 1. We searched Web of Science, EMBASE, Econlit until November 2015. We limited electronic searches to human populations and articles in English. The articles that met the search terms for each chronic disease (see exact terms for each chronic disease in each sub section) were then extracted to an excel file.

Step 2. Excel database was searched for the terms "meta-analysis" and "systematic" (for systematic review) in order to identify a smaller set of articles that would proceed to step 3.

Step 3. The abstracts of all the papers identified in Step 2 were extracted. Then the abstracts were examined for whether the exposure (independent variable or risk factor) variable in the paper was a measure of SES. At this stage the terms psychosocial was also accepted.

Step 4. Of the papers that cleared step 3 we examined whether the study was on human populations, and whether it did not focus exclusively on countries outside Europe or special groups (ethnic minorities, pregnant women, etc.)

Step 5. For papers that cleared step 4 we examined whether the outcome was the chronic disease in question.

Step 6. For papers that cleared step 5 the full version of the paper was examined further and both SES (to ensure that SES was indeed the, or one of the, exposures examined (in studies that used psychosocial as a term) and outcome measures re-examined.

Inclusion and exclusion criteria: We only included papers with a clear focus on social inequalities. SES was considered to be measured by education, occupation, income, or area level measures of SES. We also excluded reviews on specific populations such as prisoners, pregnant women, children with disabilities, or when focus was exclusively on low income countries. In all the extracted data an attempt was made to pay attention to age, sex, and European differences.

Data extraction: Eligible studies were extracted by one person (AF) in close consultation with a second person (ASM).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1.3 Results

1.3.1 Cardiovascular disease

Cardiovascular diseases affect the circulatory system, i.e. heart and blood vessels. The two most common subsets of CVD are coronary heart disease (CHD) and stroke. Coronary heart disease is a term utilised to describe diseases that specifically affect the coronary arteries, commonly manifesting in heart attacks or angina. Stroke is an important element of CVD morbidity, disability and mortality. Those who have suffered one stroke are particularly vulnerable to further episodes. Although incidence is higher for men, strokes affect women more seriously.[13] Social inequalities in CVD have been widely reported and are the subject of much research. The search terms used to identify papers for our analysis are as follows:

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

"Coronary Heart Disease" OR "Coronary artery disease" OR "Myocardial Infarction" OR "Ischaemic Heart Disease" OR "Heart disease" OR "stroke" OR "cardiovascular disease"

The search yielded a total of 5757 results (**Figure 1**). After exclusion of 433 duplicates, we undertook a first screening of articles to remove articles that were not meta-analyses or systematic reviews. This led to 12 papers which after the steps outlined above until step 5 yielded six papers that are listed below. In step 6 one of these papers was excluded (in red in the list below) because it was an abstract presented at a conference, focused on subjective social status.[14]

- Pollitt, R.A., K.M. Rose, and J.S. Kaufman, Evaluating the evidence for models of life course socioeconomic factors and cardiovascular outcomes: a systematic review. BMC Public Health, 2005. 5: p. 7.
- Galobardes, B., G.D. Smith, and J.W. Lynch, Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. Annals of Epidemiology, 2006. 16(2): p. 91-104.
- Kerr, G.D., et al., Do vascular risk factors explain the association between socioeconomic status and stroke incidence: a meta-analysis. Cerebrovasc Dis, 2011. 31(1): p. 57-63.

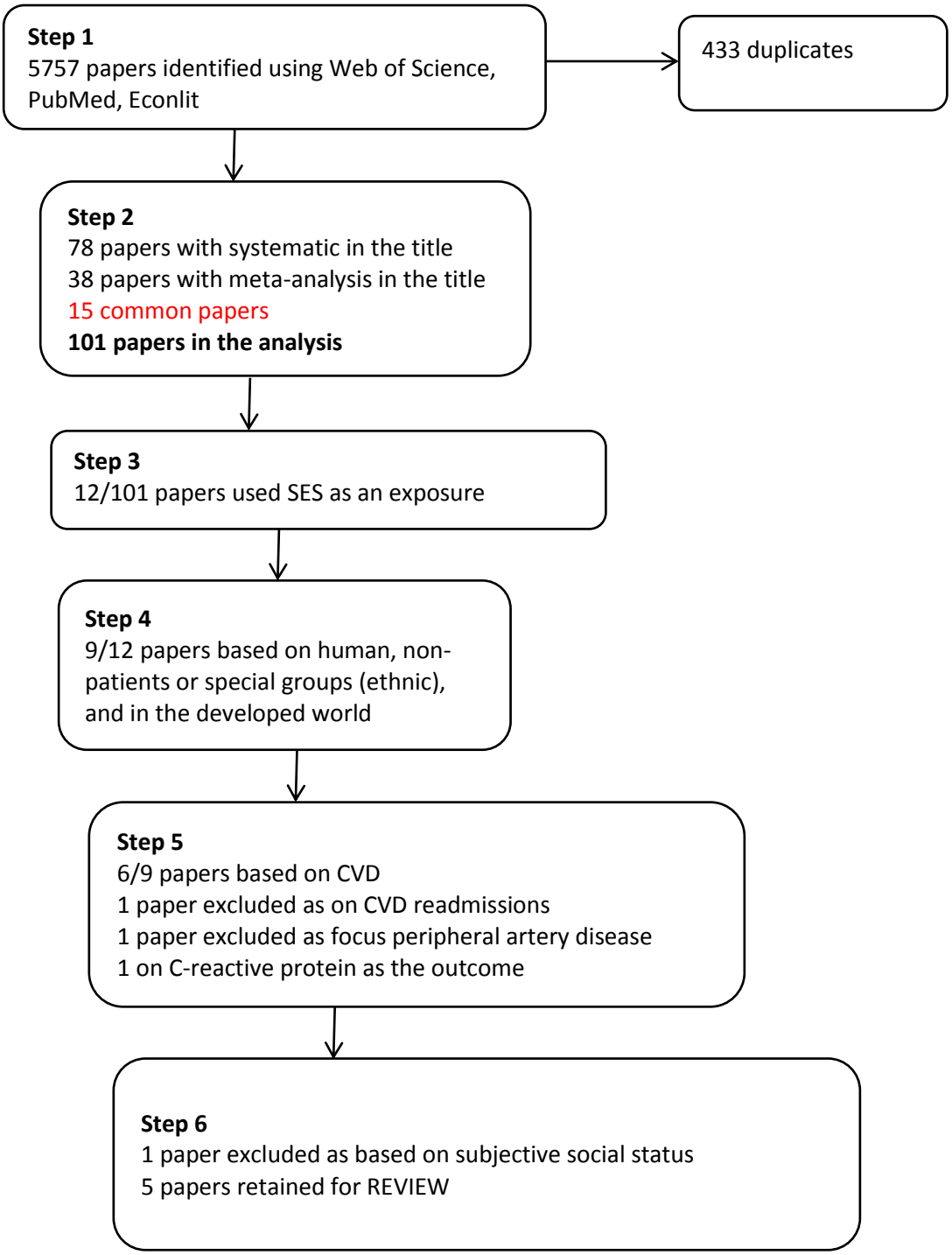
This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

- Manrique-Garcia, E., et al., Socioeconomic position and incidence of acute myocardial infarction: a meta-analysis. J Epidemiol Community Health, 2011. 65(4): p. 301-9.[15]
- Sommer et al., 2015 Socioeconomic inequalities in non-communicable diseases and their risk factors: an overview of systematic reviews.[16]
- Tang, K.R., Ruksana; Ghali, William A, *ASSOCIATION BETWEEN SUBJECTIVE SOCIAL STATUS AND CARDIOVASCULAR DISEASE AND CARDIOVASCULAR RISK FACTORS: A SYSTEMATIC REVIEW AND META-ANALYSIS.* JOURNAL OF GENERAL INTERNAL MEDICINE, 2015. **30**: p. S104-S105. [14]

Analysis of the five papers remaining in the analysis after the selection outline in **Figure 1** led us to regroup the results in two sections, one dealing with the effect of childhood SES which is constituted of papers by Pollitt et al. 2005 [17] and Galobardes et al. 2006 [18] and the other of adult SES, constituted of papers by Kerr et al. 2011 [19], Manrique-Garcia et al. 2011 [15] and Sommer et al. 2015 [16].

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 1. Results of the search to identify papers on social inequalities in CVD.



Childhood SES and CVD

The focus of Pollitt and colleagues [17] was the assessment of childhood markers of SES from a life course perspective which posits that the combination, accumulation, and/or interaction of the social environments and biological insults experienced throughout the life course impact current and future events, environments, and health conditions and thus

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

ultimately impact the development of chronic diseases such as CVD. The objective in many of the studies reviewed in this paper was to assess whether the childhood SES-adult CVD association was independent of adult SES, examined using statistical adjustment for adult SES. **Table 1** provides a summary of the results. The evidence on this research question was weak; the existence of a "direct effect" of early-life SES after adjusting for adult risk factors was not strongly supported. Most studies used retrospective cohorts or a case-control design, relying on participants' recall of early life SES. It is possible that in studies directly comparing the impact of childhood and adult SES on adult CVD risk, greater error in childhood (vs. adult) SES measures may underestimate the true impact of child SES.

Galobardes et al. 2006 [18] reviewed a total of 40 studies (24 prospective, 11 case-control, and 5 cross-sectional) of which a majority (31 in all - 19 prospective , 7 case-control and all 5 cross-sectional studies) found a robust inverse association between childhood circumstances and CVD. There was considerable heterogeneity in results as a function of the outcome in question, the SES measure, and study design. Key findings from this qualitative review were as follows:

- Outcome: Poor childhood SES was associated more strongly with stroke than CHD in five studies, the magnitude of the association was similar in two studies, and there was no association with stroke in two studies. Furthermore, the inverse association between childhood SES and haemorrhagic stroke risk did not diminish after adjusting for adult SES or risk factors. This contrasts with results for CHD, for which the risk associated with poorer childhood circumstances often diminished after accounting for adult circumstances.
- Measure of SES: Father's occupational class was the indicator used most often to measure childhood SES. However, studies also used measures such as parental education, housing conditions (e.g., having running water, type of toilet, ventilation, and cleanliness), crowding, number of siblings, living in a single-parent family, mother's marital status, inadequate food intake, parent's unemployment, self-reported economic problems during childhood, family without car, and sibling mortality. The authors conclude that there is no best measure of childhood SES, the consensus appears to be that a single indicator is unlikely to capture the multiple dimensions of SES. Sixteen of the 24 cohort studies used data on SES obtained during childhood or young-adulthood of the participant, whereas the rest obtained SES data through recall in adulthood. Studies

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

that measured SES in childhood generally showed stronger associations than those using adult recall of childhood SES.

- Study design: The majority (80%) of prospective studies, the study design that can present the strongest evidence, and all cross-sectional studies found an association between poor childhood circumstances and greater risk for CHD, angina, stroke, and atherosclerosis in adulthood. Case–control studies gave mixed results, possibly because of issues with the selection of controls.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 1. The association of early life SES with CVD outcomes, from Pollitt et al. 2005.[17]

Paper ref Study name Study size; % male	Study design; age at base-line (years)	Early life SES measures	Variables adjusted for other than age	CVD outcomes evaluated	Key findings
MI, CVD					
Burr 1980[20] South Wales hospital cohort 602; 100% M	Case-Control; 40-69	Father's occup, father unemployed (> than 1 year), family size	Current occup (3 groups)	MI (hospital patients)	In all 3 current SES groups, MI patients came from larger families ($p < 0.05$) & had higher proportion of fathers unemployed for over a year ($p < 0.05$).
Notkola 1985[21] East-West Study 1711; 100% M	Retrospective cohort; 40-59	5-level index using father's occup & farm size	Occup (6 groups), cholesterol, smoking, height	MI, IHD without MI	East Finland analysis: RR's vs. men born to large/medium farmers: small farmers: 1.24, landless: 1.63, craftsmen: 0.95, others/missing: 0.73 (no tests for statistical significance conducted). Fully adjusted RR's: small farmers: 1.22, landless: 1.31, craftsmen: 1.14, others/missing: 0.62.
Coggon 1990[22] Stoke-on-Trent & Newcastle study 351; 74% M	Case-control; 25-64	Father's occup (5 groups), height, perinatal sibling death	Current occup (5 groups), smoking	Acute MI	Somewhat elevated risk of MI for lower childhood SES; adjustment had little effect. Adjusted risk of MI vs. birth classes I-III non-manual: III manual: 1.9 (95% CI: 0.6-6.5), IV, V: 2.0 (95% CI: 0.5-7.6), military: 3.9 (95% CI: 0.8-19.2).
Hasle 1990[23] Danish worker's union study 1673; 100% M	Nested case-control; 50-67	8 variables (yes/no) on parent's occup, health, household condition, urban residence, edu, illness	None; cases were disability pensioners; controls were union members	self-reported MI	No significant differences between cases & controls. For entire group: OR for MI, less vs. more school: 1.95 (95% CI: 0.99-3.85), urban residence: 1.39 (95% CI: 0.98-1.98), broken home 1.38 (95% CI: 0.89-2.12). Among controls, broken homes & urban residence associated ($p < 0.05$) with MI.
Kaplan 1990 [24]Kuopio Study 2679; 100% M	Retrospective cohort; 42-0	Factor analysis of edu, occup, farm (yes/no), farm size, perceived wealth	Physical and behavioural CVD risk factors	IHD	Childhood SES associated ($p < 0.05$) with IHD. Adjustment for adult RF's did not attenuate association, but adjustment for adult SES attenuated association to non-significance. Age-adjusted RR's vs. High child SES: Med SES 1.35 (95% CI: 1.12-1.64), Low 1.44 (95% CI: 1.17-1.78). RR's adjusted for adult SES: Med: 1.20 (95% CI: 0.98-1.45), Low: 1.21 (95% CI: 0.97-1.51).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Paper ref Study name Study size; % male	Study design; age at base-line (years)	Early life SES measures	Variables adjusted for other than age	CVD outcomes evaluated	Key findings
Lundberg 1993[25] Swedish population cohort study 4216; 49% M	Prospective cohort; 30-75	4 yes/no variables: economic hardship, large family, broken family, dissension in family	Gender, father's social class (8 groups)	MI, HTN, weak heart, dizziness	Adjusted OR for childhood variables (for yes vs. no answer): economic hardship: 1.43 (p = 0.003), large family: 1.39 (p = 0.004), broken family: 1.64 (p = 0.001), family dissension: 2.42 (p = 0.001). Entering childhood variables into model together attenuated effect of economic hardship to non-significance.
Gliksman 1995 [26] Nurses' Health Study 117, 006; 0% M	Prospective cohort; 30-55	Father's occup (white, blue-collar, farmer, deceased) at 16 years	Husband's edu, wide range of covariates	Non-fatal MI	Increased risk of MI for women with fathers who were blue-collar: RR 1.23 (95% CI: 1.06-1.42) or deceased: RR 1.35 (95% CI: 1.08-1.69) versus white-collar, when women were 16. Adjustment for all RF's attenuated RR's to marginal statistical significance. Women with fathers who were farmers had lower RR: RR 0.93 (95% CI: 0.72-1.19); adjustment led to increased RR.
Lamont 2000 [27] Newcastle 1,000 Families Cohort 347; 44% M	Retrospective cohort; 49-51	Birth: father's occup (4 groups) 5 & 10 years: wage earner's occup, housing index, # of adverse life events in childhood	Adult SES: occup (4 groups), smoking, alcohol, diet, SBP, cholesterol, WHR, LDL, HDL, fibrinogen, insulin, more	% variance explained, carotid IMT	Independent contribution of early life was small (3.2% of variance (95% CI: 0.27-6.78) in M, 2.22% (95% CI: 0.21-5.04) in F) compared to adult biological risk markers (9.49% of variance (95% CI: 2.38-14.21) in M, 4.87% (95% CI: 1.56-7.39) in F). Higher total contribution of early life effects, including adult-mediated effects of childhood: 9.15% (95% CI: 2.42-12.26) for M, 4.73% (95% CI: 2.12-6.68) for F.
Marmot 2001[28] Whitehall II Study 10,308; 67% M	Prospective cohort; 35-55	Childhood: father's occup (4 groups), age leaving full time edu; Labour force entry: occup by civil service grade (high/middle/low)	Adult social class by civil service grade (high/ middle/low), father's SES, labour force entry SES	Self-reported CHD	Labour force entry & current occup grade both associated with CHD risk, but not childhood SES (unadjusted OR are 1.57 (95% CI: 0.9-2.7), 1.57 (95% CI: 1.0-2.4) and 1.10 (95% CI: 0.7-1.8), respectively). Adjustment for SES at other life course points attenuated all associations.
Wamala 2001 [29] Stockholm Study 584; 0% M	Case-control; 30-65	Early-life SES disadvantage index (0-3) of 3 variables: large family size, being born last, & low edu	Marital status, adult SES disadvantage, smoking, physical activity, abdominal obesity, HDL, triglycerides, HTN, fibrinogen	Acute MI, or recurrent/ unstable AP	Early life SES disadvantage somewhat associated with increased CHD risk (3 instances of disadvantage vs. none: OR = 2.65, (95% CI: 1.12-6.54); 2 instances: 1.73 (95% CI: 0.96-3.88)). After adjustment, OR for 3 instances: 2.48 (95% CI: 0.90-6.83); 2 instances: 1.34 (95% CI: 0.62-2.88). Later life SES disadvantage had greater effect on CHD risk.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Paper ref Study name Study size; % male	Study design; age at base-line (years)	Early life SES measures	Variables adjusted for other than age	CVD outcomes evaluated	Key findings
Stroke					
Gliksman 1995[26] Nurses' Health Study 117, 006; 0% M	Prospective cohort; 30-55	Father's occup (white-, blue-collar, farmer, deceased) at 16 years	Husband's edu, wide range of covariates	Stroke (fatal & non-fatal)	Women with deceased fathers when they were 16 had slightly elevated unadjusted stroke risk vs. women of white-collar fathers (RR 1.17 (95% CI: 0.91-1.47)). Women of fathers who were farmers had slightly decreased risk (RR 0.96 (95% CI: 0.74-1.23)).
Coggon 1990[22] Stoke-on-Trent & Newcastle study 351; 0% M	Case-control; > 65	Father's occup (5 groups), height, perinatal sibling death	Current occup (5 groups), smoking	Recent stroke	Slight or no elevated risk of stroke for those of lower childhood SES. Adjusted risk vs. birth classes I-IIINM: IIIM: 1.5 (0.4-6.3), IV, V: 0.9 (95% CI: 0.2-3.3), father in armed forces: 0.3 (95% CI: 0.0-3.3).
Davey Smith 1998[30] Collaborative Study 5645; 100% M	Prospective cohort; 35-64	Father's occup (4 groups), also divided into mnl vs. non-mnl groups	Adult class (6 groups), CVD RF's, area deprivation, car ownership	Stroke mortality	Lower vs. high father's SES associated with elevated stroke mortality in unadjusted analysis (p trend = 0.031). Fully adjusted RR of stroke mortality for mnl vs. non-mnl father's SES: 1.74 (95% CI: 1.05-2.90).
Frankel 1999 [31] Boyd Orr Cohort 3750; 50% M	Retrospective cohort; < 20	Father's occup (4 groups + unemployed)	Adult Townsend area deprivation score	Stroke mortality	Linear trend of increasing stroke mortality with decreasing childhood SES (p = 0.01). Adjustment for Townsend deprivation score did not alter findings.
Dedman 2001[32] Boyd Orr Cohort 4168; 50% M	Retros-pective cohort; < 20	Persons/room (crowding), tap water yes/no, toilet type (3 groups), ventilation (3 levels), cleanliness (3 levels)	Childhood SES by father's occup, per capita food expenditure & household per capita income; adult SES by Townsend area deprivation score[7]	Stroke mortality	Poorer housing conditions in childhood were not a major determinant of stroke mortality, although poorer ventilation was associated with higher stroke mortality. For higher crowding, p trend for HR = 0.53, no vs. yes tap water: p trend = 0.53, worse toilet type: p trend = 0.67, worse ventilation: p trend = 0.08, poor cleanliness: p trend = 0.07. Adjustment had minor impact.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Paper ref Study name Study size; % male	Study design; age at base-line (years)	Early life SES measures	Variables adjusted for other than age	CVD outcomes evaluated	Key findings
CHD Mortality					
Notkola 1985[21] East-West Study 1711; 100% M	Retrospective cohort; 40-59	5-level index using father's occup & farm size (large/medium farmers, small farmers, landless, craftsmen, others/missing)	Occup (6 groups), cholesterol, smoking, height	CHD mortality	East Finland analysis: Men born to small farmers and landless fathers had elevated risk of CHD death. RR's vs. men born to large/medium farmers: small farmers: 1.44, landless: 1.88, craftsmen: 0.69, others/missing: 1.17 (no tests for statistical significance conducted).
Lynch 1994[33] Kuopio Study 2636; 100% M	Pros-pective cohort; 42-60	SES index (3 groups), by parents' edu, occup, farm yes/no & size, perceived wealth	Adult SES by current income (2 groups)	CVD mortality	Childhood SES not clearly associated with CVD mortality. Low adult income vs. high adult income associated with CVD mortality (RR 2.37 (95% CI: 1.51-3.70)).
Vagero 1994[34] Uppsala Birth Cohort Study 404,450; 100% M	Retros-pective cohort; 25-40	Occup of head of household (mnl, non-mnl, unemployed)	Own occup (mnl, non-mnl, unemployed)	IHD mortality	Indication of independent effect of child SES on IHD mortality risk. Unadjusted RR vs. non-mnl child SES: mnl: 2.29 (95% CI: 1.51-3.46), unemployed: 2.23 (95% CI: 1.08-4.59). Adjusted RR, mnl: 1.99 (95% CI: 1.30-3.05), unemployed: 1.82 (95% CI: 0.88-3.77).
Gliksman 1995[26] Nurses' Health Study 117, 006; 0% M	Prospective cohort; 30-55	Father's occup (white-, blue-collar, farmer, deceased) at 16 years	Husband's edu, wide range of covariates	CVD mortality	RR vs. women of white-collar fathers: blue-collar father: 1.09 (95% CI: 0.86-1.37), farmer: 0.69 (95% CI: 0.46-1.05), father deceased: 1.20 (95% CI: 0.84-1.72). After adjustment, increased risk of children of blue-collar and deceased fathers disappeared; somewhat decreased risk of women of farmers remained.
Davey Smith 1998 [30] Collaborative Study 5645; 100% M	Prospective cohort; 35-64	Father's occup (4 groups), also divided into mnl vs. non-mnl groups	Adult class (RG, 6 groups), CVD RF's, area deprivation, car ownership	CHD mortality	Lower vs. high father's SES associated with elevated CHD mortality in unadjusted analysis (p trend 0.0003). Fully adjusted RR of CHD mortality for mnl vs. non-mnl fathers' SES: 1.26 (95% CI: 1.01-1.58).
Hart 1998[35] Collaborative Study 5567; 100% M	Prospective cohort; 35-64	Early SES: father's occup Labour force entry: occup SES at screening: occup (All 3 time points, 4 groups)	None; Relative Index of Inequality (RII) used to compare groups	CVD mortality	Increasing absolute risk of CVD mortality as childhood SES decreases (p trend < 0.0001); Relative Index of Inequality (RII) = 1.68 (95% CI: 1.30-2.17). Similar findings for labour force entry SES (p trend < 0.0001, RII = 1.62 (95% CI: 1.26-2.09)) and for SES at screening (p trend < 0.0001, RII = 1.79 (95% CI: 1.40-2.29)).
Frankel 1999 [31] Boyd Orr Cohort 3750; 50% M	Retrospective cohort; < 20	Father's occup (4 groups + unemployed)	Adult Townsend area deprivation score	CHD mortality	Linear trend of increasing CHD mortality with decreasing childhood SES (p = 0.12). Adjustment for Townsend deprivation score did not alter findings.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Paper ref Study name Study size; % male	Study design; age at base-line (years)	Early life SES measures	Variables adjusted for other than age	CVD outcomes evaluated	Key findings
Davey Smith 2001[36] Glasgow Alumni Cohort 8396; 100% M	Prospective cohort; university age	Childhood SES by father's social class, (5 groups)	SBP, smoking (most had privileged adult social environment)	CVD mortality	Strong association between childhood SES & CVD mortality. RR vs. RG class I: class II: 1.51 (95% CI: 1.08-2.11), III: 1.63 (95% CI: 1.17-2.27), IV: 1.85 (95% CI: 1.12-3.07), V: 2.36 (95% CI: 1.11-4.99). Trend of increasing CVD mortality risk with decreasing early SES (p trend = 0.002). Adjustment for SBP & smoking had little effect.
Dedman 2001 [32] Boyd Orr Cohort 4168; 50% M	Retrospectiv e cohort; < 20	Persons/room (crowding), tap water (yes/no), toilet type (3 groups), ventilation (3 levels), cleanliness (3 levels)	Childhood SES by father's occup (by RG) & per capita food expenditure & household per capita income; adult SES by Townsend area deprivation score[10]	CHD mortality	Poorer childhood housing conditions were in general associated with, but were not a major determinant of, CHD mortality. For higher crowding, p trend for HR = 0.11; no vs. yes tap water: p trend = 0.03; worse toilet type: p trend = 0.13, worse ventilation: p trend = 0.14, worse cleanliness: p trend = 0.37. Adjustment had small effect.
Davey Smith 2002[37] Collaborative Study 5628; 100% M	Prospective cohort; 35-64	Father's occup (mnl/non-mnl)	Occup (mnl/non-mnl), alcohol, smoking, area deprivation, age at leaving edu	CVD mortality	Mnl vs. non-mnl unadjusted RR for CVD mortality: 1.61 (95% CI: 1.39-1.88). Stratification by each adult risk factor did not attenuate the association between childhood SES and CVD mortality below statistical significance (p < 0.05).
Claussen 2003[38] [53] Oslo Mortality Study 101,487; 50% M	Retrospectiv e cohort; 31-50	Index of housing conditions items; Relative Index of Inequality (RII) used to compare groups	Adult household income (7 groups by income); RII used to compare groups	CVD mortality	CVD mortality more strongly related to childhood than adult SES for both M & F. RII for childhood SES: M: 2.79 (95% CI: 1.71-4.55), F: 3.96 (95% CI: 1.52-10.3). After adjusted for adult SES, RII for M: 2.68 (95% CI: 1.64-4.38), F: 3.80 (95% CI: 1.45-9.96). Supra-multiplicative interaction (p < 0.05) observed between childhood & adult SES.
Osler 2003[39] Project Metropolit 7493; 100% M	Pros-pective cohort; 49	Father's social class (3 groups: high/ middle, working, unknown) by occup status	Birth weight, cognitive function (IQ score) at age 12	CVD mortality	Men with working class & unknown class fathers had higher HR for CVD death than men with high/middle class fathers (p < 0.05). Adjustment attenuated HR (p > 0.05 for men with working class fathers).

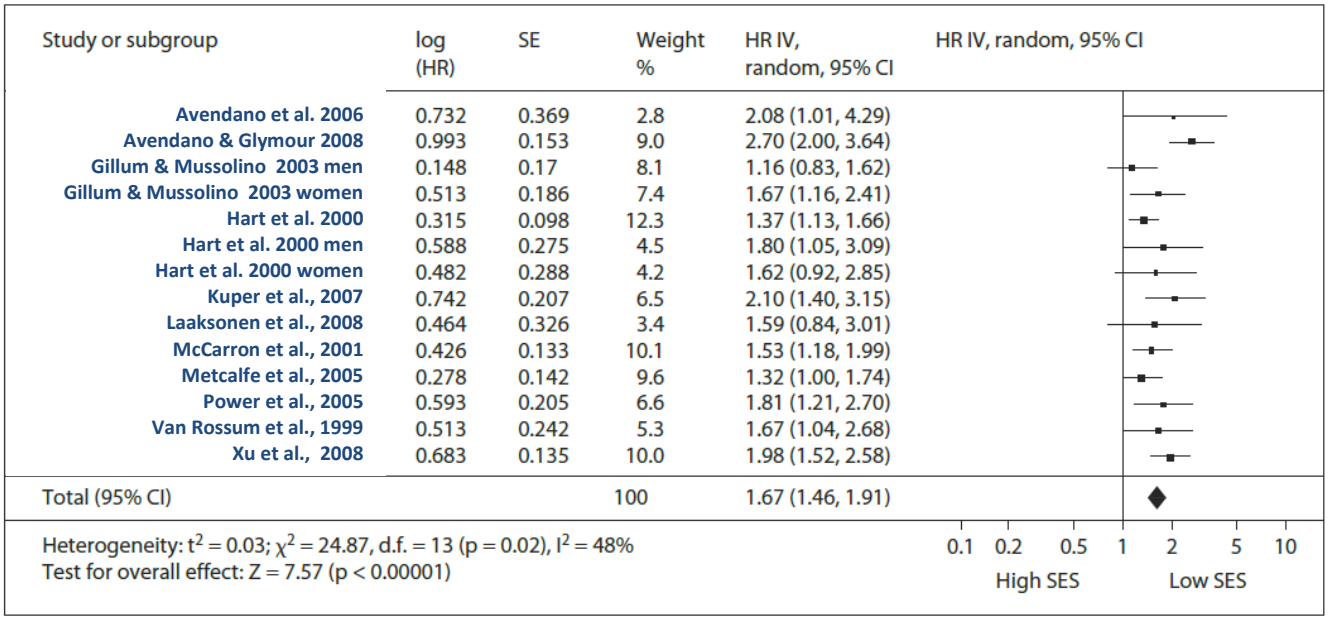
AP = Angina pectoris; BMI = Body mass index; CHD = Coronary heart disease; CVD = Cardiovascular disease; DBP = Diastolic blood pressure; Edu = Education; F = Female; FEV1 = Forced expiratory volume in 1 second; HR = Hazard ratio; HTN = Hypertension; IHD = Ischemic heart disease; M = Male; MI = Myocardial infarction; Mnl = Manual occupational class; Non-mnl = Non-manual occupational class; Occup = Occupation; OR = Odds ratio; RF = Risk factor; RG = Registrar General's social class categories; RR = Relative risk; SBP = Systolic blood pressure; SES = Socioeconomic status; WHR = Waist-to-hip ratio.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Adult SES and CVD

Kerr et al. 2011 [40] examined the role of vascular risk factors in the association between SES and stroke incidence. Their meta-analysis was based on 17 studies extracted from a search that yielded 6670 papers. Occupation (manual versus non-manual) was the preferred measure of SES but when not available other measures were used. In all studies the lowest socioeconomic category was compared with the highest. Results of the meta-analysis show that compared to those in the highest SES group those in the lowest group had a greater risk of stroke (HR 1.67; 95% CI 1.46–1.91), see **Figure 2** below. As is clear from the I^2 statistic there was considerable heterogeneity in the studies. The authors see this as being related to the use of different measures of SES, most studies used occupation to measure SES, but two studies used income, and 3 used education. Furthermore, the age of persons included in these studies covered a wide range and three of the studies examined incidence of fatal stroke while others examined non-fatal stroke.

Figure 2. Association between adult SES and stroke, from Kerr et al. 2011.[19]



List of studies in the meta-analysis, shown in Figure 2:

- Avendano M, Kawachi I, Van Lenthe F, Boshuizen HC, Mackenbach JP, Van den Bos GAM, et al: Socioeconomic status and stroke incidence in the US elderly – the role of risk factors in the EPESE study. Stroke 2006; 37: 1368–1373.[41]
- Avendano M, Glymour MM: Stroke disparities in older Americans: is wealth a more powerful indicator of risk than income and education? Stroke 2008; 39: 1533–1540.
- Gillum RF, Mussolino ME: Education, poverty, and stroke incidence in whites and blacks: the NHANES I Epidemiologic follow-up Study. J Clin Epidemiol 2003; 56: 188–195.[42]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

- Hart CL, Hole DJ, Smith GD: Influence of socioeconomic circumstances in early and later life on stroke risk among men in a Scottish cohort study. Stroke 2000; 31: 2093–2097. [43]
- Hart CL, Hole DJ, Smith GD: The contribution of risk factors to stroke differentials, by socioeconomic position in adulthood: the Renfrew/Paisley Study. Am J Public Health 2000; 90: 1788–1791.[44]
- Kuper H, Adami HO, Theorell T, Weiderpass E: The socioeconomic gradient in the incidence of stroke: a prospective study in middle-aged women in Sweden. Stroke 2007; 38: 27–33.[45]
- Laaksonen M, Talala K, Martelin T, Rahkonen O, Roos E, Helakorpi S, et al: Health behaviours as explanations for educational level differences in cardiovascular and all cause mortality: a follow-up of 60 000 men and women over 23 years. Eur J Public Health 2008; 18: 38–43.[46]
- McCarron P, Greenwood R, Elwood P, Shlomo YB, Bayer A, Baker I, et al: The incidence and aetiology of stroke in the Caerphilly and Speedwell Collaborative Studies II: risk factors for ischaemic stroke. Public Health 2001; 115: 12–20.[47]
- Metcalfe C, Davey SG, Sterne JA, Heslop P, Macleod J, Hart CL: Cause-specific hospital admission and mortality among working men: association with socioeconomic circumstances in childhood and adult life, and the mediating role of daily stress. Eur J Public Health 2005; 15: 238–244.[48]
- Power C, Hypponen E, Smith GD: Socioeconomic position in childhood and early adult life and risk of mortality: a prospective study of the mothers of the 1958 British birth cohort. Am J Public Health 2005; 95: 1396–1402.[49]
- van Rossum CTM, van de Mheen H, Breteler MMB, Grobbee DE, Mackenbach JP: Socioeconomic differences in stroke among Dutch elderly women: the Rotterdam Study. Stroke 1999; 30: 357–362.[50]
- Xu F, Ah TL, Yin X, Yu IT, Griffiths S: Impact of socio-economic factors on stroke prevalence among urban and rural residents in Mainland China. BMC Public Health 2008; 8: 170.[51]

Manrique-Garcia et al 2011 [15]conducted a review on the incidence of myocardial infarction (including MI death), mainly to rule out reverse causation effects that can be a problem in cross-sectional data. They used three measures of SES: educational attainment, income and occupation. The authors undertook pooled analysis for each of these indicators. To be included in the analyses, studies had to use original data, be designed as case control or cohort study, have incident MI as the outcome, present risk estimates with 95% CI, or report sufficient information to compute these for men, women or both. The results are for risk in the lowest compared with the highest SES category.

The overall results of this meta-analysis provided evidence of a significant increase in the risk of MI among the lowest socioeconomic categories for all three socioeconomic indicators (**Table 2** for pooled results). Heterogeneity was observed for all three SES indicators (I^2 between 77.6% and 95.9%, all $p<0.001$). This could be due to differences in study design, and assessment of exposures, confounders and the outcome. The strongest pattern was seen for the lowest income group in

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

which the incidence of MI increased by 71% compared with the high income group (RR 1.71, 95% CI 1.43, 2.05), this excess risk was 34% for education (RR 1.34, 95% CI 1.22, 1.47) and 35% for occupation (RR 1.35, 95% CI 1.19, 1.53). Further stratification by sex, adjustment strategy, study design, status of event, personal or household type of SES or publication years did not alter these overall pooled results. The results were less consistent among case control studies, particularly for the measure of occupation.

The increased incidence of MI was evident for the lowest income-based, educational and occupational SES in high-income countries and in regional areas such as the USA/Canada and Europe. The authors highlight some limitations of their study, the principal being the differences in the definition and classification of SES across studies. Use of the extreme SES categories also does not allow the social gradient to be studied.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 2. Pooled estimates for the lowest versus the highest socioeconomic category and incidence of MI, from Manrique-Garcia et al. 2011.[15]

	Income	I^2(%)	Education	I^2(%)	Occupation	I^2 (%)
Summary pooled estimate	**1.71 (1.43 to 2.05)**	**95.9**	**1.34 (1.22 to 1.47)**	**77.6**	**1.35 (1.19 to 1.53)**	**81.6**
Sex						
Male	1.50 (1.31 to 1.72)	54.8	1.24 (1.04 to 1.48)	83.7	1.34 (1.16 to 1.55)	77.3
Female	1.87 (1.48 to 2.36)	71.3	1.58 (1.25 to 2.00)	66.5	1.87 (1.34 to 2.60)	77.6
Country's income group						
High	1.76 (1.46 to 2.12)	96.3	1.39 (1.25 to 1.55)	79.3	1.41 (1.25 to 1.59)	80.6
Middle or low	1.46 (0.60 to 3.54)	81.3	1.16 (0.97 to 1.39)	54.9	0.51 (0.27 to 0.99)	37.0
Geographical region*						
USA/Canada	1.49 (1.27 to 1.75)	9.2	1.42 (1.28 to 1.57)	10.6	1.44 (1.22 to 1.70)	0.0
Europe†	1.80 (1.46 to 2.21)	97.0	1.33 (1.17 to 1.50)	82.6	1.37 (1.19 to 1.58)	4.4
Asia	1.52 (0.29 to 7.93)	88.0	1.90 (0.48 to 7.58)	86.3	0.67 (0.41 to 1.09)	
Latin America	1.27 (1.06 to 1.52)	—	1.23 (1.03 to 1.47)	59.2		
Middle East	—		1.18 (0.27 to 5.15)			
Adjustment strategy						
Unadjusted	1.79 (1.44 to 2.24)	97.5	1.37 (1.21 to 1.56)	81.3	1.27 (1.05 to 1.54)	68.1
Adjusted	1.58 (1.20 to 2.08)	70.1	1.26 (1.06 to 1.49)	68.4	1.41 (1.19 to 1.68)	80.5
Design						
Cohort	1.59 (1.45 to 1.75)	55.8	1.45 (1.27 to 1.66)	78.7	1.39 (1.24 to 1.56)	55.0
Case–control	1.91 (1.37 to 2.66)	91.3	1.23 (1.07 to 1.41)	74.1	1.17 (0.88 to 1.55)	82.8
Publication period						
Before 2000	2.64 (2.16 to 3.22)	0.0	1.43 (1.12 to 1.82)	70.7	1.34 (1.02 to 1.76)	54.6
2000 or after	1.58 (1.29 to 1.93)	97.2	1.31 (1.18 to 1.45)	80.2	1.37 (1.18 to 1.59)	87.9
Personal or household SES						
Personal	1.84 (1.49 to 2.26)	96.4	1.34 (1.22 to 1.47)	77.6	1.36 (1.20 to 1.55)	81.0
Household	1.45 (1.00 to 2.08)	89.0	—		1.35 (0.35 to 5.18)	89.1
Event						
Clearly first event ever	1.59 (1.30 to 1.94)	96.8	1.29 (1.16 to 1.43)	79.1	1.25 (1.09 to 1.43)	83.4
Potentially first event	2.47 (2.12 to 2.88)	0.0	1.75 (1.14 to 2.67)	74.4	2.04 (1.28 to 3.25)	68.5

The most recent of these studies was an overview of existing systematic reviews on socioeconomic inequalities in the incidence/prevalence as well as mortality associated with CVD by Sommer et al., 2015 [16]. Publications from 2003 until December 2013 were included and various measures of SES included: education, occupation, income, insurance status, and other indirect SES measures such as housing condition or maternal marital status. Reviews on specific populations such as prisoners, pregnant women, or children with disabilities were excluded.

The authors concluded that the evidence evaluating associations between SES and CVD is fairly consistent. This conclusion was based on the reviews by Kerr et al. 2011 [19], and Manrique-Garcia et al. 2011 [15] described above. They also reviewed results on childhood SES, focusing on the two papers we highlighted above [17,18], and there conclusion was also that the observed inverse

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

associations were often attenuated or disappeared when adjusting for CVD risk factors or adult SES.[17]

1.3.2 Diabetes

Type 2 diabetes describes a group of metabolic diseases in which the person has high blood glucose, either because insulin production is inadequate, or because the body's cells do not respond properly to insulin, or both. Patients with high blood sugar will typically experience polyuria (frequent urination), they will become increasingly thirsty (polydipsia) and hungry (polyphagia). Serious long-term complications include cardiovascular disease, stroke, chronic kidney failure, foot ulcers, and damage to the eyes. The search terms used to identify papers on social inequalities in diabetes were as follows.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

"Diabetes" OR "Diabetes Mellitus" OR "Type 2 Diabetes" OR "T2DM"

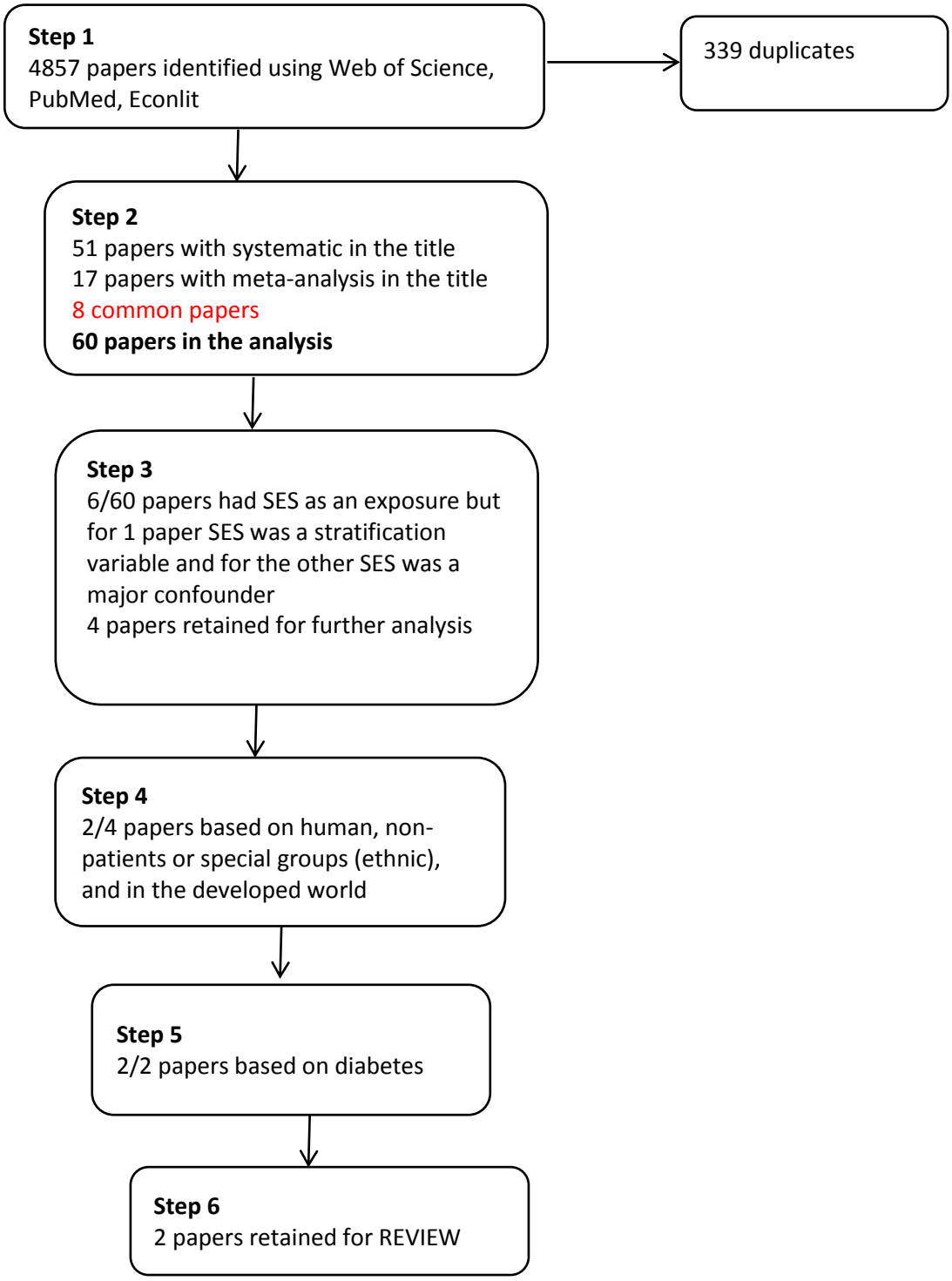
The search yielded a total of 4857 results (**Figure 3**). After exclusion of 339 duplicates, we undertook a first screening of articles to remove articles that were not meta-analyses or systematic reviews. This led to 2 papers which after the steps outlined above yielded the papers listed below.

- Agardh, E., et al., Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. Int J Epidemiol, 2011. 40(3): p. 804-18.[52]
- Tamayo, T., H. Christian, and W. Rathmann, Impact of early psychosocial factors (childhood socioeconomic factors and adversities) on future risk of type 2 diabetes, metabolic disturbances and obesity: a systematic review. BMC Public Health, 2010. 10: p. 525.[53]

Analysis of these two papers led us group the results in two sections, one dealing with the effect of childhood SES [53] and the other on adult SES.[52]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 3. Results of the search to identify papers on social inequalities in Type 2 diabetes.



Childhood SES and Type 2 Diabetes

The primary aim of the review by Tamayo et al. 2010 [53] was to evaluate the risk of psychosocial factors, including childhood SES, on type 2 diabetes incidence. As such, cross-sectional studies with data only on diabetes prevalence were excluded and so were studies with a

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

focus on type 1 diabetes. Multiple markers of SES were used: parental education, parental occupation, family income, public housing, housing conditions, house ownership, unemployment, neighbourhood deprivation indexes. Their review identified ten studies, see **Table 3**. These ten studies consisted of a total of 200,381 individuals. Eight out of ten studies indicated that low parental SES was associated with type 2 diabetes incidence or the development of metabolic abnormalities. Adjustment for adult SES and obesity tended to attenuate the childhood SES-attributable risk but the association remained statistically significant.

Sources of heterogeneity: Of the tens studies, four were birth cohorts [54-57], two were conducted in children or adolescents (age range 3-18 and 14-19 years, respectively)[58,59], the other studies measured childhood SES retrospectively. Self-reported diabetes was the most common outcome measure, only one study, Lidfeldt et al. 2007 [60], assessed diabetes using a gold-standard measure based on fasting plasma glucose levels in an originally diabetes-free cohort. In four studies, the risk of developing type 2 diabetes or metabolic disturbances in the offspring of lower social classes compared to children of higher status was only slightly elevated after adjustment for covariates with different effect measures (OR, HR and RR) ranging between 1.08 and 1.7 [56,58,60,61].

As shown in **Table 3**, the study with the smallest population size (N = 233) showed the largest protective effect (men OR 0.2 (95% CI 0.05, 0.8); women 0.6 (0.1 2.7)) from high SES group (father's occupation)[57]. This study was based on middle-aged participants of the Newcastle Thousand Families Cohort with a BMI exceeding 25 kg/m². Furthermore a large protective effect of maternal education (beyond elementary level) was found in a Mexican population (OR 0.6 (95% CI 0.5; 0,8)) [62]. In contrast, low maternal education at high school level or less was a significant factor influencing type 2 diabetes incidence in the Princeton School District Study (ß-coefficient = 4.47 (SE 0.78)). Two studies indicated small, nonsignificant protective effects of low social class. In a Finnish cohort children at the age of 7 years from blue-collar families had a reduced risk (OR 0.8 (95% CI 0.48; 1.45) of being diagnosed with type 2 diabetes in comparison with their white-collar counterparts [54]. In a British Cohort only women of the lowest SES group were less likely to have HbA1c levels exceeding 5.8% (OR 0.8 (95% CI 0.5; 1.4)). In men, no effect of SES was seen in this study (OR 1.1 (95% CI 1.0; 1.8)) [55].

Comparison of effect sizes suggests that improving SES over lifetime (spouse's high educational level and low father´s occupational status) with stable high SES as the reference resulted in a slightly reduced, albeit non-significant relative risk for type 2 diabetes (RR 0.9 (95% CI 0.7; 1.3), whereas a stable intermediate SES and a declining SES influenced the type 2 diabetes

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

relative risk negatively (RR 1.2 (95% CI 1.06; 1.4) and RR 1.18 (95% CI 1.06; 1.3), respectively). The relative risk in participants with stable low SES was comparable to those participants with stable high SES. Langenberg et al. [55]examined lifetime effects by analysing the change in the influence of the socioeconomic position on HbA1c levels with adjustment for childhood and adult SES. In both men and women, adult social class had stronger effects than childhood social class on HbA1c values exceeding 5.8%. In women childhood effects on HbA1c even reversed in the fully adjusted model. Langenberg et al. [55]interpret these findings by postulating that low childhood social class continues to influence adult social class as both variables were highly correlated. A high continuity of childhood and adult SES parameters was also observed in a Finnish cohort, where children from manual classes were more likely to work in manual or lower non-manual occupations in adulthood. [58]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 3. Overview of studies on childhood psychosocial factors and incident type 2 diabetes, from Tamayo et al. 2010 [53]

Paper ref.	Country.	N	Age at baselin	Follow up	Outcome	Effect size (95% CI or SE) (adjusted)		Study quality
Lidfeldt et al. 2007[60]	USA	100,330 females	30-55	22	**T2DM** (FPG > 140 mg/dl)	RR (CI) father labourer vs. rest	1.08 (0.95; 1.2)	1
Maty et al. 2008[61]	USA	5,913	17-94	34	Self-reported **DM**	HR (CI) for father manual vs. non-manual	m 1.2 (0.8; 1.7) w 1.7 (1.2; 2.4)	3
Gissler et al. 1999[54]	FIN	59,865	0	7	**DM** criteria register based	OR (CI) for mother blue-collar vs. upper white collar	0.83 (0.5; 1.5)	3
Hayes et al. 2006[57]	UK	233 (BMI≥25)	0	50	**"metabolically normal"** (MetS)	OR (CI) for father Class IV, V vs. I, II	m 0.2 (0.05; 0.8)* w 0.6 (0.1; 2.7)	1
Langenberg et al. 2006[55]	UK	2,629	0	53	**HbA1c** (> 5,8%)	OR (CI) for father lowest vs. highest class	m 1.1 (1.0; 1.8) w 0.8 (0.5; 1.4)	3
Kivimäki et al. 2006[63]	FIN	1,922	3-18	21	**HOMA-IR**	OR (CI) for parental SES change per descending category	m 1.3 (1.03; 1.6)* w 1.2 (0.98; 1.5)	4
Kohler et al. 2005[62]	MEX	6,423	50+	2	Self-reported **DM**	OR (CI)[h] for mother > elementary vs. rest	0.6 (0.5; 0.8)**	2
Bestet al. 2005 [64]	USA	12,589	51+	4	Self-reported **DM**	β (SE) for parental education regression coefficients (linear)	m 0.2 (0.1) w 0.05 (0.1)	2
Goodman et al. 2007 [59]	USA	1,167	13-19	3	**HOMA-IR**	β (SE) for parental education high school or less vs. rest	4.5 (0.78)**	3
Thomas et al. 2008 [56]	UK	9,310	0	45	**HbA1c** (> 6,0%);**MetS**	OR (CI) for mother: little interest in education	1.4 (0.99; 1.9)	3

T2DM: Type 2 Diabetes mellitus, DM: Diabetes mellitus, MetS: Metabolic Syndrome, HbA1c: Glycated Haemoglobin, HOMA-IR: Homeostatic Model Assessment - Insulin Resistance
B: Beta Coefficient, HR: Hazard Ratio, OR: Odds Ratio, RR: Relative Risk, CI: Confidence Interval, SE: Standard Error
[h]1 low, 5 high
ADA diagnostic criteria for type 2 diabetes mellitus: fasting plasma glucose (FPG) ≥ 126 mg/dl
** p < 0.01/* p < 0.05

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Adulthood SES and Type 2 Diabetes

Agardh et al. 2011 [52] conducted a systematic quantitative review to summarize the association between SES (measured by educational level, occupation and income) and type 2 diabetes incidence. A final 23 articles were included in the meta-analysis, involving approximately 21 978 cases.[60,61,65-85] The majority of studies (19 studies) were from high-income countries such as the USA, Great Britain, Sweden, Finland, Japan, Southern Taiwan, Germany and France, whereas three studies were from upper–middle-income countries, i.e. Mauritius, Brazil and Lithuania, referred to as middle-income, and only one was from a low-income country, Tanzania.

In the overall summary, there was an increased risk of type 2 diabetes in the lowest compared with the highest SES groups, measured by educational level (RR=1.41, 95% CI: 1.28–1.51), occupation (RR=1.31, 95% CI: 1.09–1.57) or income (RR=1.40,95% CI: 1.04–1.88) (**Table 4**). A moderate heterogeneity was observed for all three indicators, i.e. educational level (P<0.001, I^2=65.5%), occupation (P=0.020, I^2=52.8%) and income (P=0.002, I^2=71.9%) (**Table 4**). Sub-group analyses showed that socioeconomic inequalities in type 2 diabetes incidence were more pronounced in women than men (**Table 4**). The socioeconomic differential was also more consistent in high-income countries. Although increased risks were observed with lower SES also in middle- and low-income countries, data from these economies were very limited. Further comparison of adjustment for covariates showed that the SES-diabetes association survived adjustment for multiple covariates (sex, age, residence, and well-established risk factors for diabetes) only for education. The association between education and diabetes was robust to the method of ascertainment of diabetes (**Table 4**).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 4. Pooled estimates for lowest vs highest SES group and incidence of type 2 diabetes, from Agardh et al. 2011 [52]

Sub-groups	Educational level	Occupation	Income
Overall	1.41 (1.28–1.51); I^2 = 65.5, P < 0.001	1.31 (1.09–1.57); I^2 = 52.8, P = 0.020	1.40 (1.04–1.88); I^2 = 71.9, P = 0.002
Sex			
Men	1.46 (1.15–1.86); I^2 = 60.0, P = 0.020	1.19 (1.05–1.36); I^2 = 0.0, P = 0.598	1.33 (0.88–1.20); I^2 = 43.0, P = 0.185
Women	1.72 (1.26–2.35); I^2 = 87.4, P = 0.001	1.52 (0.93–2.49); I^2 = 71.0, P = 0.008	1.77 (1.29–2.41); I^2 = 0.0, P = 0.320
Combined	1.28 (1.18–1.38); I^2 = 16.6, P < 0.001	–	1.19 (0.69–2.06); I^2 = 66.6, P = 0.050
Countries, Income			
High-income	1.45 (1.28–1.63); I^2 = 70.1,P < 0.001	1.31 (1.05–1.63); I^2 = 60.7, P = 0.009	1.40 (0.81–2.42); I^2 = 79.9, P = 0.002
Middle-income	1.59 (1.28–1.97); , I^2 = 0.0, P = 0.550	1.27 (0.96–1.68); I^2 = 0.0, P = 0.360	1.39 (1.06–1.82); I^2 = 22.7, P = 0.274
Low-income	1.27 (0.99–1.62)	–	–
Geographical area			
USA	1.41 (1.24–1.62); I^2 = 79.2, P < 0.001	1.43 (0.91–2.24); I^2 = 78.9, P = 0.003	1.40 (0.18–2.42); I^2 = 79.9, P = 0.002
Europe	1.45 (1.20–1.76); I^2 = 3.5, P = 0.394	1.47 (1.06–2.05); I^2 = 0.0, P = 0.646	–
Asia/Middle East	1.43 (1.08–1.89); I^2 = 50.3, P = 0.156	1.10 (0.90–1.33); I^2 = 9.2 , P = 0.294	–
Latin America	1.43 (1.20–1.76)	–	1.80 (1.06–3.01)
Africa	1.40 (1.15–1.75); I^2 = 26.8, P = 0.255	1.27 (0.96–1.68); I^2 = 0.0, P = 0.360	1.29 (0.95–1.74); I^2 = 23.3, P = 0.253
Adjustment			
Minimally adjusted	1.50 (1.27–1.79); P < 0.001, I^2 = 68.7	1.51 (1.12–2.03); I^2 = 70.2, P = 0.009	1.50 (1.17–1.92); I^2 = 22.6, P = 0.270
Maximally adjusted	1.28 (1.17–1.40); P = 0.086, I^2 = 40.7	1.14 (0.93–1.39); I^2 = 12.1, P = 0.338	1.21 (0.62–2.38); I^2 = 83.1, P = 0.015
Publication year			
<2000s	1.35 (1.13–1.61); I^2 = 50.4, P = 0.073	1.17 (0.94–1.45)	1.18 (0.30–4.66)
≥2000s	1.44 (1.29–1.62); I^2 = 68.6, P < 0.001	1.34 (1.08–1.66); I^2 = 56.1, P = 0.015	1.41 (1.03–1.91); I^2 = 76.6, P = 0.001
Assessment of cases			
Self-report	1.13 (1.03–1.25); I^2 = 1.20, P = 0.386	1.06 (0.78–1.44); I^2 = 8.2, P = 0.297	0.90 (7.62–1.06)
Self-report verified	1.47 (1.27–1.72); I^2 = 43.8, P = 0.149	1.47 (1.06–2.05); I^2 = 0.0, P = 0.646	–
Blood glucose	1.45 (1.28–1.64); I^2 = 0.0, P = 0.560	1.15 (0.98–1.34); I^2 = 0.0, P = 0.456	1.36 (1.08–1.71); I^2 = 0.0, P = 0.452
Register	1.20 (1.15–1.26); I^2 = 0.0, P = 0.747	–	–
Medical records	1.67 (1.26–5.65); I^2 = 83.7, P = 0.013	2.00 (0.98–4.11); I^2 = 83.6, P = 0.014	1.95 (1.36–2.79); I^2 = 0.0, P = 0.592

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1.3.3 Cancer

Cancer, also known as a malignant tumour or malignant neoplasm, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. There are more than 100 types of cancer and its treatment may include chemotherapy, radiation, and/or surgery. Initial search was carried out not limiting the search to specific cancers, this search identified over a million papers. In the subsequent search, we modified the terms to focus on the common cancers, final search terms are described below.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

"Cancer" OR "neoplasm"

AND

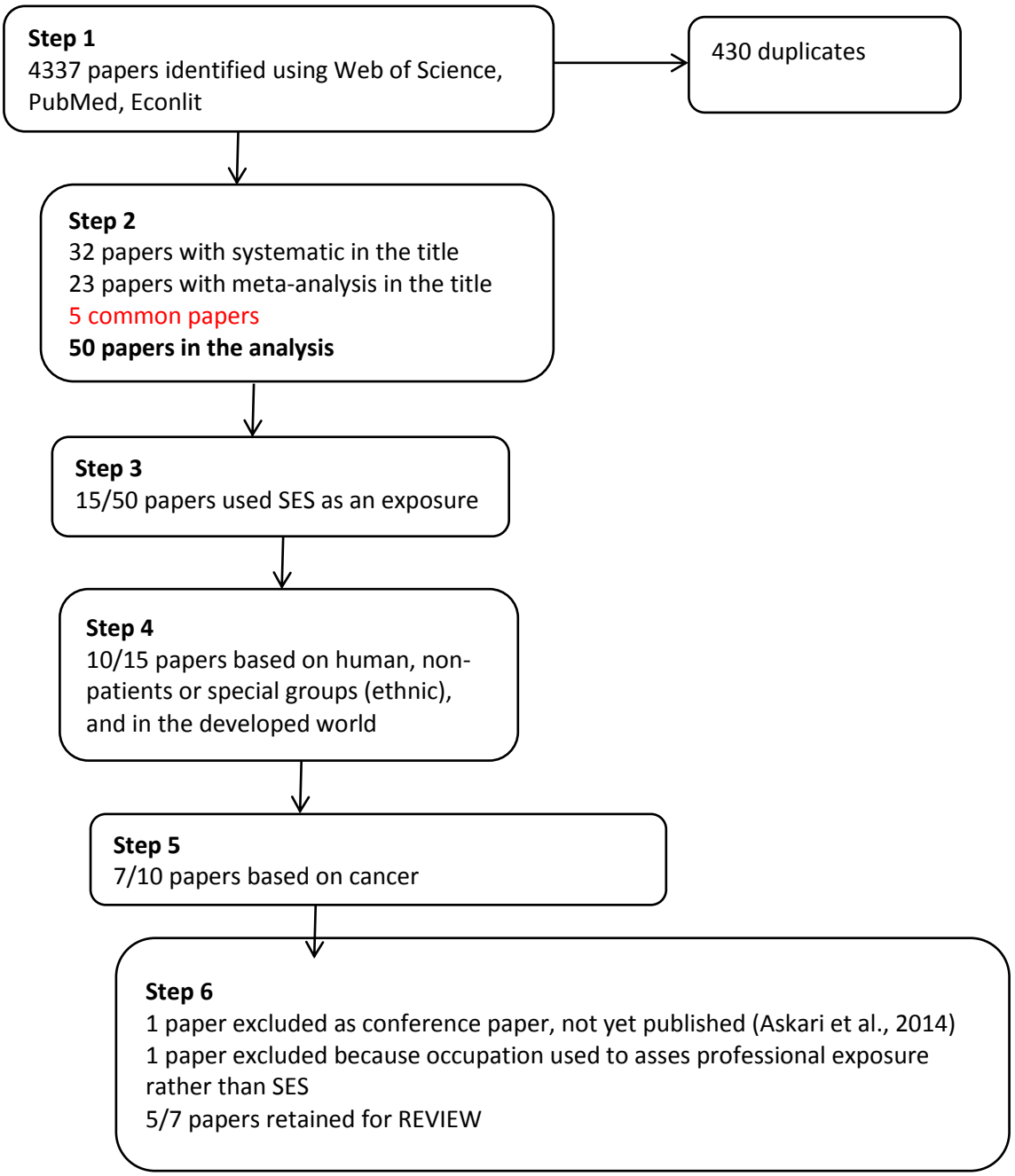
"Breast" OR "lung" OR "colorectal" OR "prostate" OR "oral"

A total of 4337 papers were identified (**Figure 4**), of which only 7 papers listed below reached step 6. Finally, two papers (in red below) were excluded as one was a conference report and the other did not use occupation as a marker of SES but for assessing exposure to noxious agents. Five papers were included in the final analysis, grouped under cancer sites.

- Askari A, Aziz O, Currie A, Nachiappan S, Athanasiou T, Faiz O. Inequalities in colorectal cancer risk and educational level in developed countries: A systematic review and metaanalysis of observational studies. Tripartite Conference Paper 2014
- Conway, D.I., et al., Socioeconomic inequalities and oral cancer risk: a systematic review and meta-analysis of case-control studies. Int J Cancer, 2008. 122(12): p. 2811-9.[86]
- Palmer, R.C. and E.C. Schneider, Social disparities across the continuum of colorectal cancer: a systematic review. Cancer Causes Control, 2005. 16(1): p. 55-61.[87]
- Pruitt, S.L., et al., Association of area socioeconomic status and breast, cervical, and colorectal cancer screening: a systematic review. Cancer Epidemiol Biomarkers Prev, 2009. 18(10): p. 2579-99.[88]
- Sidorchuk, A., et al., Socioeconomic differences in lung cancer incidence: a systematic review and meta-analysis. Cancer Causes Control, 2009. 20(4): p. 459-71.3545.[89]
- Vainshtein, J., Disparities in breast cancer incidence across racial/ethnic strata and socioeconomic status: a systematic review. J Natl Med Assoc, 2008. 100(7): p. 833-9.[90]
- Vineis, P. and L. Simonato, Proportion of lung and bladder cancers in males resulting from occupation: a systematic approach. Arch Environ Health, 1991. 46(1): p. 6-15.[91]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 4. Results of the search to identify papers on social inequalities in breast, lung, colorectal, prostate, or oral cancer.



Oral cancer

Conway et al. 2008 [86] undertook a systematic review of the literature and meta-analysis specifically on oral cancer, focusing only on case-control studies. Separate meta-analyses were performed for income, occupation, and education. They also tested the effects of age, sex, definition of oral cancer employed, and country location on this association when it was possible. A total of forty-one studies were included in the analysis

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Education: Thirty-seven studies examined the association between education and oral cancer. The combined OR was 1.85 (95%CI 1.60, 2.15), suggesting higher oral cancer risk in those with low educational attainment. However, four of the studies showed the opposite association, with high education associated with increased risk for oral cancer. There were no differences by sex and no data comparing the effect of age on this association.

Occupation: The results were based on 14 studies, the combined OR of the occupation-oral cancer association was 1.84 (95%CI 1.47, 2.31; $p < 0.001$), with no differences by sex, age-group, oral cancer definition, or location of country.

Income: The overall estimate for the income-oral cancer association (estimates from 5 studies) was an OR 2.41 (95%CI 1.59, 3.65; $p < 0.001$), with no differences by sex or age-group. There was some evidence of the association being stronger in high-income (2 out of the 5 studies) compared to lower income countries.

Comparison between SES measures: Ten studies had data on both education and occupation data, showing that the association with oral cancer was similar for both markers of SES. The education OR at 1.88 (95%CI 1.44, 2.46) was marginally, albeit not statistically significantly, lower than that for occupation (OR=1.97; 95%CI 1.49, 2.61). Five studies contained both education and income measures and these results showed stronger associations (p= 0.05) with income (OR= 2.41; 95%CI 1.59, 3.65) compared to education (OR= 1.48; 95%CI 1.15, 1.91).

Colorectal cancer

Palmer et al. 2005 [87] focused their analysis on results from the United States. Their qualitative review shows that in the US most research has focused on the race/ethnicity dimension for the exposure variable and inequalities in screening as the outcome variable. Much of the evidence consists of comparisons of whites and blacks, where the results are inconsistent. For example, compared to whites, blacks have a higher incidence of colorectal cancer but blacks have also been shown to have more favourable tumour histology than whites. In this review there was also evidence of lower SES being associated with a higher incidence of colorectal cancer, higher ensuing mortality, lower likelihood of undergoing screening, later stage at diagnosis, and less likelihood of receiving potentially life-saving treatment.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Breast cancer

The focus of the review by Vainshtein et al. 2008 [90] was to examine whether differences in SES could account for inequalities in breast cancer incidence between races in the United States. Four studies were identified and results showed that white non-Hispanic women were at the highest non-adjusted and age-adjusted risk for breast cancer, followed by black, Hispanic and Asian women. There were SES inequalities in breast cancer incidence in each ethnic group besides the black group. However, the authors note that the data and findings from the studies could not be meaningfully compared because major differences in design and analysis, it was also not possible to pool the data for an aggregate estimate.

Pruitt et al.'s 2009 [88] systematic review focused on the association between area based SES and cancer screening, with 13 studies identified on breast cancer. The findings of these studies demonstrate no consistent pattern in the association between area SES and cancer screening.

Lung cancer

Sidorchuk et al. [89] undertook a comprehensive review of the association between SES and lung cancer incidence. They included studies that were based on lung cancer incidence as the outcome, had a risk estimate with a confidence interval, and SES indicators were income, educational attainment, occupational categories or by a combination of these. Their meta-analysis, based on 64 original studies, found the most pronounced effect of a negative social gradient was seen for studies on educational attainment where the incidence of lung cancer among the group with the lowest educational background was 61% higher compared to the highest educational group (RR = 1.61; 95% CI 1.40–1.85). The corresponding pooled RRs for studies on occupational SES and income showed an increased risk in less affluent compared with most affluent categories (RR = 1.48; 95% CI 1.34–1.65) and RR = 1.37; 95% CI 1.06–1.77, respectively.

They also undertook a meta-analysis of papers that had adjusted for smoking; the overall results were only minimally modified compared to overall results from the primary analyses. The education-lung cancer RR was 1.65 (95% CI 1.19–2.28) and 1.33 (95% CI 1.14–1.55) for occupation. Stratified analyses for income did not reach statistical significance either in the analysis with or without adjustment for smoking.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1.3.4 Chronic lung disease

Chronic respiratory diseases are a group of chronic diseases affecting the airways and the other structures of the lungs. Emphysema and chronic bronchitis (referred to as Chronic Obstructive Pulmonary Disease or COPD), asthma, cystic fibrosis, and restrictive lung diseases are examples of serious lung conditions that can adversely affect the quality of a patient's life. The main symptoms are breathlessness, chronic cough and sputum production. Our search terms were intended to capture all these conditions and included conditions such as chronic lung disease, chronic obstructive pulmonary disease, asthma, and chronic bronchitis. The final search terms are described below.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

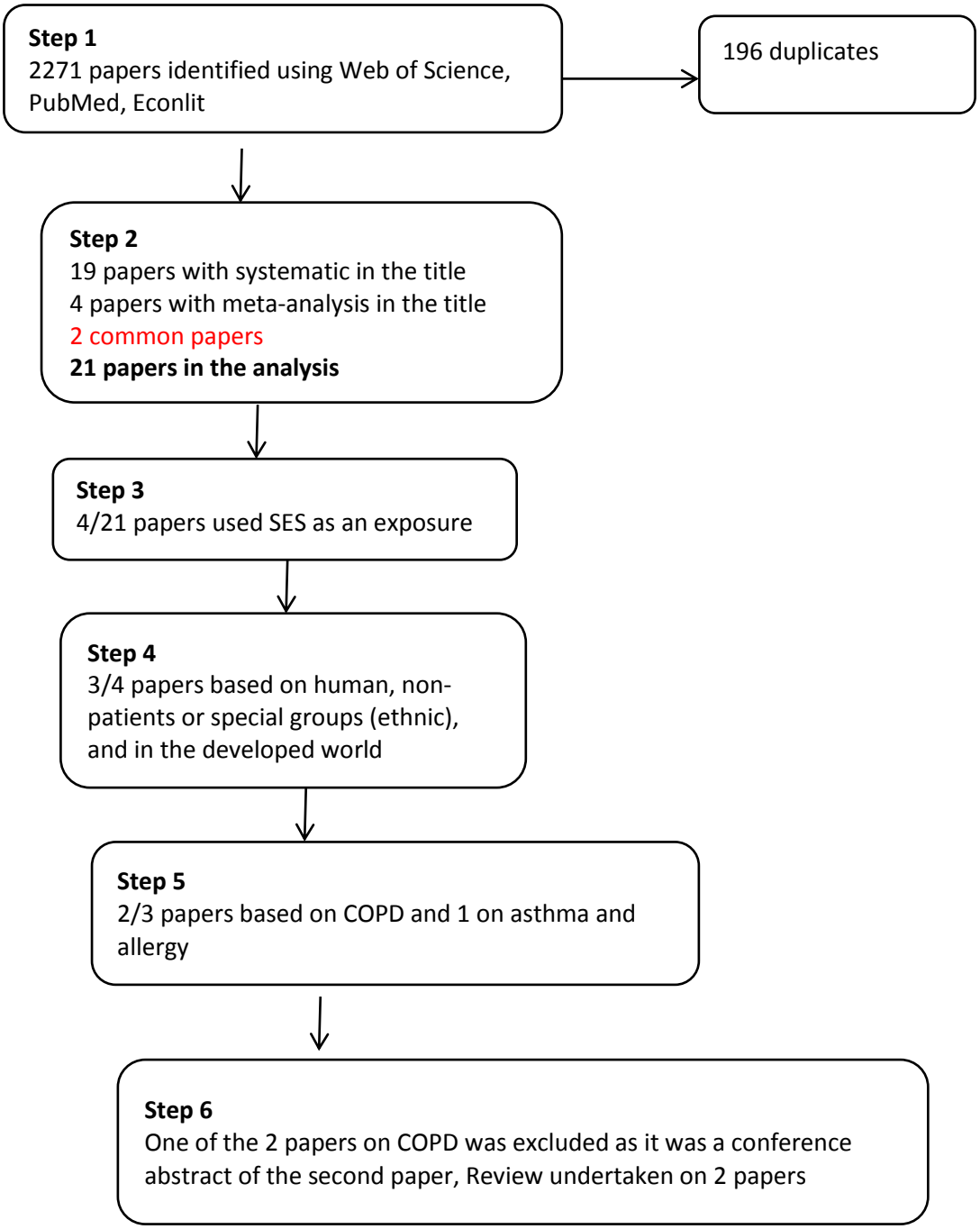
"Chronic lung disease" OR "chronic obstructive pulmonary disease" OR "asthma" OR "chronic bronchitis"

The search term identified a total of 2271 papers (**Figure 5**) which was reduced to 3 papers at step 6. One of these was a 2011 conference abstract, later published in 2012 which was included in the analysis. The second paper retained in the analysis was on asthma and allergies. We present these results separately.

- Gershon, A.S., et al., Chronic obstructive pulmonary disease and socioeconomic status: a systematic review. COPD, 2012. 9(3): p. 216-26.[92]
- Gershon A.S. 2011 Socioeconomic status (SES) and Chronic Obstructive Pulmonary Disease (COPD): A systematic literature review. Abstract Proceedings
- Uphoff E, Cabieses B, Pinart M, Valdés M,, Antó JM, Wright J. A systematic review of socioeconomic position in relation to asthma and allergic diseases. Eur Respir J. 2015; 46(2):364-74.[93]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 5. Results of the search to identify papers on social inequalities in Chronic lung disease.



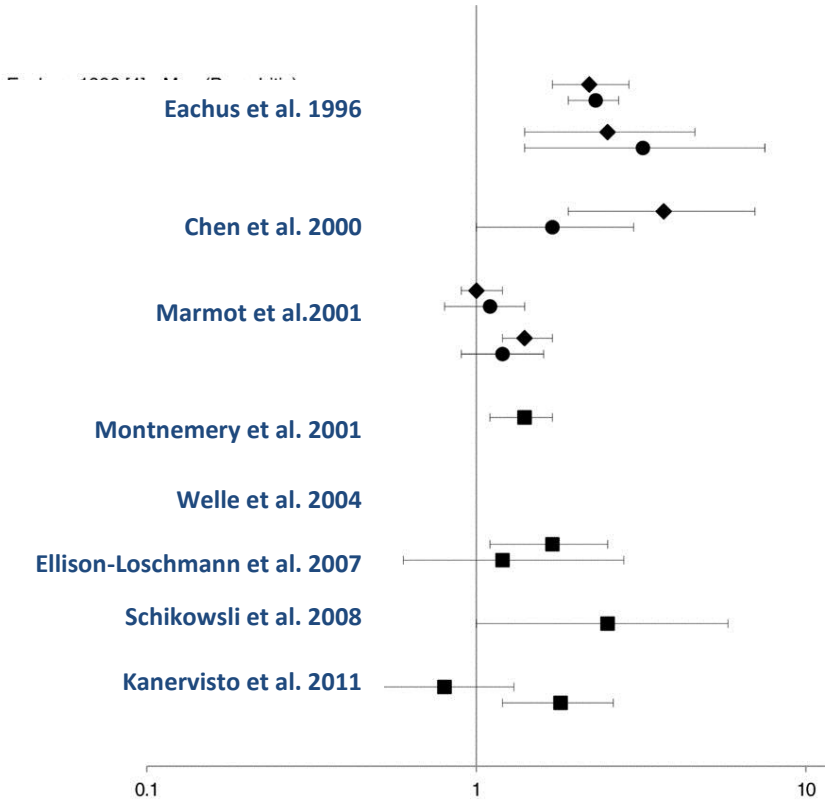
COPD

The systematic review by Gershon et al., 2012 [92] was based on 15 studies. Remarkably only one of these studies focused on SES and COPD, most studies either examined SES as one of many exposure variables and/or examined multiple diseases. Studies were mainly set in North America and Europe, with one set in China. Thirty-one outcome measures were reported in total, with 23 of them showing a significant inverse association between SES and COPD. In general terms those in the lowest SES were at least twice as likely to have poor COPD outcomes as those of the highest

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

SES. These results were consistent across gender, age, and population and appeared uninfluenced by how COPD was diagnosed, the specific measures of SES used, or the disease outcome studied (COPD incidence or mortality). Eight studies [28,94-100] focused on association of SES to either the incidence or the prevalence of COPD. The majority of these studies found individuals of the lowest SES to be significantly more likely to develop COPD (**Figure 6**).

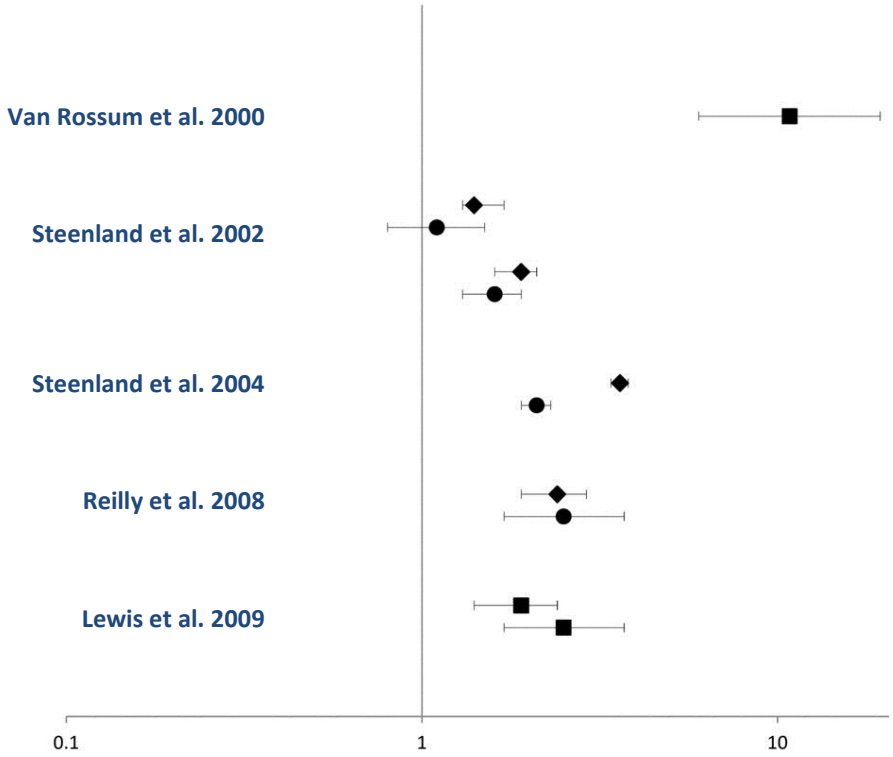
Figure 6. Associations between SES and the risk of developing COPD, from Gershon et al., 2012[95].



Five studies [108-112], reporting 11 outcome measures, examined an association between SES and COPD mortality as recorded on death certificates (**Figure 7**). Except for one outcome in women, low SES was associated with greater risk of mortality from COPD (**Figure 7**).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 7. Association between SES and COPD mortality, from Gershon et al., 2012.[92]



Asthma & Allergy

Uphoff et al. 2015 [93] conducted a systematic review to assess the association between SES and asthma and allergy. A total of 183 studies were identified, a majority (n=124) of these were cross-sectional in nature. A large part of the studies (n=119) were on children, 39 on adults and 25 on both adults and children. Results of their analysis showed 9% of their studies to show high SES to be associated with higher asthma, while 63% reported lower SES to be associated with greater risk of asthma. The pooled (children and adults) unadjusted odds ratio for the prevalence of asthma in the lowest compared with the highest SES was 1.38 (95% CI 1.37–1.39), the adjusted association was 1.11 (95% CI 1.09–1.14).

In contrast to asthma, the associations for allergy suggested high SES to be associated with greater risk of allergy; the pooled unadjusted odds ratio in the lowest compared to the highest SES was 0.67 (95% CI 0.62–0.72) and the adjusted odds ratio was 0.69 (95% CI 0.60–0.79). This was also the case for atopic dermatitis (unadjusted OR 0.72, 95% CI 0.61–0.83; adjusted OR 0.79, 95% CI 0.73–0.85) and allergic rhino conjunctivitis (unadjusted OR 0.52, 95% CI 0.46–0.59; adjusted OR 0.79, 95% CI 0.78–0.80).

The authors conclude that in their review of studies from mainly high- and middle-income countries, they found evidence confirming an association between lower SES and a higher

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

prevalence rate of asthma for children and adults. However, the evidence for the association between SES and allergic diseases points in the opposite direction, with higher SES being associated with a higher prevalence of allergies.

1.3.5 Musculoskeletal disorders (MSD)

Musculoskeletal Disorders or MSDs are injuries and disorders that affect the human body's movement or musculoskeletal system (i.e. muscles, tendons, ligaments, nerves, discs, blood vessels, etc.). They are caused, precipitated or exacerbated by sudden exertion or prolonged exposure to physical factors such as repetition, force, vibration, or awkward posture. In our search for papers on this subject we also included chronic diseases such as arthritis and osteoporosis, although the analysis of results will be undertaken separately on these constructs. The precise search terms used were the follows.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

"Musculoskeletal disease" OR "osteoarthritis" OR "osteoporosis" OR "rheumatoid arthritis" OR "spinal disorders" OR "low back pain" OR "joint disease"

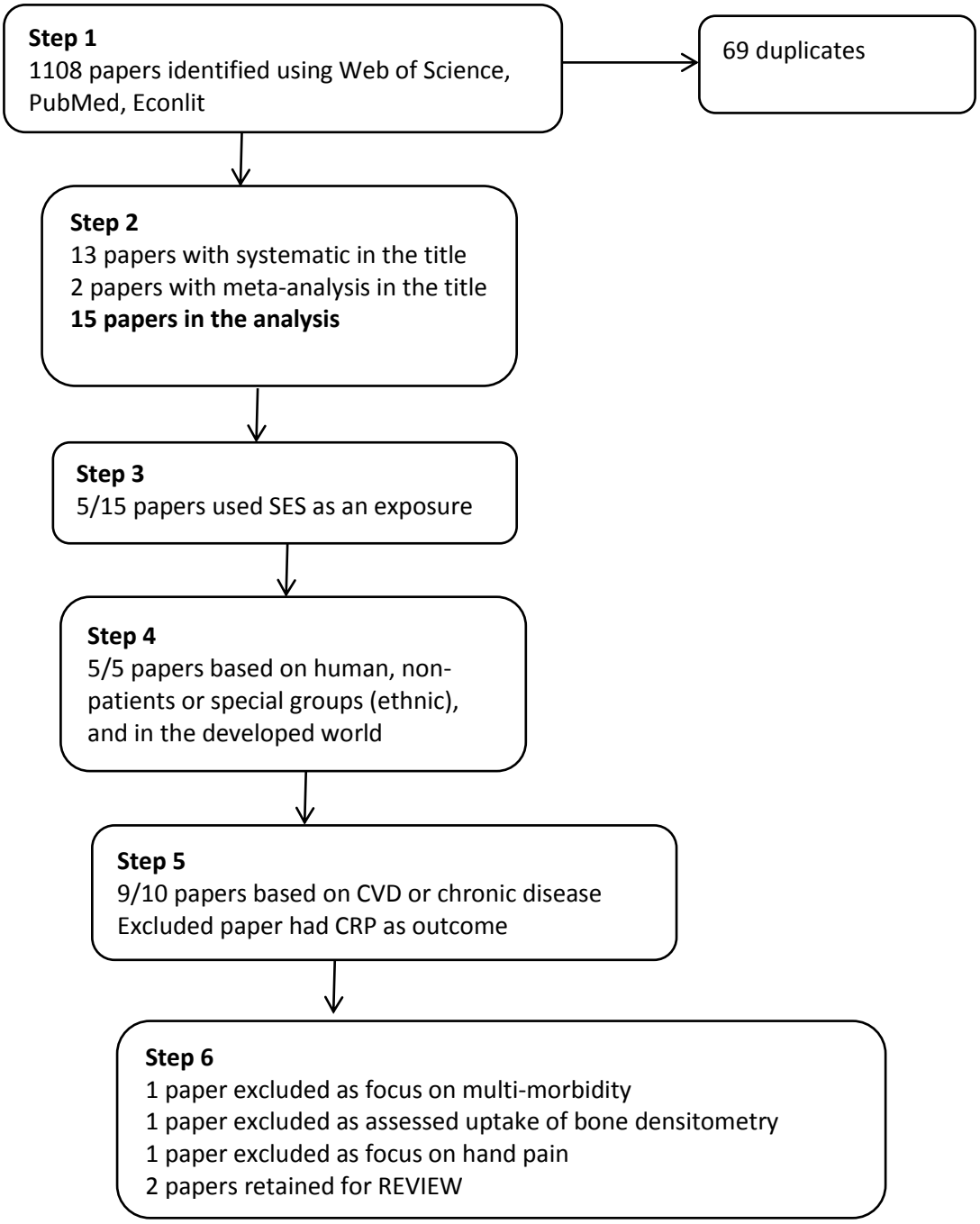
The search term identified a total of 1108 papers (**Figure 8**) which was reduced to 5 papers at step 6 (see list below). One of these was a 2011 conference abstract, later published in 2012 which was included in the analysis. The second paper retained in the analysis was on rheumatoid arthritis. We present these results separately.

- Brennan, S.L., et al., The association between socioeconomic status and osteoporotic fracture in population-based adults: a systematic review. Osteoporos Int, 2009. 20(9): p. 1487-97.[101]
- López-Castillo CA, C.-R.R., Amaya-Amaya J, DeSanVicente-Célis Z, Mantilla RB, Rojas-Villarraga A., Impact of educational level on rheumatoid arthritis: A systematic review. Rev Colomb Reumatol, 2014. 21(4): p. 201-212. [102]
- Brennan SL, Wluka AE, Gould H, Nicholson GC, Leslie WD, Ebeling PR, Oldenburg B, Kotowicz MA, Pasco JA. Social determinants of bone densitometry uptake for osteoporosis risk in patients aged 50yr and older: a systematic review. J Clin Densitom. 2012 Apr-Jun;15(2):165-75.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

- Nicholls EE, van der Windt DA, Jordan JL, Dziedzic KS, Thomas E. Factors associated with the severity and progression of self-reported hand pain and functional difficulty in community-dwelling older adults: a systematic review. Musculoskeletal Care. 2012 Mar;10(1):51-62.
- Violan C, Foguet-Boreu Q, Flores-Mateo G, Salisbury C, Blom J, Freitag M, Glynn L, Muth C, Valderas JM. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. PLoS One. 2014 Jul 21;9(7):e102149.

Figure 8. Results of the search to identify papers on social inequalities in Musculoskeletal disorders.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Osteoporotic fracture

Osteoporosis is characterized by increasing porosity and fragility of bone, which places the individual at increased risk of low trauma fracture, which are often markers of deterioration in quality of life. Brennan et al. 2009 [101] undertook a systematic review the literature to examine the relationship between different individual indicators of SES (income, education, type of occupation, type of residence) and risk of osteoporotic fracture. A total of twelve studies were identified by Brennan et al. 2009 [101], three were cohort studies, one a nested case-control study, four were case control designs, and four were cross-sectional in design. Eight of these studies used hospital, or medical, reports to confirm fracture and over three-quarter of the participants overall were women. Due to the heterogeneity of the studies, statistical pooling of the extracted data was not feasible. The review carried out by these authors did not find consistent evidence of associations between the markers of SES (income, education, occupation, and place of residence) and osteoporotic fractures.

Rheumatoid arthritis

Rheumatoid arthritis is a chronic inflammatory disorder that typically affects the small joints in hands and feet. Unlike the wear-and-tear damage of osteoarthritis, rheumatoid arthritis affects the lining of joints, causing a painful swelling that can eventually result in bone erosion and joint deformity. It is an autoimmune disorder, which in addition to causing joint problems can affect other organs of the body — such as the skin, eyes, lungs and blood vessels. López-Castillo et al. 2014 [102] undertook a systematic review of the literature to assess the impact of educational level on rheumatoid arthritis. A total of 68 studies were included in the analysis and the general conclusion of the review was that education affected the risk of developing the disease, radiographic progression, depression and anxiety, work disability, functional disability, quality of life, and mortality in relation to rheumatoid arthritis.

1.3.6 Depression

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Major depressive disorder or clinical depression affects how people feel, think, behave, and can lead to a variety of emotional and physical problems. In our review, we included terms to

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

capture depression as well as depressive symptoms, we excluded postpartum depression. The search terms used were the follows.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

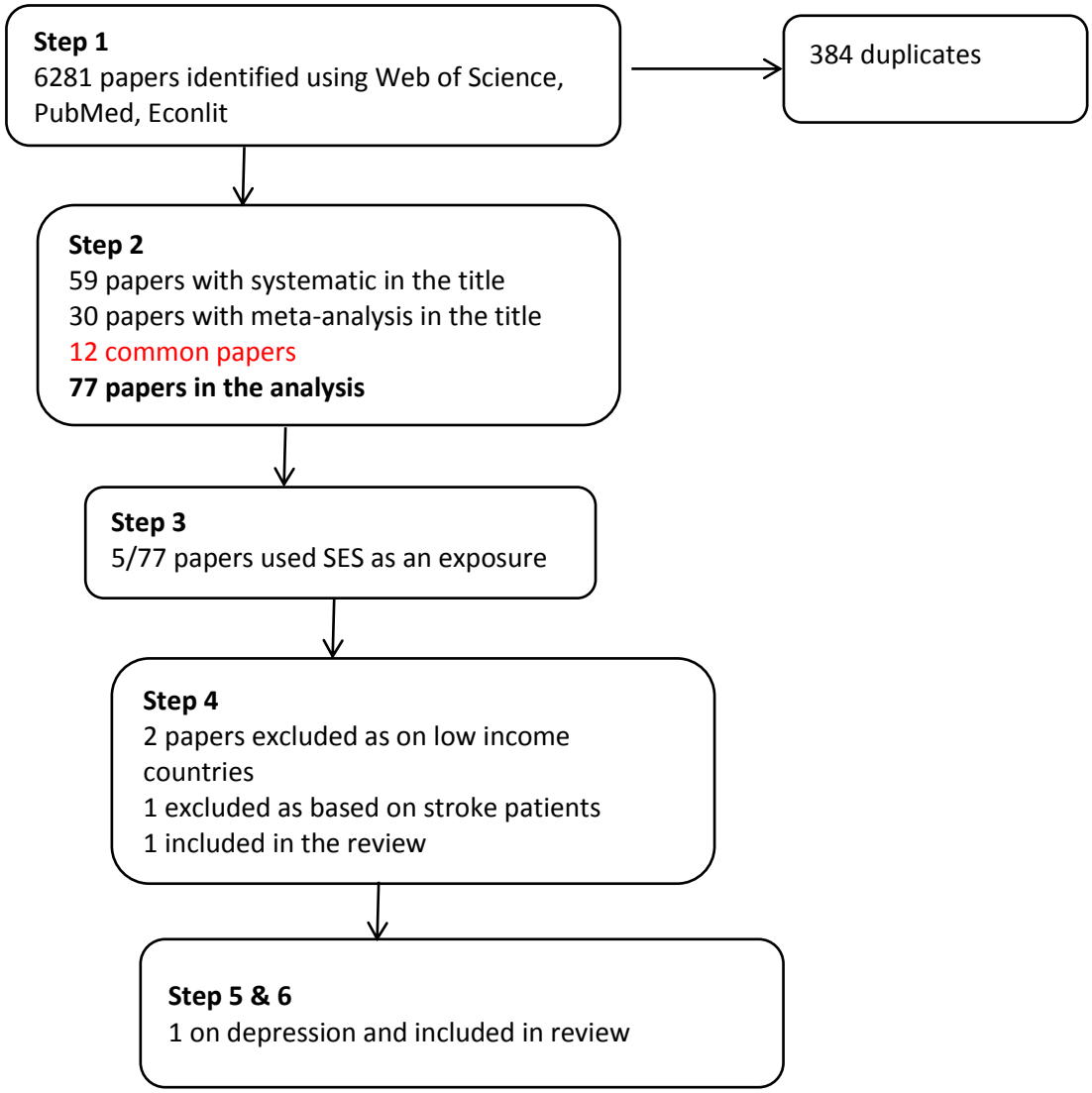
"Depression" OR "depressive disorder" OR "depressive symptoms"

The search strategy yielded a total of 6281 results but a tiny fraction were meta-analyses or systematic reviews (**Figure 9**). Only five papers had SES as the exposure and among these papers only one was suitable for analysis as it was the only one not to be based on special populations or groups. This paper by Lorant et al is listed below.

- Lorant V, Deliège D, Eaton W, Robert A, Philippot P, Ansseau M. Socioeconomic inequalities in depression: a meta-analysis. Am J Epidemiol. 2003 Jan 15;157(2):98-112.[103]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 9. Results of the search to identify papers on social inequalities in depression.



Among psychiatric disorders, depression exhibits a more controversial association with SES, mostly because much research is based on patient samples and the outcome is poorly defined. In their meta-analysis and systematic review Lorant et al. 2003 [103] assessed the impact of SES on the prevalence (n=51), incidence (n=5), and persistence (n=4). The majority of studies came from North America and Europe, were carried out around 1987, and yielded a mean prevalence of depressive disorders of 9 percent.

Thirty five of the 51 studies showed a statistically significant association between low SES and greater prevalence of depression. Individuals from lower SES groups had an overall odds ratio for being depressed of 1.81, as compared with the higher SES group (**Table 5**). Within the incidence studies, the lowest SES group turned out to have 1.24 times' greater odds of

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

experiencing a new depressive episode than the highest group. Once depressed, lower SES individuals were much more likely to persist in depression (odds ratio = 2.06). There was significant heterogeneity among the prevalence studies ($p < 0.001$), the number of studies included in the incidence and persistence analyses was too few to examine heterogeneity.

Table 5. Overall unadjusted odds ratios for major depression for the lowest socioeconomic status group versus the highest, studies published after 1979; from Lorant et al. 2003 [103].

	No. of studies	OR*	95% CI	*p*	OR**	95% CI	*p*
Prevalence	51	1.81	1.57, 2.10	< 0.001	1.68	1.49, 1.89	< 0.001
Incidence	5	1.24	1.04, 1.48	0.004	1.21	1.06, 1.38	0.001
Persistence	4	2.06	1.39, 3.05	< 0.001	1.91	1.40, 2.60	< 0.001

* Random Effects Model
**Fixed Effects Model

Although the estimates in the table above compare low to high SES, this paper also explored evidence of a dose-response association for education and income. They found that for each additional year of education, the log odds ratio of being depressed decreased by 3 percent. A 1 percent increase in relative ranking on income led to a 0.74 percent decrease in the log odds ratio of being depressed. The authors concluded that there was firm evidence for an association between low SES and prevalence of depression. The authors note that their results lack specificity regarding depression as they combined outcomes to overall psychiatric disorder in order to gain statistical power in their analysis.

1.3.7 Neurologic disorders

Neurological disorders are diseases of the central and peripheral nervous system: the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles. This group can include epilepsy, Alzheimer disease and other dementias, cerebrovascular diseases including stroke, migraine and other headache disorders, multiple sclerosis, Parkinson's disease, neuro-infections, brain tumours, traumatic disorders of the nervous system such as brain trauma, and neurological disorders as a result of

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

malnutrition. However, in order to focus our research we decided to use the following search terms.

"Educational level" OR "Socioeconomic status" OR "Socioeconomic position" OR "Social inequality" OR "Social disparity" OR "social determinant" OR "social status" OR "Income" OR "Occupation"

AND

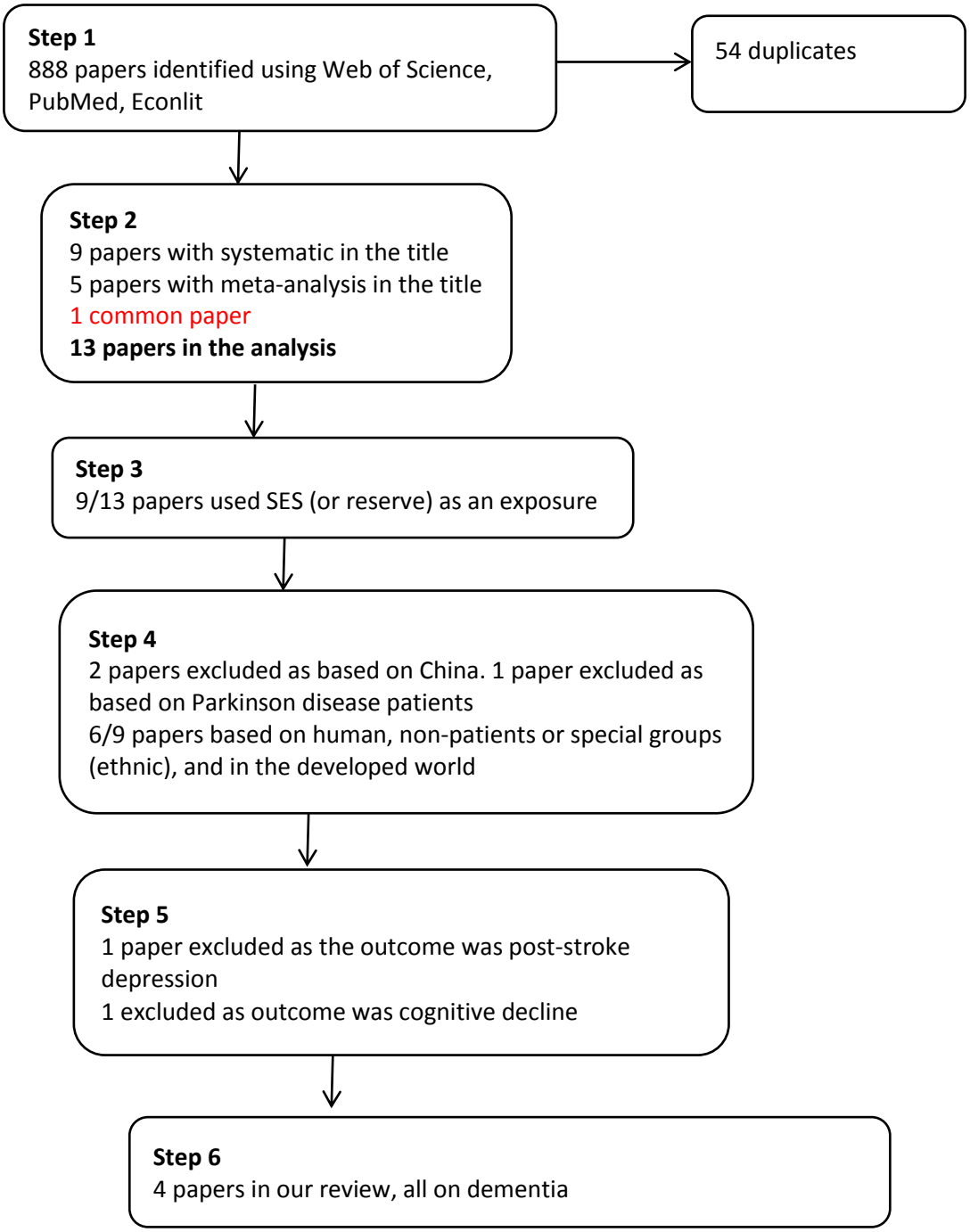
"Dementia" OR "Alzheimer" OR "Parkinson" OR "Chronic neurologic disease"

The search strategy yielded a total of 887 papers, of which 4 were included in our analysis (**Figure 10**). All three were on dementia.

- Caamaño-Isorna F1, Corral M, Montes-Martínez A, Takkouche B. Education and dementia: a meta-analytic study. Neuroepidemiology. 2006;26(4):226-32.[104]
- Valenzuela, M.J. and P. Sachdev, Brain reserve and dementia: a systematic review. Psychological Medicine, 2006. **36**(4): p. 441-454. [105]
- Sharp, E.S. and M. Gatz, Relationship between education and dementia: an updated systematic review. Alzheimer Dis Assoc Disord, 2011. 25(4): p. 289-304.[106]
- Russ, T.C., et al., Socioeconomic status as a risk factor for dementia death: individual participant meta-analysis of 86 508 men and women from the UK. Br J Psychiatry, 2013. **203**(1): p. 10-7. [107]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Figure 10. Results of the search to identify papers on social inequalities in Neurologic disorders.



Dementia is an overall term that describes a wide range of symptoms associated with a decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities. Alzheimer's disease accounts for 60 to 80 percent of cases. Vascular dementia, which occurs after a stroke, is the second most common dementia type. There are many other conditions that can cause symptoms of dementia, including some that are reversible, such as thyroid problems and vitamin deficiencies. Several studies have shown an association between

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

education and dementia. This association could be explained by a direct effect of education or brain function or delaying the clinical expression of the disease, the so called reserve hypothesis.[108]

In the systematic review and meta-analysis undertaken by Caamaño-Isorna et al. 2006 [104] a total of 19 studies were identified: 13 cohort studies and 6 case-control studies. In pooled analysis on 14 studies (9 cohort and 5 case-control studies) the risk of Alzheimer's disease in those with low compared to high education was 1.80 (95% CI: 1.43–2.27). The risk in medium compared to high education was 1.44 (95% CI: 1.24–1.67). These results also suggested that low education represents a stronger risk factor for AD than for non-AD (**Table 6**).

Valenzuela et al., 2006 [105] undertook an analysis of the effects of education and occupation, on dementia risk using data from twenty-two studies. Their results show that the combined OR for incident dementia for individuals with high compared to low education was 0.53 (95% CI 0.45–0.62, p<0.0001), indicating a decreased risk of 47%. Five out of 15 studies showed no significant effect, while 10 out of 15 demonstrated a significant protective effect. There was considerable heterogeneity in this analysis (p=0.0063). The combined OR for incident dementia for individuals with history of high occupational status compared to low was 0.56 (95% CI 0.49–0.65, p<0.0001), indicating a decreased risk of 44%. Three out of 12 studies showed no significant effect, while 9 out of 12 demonstrated a significant protective effect. There was heterogeneity in the analysis (p=0.062).

Table 6. Pooled RRs of the education-dementia association, from Caamaño-Isorna et al. 2006.[104]

		Studies	RR (95% CI)
Lowest education level versus highest education level			
AD	Cohort studies	9	1.59 (1.35–1.86)
	Case-control studies	5	2.40 (1.32–4.38)
	All studies	14	1.80 (1.43–2.27)
Non-AD	Cohort studies	4	1.32 (0.92–1.88)
All dementias	Cohort studies	10	1.62 (1.26–2.09)
	Case-control studies	2	1.33 (0.68–2.59)
	All studies	12	1.59 (1.26–2.01)
Any education level other than highest versus highest level			
AD	Cohort studies	5	1.32 (1.09–1.59)
	Case-control studies	3	1.66 (1.30–2.10)
	All studies	8	1.44 (1.24–1.67)
Non-AD	Cohort studies	3	1.23 (0.94–1.61)
All dementias	Cohort studies	6	1.45 (1.16–1.81)
	Case-control studies	1	1.75 (0.58–5.23)
	All studies	7	1.33 (1.15–1.54)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Sharp et al., 2011 [106] report a systematic review which included studies on both dementia prevalence and incidence, on a total of 71 studies. (58%) reported a significant effect of lower education on risk for dementia whereas 37 studies (42%) reported no significant relationship between lower education and a dementia outcome. Of the 46 prevalence studies, 28 studies (61%) reported a significant effect of low education on risk for dementia. Of the 42 incidence studies, 23 studies (55%) reported a significant effect of low education on dementia risk. Thus, there was no clear evidence that prevalence studies reported stronger or more consistent significant effects of education on risk for dementia compared to incidence studies. Overall, there was more consistent support for an education-dementia relationship in developed compared to developing regions of the world. However, the level of education that was most associated with dementia risk varied considerably by study region as well as by age, gender, and race/ethnicity.

The meta-analysis by Russ et al 2013 [107] was the most recent, and its methodology differed in that the analysis consisted of pooling raw data from several studies rather than estimates from studies and the focus of the analysis was dementia deaths, extracted from mortality records. Data on a total of 86508 persons was included, with 622 dementia deaths (of a total of 12952 deaths). Results show that leaving full-time education at an earlier age was associated with an increased risk of dementia death in women (fully adjusted hazard ratio (HR) for age ≤14 v. age ≥16: HR = 1.76, 95% CI 1.23–2.53) but not men. Occupational social class was not statistically significantly associated with dementia death in men or women. The results are interesting but the authors urge caution in their interpretation as the number of dementia related deaths in this study was small and is likely to have been affected by the unavoidable problems of under-diagnosis of dementia in the community, under-recording of dementia on death certificates and diagnoses being inaccurately coded.

These results taken together suggest a protective effect of SES on dementia. However, the burning question is whether low education is a risk factor for the occurrence of the disease itself or for the expression of its clinical features. There is some consensus that methodological and ascertainment biases drive the relationship between low education and an increased risk for dementia. Criticisms have also focused on confounding elements such as age and gender, and that education may be a surrogate for other unmeasured variables.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

1.4 Discussion

Synthesis of results

Our analysis of the published systematic reviews and meta-analyses on the association between SES and chronic diseases suggests the existence of social inequalities in most of these outcomes, the exceptions being some musculoskeletal conditions and allergies. Key findings from our analyses are the following.

- CVD: There is consistent evidence of an association between childhood SES and CVD, for stroke this association may be independent of adult SES. The largest association of adult SES with CVD was for income (RR 1.71) compared to occupation (RR 1.35) and education (RR 1.34). It is possible that some of this is due to reverse causation.
- Diabetes: Childhood SES is also associated with diabetes. The markers of adult SES were similarly associated with risk of diabetes (RR from 1.31 to 1.40). There is some evidence that the SES-diabetes association is stronger in women.
- Cancer: There is consistent evidence of an association of SES with oral and colorectal cancer. The evidence for breast cancer is mixed. For lung cancer the strongest association is for education (RR 1.61) compared with adult income (RR 1.37) or occupation (RR 1.48).
- Chronic lung disease: There is consistent evidence of an association of SES and COPD onset and prognosis. SES is also associated with asthma but not allergy.
- Musculoskeletal diseases: SES was not found to be associated with osteoporotic fractures; there is some evidence that it is associated with occurrence and persistence of Rheumatoid arthritis.
- Depression: There were surprisingly few reviews on depression, the one analysed by us dated from 2003. It showed SES to be associated with occurrence and persistence of depression.
- Neurologic disorders: All our analysis was based on dementia were there was consistent evidence of a protective effect of SES on dementia, including Alzheimer's disease. However, it remains unclear if SES is a risk factor or simply provides reserve against clinical expression of disease.

Socioeconomic factors also influence the prognosis of chronic diseases, in terms of greater mortality [17,18,92,109-114]. Systematic reviews on the outcome for CVDs [17-19,111,114], cancer [110,113], and chronic respiratory disease [92] show that low SES increases the risk of mortality from lung cancer, COPD, and reduces breast cancer survival. Whilst there were some systematic reviews on

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

socioeconomic inequalities and risk of chronic diseases, many of the studies were fraught with methodological shortcomings; we highlight a few of them.

- Heterogeneity: The diversity in the definition of outcome, study design, the marker of SES used in the study makes it difficult to synthesise data.
- Studies often use different markers of SES in an interchangeable way; this is problematic as the mechanisms associated with one measure of SES may be quite different from that associated with another measure.
- Most studies compare extreme SES categories; this does not allow the social gradient to be examined.
- Little attention is paid to assessing the age and sex specific effects, most studies are small and often the results are pooled across age and sex strata to increase power.
- A significant limitation to the currently available evidence on the magnitude and direction of socioeconomic inequalities in non-communicable chronic diseases (NCDs) is the widespread use of self-reported cases of physician diagnoses as source data. These self-reported data may systematically skew estimated inequalities due to reporting bias.
- Publication bias is likely to be important in this domain, making it important to encourage individual participant data type approaches, both from published and unpublished studies.

Comparative studies on social inequalities in chronic diseases in Europe

Much of the first section on systematic reviews and meta-analyses contained studies on chronic diseases conducted within individual countries and lack comparability due to differences in the SES indicator used, age groups studied, and the definition of diseases. In the past decade Johan Mackenbach and colleagues have made considerable effort to document social inequalities in European countries. [2,3,115-118] Although much of the focus in these papers is mortality, there is at least one paper that specifically examined chronic diseases.[116] In order to provide an overview of these findings we discuss two seminal papers, one on all-cause mortality[119] and the other on chronic diseases[116].

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Social inequalities in mortality

This paper by Mackenbach et al. 2008 aimed to assess the magnitude of inequalities in mortality in 22 European countries. [119] The data were drawn mostly from national populations, and the analyses based on 3.5 million deaths among more than 54 million persons ranging in age from 30 to 74 years at the beginning of the study. Socioeconomic status was measured by education, occupation, and income. Results showed that for both men and women in all countries, mortality was higher among those with less education. These inequalities were smaller than the average for Europe in southern European populations and larger than average in most countries in the eastern and Baltic regions. These effects could be attributed to smaller inequalities in the rate of death from cardiovascular disease. There was no evidence for systematically smaller inequalities in health in countries in northern Europe, despite these countries having long histories of egalitarian policies, reflected by, among other things, welfare policies. The authors suggest that lifestyle-related risk factors have an important role in premature death in high-income countries. The variability in social inequalities in mortality across Europe suggests that there in an opportunity to reduce them via the development of well targeted policies and interventions.

Social inequalities in chronic diseases

Dalstra et al. 2005 wished to highlight is a comparison of socioeconomic differences in a wide range of chronic diseases using data from eight European countries for men and women aged 25–79 years.[116] Data from non-standardized nationally representative health surveys were pooled; **table 7** below provides details on the countries and numbers included in the analysis.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 7. An overview of eight European countries in the study, from Dalstra et al. 2005.[116]

				Population share (%) by lower education level		overall non-response rate (%)
Country	**Year**	**Name**	**N**	**Men**	**Women**	
Finland	1994	Survey on Living Conditions in Finland	7385	37.8	38.5	27
Denmark	1994	The Danish Health and Morbidity Survey	3717	21.4	29.0	22
Great Britain	1995	Health Survey for England	12 556	33.8	43.8	27
The Netherlands	1997–1999	Permanent Survey on Living Conditions	19 102	38.6	53.3	43
Belgium	1997	Belgium Health Interview Survey	6960	40.9	44.7	40
France	1991–1992	Enquête sur la Santé et les Soins Médicaux	12 569	58.4	>56.7	34
Italy	1994	Condizioni di salute e ricorso ai servizi sanitari	41 240	34.4	43.7	10 (of families)
Spain[a]	1997	Encuesta Nacional de Salud	4943	44.6	48.4	1

For men the population share of the lowest education level was 55.73% and for women this was 62.37%. The overall non-response rate in this survey was 5%.

Results showed large inequalities (OR >1.50) for stroke, diseases of the nervous system, diabetes mellitus, and arthritis. There were no significant socioeconomic inequalities in cancer. Inequalities in diabetes and heart disease were larger in women. See **Table 8** for results on the outcomes relevant to the FRESHER project. There were country specific patterns (see **Table 9**)

Country specific patterns For chronic respiratory diseases there were large differences (OR > 1.5) for Belgium, Italy, and Spain, and no differences for Finland and France (see **Table 9**). For heart disease the socioeconomic differences were consistently larger in northern European countries (Great Britain, The Netherlands and Belgium) as compared with more southern European countries (France, Italy and Spain).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 8. Education differences (low vs high education) for chronic disease groups in Europe, from Dalstra et al. 2005.

Chronic disease	Total	Men (Aged 25–79)	Women (Aged 25–79)	Men & women (25–59 years)	Men & women (60–79 years)
Stroke	1.64 (1.40-1.93)	1.70 (1.35–2.14)	1.56 (1.25–1.96)	1.89 (1.43–2.51)	1.53 (1.27–1.86)
Diseases of the nervous system	1.63 (1.51–1.77)	1.57 (1.40–1.77)	1.57 (1.41–1.75)	1.81 (1.64–1.99)	1.33 (1.17–1.52)
Diabetes mellitus	1.60 (1.43–1.80)	1.30 (1.11–1.51)	2.19 (1.82–2.63)	1.64 (1.38–1.94)	1.57 (1.34–1.84)
Arthritis	1.56 (1.40–1.73)	1.50 (1.27–1.77)	1.46 (1.26–1.68)	2.04 (1.76–2.36)	1.17 (1.01–1.36)
Chronic respiratory diseases	1.24 (1.15–1.33)	1.33 (1.20–1.48)	1.19 (1.07–1.33)	1.13 (1.03–1.25)	1.42 (1.26–1.61)
Heart disease	1.22 (1.10–1.35)	1.18 (1.04–1.34)	1.51 (1.28–1.79)	1.29 (1.09–1.53)	1.18 (1.04–1.33)
Cancer	1.13 (0.98–1.30)	0.96 (0.78–1.20)	1.22 (1.02–1.46)	1.64 (1.36–1.99)	0.77 (0.64–0.93)

Table 9. Education differences (low vs high education) for chronic disease groups for persons aged 25–79, from Dalstra et al. 2005.

Chronic disease	Finland	Denmark	Great Britain	The Netherlands	Belgium	France	Italy	Spain	Interaction between education & country
Stroke			2.23 (1.29–3.86)	1.65 (1.09–2.49	1.38 (0.79–2.41)	1.30 (1.04–1.63)	1.47 (1.15–1.86)	1.31 (0.79–2.17)	$P = 0.43$
Diseases of the nervous system	1.06 (0.90–1.26)	1.14 (0.70–1.86)	1.29 (1.03–1.61)	1.39 (0.91–2.14)	1.99 (1.65–2.39)	0.97 (0.84–1.11)	1.85 (1.62–2.11)		$P < 0.0001$
Diabetes mellitus		1.16 (0.74–1.82)	1.26 (0.98–1.62)	1.60 (1.28–1.99)	1.98 (1.49–2.62)	1.45 (1.13–1.87)	1.59 (1.41–1.78)	1.99 (1.38–2.87)	$P < 0.001$
Arthritis			1.73 (1.51–1.98)	1.48 (1.26–1.75)	1.44 (1.22–1.69)				$P < 0.01$
Chronic respiratory diseases	1.07 (0.89–1.27)	1.44 (1.08–193)	1.34 (1.17–1.54)	1.23 (1.09–1.39)	1.70 (1.42–2.04)	1.19 (0.99–1.43)	1.69 (1.55–1.86)	1.82 (1.25–2.64)	$P < 0.0001$
Heart disease			1.29 (1.08–1.55)	1.20 (0.98–1.46)	1.63 (1.27–2.08)	1.07 (0.89–1.28)	1.09 (0.95–1.25)	0.89 (0.64–1.24)	$P < 0.01$
Cancer	0.86 (0.56–1.33)		1.20 (0.89–1.62)	1.23 (0.92–1.64)	1.08 (0.73–1.61)	0.90 (0.73–1.11)	0.98 (0.78–1.22)		$P = 0.18$

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Conclusion

Chronic conditions have multifactorial aetiologies, including common disease risk factors and determinants; significant latency periods and protracted clinical courses; and are seldom cured completely. Causal factors interact at an individual and at a population level to determine the degree of disease burden and illness. At different life stages, common risk factors and determinants include poor intra-uterine conditions; stress, violence and traumatic experiences; educational disadvantage; inadequate living environments that fail to promote healthy lifestyles; poor diet and lack of exercise; alcohol misuse and tobacco smoking. Social determinants are seen to be important determinants of all these intermediate risk factors, the “causes of the causes”.

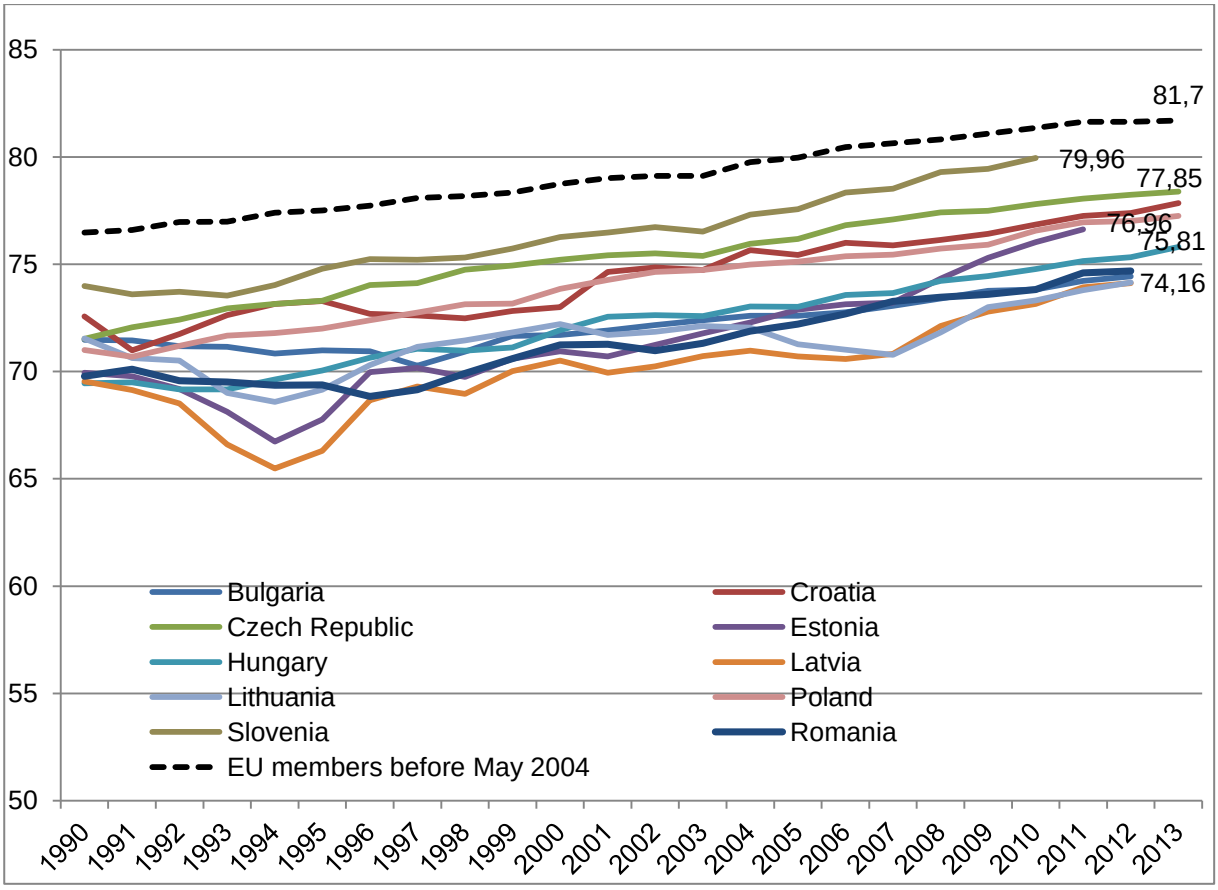
This project has received funding from the European Union’s Horizon 2020 research and innovation programme under Grant Agreement No 643576.

2 DIFFERENCES BETWEEN EASTERN & WESTERN EUROPE

2.1 Introduction

Eastern Europe is recognized as a region facing multiple health problems, with a higher burden of NCDs than Western and Northern parts of the continent. The social and economic transformation in the last decade of the 20th century in Eastern Europe and collapse of former communistic block led to an increase in health problems in many of these countries. In recent times, trends in life expectancy at birth have improved in many areas around the world, however those for Russia, as well as for some other former Soviet Union countries, have fluctuated, not showing signs of stable growth. In Eastern European EU member states significant progress has been observed (**Figure 11**), the trend being similar to that observed in Western Europe. The picture for Russia, Ukraine and many other countries of the former Soviet Union remains unsatisfactory.

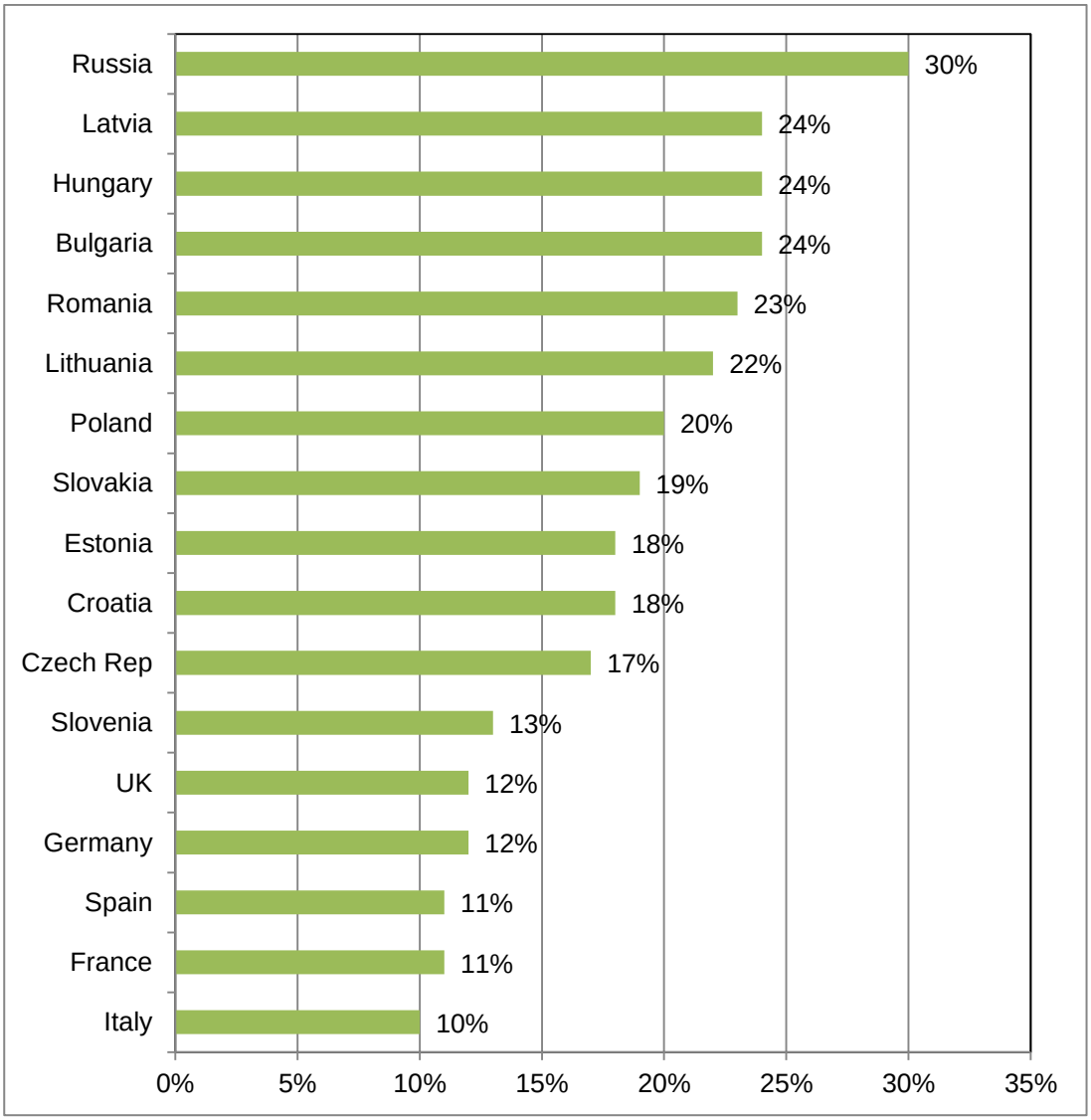
Figure 11. Life expectancy in EU Eastern countries and average for EU members before 2004 in years 1990-2013 ***(source: WHO HFA DB database 2016)***



This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

The major problem in these countries is higher premature mortality due to cardiovascular diseases (CVD) and external causes of death, especially among middle aged men. However, diabetes and malignant neoplasms morbidity in Eastern EU can very considerable between the countries compared to EU 15. Estimates by Zatoński and colleagues on the probability of death before the age of 65 years for men are of the order of 16% in Western Europe (EU member states before 2004), compared with 31% for Eastern Europe (new EU states after enlargement in 2004) and 54% in Russia.[120] In general among the all EU member states the highest rates of premature mortality are observed in Hungary, Latvia and Bulgaria (**Figure 12**).

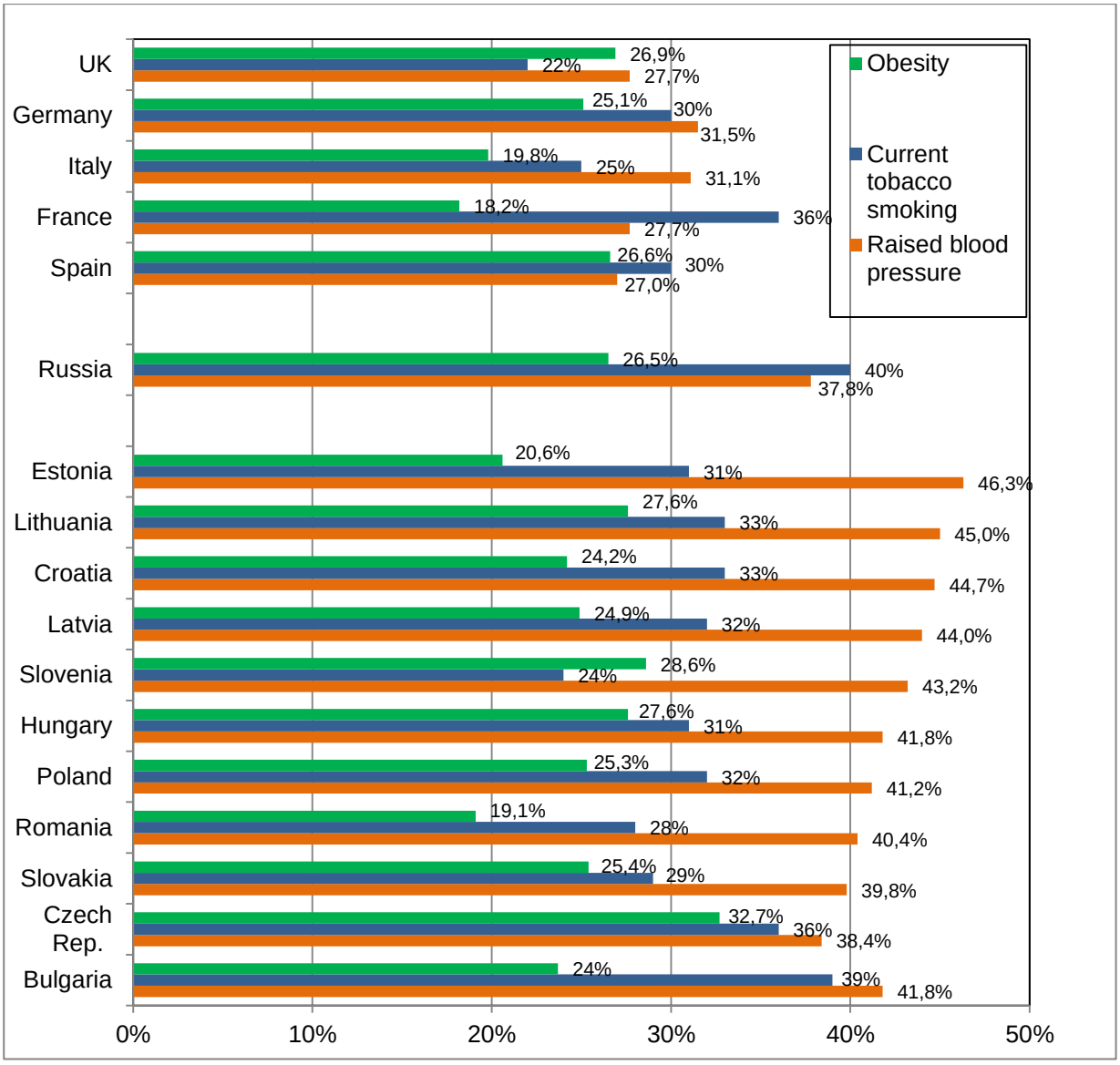
Figure 12. The probability of dying between ages 30 and 70 years from the CVD, cancer, chronic respiratory diseases and diabetes in Eastern EU countries, Russia and the biggest Western European countries *(according to estimates of WHO "Noncommunicable Diseases Country Profiles 2014")*



This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

The reasons of such an unfavorable situation can be related to relatively higher burden of NCDs risk factors in Eastern Europe, related to more frequent tobacco smoking, unhealthy dietary habits, and hypertension. The prevalence of hypertension in particular tends to be much higher in Eastern than in Western part of the continent (**Figure 13**). The patterns of alcohol consumption is also thought to play a role in the higher burden of NCDs in Northern-East part Europe.[121]

Figure 13. Frequency of smoking tobacco, obesity and hypertension in EU Eastern countries, Russia and the biggest countries of Western Europe *(according to estimates of WHO "Non-communicable Diseases Country Profiles 2014")*



Another challenge for Eastern EU countries is related to the quality of data used for monitoring health in the region. Some of the countries do not have relevant statistical systems like, for instance medical registries and do not perform adequate epidemiological studies. These

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

circumstances lead the comparison of the health situation in Eastern and Western European countries to be difficult and require special attention in the process of data interpretation.

The history of large epidemiological studies in the field of non-communicable diseases in Eastern part of European Union is fairly short compared to other western countries. More intense activity in this field started in the late 70's. In this period some countries in the region launched population based studies focused on NCDs. In the context of cardiovascular diseases in 80's the WHO MONICA study (MONItoring of trends and determinants in cardiovascular disease) under umbrella of World Health Organization (WHO) is noteworthy. In the eastern part of the EU, MONICA was performed in the Czech Republic, Lithuania, Poland and Russia. MONICA can be also recognized as a starting point for many new scientific initiatives in the field of epidemiology. Despite these attempts the number of prospective-cohort studies is still limited, not allowing us to undertake a meta-analysis regarding precise diagnosis about relationships between NCDs and biological and socioeconomic factors. It should be also taken into consideration that most of published literature from this region uses cross-sectional or case-control surveys.

Databases of the World Health Organization European Region were used in order to get a more comprehensive review of different European countries. The burden of chronic respiratory diseases, mental disorders, chronic neurological diseases and musculoskeletal conditions was reviewed using data from European Health for All Database (HFA-DB) and Mortality indicator database: mortality indicators by 67 causes of death, age and sex (HFA-MDB).

A selection criterion for the countries was a membership in the European Union (EU). Differences were evaluated between countries that were in the EU before 2004 and those eastern and central European countries that joined since 2004. EU member before 2004 were Austria, Belgium, Croatia, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden and United Kingdom. In 2004 the following countries got their membership: Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Slovakia and Slovenia, Cyprus and Malta. Romania and Bulgaria joined EU in 2007 (http://europa.eu/about-eu/countries/member-countries/index_en.htm).

The HFA-DB revealed information about morbidity and hospital discharges. The most comprehensive and recent data was attained from year 2009. The HFA-MDB was used to analyse the differences in mortality data. This database gave the most up-to-date information from year 2011. These data are reported in **Tables 10 and 11,** below.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 10. Burden of various NCDs in the European Union in 2009 (World Health Organization Regional Office for Europe 2015a).

Countries	Incidence of mental disorders per 100 000	Prevalence of mental disorders (%)	Hospital discharges, respiratory system diseases, per 100 000	Prevalence of chronic obstructive pulmonary disease (%)	Hospital discharges, musculoskeletal system and connective tissue diseases, per 100 000
Bulgaria	11.18	2.26	3224	...	932.23
Czech Republic	1010.97	4.72	1399.91	4.05	1693.77
Estonia	1776.51	7.21	1772.7	...	1097.17
Hungary	277.49	1.64	1708.92	1.39	1833.39
Latvia	382.27	5.03	2038.78	...	1290.96
Lithuania	282.08	5.22	2469.65	3.44	1258.17
Poland	1020.49	3.64	1397.41	...	936.37
Romania	1149.72	1.25	3133.88	1.41	1322.82
Slovakia	1294.24	7.27	1464.83	1.7	1065.63
Slovenia	...	...	1410.74	...	969.87
Austria	...	...	1807.08	...	3220.22
Belgium	...	1.28	...	...	...
Croatia	...	...	1050.22	0.13	584.88
Cyprus	...	...	...	...	...
Denmark	512.9	1.11	1875.62	...	1297.96
Finland	96.44	1.82	...	4.27	...
France	...	...	1278.43	...	1690.47
Germany	...	...	1497.62	0.35	2671.1
Greece	...	0.35	...	0.23	...
Ireland	...	...	1307.76	0.34	470.07
Italy	...	...	1037.36	...	818.17
Luxembourg	...	...	...	...	...
Malta	103.75	...	988.05	...	346.16
Netherlands	...	...	791.46	...	845.58
Portugal	...	...	1084.54	...	470.46
Spain	...	...	1185.65	...	737.34
Sweden	...	...	1021.54	...	934.67
United Kingdom	...	...	1199.3	1.67	831.98

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 11. Age-standardized death rate (SDR) of various NCDs in European Union per 100 000 population in 2011 (World Health Organization Regional Office for Europe 2015b).

Disease	Sex	EU	EU before 2004	EU since 2004
Diseases of the respiratory system	All	40.98	41.29	39.82
	Male	57.4	56.15	62.06
	Female	30.07	31.34	25.44
Chronic lower respiratory diseases	All	17.68	17.79	17.28
	Male	26.6	25.78	29.66
	Female	11.96	12.59	9.66
Bronchitis/emphysema/asthma (HFA)	All	17.14	17.15	17.1
	Male	25.95	25.02	29.41
	Female	11.51	12.05	9.53
Asthma	All	0.7844	0.7635	0.8617
	Male	0.7358	0.6581	1.03
	Female	0.8056	0.8209	0.7494
Mental and behavioural disorders	All	14.26	16.71	5.19
	Male	15.19	17.31	7.28
	Female	12.83	15.43	3.31
Alzheimer's disease and other degenerative diseases of nervous system	All	7.73	8.71	4.08
	Male	7.15	7.97	4.12
	Female	7.93	9	4.03
Diseases of musculoskeletal system and connective tissue	All	2.49	2.84	1.19
	Male	2.13	2.47	0.8561
	Female	2.72	3.07	1.44

2.2 Methods

The methodological framework adopted in the project was to undertake search of the PubMed scientific data. We analysed epidemiological surveys from Central-Eastern Europe from 2004 to 2015. We only included studies undertaken on large representative populations– with an N of at least 400. All publications in languages other than English were excluded. The following MeSH key-words were adopted in the search: epidemiology, Europe, eastern, cohort study, cross-sectional study, case-control study, risk factor, diabetes, CVD, metabolic syndrome. To refine outcomes of the literature research we also used filters to include only original publications in the English language.

The research literature was searched in context of findings in the WHO database. The search was undertaken separately for each disease group. Search terms for diseases were following:

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

'chronic respiratory diseases'; 'chronic obstructive pulmonary disease'; 'COPD'; 'asthma'; 'neurological disorders'; 'Alzheimer'; 'Parkinson'; 'multiple sclerosis'; 'musculoskeletal'; 'osteoporosis'; 'osteoarthritis'; 'rheumatoid arthritis'; 'mental disorder'; 'depression'.

In order to find regional differences, all disease terms were individually combined with following terms:

'Europe'; 'East AND Europe'; 'West AND Europe'; 'Eastern AND Europe'; 'Western AND Europe'; 'East AND West AND Europe'.

Besides combining disease and region terms alone, distribution terms were included:

'mortality'; 'morbidity'; 'burden'; 'prevalence'; and 'incidence'.

For this review, articles were chosen based on the content of titles and abstracts.

2.3 Results

2.3.1 Cardiovascular disease

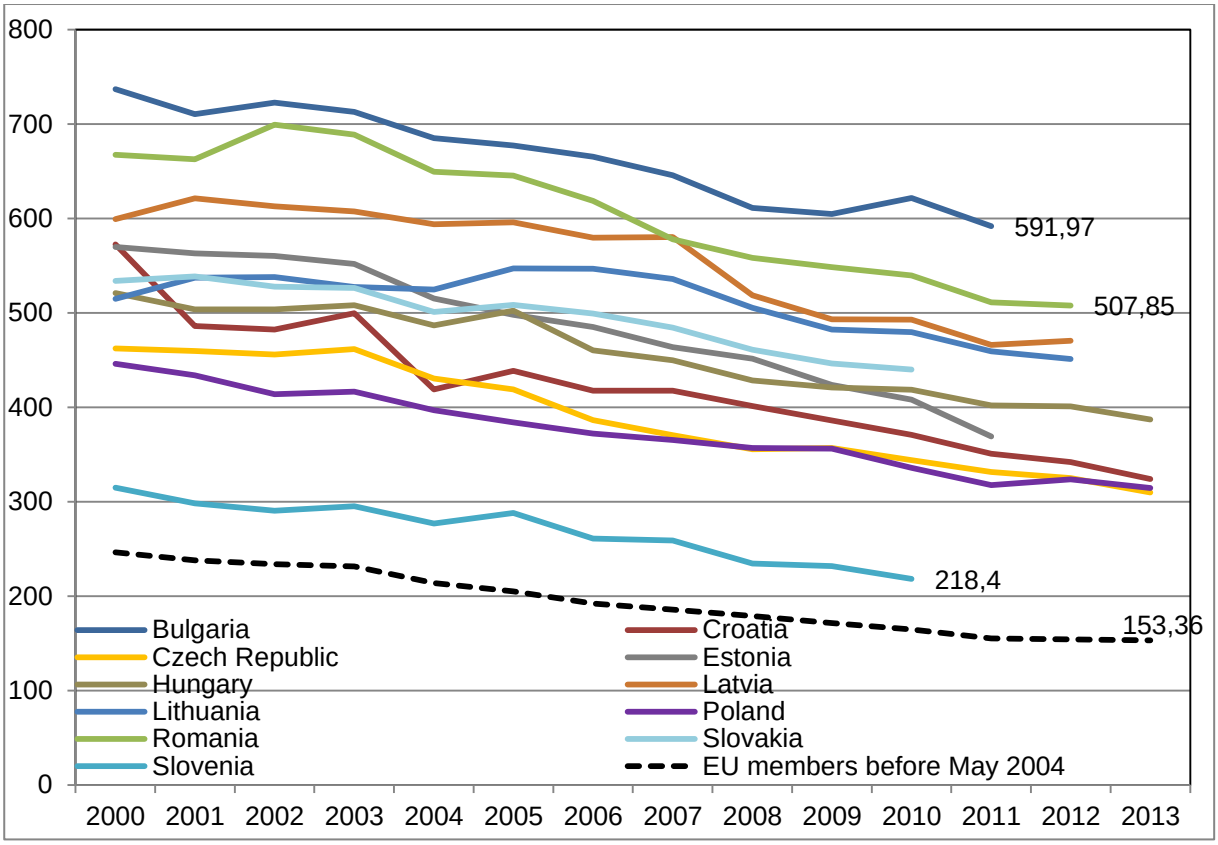
Our search revealed that the number of studies considering risk factors associations between cardiovascular diseases is limited. Most of the studies identified did not allow us to perform an umbrella review. We identified 52 publications on cardiovascular disease. Most of publications were related to cross-sectional and case-control studies (n=29 of publications) and the most significant prospective cohort study which compared different Eastern European countries were cohorts in the HAPIEE study (Health, Alcohol and Psychosocial factors In Eastern Europe). Most of the identified publications were from Poland, Lithuania, Czech Republic and Romania (see **Annexe Table 1**).

As it was mentioned above CVDs is a huge challenge for the region. The differences in CVD mortality are very high in Eastern EU countries. The highest standardized rates of mortality are observed in Bulgaria, where risk of cardiovascular death is almost approximately 4 times higher

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

than in Western EU countries, although countries of Eastern part of EU are experiencing a decline in CVD mortality and some progress is observed in most countries.

Figure 14. Standardized death rates due to CVDs in Eastern EU states and EU 15 in years per 100 000 inhabitants in years 2000-2013 ***(source: WHO Mortality Database)***



An IMPACT model for Poland proposed by O'Flaherty and colleagues has shown that modifications in lifestyle contribute substantially to decrease of CVD mortality.[122] About 37% of this decrease was attributable to treatments and 54% attributed to changes in risk factors, mainly reduction in total cholesterol concentration (39%) and an increase in leisure time physical activity (10%); however, these were partially offset by increases in body mass index (−4%) and prevalence of diabetes (−2%).

Currently one of the biggest challenges is the higher percentage of Eastern Europeans with hypertension compared to those in the Western part of the continent. Hypertension is one of the key risk factors for cardiovascular disease. Epidemiological cross-sectional studies from Poland (NATPOL2011)[123] and Romania (SEPHARII)[124] showed some progress in this area, however evidence from BP-CARE study[125] also showed that control of hypertension is weaker in Eastern

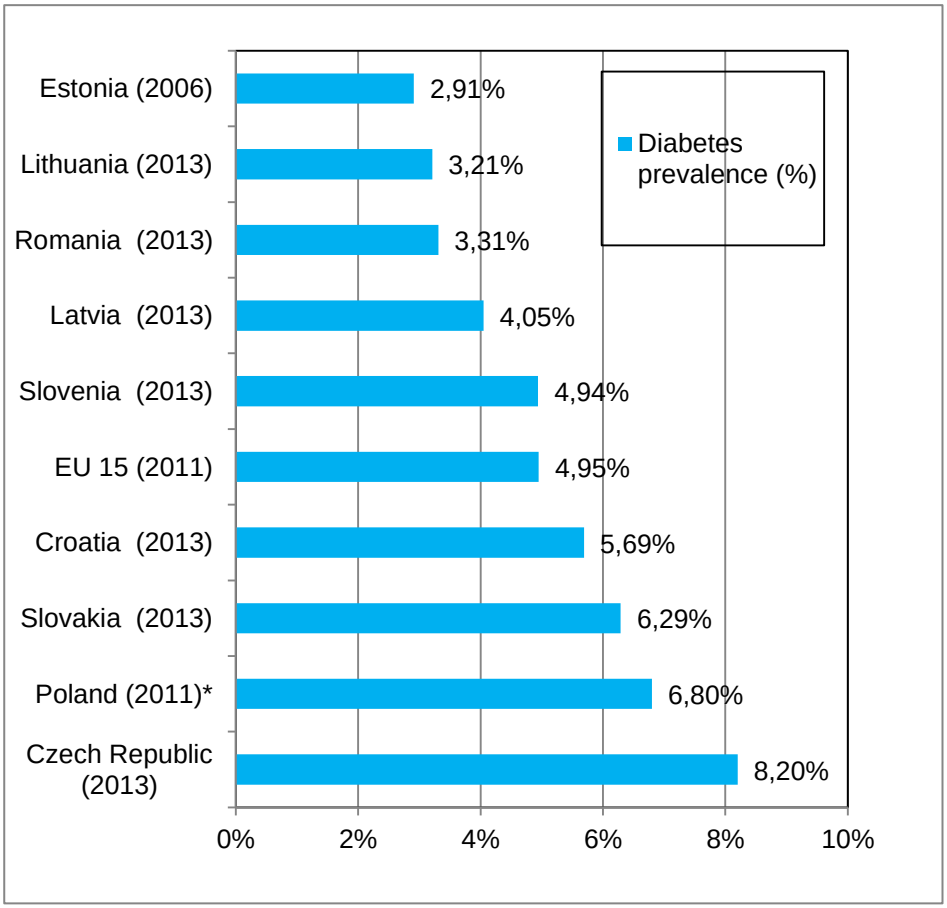
This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

than in Western Europe – 73% of hypertension patients from Eastern European countries participating in the survey had uncontrolled hypertension disease.

2.3.2 Diabetes

We identified 17 publications on epidemiology of metabolic syndrome and diabetes. Prevalence of diabetes in Eastern EU countries is similar to that observed in EU 15 countries. The highest rates are observed in Czech Republic and Poland . (**Figure 15**).

Figure 15. Prevalence of diabetes in selected countries of Eastern EU (*recent data according WHO HFA database)*



**Data from WOBASZ cross-sectional study (2011)*

A recently published systematic review on worldwide trends in diabetes including 751 studies (sample of 4 372 000 adults) from 146 countries showed that worldwide diabetes prevalence increased from 4,3% in 1980 to 9% in 2014 in men and for woman respectively from 5% to 7,9%.[126] Diabetes morbidity has increased in Central and Eastern Europe as well. The dynamics of this process was stronger than in Western part of the European continent. This state

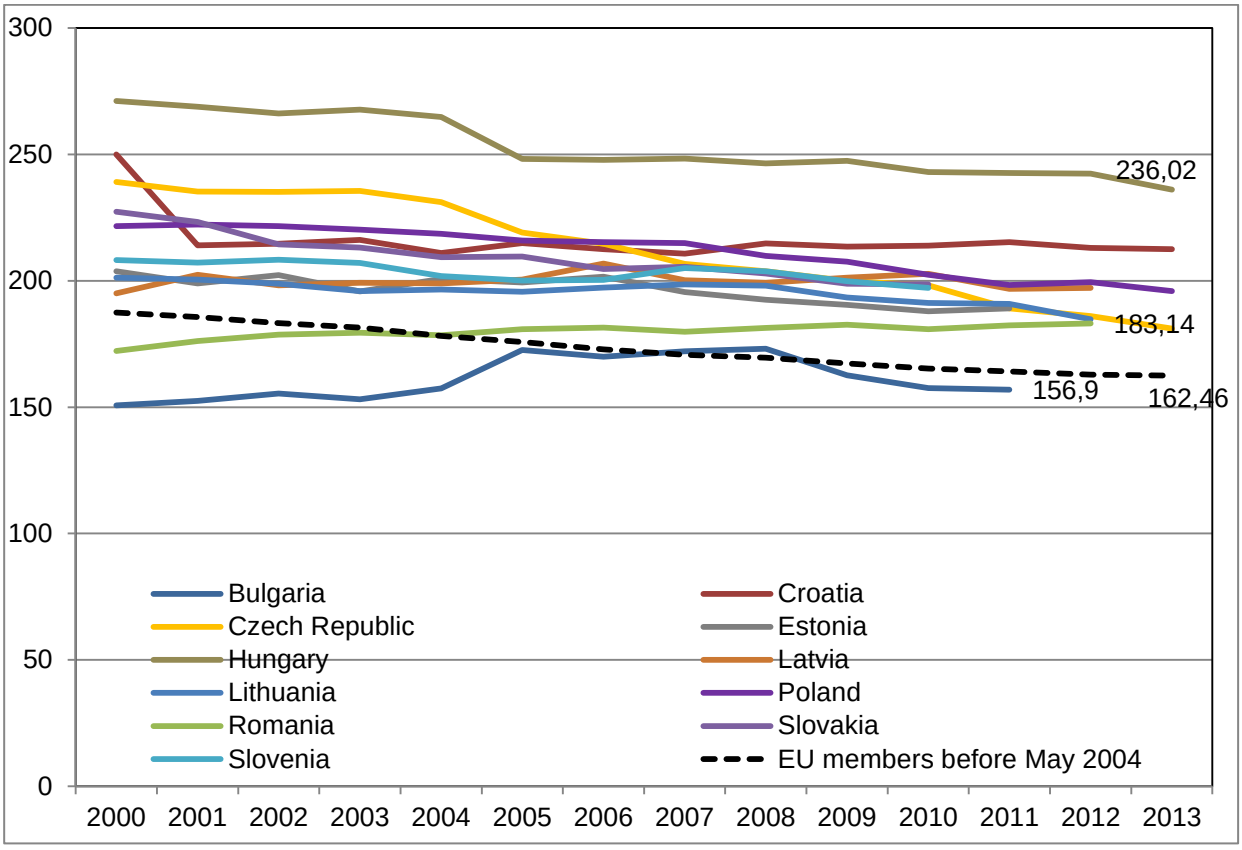
This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

of affairs is not optimistic due to the dynamic growth in overweight and obesity prevalence in the region. Findings from HBSC http://www.euro.who.int/en/hbsc-report-2016 studies performed in Eastern European countries suggests that dynamic of body mass increases among children in the region is higher than in other parts of Europe (the highest increase in rates is observed in Poland).

2.3.3 Cancer

Due to less developed systems of cancer registries it is complicated to compare situation in the field of cancer morbidity between Eastern European countries and EU15. In general standardized death rates per 100 000 in Eastern EU do not differ compared to EU 15 as much as in case of CVDs, but the situation in general is still unsatisfactory. Trends in this field seem to be stable and not changing much during last decade. The highest mortality is observed in Hungary where risk of death is 45% higher than in EU 15 (**Figure 16**).

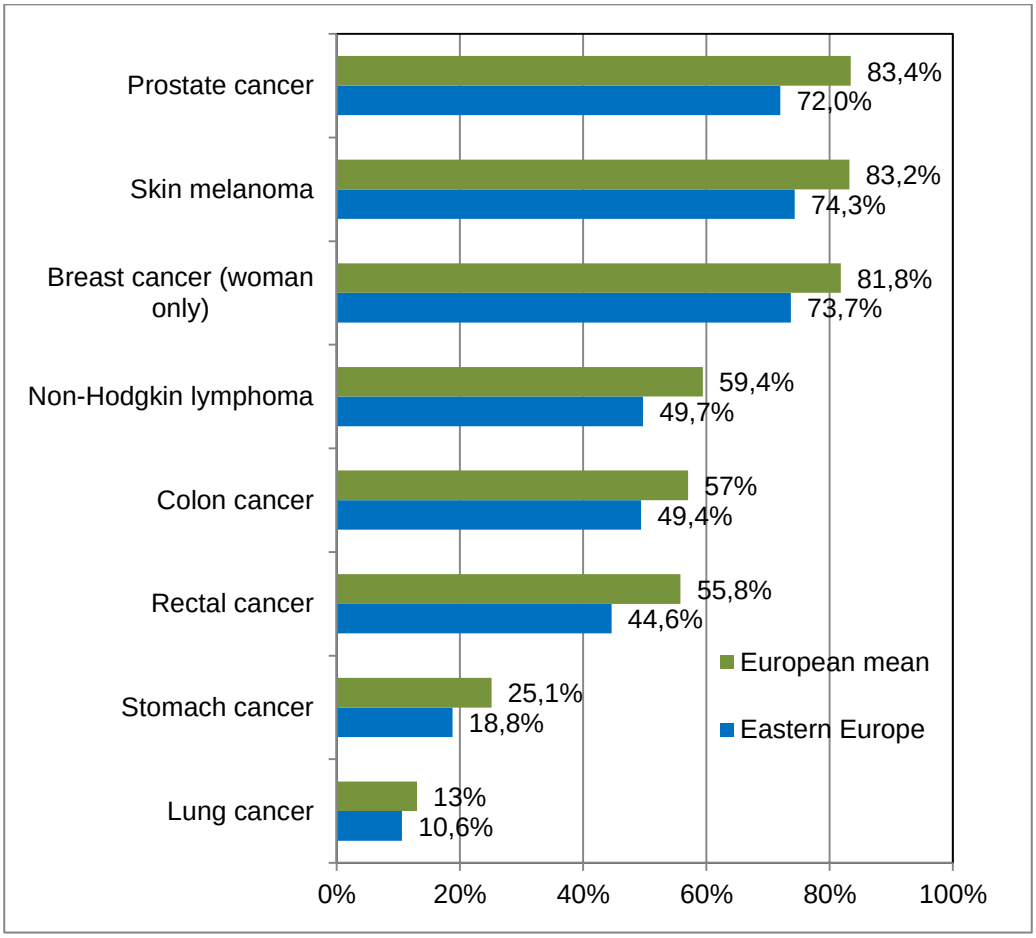
Figure 16. Standardized death rates due to CVDs in Eastern EU states and EU 15 in years per 100 000 inhabitants in years 2000-2013 ***(source: WHO Mortality Database)***



This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

The biggest concern is the unfavourable situation in the area of cancer survival. EUROCARE-5 study,[127] which measured relative survival rates in European region in years 1999-2007 availing data from cancer registries demonstrated that 5-year cancer survival in EU countries between 1999–2001 to 2005–07 has increased for prostate cancer from 73.4% to 81.7%, non-Hodgkin lymphoma from 53.8% to 60.4%, and rectal cancer from 52.1% to 57.6%. Survival in Eastern Europe was generally below the European mean, particularly for cancers with good or intermediate prognosis (**Figure 17**).

Figure 17. 5 years cancer relative survivals rates in Europe and Eastern Europe (Bulgaria, Czech Rep., Estonia, Latvia, Lithuania, Poland, Slovakia) in years 1999-2007 according EUROCARE-5 research group



2.3.4 Chronic lung disease

In the European Region, about 1 million deaths annually are attributable to respiratory diseases. Two thirds of these deaths take place in the European Union.[128] HFA-DB reveals that the

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

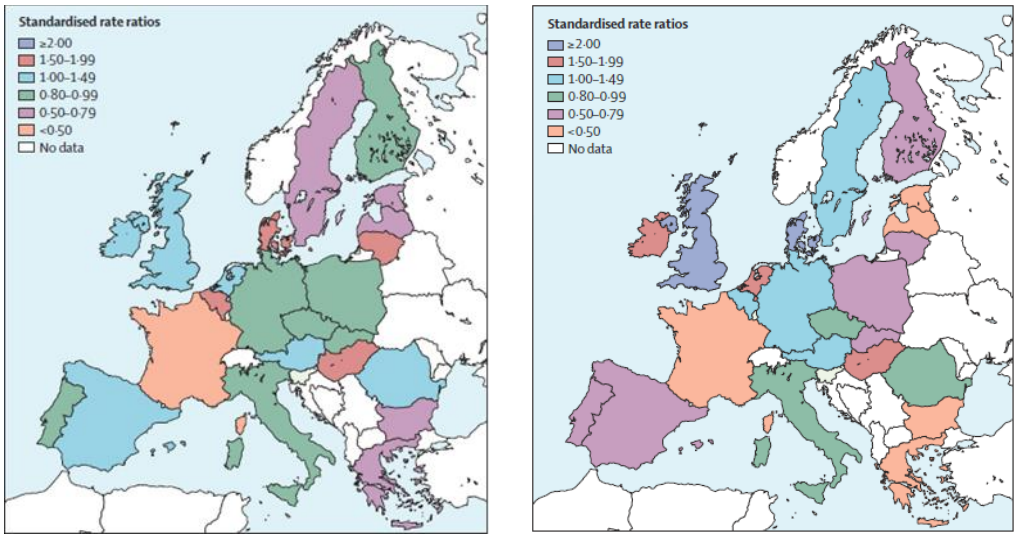
number of hospital discharges from chronic respiratory diseases is on average higher in Eastern Europe compared to the Western European countries (see **Table 10** above). Mortality data, on the other hand, is more equivalent between the Eastern and Western countries (see **Table 11** above). Death rates of respiratory diseases and more specifically chronic lower respiratory diseases were almost the same between the country groups. The estimate for respiratory diseases was around 40 and the figure for chronic lower respiratory diseases was around 17 deaths per 100 000 population. The regional differences are however noticeable in terms of gender ratio. While mortality rates among men are around two times higher both in the East and West, the gap between men and women is bigger in the Eastern countries. While the EU average is that men have around two times higher mortality, then in the Eastern countries the mortality ratio is 2,4 for respiratory diseases and 3,1 for lower chronic respiratory diseases. At the same time, the equivalent ratios in the Western countries are 1,8 and 2. The difference could be explained by cigarette smoking, which is the main risk factor for respiratory diseases. The gender gap in smoking rates is relatively smaller in Western EU compared to Eastern EU. In 2013, the difference in the prevalence of smoking between men and women was around 5% in Western Europe and 10% in the Eastern Europe (World Health Organization Regional Office for Europe 2015a).

One of the most common chronic respiratory diseases is chronic obstructive pulmonary disease (**COPD**). COPD is a condition associated with old age and as the world population is aging, it has become the third most common cause of death in the world.[128] In Europe, 23 million people have COPD and this figure is expected to increase at least until 2030.[129] Unfortunately, incomplete data from the WHO (**Table 10**) does not allow conclusions to be drawn on the regional differences between Western and Eastern countries. The prevalence of COPD seems to be higher in Eastern countries, but for example Finland has a similar prevalence as Czech Republic (4.27% and 4.05%, respectively). We found one study on COPD burden in Europe. Although Lopez-Campos et al.[130] looked at mortality instead of disease prevalence; the findings were similar to that of HFA-DB. They looked at the mortality rates of European Union population aged 40 years and older between years 1994-2010 and found that although there was a downward trend in the mortality rates, there were differences between countries prevalent throughout the years. Belgium, Denmark, Hungary, Lithuania, Netherlands, Spain, and the UK had higher male COPD mortality rates than the EU average, while Bulgaria, Cyprus, the Czech Republic, Greece, and France had mortality rates lower than the EU average (see **Figure 18**). This illustrates that there are no apparent regional differences in the burden of COPD. However, the study found a decreasing gender gap in the

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

overall disease burden. Although in 2010 mortality was over two times higher among men, the gap between men and women is decreasing and with the same trend it is expected that by the year 2031 the mortality rates will be equal in the two sexes.[130]

Figures 18. COPD mortality standardised rate ratios for every country in the EU in 2010 (men on the left and women on the right), from Lopez-Campos et al., 2014 [130]

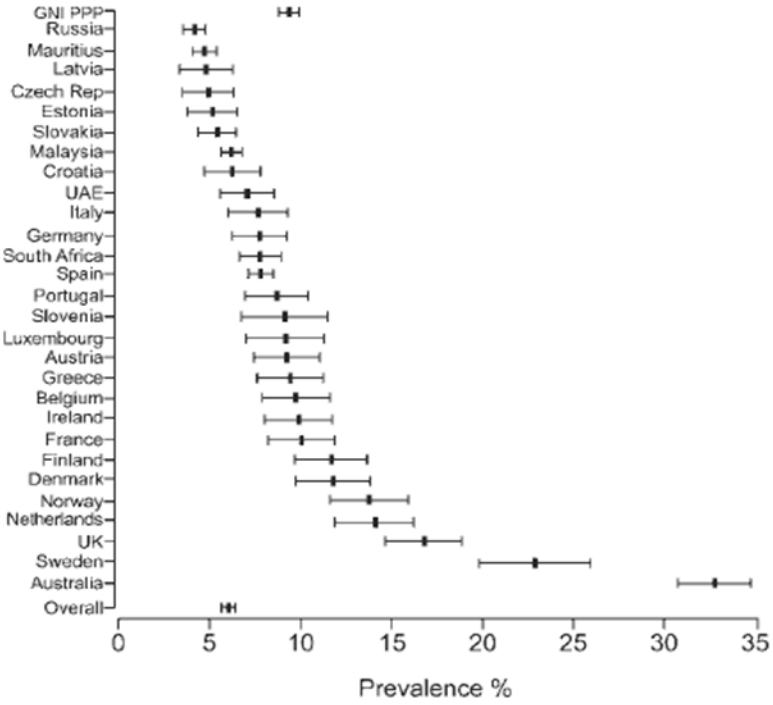


The second most common chronic respiratory disease is **asthma**. In 2013, the global prevalence of asthma was 3429,7 cases per 100 000 population (Global Burden of Disease Study 2013 Collaborators 2015). HFA-MDB provided data on asthma mortality rates. In 2011, Western European countries had the age-standardized asthma death rate of 0.7635 per 100 000 population and in the countries joining EU since 2004 the according death rate was 0.8612 per 100 000 population. These figures show that asthma mortality is rather small and no significant differences exist between regions. This can be explained by the nature of the disease. It is a condition that predominantly affects the younger age group and is predominantly associated with morbidity. For this reason it can be more informative to look at asthma prevalence. Burney et al.[128] aimed to look at the prevalence of asthma in the adult population with data from the World Health Survey. They state that compared to Eastern Europe asthma prevalence is overall higher in Western Europe. In the former group of countries, the figure varies between 5-10%, while in the latter group it reached as high as 25% (see **Figure 19**). It is suggested that the difference could be partly related to "western" lifestyle and increasing urbanization. With ongoing globalization, the prevalence of

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

asthma in the Eastern Europe is expected to approach the levels of Western Europe in the near future.[128]

Figure 19. Prevalence of asthma among adults according to the World Health Survey, from Burney et al. 2015 [128]



2.3.5 Musculoskeletal disorders

Musculoskeletal disorders are a wide spectrum of conditions, from acute to lifelong disorders. Some of the conditions with the greatest impact on society include rheumatoid arthritis, osteoarthritis, and osteoporosis. Data from WHO shows that on average, Eastern region has more hospital discharges due to musculoskeletal system and connective tissue diseases than countries in the Western region (see **Table 10** above). However, it is noticeable that in the latter group there are some outliers. For example, in France and Austria, the estimate was considerably higher compared to other countries in the same group. Despite the fact that musculoskeletal disorders are more associated with morbidity rather than mortality, an insight to mortality estimates gives us a basis for further regional comparisons. HFA-MDB shows that in 2011, Western European countries had 2,4 times higher standardized death rate than Eastern European countries with the

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

estimates of 2.84 and 1.19 deaths per 100 000 people, accordingly. Additionally, it appears that in all countries women have higher mortality than men.

Osteoporosis, one of the most common musculoskeletal disorders, is a condition that increases the fragility of bones and the risk of fractures. It is a disorder more prevalent among older age groups and significantly more pronounced among females. In Europe osteoporotic fractures account for 2 million disability adjusted life years (DALYs) annually. It is estimated that in 2010, 22 million women and 5.5 million men in the EU had osteoporosis. As it is a condition related to aging, the burden of osteoporosis is predicted to significantly increase in the near future. Findings show that there are not remarkable disparities in the prevalence of osteoporosis in Eastern and Western Europe (see **Table 12**)**.** The prevalence varies between 3.7% and 5.8% with an average of 5.5%. Compared to men, women have on average 3,3 times higher prevalence of osteoporosis.[131,132]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 12. Estimated number of men and women with osteoporosis (defined as a T-score of −2.5 SD or less at the femoral neck), prevalence in men and in women over 50 years, and prevalence in the total population, 2010, from Herlund et al. 2013[131]

Country	Men with osteoporosis	Women with osteoporosis	Men and women with osteoporosis	Prevalance in male population aged 50 or more (%)	Prevalance in female population aged 50 or more (%)	Prevalance in total population (%)
Austria	89 862	368 685	458 547	6.5	22.2	5.5
Belgium	120 695	476 875	597 570	6.6	22.4	5.6
Bulgaria	81 482	336 425	417 907	6.4	20.9	5.6
Cyprus	9 263	31 032	40 295	6.2	19.3	3.7
Czech Republic	103 114	425 944	529 058	6.0	20.4	5.0
Denmark	61 456	221 912	283 368	6.5	21.1	5.1
Estonia	11 642	65 789	77 431	6.2	22.2	5.8
Finland	61 054	243 399	304 453	6.4	21.5	5.7
France	691 112	2 784 198	3 475 310	6.7	22.5	5.5
Germany	1 006 652	4 017 260	5 023 912	6.6	22.6	6.1
Greece	135 202	507 505	642 707	6.9	22.3	5.7
Hungary	94 949	452 158	547 107	6.2	21.1	5.5
Ireland	37 127	129 309	166 436	6.2	20.0	3.7
Italy	749 237	3 042 794	3 792 031	6.9	23.4	6.3
Latvia	19 210	111 236	130 446	6.1	22.3	5.8
Lithuania	27 136	148 375	175 511	6.1	21.7	5.3
Luxembourg	4 541	17 422	21 963	6.1	21.0	4.3
Malta	4 190	16 074	20 264	5.9	19.8	4.9
Netherlands	175 244	643 258	818 502	6.3	20.8	4.9
Poland	338 756	1 509 772	1 848 528	5.8	20.1	4.8
Portugal	117 738	475 882	593 620	6.7	22.0	5.6
Romania	198 065	835 885	1 033 950	6.2	20.5	4.8
Slovakia	42 726	188 911	231 637	5.7	19.4	4.2
Slovenia	20 543	89 489	110 032	6.0	21.5	5.4
Spain	496 368	1 952 987	2 449 355	6.8	22.6	5.4
Sweden	113 722	409 373	523 095	6.9	22.4	5.6
UK	679 424	2 527 331	3 206 755	6.7	21.9	5.2
EU27	**5 490 510**	**22 029 280**	**27 519 790**	**6.6**	**22.1**	**5.5**

Another common disease in the group of musculoskeletal disorders is **rheumatoid arthritis**. Lundkvist and colleagues analysed the burden of rheumatoid arthritis with data from year 2002.[133] Rheumatoid arthritis was attributable for around 0.8% of all DALYs lost and about 0.1% of all deaths in Europe, which indicates the chronic nature of the disease. The study shows that there is not a remarkable difference in the morbidity of rheumatoid arthritis between Eastern and Western Europe. In 2002, the disease accounted for 0.84% in Western region and 0.83% in Eastern region of all disability adjusted life years (**Table 13**).[133]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 13. Health burden of RA: DALYs lost and deaths from RA per 100,000 population, from Lundkvist et al., 2008[133]

	DALYs lost due to RA (per 100 000)	Total DALYs Lost (per 100 000)	% DALYs lost due to RA	Total deaths (per 100 000)	Death due to RA (per 100 000)	% Deaths due to RA
Europe	110	13,219	0.84	969	0.9	0.09
Western Europe	103	12,379	0.83	945	1.0	0.10
Eastern Europe	138	16,528	0.84	1,064	0.6	0.06

2.3.6 Depression

In 2010, all mental disorders accounted for 5,76% of DALYs globally. Depression is by far the highest contributor to the burden of mental disorders. Depression accounted for 2.5% of global DALY's in 2010.[134] In Europe, mental disorders account for one quarter of all DALYs. Almost 21 million people in Europe have depression or a bipolar disorder .[135]

Data about the prevalence and incidence of mental disorders was insufficient to make any conclusions about the differences between European regions (see **Table 10** above). Information was available from almost all Eastern countries, but data about Western Europe was presented only for four countries. Furthermore, extreme variations were apparent between the countries. For example, in 2009 the incidence of mental disorders in Bulgaria was 11.18 per 100 000 population, while in Estonia the same indicator was 1776.51 per 100 000 population. Comparison of these estimates should be avoided. This kind of variation could be explained by differences in definition, incomplete registration in some countries or other national specificities in data recording and processing (http://data.euro.who.int/hfadb/ World Health Organization Regional Office for Europe 2015). Nevertheless, data regarding mortality was more comprehensive and it indicated a distinct regional difference (see **Table 11** above). It appeared that compared to Eastern Europe, there was a three times higher death rate in Western Europe. In 2011, there were 16.71 deaths per 100 000 population in Western EU members and 5.19 deaths per 100 000 population in countries, which joined EU since 2004. Furthermore, there was also a regional difference in gender distribution. While in the Western countries mortality was rather equally distributed, then in Eastern Europe men had about two times higher death rate compared to women.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Although, the prevalence of mental disorder could not have been evaluated from HFA-DB data, some conclusions could be drawn based on the study by Boyd and colleagues.[136] They looked at gender disparities in different mental disorders by using data from World Mental Health Surveys (EU-WMH). Ten European countries were analysed; out of which 8 were EU members before 2004 (Belgium, France, Germany, Italy, the Netherlands, Spain, Ireland and Portugal) and 2 were members since 2004 (Bulgaria and Romania). The found that depression, which is by far the most common mental disorder, was on average two times more prevalent among women in all countries (see **Table 14**). Although only two countries of Eastern region were represented, there was clear difference notable with Western European countries. The prevalence in Bulgaria and Romania varied between 4.1-8% among women; and 2.5-3.3% among males, respectively. In Western countries the same indicators varied between 12.4-26.7% among women and 6.4-14.8% among men.[136]

Table 14. Prevalence (%) of lifetime mental disorders among women and men in the EU-WMH survey, by country, from Boyd et al., 2015[136]

Country	Prevalence of major depressive episode
Belgium	W 17.7
	M 10.3
France	W 26.7
	M 14.8
Germany	W 12.4
	M 7.3
Netherlands	W 22.6
	M 13.0
Northern Ireland	W 22.6
	M 12.7
Bulgaria	W 8.0
	M 3.3
Romania	W 4.1
	M 2.5
Italy	W 13.2
	M 6.4
Portugal	W 23.9
	M 11.4
Spain	W 14.5
	M 6.4

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

2.3.7 Neurologic disorders

One of the main chronic neurological disorders is dementia, a condition of older age. It is estimated that globally in 2010, the total number of people with dementia was 35.6 million. The most common cause of dementia is Alzheimer's disease. Data about Alzheimer's disease prevalence in Europe is not provided by the WHO databases, but some information can be retrieved from a study done by Takizawa and colleagues.[137] They looked into the burden of Alzheimer's disease in Western Europe and Northern America between years 2002 up to 2012. Findings showed that although the incidence rate of the disease varied greatly between countries, the prevalence rate was more constant. They found that the prevalence of Alzheimer's disease in Western European countries (i.e. France, Germany, Italy, The Netherlands, Spain, the United Kingdom) varied around 3-6%. It was also noted that women were more likely to have the disease compared to men.[137] Studies about the prevalence of Alzheimer's disease in Eastern Europe were not found. However, Kiejna et al. attempted to conduct information about dementia prevalence in Eastern and Middle Europe, but widely diverse and incomplete findings did not allow making definite conclusions. Based on the limited findings they suggested that the prevalence of dementia in Eastern Europe is estimated to be similar to Western Europe.[138]

Among younger population, the most common cause of neurological disability worldwide is Multiple sclerosis (MS) and around half of those with disease are in Europe. Kingwell and colleagues attempted to analyse the incidence and prevalence of multiple sclerosis in Europe.[139] They found that the estimates vary a lot between countries and even regions. Although they emphasized that conclusions could not be drawn due to lack of standardization, they did suggest that prevalence and incidence were higher in the Nordic countries and in Northern regions of the British Isles.[139]

However, regional differences are clearly notable in the mortality rates of neurological disorders. Standardized death rate of Alzheimer's disease and other degenerative diseases of nervous system are remarkably lower in Eastern region (see **Table 11** above). WHO data shows that in 2011, Western European countries had 2.1 times higher age-standardized death rate compared to Eastern European countries. Furthermore, compared to men, women in Western European countries have slightly higher death rate of Alzheimer's diseases and other degenerative diseases of the nervous system. Eastern countries, on the other hand, have the similar rates in men and women.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

3 IMPACT OF INEQUALITIES IN NCDs

NCDs have become a primary health concern for most countries around the world. According to the WHO (2015) NCDs are responsible for almost 38 million global deaths each year, accounting the 63% of annual global deaths. Almost three quarters of NCDs deaths - 28 million - occur in low- and middle-income countries.[140] The global financial burden of NCDs is staggering, with an estimated 2010 global cost of $6.3 trillion (US dollars) that is projected to increase to $13 trillion by 2030, leading millions of people to be trapped in poverty (WHO, 2013). Cardiovascular diseases account for most NCD deaths, or 17.5 million people annually, followed by cancers (8.2 million), respiratory diseases (4 million), and diabetes (1.5 million). These four groups share similar risk factors (tobacco use, unhealthy diet, physical inactivity and the harmful use of alcohol).

Lifestyle is linked to 20-25% of the global burden of disease. In the next decades as the result of an epidemiological transition non-communicable diseases will replace infectious diseases and malnutrition as the leading causes of disability and premature deaths in countries of low and middle income. By the year 2020, non-communicable diseases are expected to account for seven of every ten deaths in the developing regions. In developed countries, NCDs have replaced communicable diseases as the main source of ill-health. (WHO, 2015). The epidemiologic transition from predominance of infectious diseases to NCDs is thought to arise due to a population that acquires life-styles related to economic development.

According to Krieger the social determinants of health refer to both specific features of and pathways by which societal conditions affect health and that potentially can be altered by informed action.[141] Examples are income, education, occupation, family structure, service availability, sanitation, social support, racial discrimination, and access to resources linked to health. The WHO (2004) suggests that the social determinants of health are the conditions in which people born, grow, live, work and age, including the health system. The social determinants of health are mostly responsible for health inequalities which are understood to be unfair and avoidable differences in health status within and between countries. A range of factors has been identified as social determinants of health, among them: the socio-economic context, inequality, poverty, social exclusion, socio-economic position, income, public policies, health services, employment, education, housing, transport, environment, health behaviours or lifestyles, and social and community support networks.

The aim of this chapter is to provide an overview of evidence about the effect of inequalities in the incidence and prevalence of NCDs. This evidence is particularly relevant in terms of

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

determining inequalities in the burden of these diseases and their determinants across social groups. We first describe the methodology which is common to all diseases analysed.

3.1 Methods

A systematic literature search was performed in PubMed, Cochrane Library and Web of Science (until 30 December 2015) to identify the most relevant published evidence regarding the relationship between income inequalities and NCDs. In all databases, terms related to ‘‘NCDs’’, ‘‘non-communicable diseases’’ and “inequalities”, “socioeconomic status”, or “socioeconomic position” were combined (for full search queries see **Table 15**). The search was refined to include papers published in the English language from 2005 to limit the scope of this review to the most recent evidence. Hence, we considered firstly a ten-year retrospective horizon to be sufficient.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 15. Search strategy PubMed, Cochrane Library and Web of Science

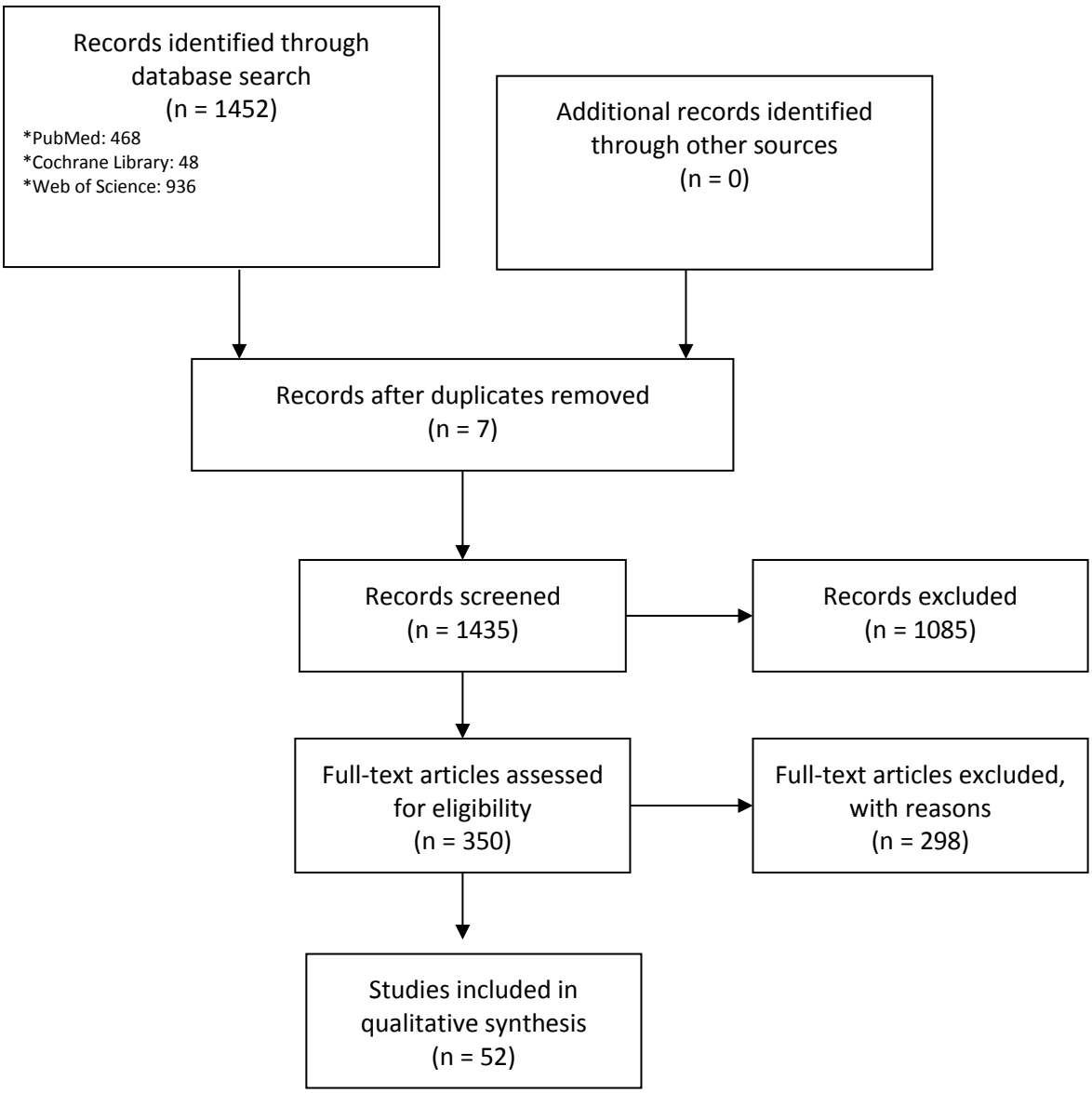
#	Search term
PubMed	
#1.	**NCDs** [Title/Abstract]
#2.	**Non-communicable diseases** [Title/Abstract]
#3.	**Inequality** [Title/Abstract]
#4.	**Socioeconomic status** [Title/Abstract]
#5.	**Socioeconomic position** [Title/Abstract]
#6.	Limit to: journal article; year of publication >= 2005; English; human subjects, free-full text
Cochrane Library	
#1.	**NCDs** [Title/Abstract]
#2.	**Non-communicable diseases** [Title/Abstract]
#3.	**Inequality** [Title/Abstract]
#4.	**Socioeconomic status** [Title/Abstract]
#5.	**Socioeconomic position** [Title/Abstract]
#6.	Limit to: year of publication >= 2005; English; free-full text
Web of Science	
#1.	**NCDs**[Topic]; [Title]
#2.	**Non-communicable diseases** [Topic]; [Title]
#3.	**Inequality** [Topic]; [Title]
#4.	**Socioeconomic status** [Title/Abstract]
#5.	**Socioeconomic position** [Title/Abstract]
#6.	Limit to: journal article; year of publication >= 2005; English; free-full text; public environmental occupational health OR social issues OR health care sciences and services

After identification of publications in electronic databases, duplicate records were removed. The final selection of papers was based on the following eligibility criteria: applied studies focusing

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

on OECD countries (included European Union and other countries) or articles referring to high- or middle-income countries. We identified 1452 publications. A total of 7 duplicates were removed, resulting in 1435 unique papers. After screening titles against the eligibility criteria, 350 papers were selected. Of these, 298 articles were excluded as they did not fit with the previously indicated criteria. Therefore a final set of 52 selected studies are fully taken into account in this review. Nevertheless, further papers are finally considered to allow for a robust overview. **Figure 20** shows the paper selection process following PRISMA.

Figure 20. Flow diagram of paper selection process



This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

3.2 Results

The selected articles varied greatly in primary purpose, design and analytic approaches, making formal homogenous synthesis impossible. The heterogeneity of studies made it difficult to synthesize the results and assess the impact of factors considered on outcomes. Despite these differences, evidence suggests that a broad number of socioeconomic factors were associated with morbidity and mortality related to non-communicable diseases.

In a recent study, Sommer et al. carried out a review of literature to study the relationship between socioeconomic inequalities, morbidity and mortality of non-communicable diseases and their risk factors.[16] The authors searched for relevant systematic reviews published between 2003 and December 2013. Of a total of 3,302 abstracts, 22 systematic reviews were chosen. The studies they analysed show that having low socioeconomic status and/or living in low- and middle-income countries increased the risk of developing cardiovascular disease, lung and gastric cancer, type 2 diabetes and chronic obstructive pulmonary disease. Furthermore, low socioeconomic status increased the risk of mortality from lung cancer and chronic obstructive pulmonary disease. It also reduced breast cancer survival in high-income countries. The literature review concludes that the studies show an association between socioeconomic inequalities and NCDs and risk factors for NCDs. However, this evidence is incomplete and is limited by the fairly low methodological quality of the reviews, including shortcomings in the study selection and quality assessment process.

The remaining evidence analysed is reported in third main groups of chronic diseases: cardiovascular and heart diseases, cancer and diabetes. Asthma and atherosclerosis are considered in a fourth group of diseases.

3.2.1 Cardiovascular Diseases

We identify 22 studies (**Table 16**) on socioeconomic inequalities and cardiovascular and heart diseases, with 4 of them reporting on CVD in general, 3 of them on stroke, one on adherence to therapy in cardiovascular medication, 3 on cardiac surgery, 3 on myocardial infarction, 5 on coronary disease and one on ischemic illness.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Socioeconomic circumstances featuring childhood may be relevant to influence risk of CVD in adulthood. Galobardes et al. retrieved individual-level studies of morbidity and mortality from CVD linked to early life influences up to 2004.[18] They searched for childhood socioeconomic circumstances as generic term and specific indicators such as parental education, parental occupation, housing conditions and overcrowding. They also consider proxy indicators of poor socioeconomic circumstances, such as number of siblings, maternal marital status or residence in an orphanage or similar. The results obtained from the analysis of 40 studies found a robust inverse association between childhood circumstances and adult CVD risk. Results present variations depending on specific outcomes, socioeconomic measures or sex.

The impact of socio-economic inequalities in CVD among people with and without diabetes was investigated for Dray-Spira and colleagues.[142] The study analyses a sample of 255,966 thousand people from 25 years or more in the National Survey of Interview of Health between 1997 and 2005 in the United States. Among adults with diabetes, the prevalence of CVD is higher for those people that do not complete high school in the University graduate, although the incidence varied throughout the period studied. Among adults without diabetes educational disparities in CVD increased significantly during the period analysed. In general, age and type of the CVD-adjusted prevalence was about 2.5 times higher in adults, facing those without diabetes, regardless of sex. Similar results were obtained by Kavanagh and colleagues,[143] who studied the associations between socio-economic position (education and household income) and biomarkers of diabetes and CVD in Australia. They concluded that low socio-economic position is more consistently associated with a worse profile of biomarkers for CVD and diabetes for women.

The study designed by Schulz et al (2008) provides evidence of a cascade effect linking socioeconomic position to anthropometric indicators of CVD risk through effects on psychosocial stress, psychological distress and health-related behaviours, and consider implications for disease prevention and health promotion.[144] Socioeconomic position was associated with multiple CVD risk factors such as smoking and physical inactivity.

Li et al.,[145] in a study on Swedish data, concluded that the incidence, recurrence, and case-fatality of stroke increased with decreasing socioeconomic status. Besides, the relationship differed by gender and subtype of events. Andersen et al. carried out a study that analysed the relationship between socioeconomic position, measured as household

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

income and length of education, and hospital admissions for a first ischemic stroke.[146] The authors also studied cardiovascular risk factor profile associated with socioeconomic position in stroke patients. The data use in the analysis cover all citizens of Denmark over the age of 40 and who had lived in that country during some or all of the period of 2003-2012 (23 517 408 individuals). The results indicated a highly significant stepwise relation between income and risk for hospitalization for stroke. The risk being almost twice as high in the lowest income group, than in the highest. Diabetes, obesity, smoking, and high alcohol consumption in particular and, to a lesser extent, previous myocardial infarction or intermittent arterial claudication were significantly overrepresented among stroke patients with lower socioeconomic position. Nordhal et al. also confirmed inequalities in stroke incidence in Denmark when studying the combined effects of socioeconomic position, smoking, and hypertension on risk of ischemic and haemorrhagic stroke.[147]

In a macro-level analysis, Sposato et al. selected population-based studies reporting incident stroke risk and/or 30-day case-fatality.[111] They use three macro-socioeconomic status indicators: per capita gross domestic product (GDP) adjusted for purchasing power parity; total health expenditure per capita at purchasing power parity; and unemployment rate. They examine the correlation of each indicator with incident risk of stroke. Age-adjusted incident risk of stroke was associated to lower per capita gross domestic product and total health expenditure per capita. Thirty-day case-fatality rates and proportion of haemorrhagic strokes were also related to lower per capita gross domestic product and total health expenditure per capita. Moreover, stroke occurred at a younger age in populations with low per capita gross domestic product and total health expenditure per capita. There was no correlation between unemployment rates and outcome measures. The authors suggest that the macroeconomic status indicators considered may be used as proxy measures of quality for primary prevention and acute care in order to improve stroke care.

Adherence to therapy in cardiovascular medication constitutes a relevant subject of study. Laba et al. developed a systematic review about the adherence to medications for cardiovascular diseases in socioeconomically disadvantaged populations in order to determine the effects of strategies to improve that adherence.[148] A total of 14 articles were analysed from a total of 945 studies identified through database searching. Disadvantage was defined by place of residence, education and income. The strategies most effectives were simultaneously directed at patients and physicians/practices, targeting physician

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

prescribing behaviour as well as interventions to reduce patient social, financial and treatment-related barriers to patients.

Literature on the relationship between socioeconomic status and cardiac surgery, find a direct effect between a better socioeconomic position and improved results in surgery. Singh et al (2009),[149] develop a retrospective cohort study in order to analyse whether low socioeconomic position is associated with outcomes in heart transplant recipients. The study was designed to provide evidence of a cascade effect linking socioeconomic position to anthropometric indicators of cardiovascular disease risk through effects on psychosocial stress, psychological distress and health-related behaviours. In a similar way, the purpose of the study of Singh et al (2010) was to assess whether low socioeconomic position is associated with outcomes in heart transplant recipients. Low socioeconomic group was associated with a greater risk of subsequent graft loss.[150] At the same time rejection episodes were more frequent in the low socioeconomic group. In this sense, Koch et al. (2010) with a 2-phase cox model and generalized propensity score techniques for the US, indicated that socioeconomically disadvantaged patients had significantly higher risk-adjusted mortality after surgery.[151]

We can also find evidence on socioeconomic position and myocardial infarction. Ljung and Hallqvist,[152] using information on Sweden, concluded that accumulated experience of adverse socioeconomic position over the entire life course increases the risk of myocardial infarction for both men and women. They pointed out that the accumulation effect is partly mediated by the acquisition of health-damaging experiences. Rosvall et al (2008) evaluated long-term survival after acute myocardial infarction in relation to socioeconomic position and use of revascularization in Sweden.[153] Adjusting socioeconomic differences for the use of revascularization procedures only marginally reduced the age adjusted HRs of death within five years for the lowest cumulative income group compared to the highest. Authors also analysed socioeconomic differences in survival through stratified analyses by use of revascularization procedures. Results show that those with low cumulative income who had no revascularization showed an increased HRR of 5-year mortality, compared to those with high cumulative income with no revascularization, after adjustment for age and sex. Malki and colleagues analysed temporal trends in the incidence of myocardial infarction and ischemic stroke in Sweden by socioeconomic position and investigated whether social

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

inequalities in incidence of these diseases changed over time.[154] Their results confirmed that there exist social inequalities in the incidence of cardiovascular diseases.

The association between cumulative socioeconomic position and ankle-brachial index was examined by Agha and colleagues although without concluding results.[155] The authors use data from a prospective analysis of 1,454 participants of the *Framingham Heart Study Offspring Cohort* (United States). The results indicated that a cumulative life-course socioeconomic position was associated with low ankle-brachial index in men but not in women. Associations with low ankle-brachial index in men were substantially driven by their own education.

Using data from the British women's heart and health study, Lawlor et al. analysed the association of socio-economic and coronary heart disease. Results showed an increased prevalence.[156,157] Again for the UK Lawlor et al. used the Aberdeen children of the 1950s cohort study to analyse the association of father's social class with coronary heart disease. Its findings provided evidence regarding how rates of coronary heart disease and stroke increased across the social class distribution from highest to lowest.[158]

Thurston et al. examined the association between socioeconomic position and coronary heart disease with data of the First National Health and Nutrition Examination Survey in USA.[159] Low education was associated with greater social and psychological risks for women than men. Models showed that education and income were inversely associated with incident coronary heart disease in age-only and multivariate models. Risk associated with education varied by gender, with less than high school education associated with stronger risk of coronary heart disease in women than in men in age-adjusted models. In a more recent study, Loucks et al. studied life-course socioeconomic position and the incidence of coronary heart disease in a well-characterized US cohort (the Framingham Offspring Study).[160] Results confirmed that cumulative socioeconomic position is associated with incident coronary heart disease after adjustment for age and sex.

Bender et al. (2014) analyse the relationship between ischemic illness of heart and socio-economic characteristics (education, income available, relation to employment, property of home, civil status).[161] The study analyses the total effect of socioeconomic factors on the first participation of visitors and its subsequent follow-up. Results show that the participants at increased risk of suffering an ischemic heart disease have socioeconomic characteristics less favourable than the average of all participants.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Calvillo-King et al. developed a systematic review that considers the impact of social factors on the risk of readmission or mortality in pneumonia (CAP) and heart failure (HF).[114] The authors analyse 72 articles (20 CAP and 52 HF) that evaluate the variables of age, gender and race and their association with readmission and mortality in patients hospitalised with CAP or HF. A classification of sociodemographic characteristics is made on three levels. Level 1 factors include gender and race; level 2 factors include socioeconomic variables, such as education, employment, income, insurance, and marital status; level 3 considers factors related to the underlying social environment (social support, housing situation), behavioural factors (diet, smoking, medication, substance use), socio-cognitive factors (health, literacy) and neighbourhood factors (urban/rural, community poverty, proximity to healthcare). For level 1, older age was the most common risk factor. Among level 2 factors, low income and education and Medicaid insurance increased risk. There was little evidence about the variables of level 3, but housing stability and social support (environment), smoking and substance abuse (behavioural), and rurality and distance to hospital (neighbourhood) were predictors of poor post-hospital outcomes. Roberts et al. (2010) showed the relation between early-life socioeconomic position and incident, hospitalized heart failure among middle-aged US (black and white) participants.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 16. Summary of results for socioeconomic inequalities and Cardiovascular Diseases

STUDY	YEAR	COUNTRY	METHODOLOGY	RESULTS (COMPARATIVE RISKS)
Agha et al (2011)	1971-1998	United States	**Multivariable logistic regression analyses** to evaluate associations between cumulative Socioeconomic Position (SEP) and ankle–brachial index (ABI). Prospective analysis of 1,454 participants from the Framingham Heart Study Offspring Cohort.	Cumulative life-course **SEP** was associated with low ABI in men (OR= 2.04) but not in women (OR 0.86). Associations with low ABI in men were substantially driven by their own **education** (OR 4.13).
Andersen et al (2008)	2003-2012	Denmark	**Log-linear Poisson regression models** to estimate incidence rate ratios for education and disposable income. **Logistic regression models** to estimate the association between socioeconomic position and cardiovascular risk factors for stroke.	A highly significant stepwise relation was found between **income** and risk for hospitalization for stroke. The risk being almost twice as high in the lowest income group than in the highest. Adjusted analysis: RR=0.85 for higher **education** and RR=0.99 for vocational education (reference = basic education). The risk of stroke hospitalization of the higher education groups was lower than in the vocational and short education group. Adjusted analysis: RR=0.56 for level of income 5 and RR=0.83 for level of income 2 (reference = level of income 1). Diabetes, obesity, smoking, and high alcohol consumption in particular and, to a lesser extent, previous myocardial infarction or intermittent arterial claudication were significantly overrepresented among stroke patients with lower **socioeconomic position**. Atrial fibrillation and hypertension were not.
Bender et al. (2014)	1999-2001	Denmark	The aim of this paper is to investigate which socioeconomic factors influence participation at baseline and follow-up visits in the Inter99 study. The overall aim of the Inter99 study was to estimate the effects of a lifestyle intervention on the risk of Ischemic Heart Disease (IHD).	In the current study we find large socioeconomic inequality in participation in a lifestyle intervention aimed at investigating factors that prevent IHD. The socioeconomic inequality was largest at baseline; however, in the high-risk population the socioeconomic inequality in participation increased a
Calvillo-King et al. (2013)	1980-2012	Several countries	Authors developed a **systematic review** that considers the impact of social factors on risk of readmission or mortality in cases of pneumonia (CAP) and heart failure (HF). Authors analyse 72 articles (20 CAP and 52 HF) that evaluate variables of age, gender and race and their association with readmission and mortality in patients hospitalised with CAP or HF.	A broad range of social factors affect the risk of post-discharge readmission and mortality in CAP and HF. Older age was the most common risk factor. Low **income** and **education** and Medicaid **insurance** increased risk. Housing stability, social support, smoking, substance abuse, rurality and distance to hospital were predictors of poor post-hospital outcomes. For Heart Failure (HF), there were 36 retrospective and 14 prospective cohort studies, one case control and one cross-sectional. Focus on social factors associated with readmission and short-term mortality in Heart Failure (HF), several related measures of low socioeconomic status were found to significantly increase readmission. Insurance, education and socioeconomic status were examined but were not significant in the association between social factors and short-term mortality in HF.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Dray-Spira et al. (2007)	1997-2005	United States	**Regression models**	Among adults with diabetes, disparities in Cardiovascular Disease (CVD) prevalence was persistently higher in those who did not complete **high school** (HS) than in college graduates (adjusted prevalence rate ratios [aPRR] 1.20, 95% confidence interval [95%CI] 1.05–1.38 in 1997–1999, and aPRR 1.12, 95% CI 1.00–1.25 in 2003–2005). However, the HS vs. college graduates disparity in CVD declined from 1997–1999 (aPRR 1.20, 95% CI 1.04–1.37) to 2003–2005 (aPRR 1.01, 95% CI 0.90–1.12). Among adults without diabetes educational disparities in CVD widened markedly over time.
Dzayee et al (2014)	1987-2007	Sweden	**Cox proportional hazard model** to analyse trends in, and risk of Second myocardial infarction (SMI) after day 28 of first myocardial infarction (FMI) association with gender, educational level, and country of birth were analysed. Nationwide cohort study of 331,748 men and 186,755 women aged 30-84, living in Sweden, and diagnosed with first myocardial infarction (FMI)	Men had a higher risk of SMI than women (HR 1.14, 95% CI 1.12-1.55) with a downward trend over time, regardless of country of birth (p-trend <0.0001). Low educational level increased the HR of SMI irrespective of gender or country of birth. Foreign-born men and women had a slightly increased HR than Sweden-born. Foreign-born who had lived in Sweden for less than 35 years had a higher risk than those that had lived there for 35 years or longer.
Fischbacher et al. (2014)	2001	Scotland	To link self-reported Socio Economic Position (SEP) and ethnicity data on 4.65 million individuals from the 2001 Scottish Census to hospital admission and mortality data for cardiovascular disease (CVD) in 10 ethnic groups. **Poisson regression** with robust variance was used to calculate CVD incidence rate ratios.	Wide socioeconomic variation between groups. Multiple SEP adjustment had little effect on relative risk of CVD for most groups. Where it did, the effect varied in direction and magnitude. Across groups, SEP measures were inconsistently associated with CVD hospitalization or death.
Fiska et al. (2015)	1994-2003	Norway	130,066 participants were examined. A subgroup (n = 84,631) had additional life course socioeconomic data. **Using Cox proportional hazard analyses**, the authors calculated hazard ratios (HR) for coronary heart disease (CHD) mortality, assessed by linkages to the Norwegian Cause of Death Registry. For subgroup analyses, the authors created an index of life course socioeconomic position.	For men, myocardial infarction (MI) in parents and siblings were a risk factor for CHD mortality after adjusting for established risk factors and socioeconomic conditions; the highest risk was with MI in siblings (HR: 1.44 [1.19–1.75]). For women, self-reported family history (FH) constituted significant risk after similar adjustment only for those with MI in parents plus siblings (HR: 1.78 [1.16–2.73]). Adjusting for life course socioeconomic conditions marginally lowered the estimates, and those with FH did not have worse life course socioeconomic position than those without.
Galobardes et al (2006)	2004	Several countries	**Systematic review** in order to evaluate evidence for an association between socioeconomic circumstances during childhood and specific CVD subtypes, independent of adult socioeconomic position (MEDLINE, EMBASE and ISI Web of Science).	Of the 40 studies located, 31 found a robust inverse association between childhood circumstances and CVD risk, although findings varied among specific outcomes, socioeconomic measures and sex. The association was stronger for stroke (in particular for hemorrahgic stroke) than for CHD.
Gebreab et al. (2015)	2000-2004	United States	It is used data from the Jackson Heart Study (JHS) to examine the associations of multiple measures of lifecourse socioeconomic position (SEP) with cardiovascular disease (CVD) events in a large cohort of African Americans. During a median of 7.2-year follow-up, 362 new or recurrent CVD events occurred in a sample of 5301	Adult SEP was more associated with CVD risk in women than in men: age-adjusted hazard ratios for low versus high income (95% CIs), 2.46 (1.19 to 5.09) in women and 1.50 (0.87 to 2.58) in men, *P* for interaction=0.1244, and hazard ratio for low versus high wealth, 2.14 (1.39 to 3.29) in women and 1.06 (0.62 to 1.81) in men, *P* for interaction=0.0224. After adjustment

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

			participants aged 21 to 94. Childhood SEP was assessed by mother's education, parental home ownership, and childhood amenities. Adult SEP was assessed by education, income, wealth, and public assistance.	for all adult SEP measures, wealth remained a significant predictor of CVD events in women (HR=1.73 [1.04, 2.85] for low versus high). Education and public assistance were less associated with CVD. Adult SEP was a stronger predictor of CVD events in younger than in older participants (HR for high versus low summary adult SEP score 3.28 [1.43, 7.53] for participants ≤50 years, and 1.90 (1.36 to 2.66) for participants >50 years, *P* for interaction 0.0846). Childhood SEP was not associated with CVD risk in women or men.
Kavanagh et el. (2010)	1999-2000	Australia	**Multi-level linear regression model** to study the associations between socio-economic position (education and household income) and biomarkers of diabetes and cardiovascular disease (CVD).	**Low socio-economic position** is more consistently associated with a worse profile of biomarkers for CVD and diabetes for women. Lower levels of **education** were associated with higher glucose tolerance (some high school: 0.08, 95% CI 0.05-0.12 and no high school: 0.17, 95% CI 0.06-0.27); lower levels of education had higher systolic blood pressure (some high school: 1.94 mmHg, 95% CI 0.91-2.97 whereas lower 4.47 mmHg, 95% CI 1.58-7.36).
Koch et al. (2010)	1995-2005	United States	**2-phase cox model** and **generalized propensity score techniques** are used to analysed the effect of race, sex, and socio-economic position on mortality after cardiac surgery.	**Socioeconomically disadvantaged patients** had significantly higher risk-adjusted mortality after surgery (-0.010 [-0.02 – 0.009]).
Laba et al (2013)	1996-2012	Several countries	**Systematic review** to determine the effects of strategies to improve adherence to cardiovascular disease (CVD) related medications in socioeconomically disadvantaged groups.	Strategies to improve adherence in general population have shown to have had moderate effectiveness and cost-effetiveness. There is evidence that among socioeconomically disadvantaged groups, strategies that simultaneously target patients and physicians are highly effective.
Lawlor (2005a)	1999-2001	United Kingdom	**Multilevel logistic regression models** are used to assess the association between area-level socioeconomic characteristics and coronary heart disease.	All measurements of **socioeconomic position** were associated with increased prevalent (1.11 (95% confidence interval: 1.06 – 1.16)) and incident (7.9%-23.8%).
Lawlor (2005b)	1999-2001	United Kingdom	**Cox proportional hazards regression models** are used to analyse the association of father's social class with coronary heart disease.	Odds of coronary heart disease was 27% greater among those living in wards with a **deprivation score** above the median compared with those living in a ward with a deprivation score equal to or below the median (odds ratio=1.27; 95% confidence interval=1.02-1.57).
Lawlor (2006)	2000-2002	United Kingdom	**ANOVA, chi-square statistic and multiple linear regression models** are used to we examined the relation between childhood and adulthood socio-economic position and the prevalence of subclinical atherosclerosis.	The gender-adjusted hazard ratio of experiencing coronary heart disease or stroke comparing the manual and non-manual **social class categories** was 1.52 (95% confidence interval=1.14- 2.02).
Li et al. (2008)	1990-2000	Sweden	**Cox regression model** was used to assess the associations between socio-economic position and stroke incidence, subtype, recurrence, and case-fatality.	The incidence of stroke increased with decreasing annual **income** [women (relative risk: 1.75, 95% CI: 1.36 to 2.25); men (relative risk: 1.29, 95% - CI: 1.06 to 1.58)].
Ljung and Hallqvist	1992-1994	Sweeden	**Case-control study** of risk factors for incident myocardial infarction. Every year in manual work was added to calculate a proportion of the	With increasing proportion of life spent in adverse **socioeconomic position**, it is found an increasing risk of myocardial infarction. The relative

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

(2006)			whole life course spent in adverse socioeconomic position.	risk of myocardial infarction was 2.36 (95% confidence interval (CI) = 1.79 to 3.11) for men and 2.54 (95% CI = 1.70 to 3.78) for women who, over the entire life course, had always been in adverse socioeconomic position compared with those who had never been in adversity. They also found a strong increase in risk from being in adversity for only a few years, which showed an important selection processes.
Loucks et al. (2009)	1971-2003	United States	**Cox proportional hazards analyses** to determine whether cumulative life-course socioeconomic position is associated with coronary heart disease incidence.	Cumulative **socioeconomic position** it is found as being associated with incident coronary heart disease (CHD) after adjustment for age and sex (hazard ratio = 1.82, 95% confidence interval: 1.17, 2.85 for low vs. high cumulative socioeconomic position score). Adjustment for CHD risk factors reduced that magnitude of association (hazard ratio = 1.29, 95% confidence interval: 0.78, 2.13).
Malki et al. (2014)	1987-2010	Sweden	**Flexible parametric survival models** adjusted for calendar year, attained age, sex, and birth country to study incidence rates of myocardial infarction and ischemic stroke and incidence rate ratios comparing levels of socioeconomic position.	Overall incidences of myocardial infarction and ischemic stroke decreased over time among men, but were stable among women. Regarding ischemic stroke incidence, **socioeconomic inequality** increased over time in the age group 55 to 59. The incidence rate ratios for low manual compared to high non-manual increased from 1.3 (95% CI: 1.2–1.4) in 1997 to 1.5 (1.4–1.7) in 2010 among men, and from 1.4 (1.3–1.6) in 1997 to 2.1 (1.8–2.5) in 2010 among women. The socioeconomic inequality in incidence of myocardial infarction was stable over time for both.
Nordhal et al. (2014)	7 existing population-based cohort studies (14 years until 2001)	Denmark	**Additive hazards models** to study the combined effect and interaction between socioeconomic position, smoking, and hypertension on ischemic and hemorrhagic stroke incidence.	It is obtained that the combined effect of **socioeconomic position** and smoking exceeded the sum of their separate absolute effect on risk of ischemic stroke, particularly among men (134 (95% confidence interval, 49–219)). They found evidence of an interaction between smoking and hypertension on risk of both ischemic and hemorrhagic stroke.
Roberts et al. (2010)	1987-1989; 2000-2001	United States	**Cox proportional hazards regression** to study the influence of life-course socioeconomic position on incident heart failure (in blacks and whites).	Broadly, a graded linear association was observed between the incidence rate of heart failure and summary early-life **socioeconomic position** in both blacks and whites (for blacks, hazard ratio (HR) = 1.39, 95% confidence interval (CI): 1.00, 1.95; for whites, HR = 1.32, 95% CI: 1.06, 1.64).
Rosvall et al. (2008)	1993-1996	Sweden	Authors wanted to evaluate, based on a **Retrospective Cohort Study**, long-term survival after acute myocardial infarction AMI in relation to socioeconomic position (SEP) and use of revascularization.	Adjusting socioeconomic differences for the use of revascularization procedures only marginally reduced the age adjusted HRRs of death within five years for the lowest cumulative **income** group compared to the highest, with in average 1% in men and women (data not shown). Authors also analysed **socioeconomic differences** in survival through stratified analyses by use of revascularization procedures. Authors therefore divided the population into four groups, i.e., by cumulative income (divided into

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

				low and high at the median) and by the use of revascularization procedures. Those with low cumulative income who had no revascularization showed an increased HRR of 5-year mortality, 1.35 (95% CI: 1.29 – 1.40), compared to those with high cumulative income with no revascularization (reference group), after adjustment for age and sex. For those with high cumulative income who had a revascularization the HRR was 0.60 (95% CI: 0.48, 0.75). Having a low cumulative income and having had a revascularization was associated with an HRR of 0.69 (95% CI: 0.56, 0.86). Among those with revascularization, there were no statistically significant mortality differences between those with high and low cumulative income.
Schulz et al. (2008)	2001-2003	United States	A **cross-sectional study** was designed to provide evidence of a cascade effect linking socioeconomic position to anthropometric indicators of cardiovascular disease (CVD) risk, through effects on psychosocial stress, psychological distress and health-related behaviours.	Socio-Economic Position (SEP) is associated with multiple CVD risk factors. **Household income** <$10K was positively associated with depressive symptoms (p<0.001), current smoking (p = 0.05), physical inactivity (p<0.05) and waist circumference (p<0.05). Income $10–19K was also positively associated with depressive symptoms (p<0.01). Relationships between income and BMI were in the expected direction but not statistically significant. Participants who had completed **high school** were more likely than those with some college to report current smoking (p<0.01), and those with less than a high school education were less likely to report physical activity (p<0.05). A significant association between <12 years of education and depressive symptoms when income was not included in the model (results not shown) was no longer significant when income was included in the model. Coefficients for relationships between education and psychosocial stressors and anthropometric indicators were not statistically significant.
Sposato and Saposnik (2012)	2000-2011	Several countries	Authors developed a systematic review and selected population-based studies reporting incident stroke risk and/or 30-day case-fatality. They use three macro-socioeconomic status indicators: per capita gross domestic product adjusted for purchasing power parity; total health expenditure per capita at purchasing power parity; and unemployment rate. They examine the correlation of each indicator with incident risk of stroke.	Age-adjusted incident risk of stroke was associated to lower **per capita gross domestic product** (p=0.661, P=0.027, R2=0.32) and total **health expenditure per capita** (p=0.623, P=0.040, R2=0.26). Thirty-day case-fatality rates and proportion of haemorrhagic strokes were also related to lower per capita gross domestic product and total health expenditure per capita. Moreover, stroke occurred at a younger age in populations with low per capita gross domestic product and total health expenditure per capita. There was no correlation between unemployment rates and outcome measures.
Tajinder P. Singh et al (2009)	1996-2005	United States	The purpose of the study was to assess whether a low socioeconomic (SE) position is associated with outcomes in heart transplant recipients (**retrospective cohort study**)	Predictors of early hospital deaths (odds ratio): Low socioeconomic group and graft failure (hazard ratio: 0.8 (0.3–1.7)) Low socioeconomic group 1.5 (1.0–2.4) in survivors of transplant hospitalization. Predictors of rejection risk (odds ratio): Low socioeconomic group 1.4 (1.0-1.9). After transplantation, predischarge hospital mortality was not affected by

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

				race/ethnicity or SE position. However, among the recipients who survived the transplant hospitalization, nonwhite patients and those living in low SE neighborhoods were at a greater risk of subsequent allograft loss. These groups also had a greater incidence rate of rejection.
Tajinder P. Singh et al (2010)	1996-2005	United States	The purpose of the study (cross-sectional study) was to assess whether a low socioeconomic position (SE) is associated with outcomes in heart transplant recipients.	Low **SE** group (hazard ratio 1.7, 95% confidence interval 1.1 to 2.5) were associated with a greater risk of subsequent graft loss. In the adjusted analysis, the risk of graft loss remained greater for low SE position (hazard ratio 1.5, 95% confidence interval 1.0 to 2.4). Rejection episodes were more frequent in the low SE group.
Thurston et al. (2005)	1971-1993	United States	The authors examined association between socioeconomic position and health in the First National Health and Nutrition Examination Survey (**retrospective cohort study**)	Low **education** was associated with greater social and psychological risks for women than men. Cox's proportional hazards models showed that education and **income** were inversely associated with incident coronary heart disease in age-only and multivariate models. Risk associated with education varied by gender (p = 0.01), with less than high school education associated with stronger risk of coronary heart disease in women (relative risk = 2.15, 95% confidence interval: 1.46 - 3.17) than in men (relative risk = 1.58, 95% confidence interval: 1.18 - 2.12) in age-adjusted models.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

3.2.2 Cancer

We found 15 studies that presented evidence on SES and cancer outcomes (**Table 17**). Most of them are referred to lung cancer (5) and breast cancer (6). Two of the revised articles consider the gastric cancer and one of them consider diagnostic procedures, particularly fact of repeated mammography. One study considered all-site cancer mortality.

The risks of mortality due to cancer by individual birth country, sex, and socioeconomic position was examined by Abdoli et al. in the total Swedish population and in subgroups of the foreign-born population.[162] They used data from the Migration and Health Cohort (1961-2009) and a *Poisson* regression models to calculate *Cancer Mortality Rate Ratio* and *Age-Standardized Rates*. Their main finding is that all-site cancer mortality decreased with increasing level of education irrespective of sex and country of birth. The risk was more prominent among foreign-born than Sweden-born men but in women, it was more noticeable among Sweden-born low versus high education level.

Sidorchuk et al. investigated the association between socioeconomic indicators and lung cancer incidence through a systematic revision and meta-analysis from 1966 from 2007.[89] The inclusion terms were “socioeconomic position”, “socioeconomic status”, “social class”, “occupational category”, “occupational classification”, “educational level”, or “income”, versus “lung cancer”, “lung neoplasm” “lung cancer incidence”, and “lung neoplasm incidence”. To be included in the meta-analysis studies had to give original data using a case-control o cohort methodology, consider as an outcome lung cancer incidence, and provide risk estimates with 95% confidence intervals. Authors identify 64 studies eligible for inclusion of the 3,288 articles obtained from the search from PubMed and EMBASE databases. The information on country was classified for geographical area and country´s income level. Results supported a significant increase in the risk of lung cancer among the lowest socioeconomic categories for the socioeconomic indicators considered (education attainment, occupational categories and income). Results were particularly relevant for the educational attainment indicator. Results are consistent when the associations are adjusted for smoking.

Forrest et al. (2013) developed a systematic revision and meta-analysis for a cohort of studies of participants with a primary diagnosis of lung cancer, in order to examine the existence of socioeconomic inequalities in treatment.[163] The outcome was receipt of a

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under Grant Agreement No 643576.

treatment and was reported as a measure of socioeconomic position. Authors identify 1483 records through data base searching up to 2012 developed in 10 countries. Of the papers analysed 46 met the inclusion criteria and 23 papers were considered in the meta-analysis. Most of studies used area-level measures of deprivation, income, poverty or education level (only one of the uses education as an individual measure of socioeconomic status). Most of studies analysed by the authors, included three treatments in the analysis: surgery, chemotherapy and radiotherapy. The principal finding of the study is that a low socioeconomic position increases the probability to receive any type of treatment for patients with lung cancer. Patients living in worse socioeconomically circumstances are less likely to receive any treatment of surgery and chemotherapy. These differences remain in both, universal and non-universal health care systems.

In relation to lung cancer Dalton et al. analysed a sample of 25,648 people born between 1920-1982, that were diagnosed with a long cancer between 2001 and 2008.[164] The data based analysed was the Denmark lung cancer registry. Among people with a medium to high level of education, was diagnosed more men than women with lung cancer. Odds ratios for patients with lung cancer in an advanced stage are lower for those who have higher education, are increased for people who live alone and are decreasing average which increases the associated morbidity. Men and older people have odds ratios higher in relation to the detection of lung cancer in an advanced state. Another study was conducted by Dalton et al. (2015) based on the same data base.[165] In this article the authors identified 13.045 patients with lung cancer diagnosed between 2004 and 2010. They considered information about the different stages, histology, functional status and treatment. This information was completed with educational data and income. They analysed associations between the previous socio-economic indicators and the possibilities of receiving an initial treatment. Odds ratios in the detection of lung cancer, both in the advanced status as in the early stages they are lower in patients with low level of education and low income. Patients who lived alone had a lower probability that was detected in early stage lung cancer, the same goes for individuals with low income levels, which have a lower probability of detection than those with higher incomes.

Nkosi et al. after making an analysis for the Canadian case highlighted the importance of adjusting for several dimensions of smoking behaviour to make correct inferences for the relationship between low socioeconomic position and lung cancer.[166]

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Social factors explain ethnic or racial inequalities in breast cancer survival are analysed by McKenzie and Jeffreys.[167] The authors developed a systematic review of literature to identify studies that investigate the influence of socioeconomic position, jointly other variables such as smoking, alcohol consumption and body mass index in breast cancer survival. The study reviewed published studies from 1996 to 2008 including 16 studies from the 673 papers identified initially. The majority of papers included analysed the effect of socioeconomic position on breast cancer survival using census-derived measures. To investigate the effect of socioeconomic position on ethnic inequalities in survival, the percentage of change in the minority versus majority survival disparity was estimated. General results indicate that socioeconomic position would explain approximately half of the inequality in breast cancer survival (all causes) between ethnic groups. Nevertheless results indicate that socioeconomic position is not a determinant explicative variable once clinical factors have been accounted for.

Mortality after breast cancer was also analysed by Larsen et al. (2015) in a study developed for Denmark. The article considered the influence of metabolic indicators, such as smoking, alcohol and socioeconomic position in breast cancer survival. Results from Cox proportional hazard models demonstrated that these considered factors could explain some (but not all) the social inequality in survival. Besides, that improvement of lifestyle would improve survival among women with low socioeconomic position.

Schliching et al. analysed the association between county-level percent of persons below the poverty level and breast cancer specific survival for cases diagnosed from 1990 to 2008.[168] The information was obtained from the Surveillance, Epidemiology, and End Results (SEER) database linked to census derived county attributes in USA. Results showed non n-IBC cases residing in low poverty, high SEP, metro counties had better overall survival, with survival differences between IBC and non-IBC and SEP groups appearing to be larger for stage III cancers. Log-rank test statistics indicated significant survival differences ($p < 0.0001$) between the survival curves. For stage III IBC and non-IBC by county-level percent of persons below the poverty level for cases diagnosed from 1990 to 2008. The median BCS survival for stage III IBC cases residing in counties with <20 % poverty was 4.8 years (range: 0–18.8 years), while median BCS survival for stage III IBC cases in counties with ≥20 % poverty was 4.1 years (range: 0–17.2 years). The corresponding values for non-IBC were 14.0 years (range: 0–18.9 years) and 10.6 years (range: 0–18.75 years), respectively. For

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

stage IV IBC and non-IBC by county-level percent of persons below the poverty level for cases diagnosed from 1990 to 2008. The median BCS survival for stage IV IBC cases residing in counties with <20 % poverty was 1.75 years (range: 0–15.7 years), while median BCS survival for stage IV IBC cases residing in counties with ≥20 % poverty was 1.6 years (range: 0–8.75 years). The corresponding values for non-IBC were 2.3 years (range: 0–18.9 years) and 2.0 years (range: 0–18.1 years), respectively. For stage III IBC and non-IBC by the county-level poverty-high school index for cases diagnosed from 2000 to 2008. The median BCS survival for stage III IBC cases residing in high SEP counties was 6.9 years (range: 0–8.9 years), while median BCS survival for stage III IBC cases in lower SEP counties was 5.2 years (range: 0–8.9 years). The median survival time for stage III non-IBC cases for both SEP groups had not been reached and therefore not estimated (range for both groups: 0–8.9 years). For stage IV IBC and non-IBC by the county-level poverty-high school index for cases diagnosed from 2000 to 2008. The median BCS survival for stage IV IBC cases residing in high SEP counties was 1.75 years (range: 0–7.2 years), while median BCS survival for stage IV IBC cases residing in lower SEP counties was 1.9 years (range: 0–8.75 years). The corresponding values for non-IBC were 2.6 years (range: 0–8.9 years) and 2.4 years (range: 0–8.9 years), respectively.

Evidence backing up the existence of differences in breast cancer prognostic factors between ethnic and socioeconomic groups is reported by McKenzie et al. for New Zealand.[169] Other authors find differences on incidence of cancer in relation to environmental characteristics such as the neighbourhood of residence. In this sense, Meijer et al. (2013) evaluated the influence of neighbourhood characteristics on breast, prostate and lung cancer incidence in Denmark.[170] Their results pointed out that in addition to individual socioeconomic status, higher breast cancer incidence appear in areas with highest population density. Furthermore, increased prostate cancer incidence was found in areas with higher socioeconomic status. Besides, higher lung cancer incidence was associated with high population density and low socioeconomic status on the area level. In the same way Olsen et al. (2015) obtained for Denmark that advanced stage at diagnosis were increased for patients with low income and for men living alone.[171]

In relation to diagnostics procedures related to cancer the study by Dailey et al. (2011), examine the relationship between the socio-economic situation of a given area and the fact of repeated mammography.[172] The authors use socio-economic data from the

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

United States Census, from a nationally representative sample of women who participated in the 2005 national survey of health (NHIS). Study gets that women living in disadvantaged socio-economic areas have a lower probability of repeat mammography, even after having adjusted its probability according to their socio-economic characteristics individuals and access to the health system.

Socioeconomic position and incidence of gastric cancer was analysed by Uthman et al by means of a systematic review and meta-analysis from 1966 to 2013.[173] They use socioeconomic determinants in the search such as "socioeconomic position", "socioeconomic status", "social class", "occupational category", "occupational classification", "educational level" or "income". The population of study was patients with diagnosed gastric cancer in case-control or cohort studies. With these criteria authors included 64 studies in a qualitative synthesis and 36 studies in the meta-analysis. Results indicate a negative social gradient with all studies socioeconomic position analysed. The risk in gastric cancer increased among individuals with low levels of educational attainment, income, occupation and combined socioeconomic position. These results were consistent for most of pooled estimations.

Later, Uthman et al. investigated the associations between gastric cancer incidence and education, occupation and income as indicators for socioeconomic position.[173] Authors observed an increased risk of gastric cancer among the lowest socioeconomic position categories in education, occupation, and combined socioeconomic position, compared with the highest categories. Although the association between the incidence of gastric cancer and the level of income is evident, it did not reach a statistically significant level.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 17. Summary of results for socioeconomic inequalities and Cancer

STUDY	YEAR	COUNTRY	METHODOLOGY	RESULTS (COMPARATIVE RISKS)
Abdoli et al (2014)	1961-2009	Sweden	**Poisson regression models** to calculate Cancer Mortality Rate Ratio (MRR) and Age-standardized rates (ASRs).	All-site cancer mortality decreased with increasing level of **education** irrespective of sex and country of birth. The risk was more prominent among foreign-born than Sweden-born men (foreign-born: MRR=1.42; Sweden-born: MRR= 1.28) but in women, it was more noticeable among Sweden-born (Sweden-born: MRR=1.39; foreign-born: MRR= 1.28) low versus high education level. Age-specific analysis revealed a lower cancer mortality risk among foreign-born women in all age strata whereas the increased mortality among foreign-born men was limited to those aged between 50 and 70 years.
Dailey et al. (2011)	2000 and 2005	United States	**Ordinary multivariable logistic regression** for survey data. A **multilevel modelling method**, estimating area-specific effects of covariates, was also undertaken.	In a model adjusted for sociodemographic, health care factors, and known correlates of mammography screening, women living in more **disadvantaged areas** had lower odds of engaging in repeat mammography than women living in the most advantaged areas. The results of this nationwide study support the hypothesis that area-level SEP is independently associated with mammography utilization. The results suggest that intervening on community, policy, or structural levels may be an appropriate way to increase early detection of breast cancer in the most socioeconomically vulnerable populations.
Dalton et al. (2011)	2001-2008	Denmark	**Logistic regression models** were used to examine the simultaneous influence of all socioeconomic and demographic factors of interest on the likelihood of receiving a diagnosis of advanced-stage lung cancer.	The adjusted OR (Odds ratios) for advanced-stage lung cancer was reduced among persons with higher **education** (OR, 0.92; 95% confidence interval (CI), 0.84–0.99). Higher education was associated with a reduced OR for 428 days between referral and diagnosis as was high **income** in early-stage patients. Male gender, age and severe comorbidity were associated with increased ORs in advanced stage patients.
Dalton et al. (2015)	2004-2010	Denmark	Associations between SEP and receipt of first-line treatment of lung cancer were analysed in **multivariate logistic regression models** and those with overall mortality in **Cox regression models** with stepwise inclusion of possible mediators.	For both low- and high-stage lung cancer, adjusted ORs for first-line treatment were reduced in patients with short **education** and low **income**, although the OR for education did not reach statistical significance in men with high stage disease. The socioeconomic difference in overall survival was partly explained by differences in

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

				stage, treatment and comorbidity, although some differences remained after adjustment. Among patients with high-stage disease, the hazard ratio (HR) for death of those with low income was 1.12 (95% CI 1.05–1.19) in comparison with those with high income. The differences in risk for death by SEP were greatest in the first six months after diagnosis Socioeconomic differences in survival after lung cancer are partly explained by social inequality in stage, first-line treatment and comorbidity.
Forrest et al (2013)	Up to September 2012	Various countries	**Systematic Review** and **Meta-Analysis** of existing research on socioeconomic inequalities in receipt of treatment of lung cancer (MEDLINE, EMBASE, and SCOPUS).	Lower **SEP** was associated with a reduced likelihood of receiving any treatment (odds ratio (OR=0.79 [95% CI 0.73 to 0.86], p<0.001), surgery (OR=0.68 [CI 0.63 to 0.75], p<0.001) and chemotherapy (OR=0.82 [95% CI 0.72 to 0.93], p=0.003), but not radiotherapy (OR= 0.99 [95% CI 0.86 to 1.14], p=0.89) for lung cancer. The association was found in both universal and non-universal health care systems.
Frederiksen et al. (2012)	2000-2008	Denmark	A **registry-based cohort study** links clinical data on prognostic factors and treatment from the national lymphoma database to individual socioeconomic information in Statistics Denmark including 6234 patients diagnosed with non-Hodgkin lymphoma (NHL).	All-cause mortality was 40% higher in NHL patients with short vs higher education diagnosed in 2000-2004 (hazard ratio (HR)=1.40 (1.27-1.54)), and 63% higher in 2005-2008 (HR=1.63 (1.40-1.90)). Mortality was increased in unemployed and disability pensioners, those with low income, and singles. Clinical prognostic factors attenuated, but did not eliminate the association between education and mortality. Radiotherapy was less frequently given to those with short education (odds ratio (OR)= 0.84 (0.77-0.92)), low income (OR=0.80 (0.70-0.91)), and less frequent to singles (OR=0.79 (0.64-0.96)). Patients living alone were less likely to receive all treatment modalities.
Ibfelt et al. (2012)	2005-2009	Denmark	1,651 cervical cancer cases from the Danish Gynaecological Cancer Database. Date of diagnosis, clinical cancer stage, tumour histology, and treating hospital were retrieved; **Logistic regression models** were used to analyse the relations between socioeconomic factors and cancer stage in a four-step model, with stepwise inclusion of mediators.	The risk for advanced (stage II-IV) compared with early-stage cancer (stage I) was increased for women with short and medium education (OR = 2.40; 1.67-3.45 and 1.76; 1.44-2.16), women living without a partner (OR = 1.31; 1.10-1.55), and older women (OR = 1.07; 1.06-1.08 increase per year). Relations between socioeconomic factors and cancer stage were partly mediated by time since last Pap smear test and to a lesser extent by comorbidity.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Ibfelt et al. (2013)	2005-2010	Denmark	1961 cases of cervical cancer diagnosed in the Danish Gynaecological Cancer database, with information on prognostic factors, treatment and lifestyle. Age, vital status, comorbidity and socioeconomic data were obtained from nationwide administrative registers. Associations between socioeconomic indicators (education, income and cohabitation status) and mortality by all causes were analysed in **Cox regression models** with inclusion of possible mediators.	All mortality cause was higher in women with shorter rather than longer education (hazard ratio (HR), 1.46; 1.20-1.77), among those with lower rather than higher income (HR, 1.32; 1.07-1.63) and among women aged<60 years without a partner rather than those who cohabited (HR, 1.60; 1.29-1.98). Socioeconomic differences in survival were partly explained by cancer stage and less by comorbidity or smoking (stage- and comorbidity-adjusted HRs being 1.07; 0.96-1.19 for education and 1.15; 0.86-1.52 for income).
Larsen et al. (2015)	1993-1997	Denmark	**Cox proportional hazard models** are used to study the influence of metabolic indicators, smoking, alcohol and socioeconomic position on mortality after breast cancer.	The age-stratified hazard ratio (HR) for women with basic or high school **education** was 1.40 (95% CI 1.05 - 1.86) compared to those with higher education. As for **income**, there was no significant trend in death from all causes between the income quartiles and adjustments only had minor effects on the estimates, although a significantly increased HR of 1.32 (95% CI 1.02 - 1.72) was observed among those with 2nd – 3rd quartile income.
McKenzie et al. (2008)	1994-2004	New Zealand	**Logistic regressions** are used to study differences in breast cancer prognostic factors between ethnic and socioeconomic groups.	Results confirm that Maori, Pacific and low **socioeconomic** women present with poor prognosis breast tumours. Precisely, women living in more deprived areas (NZDep 9–10 OR 1.22, 95% CI 1.10–1.35) were more likely to have non-local stage breast tumours than those living in less deprived areas.
McKencie and Jeffreys (2009)	1966-2008	Various countries	**Systematic review** of studies indexed in MEDLINE to identify studies that investigated the explanatory power of ethnic/racial inequalities, among them socioeconomic position (SEP) on ethnic inequalities on breast cancer survival.	In the systematic review, authors found that **SEP** explains part of the ethnic inequality in survival from all causes but this finding was not evident for breast-cancer-specific survival. The role of SEP appears to be smaller in the more recently papers analysed. SEP explains more of the disparities for African-American versus white women in the United States compared with other ethnic comparisons.
Meijer et al. (2013)	2004-2008	Denmark	Hazard rates (HR) using shared frailty models, which are **multilevel random effect models** for survival data accounting for a latent multiplicative effect on the hazard function, the 'frailty' were used to evaluate the influence of neighbourhood characteristics on breast, prostate and lung cancer incidence.	Lower HR of breast cancer was found in areas with low population density (HR¼0.93; CI 0.88 to 0.99), while neighbourhood **unemployment** had no effect. Inhabitants of lower unemployment areas had a higher risk of prostate cancer (HR¼1.14; CI 1.08 to 1.21) compared with those in higher unemployment areas, whereas population density had no effect. Risk of lung cancer was lower in areas with lowest population density

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

				(HR¼0.80; CI 0.74 to 0.85) and lowest in areas with lowest unemployment (HR¼0.88; CI 0.84 to 0.92).
Newmann and Garner (2005)	1990-2005	United States	**Structured review** for US based research on cervical cancer and social inequities (Medline).	Despite overlap with other social domains of inequality, such race/ethnicity, age, literacy, and insurance status, socioeconomic deprivation was frequently found to be a strong predictor of screening diagnosis, treatment, and survival differentials regardless of other social domains.
Nkosi et al. (2012)	1996-2002	Canada	**Logistic regression** to study associations between socioeconomic position and lung cancer when adjusting for smoking.	Comparisons of the highest to lowest categories of census-based **income**, the OR for lung cancer was 0.58 (95% CI = 0.32–1.05) when adjusting only for smoking status, but 0.97 (0.51–1.86) when adjusting for smoking status, cigarette-years, and time since cessation. Regarding comparisons of highest to lowest levels of **education**, the ORs for lung cancer were 0.50 (0.38–0.65) and 0.76 (0.57–1.02), when making the least and most comprehensive adjustments for smoking, respectively. Comparing highly skilled with unskilled manual workers, the ORs were 0.78 (0.54 –1.12) and 1.00 (0.68 –1.47), respectively.
Schlichting et al (2012)	1990-2008	United States	A **retrospective cohort study** to examined the association between county-level percent of persons below the poverty level and BC-specific (BCS) survival for cases diagnosed from 1990 to 2008.	Residing in a lower SEP, non-metro county significantly worsens BCS survival for non-IBC in multivariate proportional hazards models. African American cases appear to have worse survival than non-Hispanic Whites regardless of inflammatory status, stage, county-level SEP, tumor, or treatment characteristics.
Sidorchuk et al (2009)	1966-2007	Various countries	**Systematic review** and **meta-analysis** to investigate the associations between various socioeconomic indicators and lung cancer incidence. The authors systematically searched PubMed and EMBASE databases for articles published in English-speaking peer review journals.	Results indicate an overall increased risk in lung cancer incidence among people with low **educational** socioeconomic position (SEP), low **occupational** SEP and low **income-based** SEP. Lung cancer incidence was inversely associated with educational, occupational and income-based socioeconomic position (SEP) regardless of smoking adjustment.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Uthman et al (2013)	1966-2013	XXX	Residing in a lower SEP, non-metro county significantly worsens BCS survival for non-IBC in **multivariate proportional hazards models**. African American cases appear to have worse survival than non-Hispanic Whites regardless of inflammatory status, stage, county-level SEP, tumour, or treatment characteristics.	Authors observed an increased risk of gastric cancer among the lowest SEP categories in **education** (RII=2.97; 95% CI 1.923 to 4.58), **occupation** (RII=4.33; 95% CI 2.57 to 7.29) and **combined SEP** (RII=2.64; 95% CI 1.05 to 6.63) compared with the highest SEP categories. Although the association between the incidence of gastric cancer and the level of **income** is evident, it did not reach a statistically significant level (RII=1.25; 95% CI 0.93 to 1.68).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

3.2.3 Diabetes

Among the studies (**Table 18**) that performed reviews of literature that analyse the relationship between inequalities and non-communicable diseases, Tamayo et al. carried out two systematic reviews that included longitudinal, population- or community-based studies if they contained data on psychosocial factors in childhood and either diabetes incidence or obesity risk.[53] Searches were limited to studies published between 1995 and 2010. Eight of the considered studies indicated that low parental status was associated with type 2 diabetes incidence or the development of metabolic anomalies. For obesity, the eleven studies included observed an independent association of low childhood SES with the risk for overweight and obesity later in life. Although authors underline the limited comparability among the included studies, they state evidence on the association between childhood SES and type 2 diabetes and obesity in later life. In this sense, psychosocial discrepancies in childhood seem to have an unfavourable impact on future type 2 diabetes incidence. Adjustment for adult SES and BMI attenuated this association.

Agardh et al. conducted a systematic review and meta-analysis between 1966 and 2010 in order to identify published evidence on associations between type 2 diabetes incidence and socioeconomic position (SES) measured by educational level, occupation and income.[52] The countries considered in the article were sub-divided into high-, middle- and low-income countries. Twenty-three studies including 41 measures of association were considered relevant. Results suggest an overall increased risk of type 2 diabetes in low socioeconomic groups, measured by educational level, occupation or income. This association is consistent in high-income countries, although the available data are limited in middle- and low-income countries.

Dalsgaard et al. analysed the incidence of diabetes type 2 for a sample of 1.533 people from the Addition Study Denmark, during the period 2000-2006. In the study the levels in HbA1c, cholesterol, blood pressure and muscle mass are virtually identical regardless of the level of education, level of income, occupational or State civil status.[174] A greater proportion of people with lower levels of income level or a lower level of education have a greater attention in the unit of intensive care compared with people with higher levels of income and education. In general is checked as the ability to meet the goals of treatment for HbA1c, cholesterol, and blood pressure was not changed by the socio-economic

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

characteristics. The study noted that type 2 diabetes does not depend on the socio-economic characteristics.

In a posterior study, Dalsgaard et al. used a cohort of the Danish population to 40-69 years, all of them without a history of diabetes between the years 2001-2006.[175] The authors estimate the mortality rate by level of education, income, and coexistence between people with and without diabetes type 2 in Denmark. The age standardized mortality rate decreases to improve the socio-economic indicators. Together the effects of type 2 diabetes and socioeconomic indicators have a strong impact on the death rate. The combined effects yield multiplicative increase rates of mortality. In this sense, people with type 2 diabetes and low socio-economic indicators (low education, low income level or who live alone) have a death rate more than twice as many people with high socio-economic indicators (higher educational level, high incomes and living with others).

Demakokos et al. explored the association between the socioeconomic situation of children and adults and the incidence of diabetes to a sample of 7.432 individuals of 50 years or older from the English Longitudinal Study of Ageing (ELSA).[176] The article indicated that psychosocial factors in women and unhealthy behaviours and obesity, both women and men, partially explain the relationship between the socioeconomic status of adults and children (education, type of occupation, income, health and subjective social status) and the incidence of diabetes. The type of occupation, income and subjective social status are not significant in relation to the incidence of diabetes, once adjusted for factors psychosocial, obesity or unhealthy behaviours. However, the level of health (measured in degrees) that is significant in relation to the incidence of diabetes, what happens when analysing the incidence of education and socioeconomic position. In men the subjective social status and health are only statistical have effect on diabetes.

Smith et al. investigated associations between cumulative socioeconomic position and the incidence of T2D in the Framingham Offspring Study in Canada.[177] Analyses demonstrated that age-adjusted cumulative socioeconomic position was associated with T2D in women. Age-adjusted analyses for young-adulthood SEP, active professional life socioeconomic position, and social-mobility frameworks all demonstrated associations between low socioeconomic position and T2D incidence in women. No association was observed between childhood SEP and T2D in women for father's education. In men, there

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

was little evidence of associations between life-course socioeconomic position and T2D incidence.

Spadea et al. analysed associations between cumulative low socioeconomic position and the incidence of type 2 diabetes mellitus T2D in the Framingham Offspring Study in Italy.[178] Analyses demonstrated that age-adjusted socioeconomic position cumulative was associated with T2D in women. Age-adjusted analyses for young-adulthood socioeconomic position, active professional life SEP and social-mobility frameworks all demonstrated associations between low SEP and T2D incidence in women. No association was observed between childhood SEP and T2D in women for father's. In men, there was little evidence of associations between life-course SEP and T2D incidence. These findings suggest that cumulative SEP is inversely associated with incidence of T2D in women, and that this association may be primarily due to the women's educational levels and occupations.

Maty, James and Kaplan analysed associations between several life course socioeconomic position measures and diabetes incidence in a sample of 5,422 diabetes-free black and white participants in the Alameda County Study (US).[179] Their results confirmed the important role for life-course socioeconomic position measures in determining risk of diabetes.

Other authors analyse the influence of socioeconomic status in the care of diabetes. In this sense, Brow et al. (2005) found the existence of differences in the care of diabetes due to socio-economic or racial/ethnic disparities. The source of information is the Translating Research Action for Diabetes (TRIAD). Compared with white patients, African Americans have indicators lower A1C and LDL, a lower rate of vaccination against flu and lower blood pressure and lipids controls. In almost all cases, racial minorities / ethnic or blood pressure problems or lipid controls received similar or more intensified regarding care patients from whites or those with better socio-economic indicators.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

Table 18. Summary of results for socioeconomic inequalities and Diabetes

STUDY	YEAR	COUNTRY	METHODOLOGY	RESULTS (COMPARATIVE RISKS)
Agardh et al. (2011)	1966-2010	Several countries	Authors conducted a **systematic review** and **meta-analysis** on associations between type 2 diabetes incidence and socioeconomic position (SEP) measured by educational level, occupation and income.	Out of 5120 citations, 23 studies, including 41 measures of association, were found to be relevant. Compared with high **educational level**, **occupation** and **income**, low levels of these determinants were associated with an overall increased risk of type 2 diabetes; [relative risk (RR)=1.41, 95% confidence interval (CI): 1.28–1.51], (RR=1.31, 95% CI: 1.09–1.57) and (RR=1.40, 95% CI: 1.04– 1.88), respectively. The increased risks were independent of the income levels of countries, although based on limited data in middle- and low-income countries. The risk of getting type 2 diabetes was associated with low **SEP** in high-, middle- and low-income countries and overall. The strength of the associations was consistent in high-income countries, whereas there is a strong need for further investigation in middle- and low-income countries.
Brown et al. (2005)	2000-2001	United States	**Bivariate tests of association** were used to compare processes of diabetes care and intermediate health outcomes among the racial/ ethnic groups and by education and income. **Hierarchical regression models** were constructed to adjust for the clustering of patients within health plans.	The principal finding of this study is that in this large, diverse cohort of insured patients, there were few racial/ethnic or socioeconomic disparities in diabetes care. For dichotomous outcomes, because odds ratios are poor estimates of relative risk when outcomes are common, we report the adjusted estimated conditional probabilities for each category of race/ethnicity, income, and education. We evaluated separate models for each of the three main predictors and a full model that included all three predictors
Dalsgaard et al. (2014)	2001–2006	Denmark	Baseline characteristic were described using means (SDs) and compared using Anova-test for normally distributed variables, by the median and Kruskal–Wallis one-way analysis of variance for non-normally distributed variables, and the chi-squared test were applied for categorical variables.	The change in HbA1c, cholesterol, blood pressure and BMI were virtually the same across **educational level**, **income level**, **occupational status** or cohabiting status. Overall, the ability to meet treatment targets for HbA1c, cholesterol and blood pressure was not modified by socioeconomic position group. A higher proportion of people with lower educational level or lower income level in the intensive care redeemed anti-hypertensive treatment compared to people with higher educational or income levels.
Dalsgaard et al. (2015)	2001-2006	Denmark	The study population was characterised using the chi-square test and the t-test.	People with type2 diabetes and the lowest SEP (lowest educational level, lowest income level, or living alone) had a more than two-fold higher Mortality Rate Ratio than people without diabetes and the highest SEP (highest educational level, high income level, or cohabiting).
Demakakos et al. (2012)	2002-2003	United Kingdom	The authors examined the associations between childhood and adult socioeconomic position (SEP) and incident diabetes in 7,432 individuals aged 50 or older from the English Longitudinal Study of Ageing (ELSA). **Cox**	The descriptive analysis revealed graded associations between baseline characteristics and tertiles of total net household wealth (in almost all cases P value B0.001). The wealthier the participant, the higher their chances of being younger, married, still in paid employment (only in men), and physically active, having lower BMI (only in women), receiving

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

			proportional hazards regression models are used to assess the adjusted associations between each of the six SEP measures and incidence of self-reported doctor diagnosed type 2 diabetes.	more social support (only in men), having greater sense of control in their lives and at home, and consuming alcohol more frequently. Also, the wealthier the participant, the lower their chances of being smokers, experiencing problems in their social relationships (only in men), and reporting cardiovascular or non-cardiovascular diseases and elevated depressive symptoms. Moreover, as expected, the associations between wealth and all other SEP measures were linear and grade In women, all measures of SEP were inversely associated with incident diabetes in models that were adjusted for age, marital status, retirement status, and comorbidities (in all models P value for linear trend\0.05).
Gary and Brancati (2005)	Commentary	United States	The paper shows how time-dependent measures of socioeconomic position (SEP) might be associated with incident diabetes	After adjustment for demographics, respondents with <12 years of education had a 50% excess risk of diabetes compared with those with more education, but income and occupation were not significantly associated. Time-dependent effects were not statistically significant after adjustment for demographics and other potential factors.
Hussen et al. (2013)	1969-2008	Sweden	The authors followed a nation-wide cohort of 4 469 671 males and 4 231 680 females aged 0-30 years. Incidence rate ratios (IRRs) with 95% confidence intervals (CIs) for type 1 diabetes mellitus (T1DM) were calculated using **Poisson regression models**. They further calculated age-standardized rates (ASRs) of T1DM, using the world population as standard.	ASR of T1DM increased among children younger than 15 years, but not among young adults (15-30 years). Compared with Swedish-born children, male and female immigrant children had 44 and 42% lower IRR of TIDM, respectively. Among offspring to immigrants, corresponding decreases in IRRs were 27 and 24%. Compared with children to parents with high education, male children to parents with low education had a 10% decreased IRR of T1DM, while no effect was observed among females. IRR of T1DM increased with increasing age and calendar time of follow-up in both sexes (p-for trend <0.0001). In young adults, IRR among immigrants decreased by 32% in males and 22% in females, while reductions in IRRs were less in offspring to immigrants.
Insaf et al. (2014)	Research report	United States	**A generalised estimating equations approach** was used with a sample of 3497 adults from the Americans' Changing Lives study. Sex-specific models were calculated to compute prevalence ratios (PR) for associations of race and SEP with self-reported diagnoses of diabetes.	For men, childhood and adult SEP were unrelated to diabetes, and adjustment for lifecourse SEP had little effect on the excess diabetes in blacks (PR=1.56, 95% CI 1.11 to 2.21). Adjustment for measures of lifecourse SEP reduced the PR for the association between race and diabetes in women from 1.96 (95% CI 1.52 to 2.54) to 1.40 (95% CI 1.04 to 1.87) with the respondent's education responsible for most of the reduction in the association. Diabetes was also inversely associated with father's education, and low SEP throughout the lifecourse was associated with a nearly threefold increase in diabetes (PR=2.89, 95% CI 2.10 to 3.99).
Leat et al (2010)	1985-2009	Several countries	**Qualitative systematic review** of the literature on geographic life environments and Cardiometabolic Risk Factors (CMRFs), such as obesity, hypertension type 2	Low area socioeconomic level was generally significantly associated with an increased risk of CMRFs (in 42 of the 56 studies on obesity, 8 of the 12 studies on hypertension, 3 of the 4 studies on diabetes and dyslipidemia and 2 of the 2 studies on metabolic syndrome).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

			diabetes, syslipidemias and the metabolic syndrome in industrialized countries.	
Maty et al (2010)	1965-1999	United States	**Cox proportional hazards analyses** to study associations between several life course socioeconomic position measures and diabetes incidence.	**Income** was protective for whites, but not related to incidence among blacks. Low **education** and blue-collar occupation were protective for blacks, but increased risk for whites. Among white participants, diabetes incidence was significantly associated with low childhood **SEP**, education (≤12 years versus >12), and income, as well as high blood pressure, excess body mass, and former or current smoking status (HR range 1.6–6.4 and 95% CI range 1.1–9.3); low education and blue-collar occupation were protective against diabetes (low education HR=0.5, 95% CI=0.3–1.0; blue-collar occupation HR=0.7, 95% CI=0.4–1.4).
Smith et al. (2011)	1971-2001	Canada	**Pooled logistic regression analyses** are used to investigate associations between cumulative SEP and the incidence of T2D in the Framingham Offspring Study.	The authors demonstrated that age-adjusted cumulative **SEP** was associated with T2D in women (for low vs. high cumulative SEP, odds ratio (OR) = 1.92, 95% confidence interval (CI): 1.08 - 3.42). Age-adjusted analyses for young-adulthood SEP (7.85 for _12 vs. >16 years of education, OR = 2.84, 95% CI: 1.03 – 7.85), active professional life SEP (for laborer vs. professional/executive/supervisory/technical occupations, OR = 2.40, 95% CI: 1.05 - 5.47), and social-mobility frameworks (for declining life-course SEP, OR = 2.99, 95% CI: 1.39 - 6.44; for stable low vs. stable high life-course SEP, OR = 1.85, 95% CI: 1.02 - 3.35) all demonstrated associations between low SEP and T2D incidence in women. No association was observed between childhood SEP and T2D in women for father's education (some high school or less vs. any postsecondary education, OR = 1.26, 95% CI: 0.72 - 2.22). In men, there was little evidence of associations between life-course SEP and T2D incidence.
Spadea et al (2010)				
Tamayo et al. (2010)	1994-2010	Several countries	**Two systematic reviews** were carried out by the authors. They included longitudinal, population- or community-based studies if they contained data on psychosocial factors in childhood and either diabetes incidence or obesity risk.	The search strategy yielded a total of 19,504 results. 14 publications for obesity and 10 for diabetes mellitus were included in the final reviews. Psychosocial discrepancies in childhood seem to have an unfavourable impact on future type 2 diabetes incidence. Adjustment for adult **SES** and BMI attenuated these associations considerably. This finding raises the question if a favourable life course may be beneficial for the participants' metabolic status. The authors found the family **income** and the father´s **occupation** of relevance for overweight and obesity. Surprisingly, in contrast to their findings on diabetes incidence parental education seemed to have less impact on future obesity risk. However, lower parental **education** was linked to an earlier age at onset of obesity in one study.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 643576.

3.3 Discussion

This systematic review summarizes the methods and findings of studied associations between socioeconomic status (SES) and NCDs, published between 2005 and 2015. SES is proxied with different indicators, mainly education attainment, occupational categories and income. Different NCDs are considered, but most of literature reviewed is referred to CVDs, cancer, and diabetes. Overall the evidence suggest that having low SES increased the risk of developing CVDs, lung and breast cancer and type 2 diabetes. Socioeconomic position is also associated with multiple NCDs risk factors such as smoking and physical inactivity.

Socioeconomic circumstances during childhood appear to be relevant to influence CVD in adulthood. Among adults with diabetes, a high prevalence of CVD is associated to a lower socioeconomic position. Socioeconomic status also presents a negative relationship with the incidence, recurrence and mortality of stroke, according to the most of literature revised. From a macroeconomic perspective risk of stroke was associated to lower per capita GDP and health expenditure per capita.

Revised studies find that higher SES is related to improved adherence to therapy in cardiovascular mediation and improved results in cardiac surgery. Most of analysed studies find that increased prevalence in coronary heart disease vary across social class distribution showing that education and income are inversely associated with coronary heart disease.

Literature that examined the association between cancer incidence or prevalence and SES are based mainly on lung, breast and gastric cancers. Results suggest that low SES is correlated with an increased risk for cancer incidence and mortality in the type of cancer refereed. Socio-economic differences in survival after cancer detection are explained, partly, by the social inequality in the stage of detection, in the early stages of the treatment and the comorbidity. According to the results of the revised literature recommended efforts to improve early diagnosis and follow-up of the recommendations in the first stage of treatment in patients with cancer with low socio-economic indicators. Evidence refers that patients with lower socio-economic indicators are a first treatment with less intensity than those with higher indicators.

In relation to the studies that analyse the relationship between SES and diabetes most of the results suggest an overall increased risk of type 2 diabetes in low socioeconomic groups, measured by educational level, occupation or income. Results also find a direct

relationship between the age standardized mortality rate and SES that decreases to improve the socio-economic indicators. In this sense the effects of type 2 diabetes and socioeconomic indicators have a strong impact on the death rate.

Conclusion

Published literature on inequalities, health and NCDs is characterised by a large number of heterogeneous papers, which determine the complexity of this kind of relationship. Improving this information is crucial to capture fully the value of the socioeconomic measures, and to inform the most relevant as determinants of health and non-communicable diseases.

Several types of analysis produce very different results for the role of health determinants. The differences are particularly relevant when the results are presented in terms of effectiveness in health policies and welfare. Although the determinants of health identified in individual studies are important variables in an aggregate analysis, there are specific factors that influence social groups. Each individual factor measures different components and the selection of indicators is frequently influenced by the availability of data.

Nevertheless, according to the literature, social and economic disadvantage appears to have a significant consistent impact on mortality and morbidity caused by NCDs. Low socioeconomic status is associated with health inequalities in terms of access to care, increased incident risk of NCDs and early death. These findings point to the need for public health strategies and research to address socioeconomic status disparity among individuals. Strategies to reduce socioeconomic inequalities in NCD should be investigated in relation to the disparities in risk, diagnosis, and effective intervention among the highest prevalence groups. The global burden of diseases and the individual habits are changing because of globalisation, urbanisation, and economic development. In this sense, it would be relevant to consider the potential of individual studies to analyse the hypothesis of a more detailed relationship between socioeconomic status, health and NCDs.

3.4 References

1. Marmot M. Social determinants of health inequalities. *Lancet.* 2005;365(9464):1099-1104.

2. Cavelaars AE, Kunst AE, Geurts JJ, et al. Differences in self reported morbidity by educational level: a comparison of 11 western European countries. *J. Epidemiol. Community Health.* 1998;52(4):219-227.

3. Kunst AE, Groenhof F, Mackenbach JP, Health EW. Occupational class and cause specific mortality in middle aged men in 11 European countries: comparison of population based studies. EU Working Group on Socioeconomic Inequalities in Health. *BMJ.* 1998;316(7145):1636-1642.

4. Huisman M, Kunst AE, Andersen O, et al. Socioeconomic inequalities in mortality among elderly people in 11 European populations. *J Epidemiol. Community Health.* 2004;58(6):468-475.

5. Burnley IH. Disadvantage and male cancer incidence and mortality in New South Wales 1985-1993. *Soc Sci Med.* 1997;45(3):465-476.

6. Pukkala E, Weiderpass E. Socio-economic differences in incidence rates of cancers of the male genital organs in Finland, 1971-95. *Int J Cancer.* 2002;102(6):643-648.

7. Pukkala E, Teppo L. Socioeconomic status and education as risk determinants of gastrointestinal cancer. *Prev Med.* 1986;15(2):127-138.

8. Chandola T. Social inequality in coronary heart disease: a comparison of occupational classifications. *Soc Sci Med.* 1998;47(4):525-533.

9. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet.* 2006;367(9524):1747-1757.

10. Lynch JW, Kaplan GA, Cohen RD, Tuomilehto J, Salonen JT. Do cardiovascular risk factors explain the relation between socioeconomic status, risk of all-cause mortality, cardiovascular mortality, and acute myocardial infarction? *Am. J Epidemiol.* 1996;144(10):934-942.

11. Menvielle G, Boshuizen H, Kunst AE, et al. The role of smoking and diet in explaining educational inequalities in lung cancer incidence. *J Natl Cancer Inst.* 2009;101(5):321-330.

12. Karlamangla AS, Merkin SS, Crimmins EM, Seeman TE. Socioeconomic and ethnic disparities in cardiovascular risk in the United States, 2001-2006. *Ann Epidemiol.* 2010;20(8):617-628.

13. Appelros P, Stegmayr B, Terent A. Sex differences in stroke epidemiology: a systematic review. *Stroke.* 2009;40(4):1082-1090.

14. Tang KR, Ruksana; Ghali, William A. ASSOCIATION BETWEEN SUBJECTIVE SOCIAL STATUS AND CARDIOVASCULAR DISEASE AND CARDIOVASCULAR RISK FACTORS: A SYSTEMATIC REVIEW AND META-ANALYSIS. *JOURNAL OF GENERAL INTERNAL MEDICINE.* 2015;30:S104-S105.

15. Manrique-Garcia E, Sidorchuk A, Hallqvist J, Moradi T. Socioeconomic position and incidence of acute myocardial infarction: a meta-analysis. *J Epidemiol Community Health.* 2011;65(4):301-309.

16. Sommer I, Griebler U, Mahlknecht P, et al. Socioeconomic inequalities in non-communicable diseases and their risk factors: an overview of systematic reviews. *BMC Public Health.* 2015;15(1):914.

17. Pollitt RA, Rose KM, Kaufman JS. Evaluating the evidence for models of life course socioeconomic factors and cardiovascular outcomes: a systematic review. *BMC Public Health.* 2005;5:7.

18. Galobardes B, Smith GD, Lynch JW. Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. *Annals of Epidemiology.* 2006;16(2):91-104.

19. Kerr GD, Slavin H, Clark D, Coupar F, Langhorne P, Stott DJ. Do vascular risk factors explain the association between socioeconomic status and stroke incidence: a meta-analysis. *Cerebrovasc Dis.* 2011;31(1):57-63.

20. Burr ML, Sweetnam PM. Family size and paternal unemployment in relation to myocardial infarction. *J Epidemiol Community Health.* 1980;34(2):93-95.

21. Notkola V, Punsar S, Karvonen MJ, Haapakoski J. Socio-economic conditions in childhood and mortality and morbidity caused by coronary heart disease in adulthood in rural Finland. *Soc Sci Med.* 1985;21(5):517-523.

22. Coggon D, Margetts B, Barker DJ, et al. Childhood risk factors for ischaemic heart disease and stroke. *Paediatr Perinat Epidemiol.* 1990;4(4):464-469.

23. Hasle H. Association between living conditions in childhood and myocardial infarction. *BMJ.* 1990;300(6723):512-513.

24. Kaplan GA, Salonen JT. Socioeconomic conditions in childhood and ischaemic heart disease during middle age. *BMJ.* 1990;301(6761):1121-1123.

25. Lundberg O. The impact of childhood living conditions on illness and mortality in adulthood. *Soc Sci Med.* 1993;36(8):1047-1052.

26. Gliksman MD, Kawachi I, Hunter D, et al. Childhood socioeconomic status and risk of cardiovascular disease in middle aged US women: a prospective study. *J Epidemiol Community Health.* 1995;49(1):10-15.

27. Lamont D, Parker L, White M, et al. Risk of cardiovascular disease measured by carotid intima-media thickness at age 49-51: lifecourse study. *BMJ.* 2000;320(7230):273-278.

28. Marmot M, Shipley M, E B, Hemingway H. Relative contribution of early life and adult socioeconomic factors to adult morbidity in the Whitehall II study. *J Epidemiol. Community Health.* 2001;55:301-307.

29. Wamala SP, Lynch J, Kaplan GA. Women's exposure to early and later life socioeconomic disadvantage and coronary heart disease risk: the Stockholm Female Coronary Risk Study. *Int. J Epidemiol.* 2001;30(2):275-284.

30. Davey Smith G, Hart C, Blane D, Hole D. Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective observational study. *BMJ.* 1998;316(7145):1631-1635.

31. Frankel S, Smith GD, Gunnell D. Childhood socioeconomic position and adult cardiovascular mortality: the Boyd Orr Cohort. *Am J Epidemiol.* 1999;150(10):1081-1084.

32. Dedman DJ, Gunnell D, Davey Smith G, Frankel S. Childhood housing conditions and later mortality in the Boyd Orr cohort. *J Epidemiol Community Health.* 2001;55(1):10-15.

33. Lynch JW, Kaplan GA, Cohen RD, et al. Childhood and adult socioeconomic status as predictors of mortality in Finland. *The Lancet.* 1994;343(8896):524-527.

34. Vagero D, Leon D. Effect of social class in childhood and adulthood on adult mortality. *Lancet.* 1994;343(8907):1224-1225.

35. Hart CL, Smith GD, Blane D. Inequalities in mortality by social class measured at 3 stages of the lifecourse. *American Journal of Public Health.* 1998;88(3):471-474.

36. Davey Smith G, McCarron P, McEwen J. Social circumstances in childhood and cardiovascular disease mortality: prospective observational study of Glasgow University students. *J Epidemiol. Community Health.* 2001;55:340-341.

37. Smith GD, Hart C. Life-course socioeconomic and behavioral influences on cardiovascular disease mortality: the collaborative study. *Am J Public Health.* 2002;92(8):1295-1298.

38. Claussen B, Smith GD, Thelle DS. Impact of childhood and adulthood socioeconomic position on cause specific mortality: the Oslo Mortality Study. *J Epidemiol. Community Health.* 2003;57(1):40-45.

39. Osler M, Andersen AM, Due P, Lund R, Damsgaard MT, Holstein BE. Socioeconomic position in early life, birth weight, childhood cognitive function, and adult mortality. A longitudinal study of Danish men born in 1953. *J. Epidemiol. Community Health.* 2003;57(9):681-686.

40. Galobardes B, Costanza MC, Bernstein MS, Delhumeau C, Morabia A. Trends in risk factors for lifestyle-related diseases by socioeconomic position in Geneva, Switzerland, 1993-2000: health inequalities persist. *Am. J Public Health.* 2003;93(8):1302-1309.

41. Avendano M, Kawachi I, Van Lenthe F, et al. Socioeconomic status and stroke incidence in the US elderly: the role of risk factors in the EPESE study. *Stroke.* 2006;37(6):1368-1373.

42. Avendano M, Glymour MM. Stroke disparities in older Americans: is wealth a more powerful indicator of risk than income and education? *Stroke.* 2008;39(5):1533-1540.

43. Hart CL, Hole DJ, Smith GD. Influence of socioeconomic circumstances in early and later life on stroke risk among men in a Scottish cohort study. *Stroke.* 2000;31(9):2093-2097.

44. Hart CL, Hole DJ, Smith GD. The contribution of risk factors to stroke differentials, by socioeconomic position in adulthood: the Renfrew/Paisley Study. *Am J Public Health.* 2000;90(11):1788-1791.

45. Kuper H, Adami HO, Theorell T, Weiderpass E. The socioeconomic gradient in the incidence of stroke: a prospective study in middle-aged women in Sweden. *Stroke.* 2007;38(1):27-33.

46. Laaksonen M, Talala K, Martelin T, et al. Health behaviours as explanations for educational level differences in cardiovascular and all-cause mortality: a follow-up of 60 000 men and women over 23 years. *Eur. J Public Health.* 2008;18(1):38-43.

47. McCarron P, Greenwood R, Elwood P, et al. The incidence and aetiology of stroke in the Caerphilly and Speedwell Collaborative Studies II: risk factors for ischaemic stroke. *Public Health.* 2001;115(1):12-20.

48. Metcalfe C, Davey Smith G, Sterne JA, Heslop P, Macleod J, Hart CL. Cause-specific hospital admission and mortality among working men: association with socioeconomic circumstances in childhood and adult life, and the mediating role of daily stress. *Eur J Public Health.* 2005;15(3):238-244.

49. Power C, Hypponen E, Smith GD. Socioeconomic position in childhood and early adult life and risk of mortality: a prospective study of the mothers of the 1958 British birth cohort. *Am J Public Health.* 2005;95(8):1396-1402.

50. van Rossum CT, van de Mheen H, Breteler MM, Grobbee DE, Mackenbach JP. Socioeconomic differences in stroke among Dutch elderly women: the Rotterdam Study. *Stroke.* 1999;30(2):357-362.

51. Xu F, Ah Tse L, Yin X, Yu IT, Griffiths S. Impact of socio-economic factors on stroke prevalence among urban and rural residents in Mainland China. *BMC Public Health.* 2008;8:170.

52. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. *Int J Epidemiol.* 2011;40(3):804-818.

53. Tamayo T, Christian H, Rathmann W. Impact of early psychosocial factors (childhood socioeconomic factors and adversities) on future risk of type 2 diabetes, metabolic disturbances and obesity: a systematic review. *BMC Public Health.* 2010;10:525.

54. Gissler M, Rahkonen O, Jarvelin MR, Hemminki E. Social class differences in health until the age of seven years among the Finnish 1987 birth cohort. *Soc Sci Med.* 1998;46(12):1543-1552.

55. Langenberg C, Kuh D, Wadsworth ME, Brunner E, Hardy R. Social circumstances and education: life course origins of social inequalities in metabolic risk in a prospective national birth cohort. *Am J Public Health.* 2006;96(12):2216-2221.

56. Thomas C, Hypponen E, Power C. Obesity and type 2 diabetes risk in midadult life: the role of childhood adversity. *Pediatrics.* 2008;121(5):e1240-1249.

57. Hayes L, Pearce MS, Unwin NC. Lifecourse predictors of normal metabolic parameters in overweight and obese adults. *Int J Obes (Lond).* 2006;30(6):970-976.

58. Kivimaki M, Smith GD, Juonala M, et al. Socioeconomic position in childhood and adult cardiovascular risk factors, vascular structure, and function: cardiovascular risk in young Finns study. *Heart.* 2006;92(4):474-480.

59. Goodman E, Daniels SR, Dolan LM. Socioeconomic disparities in insulin resistance: results from the Princeton School District Study. *Psychosom Med.* 2007;69(1):61-67.

60. Lidfeldt J, Li TY, Hu FB, Manson JE, Kawachi I. A prospective study of childhood and adult socioeconomic status and incidence of type 2 diabetes in women. *Am J Epidemiol.* 2007;165(8):882-889.

61. Maty SC, Everson-Rose SA, Haan MN, Raghunathan TE, Kaplan GA. Education, income, occupation, and the 34-year incidence (1965-99) of Type 2 diabetes in the Alameda County Study. *Int J Epidemiol.* 2005;34(6):1274-1281.

62. Kohler IV, Soldo BJ. Childhood predictors of late-life diabetes: the case of Mexico. *Soc Biol.* 2005;52(3-4):112-131.

63. Kivimaki M, Smith GD, Juonala M, et al. Socioeconomic position in childhood and adult cardiovascular risk factors, vascular structure, and function: cardiovascular risk in young Finns study. *Heart.* 2006;92(4):474-480.

64. Best LE, Hayward MD, Hidajat MM. Life course pathways to adult-onset diabetes. *Soc Biol.* 2005;52(3-4):94-111.

65. Bourdel-Marchasson I, Dubroca B, Letenneur L, et al. Incidence and predictors of drug-treated diabetes in elderly French subjects. The PAQUID Epidemiological Survey. *Diabet Med.* 2000;17(9):675-681.

66. Burchfiel CM, Curb JD, Rodriguez BL, et al. Incidence and predictors of diabetes in Japanese-American men. The Honolulu Heart Program. *Ann Epidemiol.* 1995;5(1):33-43.

67. Cabrera C, Hakeberg M, Ahlqwist M, et al. Can the relation between tooth loss and chronic disease be explained by socio-economic status? A 24-year follow-up from the population study of women in Gothenburg, Sweden. *Eur J Epidemiol.* 2005;20(3):229-236.

68. Costa LM, Mussi AD, Brianeze MR, Souto FJ. Hepatitis C as a risk factor for diabetes type 2: lack of evidence in a hospital in central-west Brazil. *Braz J Infect Dis.* 2008;12(1):24-26.

69. Ezeamama AE, Viali S, Tuitele J, McGarvey ST. The influence of socioeconomic factors on cardiovascular disease risk factors in the context of economic development in the Samoan archipelago. *Soc Sci Med.* 2006;63(10):2533-2545.

70. Gaillard TR, Schuster DP, Bossetti BM, Green PA, Osei K. Do sociodemographics and economic status predict risks for type II diabetes in African Americans? *Diabetes Educ.* 1997;23(3):294-300.

71. Gao WG, Qiao Q, Pitkaniemi J, et al. Risk prediction models for the development of diabetes in Mauritian Indians. *Diabet Med.* 2009;26(10):996-1002.

72. Haffner SM, Hazuda HP, Mitchell BD, Patterson JK, Stern MP. Increased incidence of type II diabetes mellitus in Mexican Americans. *Diabetes Care.* 1991;14(2):102-108.

73. Heidemann C, Hoffmann K, Spranger J, et al. A dietary pattern protective against type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)--Potsdam Study cohort. *Diabetologia.* 2005;48(6):1126-1134.

74. Kaye SA, Folsom AR, Sprafka JM, Prineas RJ, Wallace RB. Increased incidence of diabetes mellitus in relation to abdominal adiposity in older women. *J Clin Epidemiol.* 1991;44(3):329-334.

75. Kouvonen AM, Vaananen A, Woods SA, Heponiemi T, Koskinen A, Toppinen-Tanner S. Sense of coherence and diabetes: a prospective occupational cohort study. *BMC Public Health.* 2008;8:46.

76. Kumari M, Head J, Marmot M. Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II study. *Archives of Internal Medicine.* 2004;164(17):1873-1880.

77. Maskarinec G, Erber E, Grandinetti A, et al. Diabetes incidence based on linkages with health plans: the multiethnic cohort. *Diabetes.* 2009;58(8):1732-1738.

78. Medalie JH, Papier C, Herman JB, et al. Diabetes mellitus among 10,000 adult men. I. Five-year incidence and associated variables. *Isr J Med Sci.* 1974;10(7):681-697.

79. Mehta SH, Brancati FL, Strathdee SA, et al. Hepatitis C virus infection and incident type 2 diabetes. *Hepatology.* 2003;38(1):50-56.

80. Nagaya T, Yoshida H, Takahashi H, Kawai M. Policemen and firefighters have increased risk for type-2 diabetes mellitus probably due to their large body mass index: a follow-up study in Japanese men. *Am J Ind Med.* 2006;49(1):30-35.

81. Norberg M, Stenlund H, Lindahl B, Andersson C, Eriksson JW, Weinehall L. Work stress and low emotional support is associated with increased risk of future type 2 diabetes in women. *Diabetes Res Clin Pract.* 2007;76(3):368-377.

82. Radzeviciene L, Ostrauskas R. Smoking habits and the risk of type 2 diabetes: a case-control study. *Diabetes Metab.* 2009;35(3):192-197.

83. Robbins JM, Vaccarino V, Zhang H, Kasl SV. Socioeconomic status and diagnosed diabetes incidence. *Diabetes Res Clin Pract.* 2005;68(3):230-236.

84. Swai AB, Lutale J, McLarty DG. Diabetes in tropical Africa: a prospective study, 1981-7. I. Characteristics of newly presenting patients in Dar es Salaam, Tanzania, 1981-7. *BMJ.* 1990;300(6732):1103-1106.

85. Wang CS, Wang ST, Yao WJ, Chang TT, Chou P. Hepatitis C virus infection and the development of type 2 diabetes in a community-based longitudinal study. *Am J Epidemiol.* 2007;166(2):196-203.

86. Conway DI, Petticrew M, Marlborough H, Berthiller J, Hashibe M, Macpherson LM. Socioeconomic inequalities and oral cancer risk: a systematic review and meta-analysis of case-control studies. *Int J Cancer.* 2008;122(12):2811-2819.

87. Palmer RC, Schneider EC. Social disparities across the continuum of colorectal cancer: a systematic review. *Cancer Causes Control.* 2005;16(1):55-61.

88. Pruitt SL, Shim MJ, Mullen PD, Vernon SW, Amick BC, 3rd. Association of area socioeconomic status and breast, cervical, and colorectal cancer screening: a systematic review. *Cancer Epidemiol Biomarkers Prev.* 2009;18(10):2579-2599.

89. Sidorchuk A, Agardh EE, Aremu O, Hallqvist J, Allebeck P, Moradi T. Socioeconomic differences in lung cancer incidence: a systematic review and meta-analysis. *Cancer Causes Control.* 2009;20(4):459-471.

90. Vainshtein J. Disparities in breast cancer incidence across racial/ethnic strata and socioeconomic status: a systematic review. *J Natl Med Assoc.* 2008;100(7):833-839.

91. Vineis P, Simonato L. Proportion of lung and bladder cancers in males resulting from occupation: a systematic approach. *Arch Environ Health.* 1991;46(1):6-15.

92. Gershon AS, Dolmage TE, Stephenson A, Jackson B. Chronic obstructive pulmonary disease and socioeconomic status: a systematic review. *COPD.* 2012;9(3):216-226.

93. Uphoff E, Cabieses B, Pinart M, Valdes M, Anto JM, Wright J. A systematic review of socioeconomic position in relation to asthma and allergic diseases. *Eur Respir J.* 2015;46(2):364-374.

94. Eachus J, Williams M, Chan P, et al. Deprivation and cause specific morbidity: evidence from the Somerset and Avon survey of health. *BMJ.* 1996;312(7026):287-292.

95. Chen Y, Breithaupt K, Muhajarine N. Occurrence of chronic obstructive pulmonary disease among Canadians and sex-related risk factors. *J Clin Epidemiol.* 2000;53(7):755-761.

96. Montnemery P, Bengtsson P, Elliot A, Lindholm LH, Nyberg P, Lofdahl CG. Prevalence of obstructive lung diseases and respiratory symptoms in relation to living environment and socio-economic group. *Respir Med.* 2001;95(9):744-752.

97. Welle I, Eide GE, Gulsvik A, Bakke PS. Pulmonary gas exchange and educational level: a community study. *Eur Respir J.* 2004;23(4):583-588.

98. Ellison-Loschmann L, Sunyer J, Plana E, et al. Socioeconomic status, asthma and chronic bronchitis in a large community-based study. *Eur Respir J.* 2007;29(5):897-905.

99. Schikowski T, Sugiri D, Reimann V, Pesch B, Ranft U, Kramer U. Contribution of smoking and air pollution exposure in urban areas to social differences in respiratory health. *BMC Public Health.* 2008;8:179.

100. Kanervisto M, Vasankari T, Laitinen T, Heliovaara M, Jousilahti P, Saarelainen S. Low socioeconomic status is associated with chronic obstructive airway diseases. *Respir Med.* 2011;105(8):1140-1146.

101. Brennan SL, Pasco JA, Urquhart DM, Oldenburg B, Hanna F, Wluka AE. The association between socioeconomic status and osteoporotic fracture in population-based adults: a systematic review. *Osteoporos Int.* 2009;20(9):1487-1497.

102. López-Castillo CA C-RR, Amaya-Amaya J, DeSanVicente-Célis Z, Mantilla RB, Rojas-Villarraga A. Impact of educational level on rheumatoid arthritis: A systematic review. *Rev Colomb Reumatol.* 2014;21(4):201-212.

103. Lorant V, Deliege D, Eaton W, Robert A, Philippot P, Ansseau M. Socioeconomic inequalities in depression: a meta-analysis. *Am J Epidemiol.* 2003;157(2):98-112.

104. Caamano-Isorna F, Corral M, Montes-Martinez A, Takkouche B. Education and dementia: a meta-analytic study. *Neuroepidemiology.* 2006;26(4):226-232.

105. Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. *Psychological Medicine.* 2006;36(4):441-454.

106. Sharp ES, Gatz M. Relationship between education and dementia: an updated systematic review. *Alzheimer Dis Assoc Disord.* 2011;25(4):289-304.

107. Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimaki M, Batty GD. Socioeconomic status as a risk factor for dementia death: individual participant meta-analysis of 86 508 men and women from the UK. *Br J Psychiatry.* 2013;203(1):10-17.

108. Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. *J. Int. Neuropsychol. Soc.* 2002;8(3):448-460.

109. Galobardes B, Lynch JW, Smith GD. Childhood Socioeconomic Circumstances and Cause-specific Mortality in Adulthood: Systematic Review and Interpretation. *Epidemiol. Rev.* 2004;26:7-21.

110. Gorey KM. Breast cancer survival in Canada and the USA: meta-analytic evidence of a Canadian advantage in low-income areas. *Int J Epidemiol.* 2009;38(6):1543-1551.

111. Sposato LA, Saposnik G. Gross domestic product and health expenditure associated with incidence, 30-day fatality, and age at stroke onset: a systematic review. *Stroke.* 2012;43(1):170-177.

112. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol.* 2009;8(4):355-369.

113. Slatore CG, Au DH, Gould MK, American Thoracic Society Disparities in Healthcare G. An official American Thoracic Society systematic review: insurance status and disparities in lung cancer practices and outcomes. *Am J Respir Crit Care Med.* 2010;182(9):1195-1205.

114. Calvillo-King L, Arnold D, Eubank KJ, et al. Impact of social factors on risk of readmission or mortality in pneumonia and heart failure: systematic review. *J Gen Intern Med.* 2013;28(2):269-282.

115. Mackenbach JP, Kunst AE, Cavelaars AE, Groenhof F, Geurts JJ. Socioeconomic inequalities in morbidity and mortality in western Europe. *Lancet.* 1997;349(9066):1655-1659.

116. Dalstra JA, Kunst AE, Borrell C, et al. Socioeconomic differences in the prevalence of common chronic diseases: an overview of eight European countries. *Int J Epidemiol.* 2005;34(2):316-326.

117. Cavelaars AE, Kunst AE, Geurts JJ, et al. Educational differences in smoking: international comparison. *BMJ.* 2000;320(7242):1102-1107.

118. Cavelaars AEJM, Kunst AE, Mackenbach JP. Socio-economic Differences in Risk Factors for Morbidity and Mortality in the European Community: An International Comparison. *Journal of Health Psychology.* 1997;2(3):353-372.

119. Mackenbach JP, Stirbu I, Roskam AJ, et al. Socioeconomic Inequalities in Health in 22 European Countries. *The New England Journal of Medicine.* 2008;358(23):2468-2481.

120. Zatonski WA, Bhala N. Changing trends of diseases in Eastern Europe: closing the gap. *Public Health.* 2012;126(3):248-252.

121. Rehm J, Sulkowska U, Manczuk M, et al. Alcohol accounts for a high proportion of premature mortality in central and eastern Europe. *Int J Epidemiol.* 2007;36(2):458-467.

122. O'Flaherty M, Bandosz P, Critchley J, et al. Exploring potential mortality reductions in 9 European countries by improving diet and lifestyle: A modelling approach. *Int J Cardiol.* 2016;207:286-291.

123. Zdrojewski T, Rutkowski M, Bandosz P, et al. Prevalence and control of cardiovascular risk factors in Poland. Assumptions and objectives of the NATPOL 2011 Survey. *Kardiol Pol.* 2013;71(4):381-392.

124. Dorobantu M, Darabont R, Ghiorghe S, et al. Hypertension prevalence and control in Romania at a seven-year interval. Comparison of SEPHAR I and II surveys. *J Hypertens.* 2014;32(1):39-47.

125. Grassi G, Cifkova R, Laurent S, et al. Blood pressure control and cardiovascular risk profile in hypertensive patients from central and eastern European countries: results of the BP-CARE study. *Eur Heart J.* 2011;32(2):218-225.

126. Collaboration NCDRF. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet.* 2016;387(10027):1513-1530.

127. De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based study. *Lancet Oncol.* 2014;15(1):23-34.

128. Burney P, Jarvis D, Perez-Padilla R. The global burden of chronic respiratory disease in adults. *Int J Tuberc Lung Dis.* 2015;19(1):10-20.

129. Gibson GJ, Loddenkemper R, Lundback B, Sibille Y. Respiratory health and disease in Europe: the new European Lung White Book. *Eur Respir J.* 2013;42(3):559-563.

130. Lopez-Campos JL, Ruiz-Ramos M, Soriano JB. Mortality trends in chronic obstructive pulmonary disease in Europe, 1994-2010: a joinpoint regression analysis. *Lancet Respir Med.* 2014;2(1):54-62.

131. Hernlund E, Svedbom A, Ivergard M, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos.* 2013;8:136.

132. Svedbom A, Hernlund E, Ivergard M, et al. Osteoporosis in the European Union: a compendium of country-specific reports. *Arch Osteoporos.* 2013;8:137.

133. Lundkvist J, Kastang F, Kobelt G. The burden of rheumatoid arthritis and access to treatment: health burden and costs. *Eur J Health Econ.* 2008;8 Suppl 2:S49-60.

134. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. *PLoS One.* 2015;10(2):e0116820.

135. Miret M, Ayuso-Mateos JL, Sanchez-Moreno J, Vieta E. Depressive disorders and suicide: Epidemiology, risk factors, and burden. *Neurosci Biobehav Rev.* 2013;37(10 Pt 1):2372-2374.

136. Boyd A, Van de Velde S, Vilagut G, et al. Gender differences in mental disorders and suicidality in Europe: results from a large cross-sectional population-based study. *J Affect Disord.* 2015;173:245-254.

137. Takizawa C, Thompson PL, van Walsem A, Faure C, Maier WC. Epidemiological and economic burden of Alzheimer's disease: a systematic literature review of data across Europe and the United States of America. *J Alzheimers Dis.* 2015;43(4):1271-1284.

138. Kiejna A, Frydecka D, Adamowski T, et al. Epidemiological studies of cognitive impairment and dementia across Eastern and Middle European countries (epidemiology of dementia in Eastern and Middle European Countries). *Int J Geriatr Psychiatry.* 2011;26(2):111-117.

139. Kingwell E, Marriott JJ, Jette N, et al. Incidence and prevalence of multiple sclerosis in Europe: a systematic review. *BMC Neurol.* 2013;13:128.

140. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012;380(9859):2095-2128.

141. Krieger N. Theories for social epidemiology in the 21st century: an ecosocial perspective. *Int. J Epidemiol.* 2001;30(4):668-677.

142. Dray-Spira R, Gary TL, Brancati FL. Socioeconomic position and cardiovascular disease in adults with and without diabetes: United States trends, 1997-2005. *J Gen Intern Med.* 2008;23(10):1634-1641.

143. Kavanagh A, Bentley RJ, Turrell G, Shaw J, Dunstan D, Subramanian SV. Socioeconomic position, gender, health behaviours and biomarkers of cardiovascular disease and diabetes. *Soc Sci Med.* 2010;71(6):1150-1160.

144. Schulz AJ, House JS, Israel BA, et al. Relational pathways between socioeconomic position and cardiovascular risk in a multiethnic urban sample: complexities and their implications for improving health in economically disadvantaged populations. *J Epidemiol Community Health.* 2008;62(7):638-646.

145. Li C, Hedblad B, Rosvall M, Buchwald F, Khan FA, Engstrom G. Stroke incidence, recurrence, and case-fatality in relation to socioeconomic position: a population-based study of middle-aged Swedish men and women. *Stroke.* 2008;39(8):2191-2196.

146. Andersen A, Holstein BE, Due P. Large-scale alcohol use and socioeconomic position of origin: longitudinal study from ages 15 to 19 years. *Scand J Public Health.* 2008;36(3):326-329.

147. Nordahl H, Osler M, Frederiksen BL, et al. Combined effects of socioeconomic position, smoking, and hypertension on risk of ischemic and hemorrhagic stroke. *Stroke.* 2014;45(9):2582-2587.

148. Laba TL, Bleasel J, Brien JA, et al. Strategies to improve adherence to medications for cardiovascular diseases in socioeconomically disadvantaged populations: a systematic review. *Int J Cardiol.* 2013;167(6):2430-2440.

149. Singh TP, Gauvreau K, Bastardi HJ, Blume ED, Mayer JE. Socioeconomic position and graft failure in pediatric heart transplant recipients. *Circ Heart Fail.* 2009;2(3):160-165.

150. Singh TP, Givertz MM, Semigran M, Denofrio D, Costantino F, Gauvreau K. Socioeconomic position, ethnicity, and outcomes in heart transplant recipients. *Am J Cardiol.* 2010;105(7):1024-1029.

151. Koch CG, Li L, Kaplan GA, et al. Socioeconomic position, not race, is linked to death after cardiac surgery. *Circ Cardiovasc Qual Outcomes.* 2010;3(3):267-276.

152. Ljung R, Hallqvist J. Accumulation of adverse socioeconomic position over the entire life course and the risk of myocardial infarction among men and women: results from the Stockholm Heart Epidemiology Program (SHEEP). *J Epidemiol Community Health.* 2006;60(12):1080-1084.

153. Rosvall M, Chaix B, Lynch J, Lindstrom M, Merlo J. The association between socioeconomic position, use of revascularization procedures and five-year survival after recovery from acute myocardial infarction. *BMC Public Health.* 2008;8:44.

154. Malki N, Koupil I, Eloranta S, et al. Temporal trends in incidence of myocardial infarction and ischemic stroke by socioeconomic position in Sweden 1987-2010. *PLoS One.* 2014;9(8):e105279.

155. Agha G, Murabito JM, Lynch JW, Abrahamowicz M, Harper SB, Loucks EB. Relation of socioeconomic position with ankle-brachial index. *Am J Cardiol.* 2011;108(11):1651-1657.

156. Lawlor DA, Ebrahim S, Davey Smith G. Adverse socioeconomic position across the lifecourse increases coronary heart disease risk cumulatively: findings from the British women's heart and health study. *J Epidemiol Community Health.* 2005;59(9):785-793.

157. Lawlor DA, Davey Smith G, Patel R, Ebrahim S. Life-course socioeconomic position, area deprivation, and coronary heart disease: findings from the British Women's Heart and Health Study. *Am J Public Health.* 2005;95(1):91-97.

158. Lawlor DA, Ronalds G, Macintyre S, Clark H, Leon DA. Family Socioeconomic Position at Birth and Future Cardiovascular Disease Risk: Findings From the Aberdeen Children of the 1950s Cohort Study. *American Journal of Public Health.* 2006;96(7):1271-1277.

159. Thurston RC, Kubzansky LD, Kawachi I, Berkman LF. Is the association between socioeconomic position and coronary heart disease stronger in women than in men? *Am J Epidemiol.* 2005;162(1):57-65.

160. Loucks EB, Lynch JW, Pilote L, et al. Life-course socioeconomic position and incidence of coronary heart disease: the Framingham Offspring Study. *Am. J. Epidemiol.* 2009;169(7):829-836.

161. Bender AM, Jorgensen T, Helbech B, Linneberg A, Pisinger C. Socioeconomic position and participation in baseline and follow-up visits: the Inter99 study. *Eur J Prev Cardiol.* 2014;21(7):899-905.

162. Abdoli G, Bottai M, Moradi T. Cancer mortality by country of birth, sex, and socioeconomic position in Sweden, 1961-2009. *PLoS One.* 2014;9(3):e93174.

163. Forrest LF, Adams J, Wareham H, Rubin G, White M. Socioeconomic inequalities in lung cancer treatment: systematic review and meta-analysis. *PLoS Med.* 2013;10(2):e1001376.

164. Dalton SO, Frederiksen BL, Jacobsen E, et al. Socioeconomic position, stage of lung cancer and time between referral and diagnosis in Denmark, 2001-2008. *Br J Cancer.* 2011;105(7):1042-1048.

165. Dalton SO, Steding-Jessen M, Jakobsen E, et al. Socioeconomic position and survival after lung cancer: Influence of stage, treatment and comorbidity among Danish patients with lung cancer diagnosed in 2004-2010. *Acta Oncol.* 2015;54(5):797-804.

166. Nkosi TM, Parent ME, Siemiatycki J, Rousseau MC. Socioeconomic position and lung cancer risk: how important is the modeling of smoking? *Epidemiology.* 2012;23(3):377-385.

167. McKenzie F, Jeffreys M. Do lifestyle or social factors explain ethnic/racial inequalities in breast cancer survival? *Epidemiol Rev.* 2009;31:52-66.

168. Schlichting JA, Soliman AS, Schairer C, Schottenfeld D, Merajver SD. Inflammatory and non-inflammatory breast cancer survival by socioeconomic position in the Surveillance, Epidemiology, and End Results database, 1990-2008. *Breast Cancer Res Treat.* 2012;134(3):1257-1268.

169. McKenzie F, Jeffreys M, t Mannetje A, Pearce N. Prognostic factors in women with breast cancer: inequalities by ethnicity and socioeconomic position in New Zealand. *Cancer Causes Control.* 2008;19(4):403-411.

170. Meijer M, Bloomfield K, Engholm G. Neighbourhoods matter too: the association between neighbourhood socioeconomic position, population density and breast, prostate and lung cancer incidence in Denmark between 2004 and 2008. *J Epidemiol Community Health.* 2013;67(1):6-13.

171. Olsen MH, Boje CR, Kjaer TK, et al. Socioeconomic position and stage at diagnosis of head and neck cancer - a nationwide study from DAHANCA. *Acta Oncol.* 2015;54(5):759-766.

172. Dailey AB, Brumback BA, Livingston MD, Jones BA, Curbow BA, Xu X. Area-level socioeconomic position and repeat mammography screening use: results from the 2005 National Health Interview Survey. *Cancer Epidemiol Biomarkers Prev.* 2011;20(11):2331-2344.

173. Uthman OA, Jadidi E, Moradi T. Socioeconomic position and incidence of gastric cancer: a systematic review and meta-analysis. *J Epidemiol Community Health.* 2013;67(10):854-860.

174. Dalsgaard EM, Vestergaard M, Skriver MV, Borch-Johnsen K, Lauritzen T, Sandbaek A. Socioeconomic position and cardiovascular risk factors among people with screen-detected Type 2 DM: six-year follow-up of the ADDITION-Denmark trial. *Prim Care Diabetes.* 2014;8(4):322-329.

175. Dalsgaard EM, Skriver MV, Sandbaek A, Vestergaard M. Socioeconomic position, type 2 diabetes and long-term risk of death. *PLoS One.* 2015;10(5):e0124829.

176. Demakakos P, Marmot M, Steptoe A. Socioeconomic position and the incidence of type 2 diabetes: the ELSA study. *Eur J Epidemiol.* 2012;27(5):367-378.

177. Smith BT, Lynch JW, Fox CS, et al. Life-course socioeconomic position and type 2 diabetes mellitus: The Framingham Offspring Study. *Am J Epidemiol.* 2011;173(4):438-447.

178. Spadea T, Zengarini N, Kunst A, Zanetti R, Rosso S, Costa G. Cancer risk in relationship to different indicators of adult socioeconomic position in Turin, Italy. *Cancer Causes Control.* 2010;21(7):1117-1130.

179. Maty SC, James SA, Kaplan GA. Life-course socioeconomic position and incidence of diabetes mellitus among blacks and whites: the Alameda County Study, 1965-1999. *Am J Public Health.* 2010;100(1):137-145.

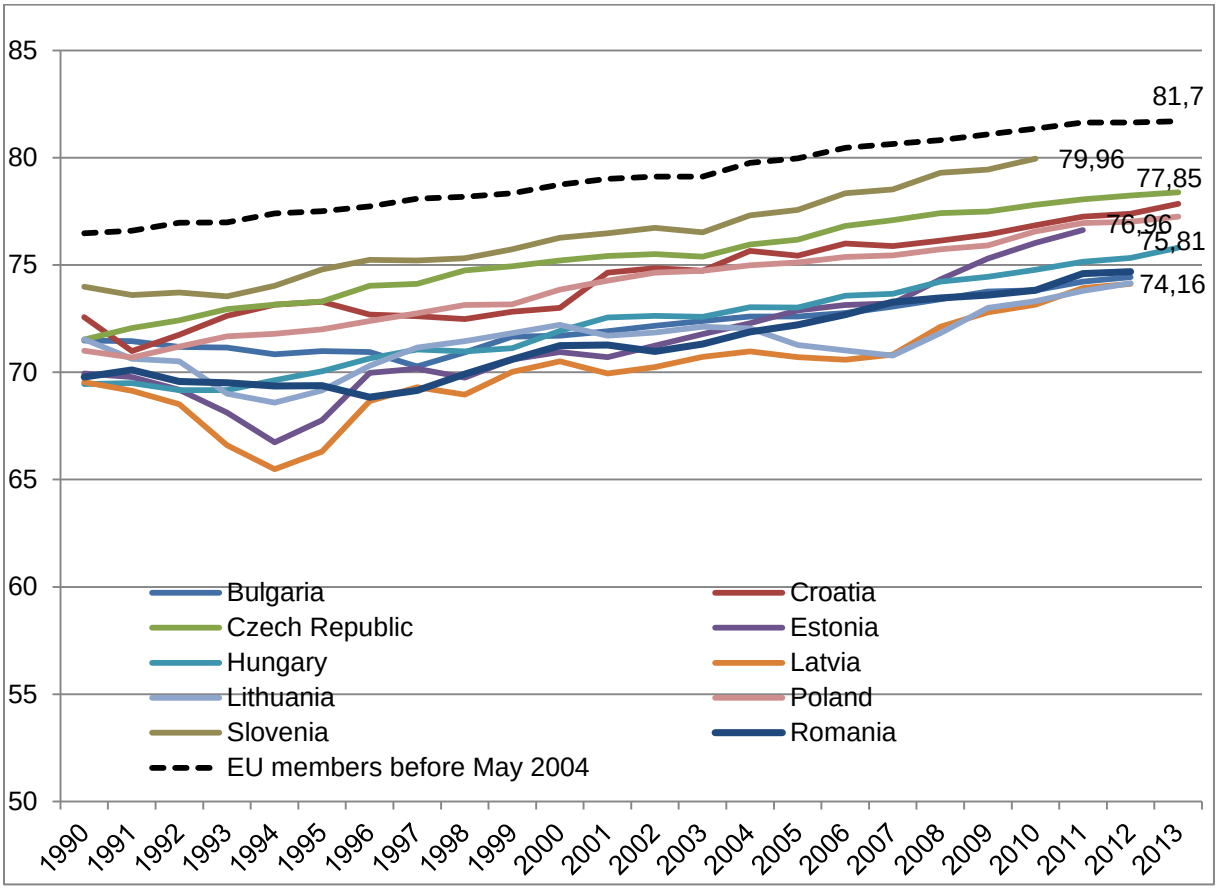
4 ANNEXES

4.1 DIFFERENCES BETWEEN EASTERN & WESTERN EUROPE

4.1.1 Introduction

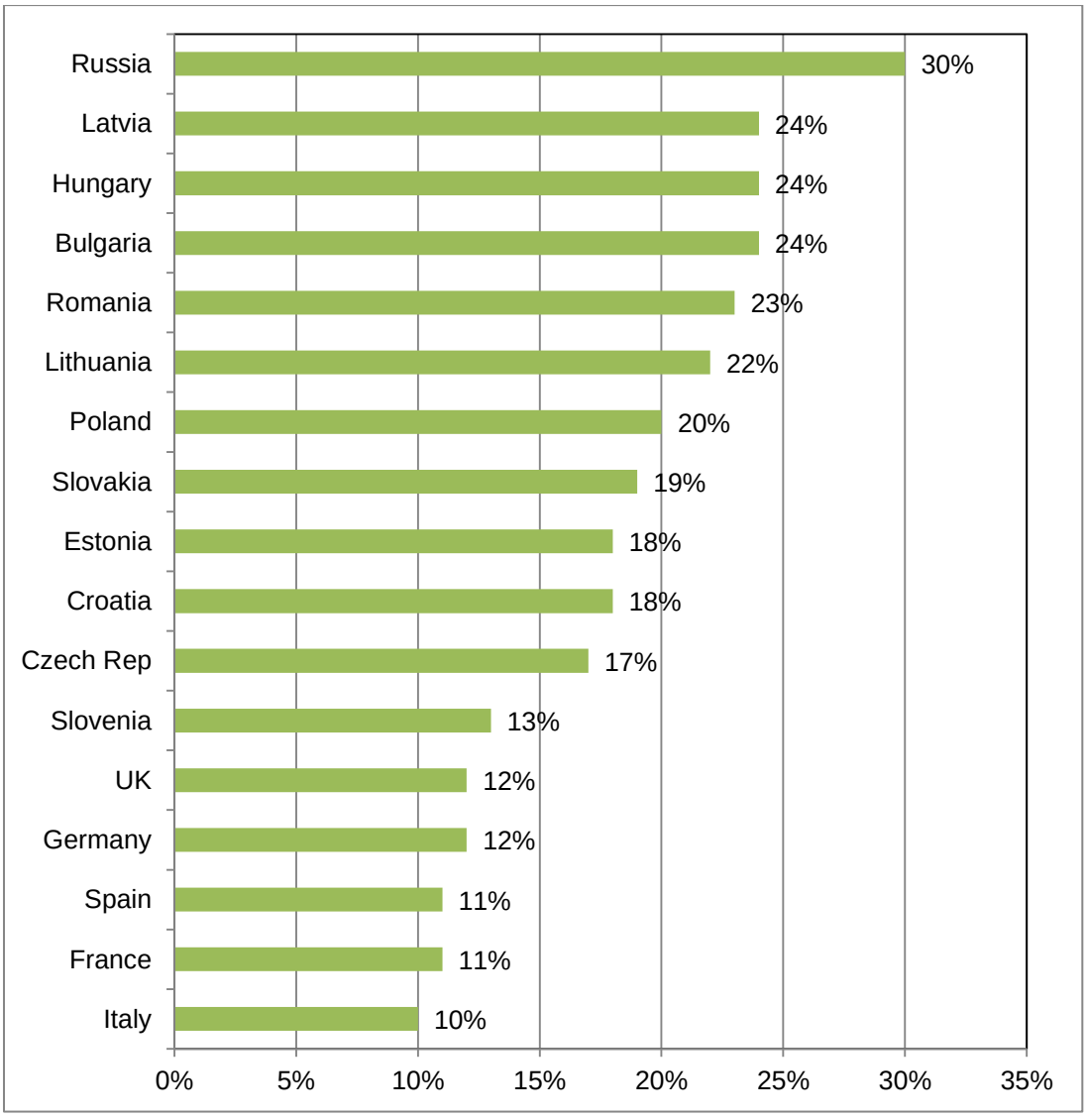
Eastern Europe is recognized as a region facing multiple health problems and with higher burden of non-communicable diseases (NCD) than Western and Northern part of the continent. The social and economic transformation in the last decade of the 20th century in Eastern Europe and collapse of former communistic block led to an increase in the health problems in many of these countries. In recent times, trends in life expectancy at birth have improved in many areas around the world, however those for Russia, as well as for some other former Soviet Union countries, have fluctuated, not showing signs of stable growth. In Eastern European EU member states significant progress has been observed (**Figure 1**), the changing trends being similar to that observed in Western Europe. The picture for Russia, Ukraine and many other countries of the former Soviet Union remains unsatisfactory.

Figure 1. Life expectancy in EU Eastern countries and average for EU members before 2004 in years 1990-2013 ***(source: WHO HFA DB database 2016)***



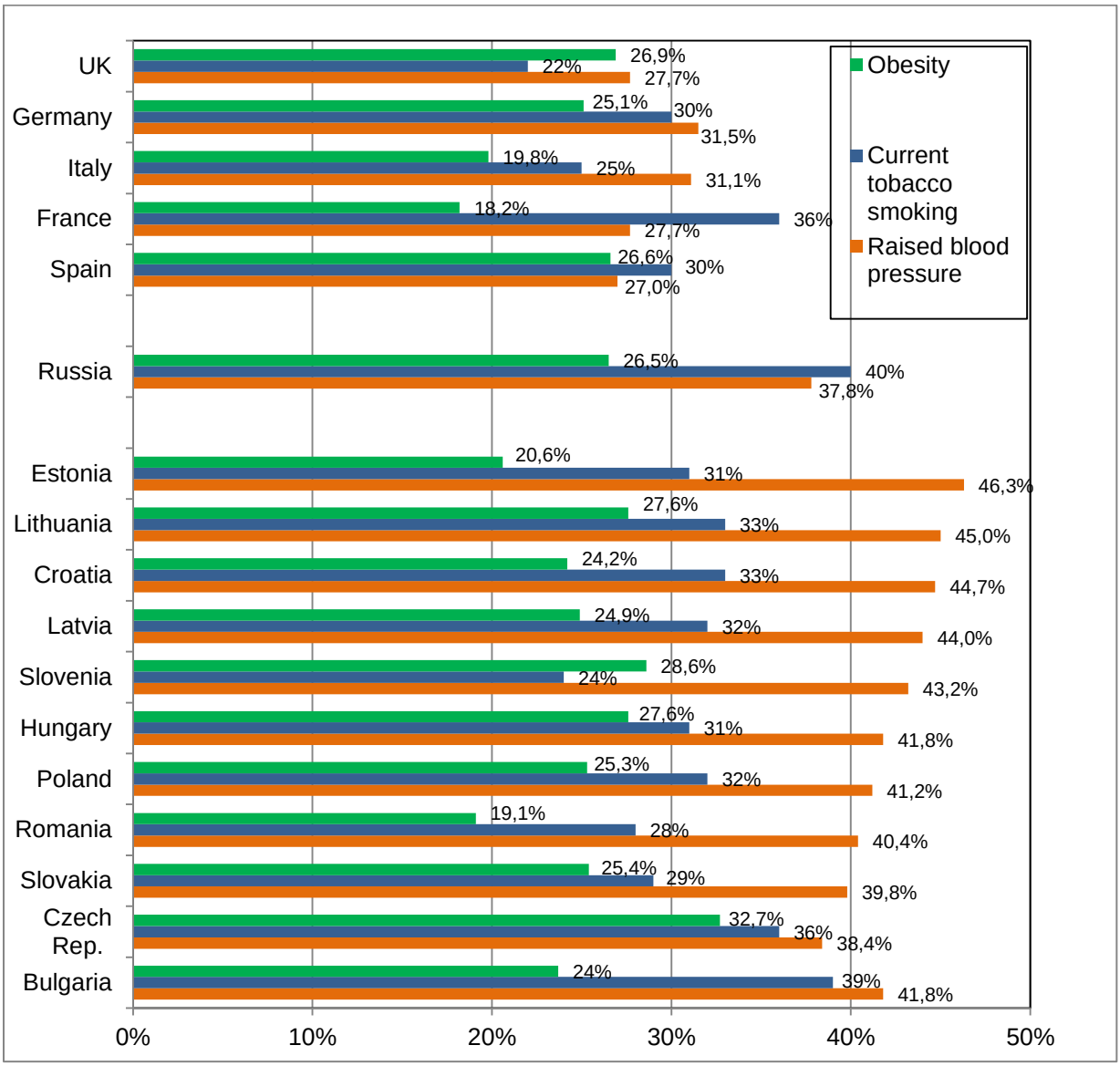
The major problem in these countries is higher premature mortality due to cardiovascular diseases (CVD) and external causes of death, especially among males in middle age. However, diabetes and malignant neoplasms morbidity in Eastern EU can very randomly compared to EU 15. Estimates from 2008 by Zatoński and al. [1] on the probability of death before the age of 65 years for men are of the order of 16% in Western Europe (EU member states before 2004) , compared with 31% for Eastern Europe (new EU states after enlargement in 2004) and 54% in Russia. In general among the all EU member states the highest rates of premature mortality are observed in Hungary, Latvia and Bulgaria (**Figure 2**).

Figure 2. The probability of dying between ages 30 and 70 years from the CVD, cancer, chronic respiratory diseases and diabetes in Eastern EU countries, Russia and the biggest Western European countries *(according to estimates of WHO "Noncommunicable Diseases Country Profiles 2014")*



The reasons of such an unfavorable situation can be related to relatively higher burden of NCDs risk factors in Eastern Europe, related to more frequent tobacco smoking, unhealthy diet habits and hypertension. The prevalence of hypertension in particular tends to be much higher in Eastern than in Western part of the continent (Figure 3). The patterns of alcohol consumption is also thought to play a role in higher burden of NCDs in Northern-East part Europe [2]

Figure 3. Frequency of smoking tobacco, obesity and hypertension in EU Eastern countries, Russia and the biggest countries of Western Europe *(according to estimates of WHO "Noncommunicable Diseases Country Profiles 2014")*



Another challenge for Eastern EU is issue regarding quality of data used for reporting health situation in the region. Some of the countries do not run relevant statistical systems like for instance medical registries and do not perform adequate epidemiological studies.

These circumstances cause that comparison of health situation in Eastern and Western European countries could be difficult or need special attention in the process of data interpretation.

4.1.2 Methods

The history of large epidemiological studies in the field of non-communicable diseases in Eastern part of European Union (UE) is fairly short comparing to other western countries. More intense activity in this field started in the late 70's. In this period some countries in the region launched population based studies focused on NCDs. In the context of cardiovascular diseases in 80's the WHO MONICA study (MONItoring of trends and determinants in cardiovascular disease) under umbrella of World Health Organization (WHO) is noteworthy. In eastern part of the EU, MONICA was performed in Czech Republic, Lithuania, Poland and Russia. MONICA can be also recognized as a starting point for many new scientific initiatives in the field of epidemiology. Despite all the described attempts the number of prospective-cohort studies is still limited, not allowing us to undertake a meta-analysis regarding precise diagnosis about relationships between NCDs and biological and socioeconomic factors. It should be also taken i to consideration that most of published in the region are cross-sectional or case-control surveys. Thus, it was important to the search criteria of publications for FRESHER.

Search strategy

The methodological framework adopted in the project was to undertake search of the PubMed scientific data. We analyzed epidemiological surveys from Central-Eastern Europe from 2004 to 2015. We only included studies undertaken on large representative populations– with an N of at least 400. All publications in languages other than English were excluded. The following MeSH key-words were adopted in the search: epidemiology, Europe, eastern, cohort study, cross-sectional study, case-control study, risk factor, diabetes, CVD, metabolic syndrome. To refine outcomes of the literature research we also used filters to include only original publications in the English language.

4.1.3 Results

Our search revealed that the number of studies considering risk factors associations between cardiovascular diseases and diabetes is limited. Most of the studies identified did not allow us to perform an umbrella review. We identified 17 publications on epidemiology of metabolic syndrome and diabetes and 52 publications on cardiovascular disease. Most of publications were related to cross-sectional and case-control studies (n=29 of publications) and the most significant prospective cohort study which was comparing situation of different. Eastern European countries were cohorts in the HAPIEE study (Health, Alcohol and

Psychosocial factors In Eastern Europe).Most of the identified publications were from Poland, Lithuania, Czech Republic and Romania. **Table 1 & 2** below describes main outcomes of reviewed publications grouping.

Table 1. Outcomes of literature review in the area of CVDs epidemiology in Eastern European countries

No.	Title	First author	Bibliographical informations	Years of study	Type of study	Population	Countries from Eastern Europe involved in study	Health problems	Main risk factors	Main outcomes
1	Educational class inequalities in the incidence of coronary heart disease in Europe	Veronesi G	Heart. 2016 Feb 5. pii: heartjnl-2015-308909.	2015	meta-analyze	49 cohorts of middle-aged European adults free of CHD (110 928 individuals) recruited mostly in the mid-1980s and 1990s,		Cardivascular diseases	Gender, Educational class	Educational class inequalities accounted for 343 and 170 additional CHD events per 100 000 person-years in the least educated men and women compared with the most educated, respectively. These figures corresponded to 48% and 71% of the average event rates in each gender group. Inequalities in CHD mortality were mainly driven byincidence in the Nordic countries, Scotland and Lithuania, and by 28-day case-fatality in the remaining central/South European populations. The pooled RIIs were 1.6 (95% CI 1.4 to 1.8) in men and 2.0 (1.7 to 2.4) in women, consistently across population. Risk factors accounted for a third ofinequalities in CHD incidence; smoking was the major mediator in men, and High-Density-Lipoprotein (HDL) cholesterol in women
2	Exploring potential mortality reductions in 9 European countries by improving diet and lifestyle: A modelling approach	O'Flaherty M	Int J Cardiol. 2016 Mar 15;207:286-91	2015	case study	9 European countries including 2 Eastern European countries	Czech republic, Poland	Mortality due to cardivascular diseases	Smoking, Saturated fats intake, Salt intake, Physical inactivity	Under the conservative, intermediate and optimistic scenarios, we estimated 10.8% (95% CI: 7.3-14.0), 20.7% (95% CI: 15.6-25.2) and 29.1% (95% CI: 22.6-35.0) fewer Coronary Heart Diseas (CHD) deaths in 2020. For the optimistic scenario, 15% absolute reductions in smoking could decrease CHD deaths by 8.9%-11.6%, Salt intake relative reductions of 30% by approximately 5.9-8.9%; 3% reductions in saturated fat intake by 6.3-7.5%, and 15% absolute increases in physical activity by 3.7-5.3%

3	Mediterranean diet score and total and cardiovascular mortality in Eastern Europe: the HAPIEE study.	Stefler D	Eur J Nutr. 2015 Nov 17. [Epub ahead of print]	2002-2004	cohort	19 333 men and women participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	Dietary pattern	Over the median follow-up time of 7 years, 1314 participants died. The proportion of participants with high adherence to Mediterraneandiet (MDS) was low (25 %). One standard deviation (SD) increase in the MDS (equivalent to 2.2 point increase in the score) was found to be inversely associated with death from all causes (HR, 95 % CI 0.93, 0.88-0.98) and CVD (0.90, 0.81-0.99) even after multivariable adjustment. Inverse but statistically not significant link was found for CHD (0.90, 0.78-1.03) and stroke (0.87, 0.71-1.07). The MDS effects were similar in each country cohort.
4	Alcohol, drinking pattern and all-cause, cardiovascular and alcohol-related mortality in Eastern Europe.	Bobak M	Eur J Epidemiol. 2015 Oct 14. [Epub ahead of print]	2002-2005	cohort	34 304 men and women aged 45-69 years participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases and alcohol-related causes	Alcohol, Drinking pattern	In fully-adjusted models, abstainers had 30-50 % increased mortality risk compared to light-to-moderate drinkers. Adjusted hazard ratios (HR) in mendrinking on average ≥60 g of ethanol/day (3 % of men) were 1.23 (95 % CI 0.95-1.59) for all-cause, 1.38 (0.95-2.02) for CVD, 1.64 (1.02-2.64) for CHD and 2.03 (1.28-3.23) for ARD mortality. Corresponding HRs in women drinking on average ≥20 g/day (2 % of women) were 1.92 (1.25-2.93), 1.74 (0.76-3.99), 1.39 (0.34-5.76) and 3.00 (1.26-7.10). Binge drinking increased ARD mortality in men only. Mortality was associated with high averagealcohol intake but not binge drinking, except for ARD in men.
5	Fruit and vegetable consumption and mortality in Eastern Europe: Longitudinal results from the Health, Alcohol and Psychosocial Factors in Eastern Europe study	Stefler D	Eur J Prev Cardiol. 2015 Apr 22. pii: 2047487315582320. [Epub ahead of print]	2002-2005	cohort	19333 men and women participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	Smoking, Fruits and vegetables intake	Among 19,333 disease-free participants at baseline, 1314 died over the mean follow-up of 7.1 years. After multivariable adjustment, was found statistically significant inverse association between cohort-specific quartiles of Fruits and Vegetables (F&V) intake and stroke mortality: the highest vs lowest quartile hazard ratio (HR) was 0.52 (95% confidence interval (CI): 0.28-0.98). For total mortality, significant interaction (p = 0.008) between F&V intake and smoking was found. The associations were statistically significant in smokers, with HR 0.70 (0.53-0.91, p for trend: 0.011) for total mortality, and 0.62 (0.40-0.97, p for trend: 0.037) for cardiovascular disease (CVD) mortality. The association was appeared to be mediated by blood pressure, and F&V intake

										explained a considerable proportion of the mortality differences between the Czech and Russian cohorts
6	Cardiovascular disease (CVD) risk factors in Kraków and in the whole Poland adult population. Results from the WOBASZ study and Polish arm of the HAPIEE project	Doryńska A	Przegl Epidemiol. 2015;69(1):79-86, 175-80	2002-2005	cohort	19333 men and women aged 45-69 years participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) from Krakow and sample of 992 residents of big towns other than Krakow from Multicenter Polish Population Health Status Study-WOBASZ	Poland	SCORE risk assessment	Socioeconomic status, BMI	The striking observation was that in Krakow proportions of participants with university education were substantially higher than average for the other big towns and the whole Poland. Also, the proportion of occupationally active men and women was the highest in Krakow. In both sexes, prevalence of smoking, hypercholesterolemia and hypertension in Krakow was similar to the other big towns but the prevalence of hypercholesterolemia and hypertension (in men only) was lower than average for Poland. The distribution by SCORE risk categories were similar in all three samples studied. In general, the distribution by BMI categories was less favourable but the prevalence of central obesity was lower among residents of Kraków than among residents of the other big towns and citizens of the whole Poland. Prevalence of diabetes was higher in Krakow than in the other samples studied. The differences between population of Krakow and population of other parts of Poland in the exposure to the main riskfactors were found diverse and not big enough to be followed by differences in the distribution by the categories of SCORE risk assessment. Thestudy suggested the importance of obesity and diabetes which are not used for the SCORE risk assessment and especially the importance of psychosocial and economic factors which may influence CVD risk and contribute more to the explanation of the regional differences in CVDmortality

7	A High Burden of Ischemic Stroke in Regions of Eastern/Central Europe is Largely Due to Modifiable Risk Factors.	Pikija S	Curr Neurovasc Res. 2015;12(4)	2007-2010	cohort and case control	Ischemic stroke patients identified in a population-based incidence study (N=751) (study 1, S1) and a concurrent case-control trial (215 patients, 125 controls, S2) were conducted in the county of Varazdin from 2007-2010	Croatia	Ischemic stroke, Atrial fibrillation	Dietary pattern, Smoking, Alcohol consumption, Dyslipidaemia	Atrial fibrillation (AF) was common (36.1% in S1, 40.9% in S2) and mostly (>50%) unrecognized before the index event. In a multivariate analysis, odds of stroke increased with tobacco smoking (OR=3.95, 95%CI 1.33-10.8), unhealthy diet (OR=2.12, 1.12-4.01) and AF (OR=9.40, 4.01-22.0), and decreased with higher education (OR=0.33, 0.11-0.98), moderate alcohol consumption (OR=0.48, 0.25-0.93), higher fasting HDL (OR=0.14, 0.07-0.30) and pre-stroke use of anticoagulants (OR=0.09, 0.01-0.59), antihypertensive drugs (OR=0.52, 0.27-1.00) and statins (OR=0.29, 0.12-0.69). Fourteen-day case fatality was 10.8% (S1) and 6.1% (S2) and the risk was higher with AF, cardioembolic stroke, older age, higher fasting serum glucose, and lower with acute aspirin. Among the acute phase survivors, 30.9% died over the subsequent 1-3 years ($p<0.05$). We conclude that the incidence of ischemic stroke in Croatia is related to conventional risk factors and largely due to a high rate of unawareness and inadequate treatment of predisposing morbidity -
8	Hypertension prevalence and control in Romania at a seven-year interval. Comparison of SEPHAR I and II surveys	Dorobanţu M	J Hypertens. 2014 Jan;32(1):39-47	2005-2012	cross-sectional	The representative sample for the Romanian adult population. SEPHAR I study (Study for the Evaluation of Prevalence of Hypertension and Cardiovascular Risk in Romania): 2017 individuals aged 18-85 years SEPHAR II: 1975 individuals aged 18-80 year	Romania	Hypertension	Age, Gender	Prevalence of hypertension in Romanian is 40.41%, awareness of hypertension is 69.55%, with 59.15% hypertensive individuals under current treatment with a control rate of 25%. In the last 7 years, there has been a 10.7% decrease in hypertension's prevalence together with an increase by 57% in awareness of hypertension and an increase by 52% in treatment of hypertension, leading to almost doubling of the hypertension'scontrol rate in all hypertensive individuals.

9	Diversity of metabolic syndrome criteria in association with cardiovascular diseases-a family medicine-based investigation	Ivezić-Lalić D	Med Sci Monit. 2013 Jul 12;19:571-8	2008	cross-sectional	3245 participants≥40 years from Cardiovascular Risk and Intervention Study in Croatia	Croatia	Cardivascular diseases	Metabolic syndrome	All analyzed Metabolic Syndrome definitions showed an association with CVD, but the strongest was shown by NCEP ATP III; coronary disease OR 2.48 (95% CI 1.80-3.82), cerebrovascular disease OR 2.14 (1.19-3.86), and peripheral artery disease OR 1.55 (1.04-2.32), especially for age and male sex. According to the NCEP ATP III (IDF), the prevalence was 38.7% (45.9%) [15.9% (18.6%) in men, and 22.7% (27.3%) in women, and 28.4% (33.9%) in the continental region, 10.2% (10.9%) in the coastal region, 26.2% (31.5%) in urban areas, and 12.4% (14.4%) in rural areas. Older age, male sex, and residence in the continental area were positively associated with MetS diagnosis according to NCEP ATP III, and current smoking and Mediterranean diet adherence have protective effects
10	All-cause and cardiovascular mortality risk estimation using different definitions of metabolic syndrome in Lithuanian urban population	Luksiene D	Prev Med. 2012 Oct;55(4):299-304	1992–2009	cohort and cross sectional	2455 men and women aged 35-64	Lithuania	Mortality due to cardivascular diseases	Metabolic syndrome	Cox regressions demonstrated that metabolic syndrome defined by IDF and JIS definitions remained the only significant determinants for all-causemortality (RR=1.48 and RR=1.41; p<0.05) and cardiovascular disease (CVD) mortality in men (RR=1.81 and RR=1.66; p<0.05). In men (without previous CVD) the NCEP-ATPIII definition had increased mortality risk from CVD (RR=1.98; p=0.012), than in men with identified MS by the IDF and the new JIS definition. In women the MS was not associated with risk of mortality from CVD
11	Determinants of cardiovascular and all-cause mortality in northwest Russia: a 10-year follow-up study	Sidorenkov O	Ann Epidemiol. 2012 Jan;22(1):57-65.	1999-2010	cohort and cross sectional	1966 men and 1738 women ages 18 years or older	Russia	Mortality due to cardivascular diseases	Gender, Alcohol Intake, Apolipoproteins, BMI	Women reporting consumption of at least 80 g of alcohol monthly and consumption of 5 or more alcohol units during one drinking episode had a greater risk of cardiovascular death than abstainers; relative risk (RR) was 5.06 (95% confidence interval [95% CI], 1.54–16.7) and 3.21 (95% CI, 1.07–9.58), respectively. ApoB/ApoA1-ratio was the strongest predictor of CVD and all-cause death in men (RR, 7.62; 95% CI, 3.15–18.4; and RR, 4.39; 95% CI, 2.22–8.68, respectively) and CVD death in women (RR 3.12; 95% CI, 1.08–8.98). Men who were obese and had obtained a university education had a 40% lower risk of all-

										cause death. Low serum albumin was associated with high mortality in both genders
12	Estimation of all-cause and cardiovascular mortality risk in relation to leisure-time physical activity: a cohort study	Bacevičienė M	Medicina (Kaunas). 2012;48 (12):632-9	1992–2009	cohort and cross sectional	2642 men and women aged 35-64	Lithuania	Mortality due to cardivascular diseases	Physical activity	Multivariate adjusted Cox proportional hazards analyses revealed an HR of 1.46 (95% CI, 1.15-1.85) for all-cause mortality and 1.73 (95% CI, 1.23-2.45) for CVD mortality in the lowest quartile of leisure-time physical activity compared with the higher ones. As much as 16.2% of all-causemortality and 22.2% of CVD mortality was attributable to the lowest quartile of leisure-time physical activity
13	HYPEST study: profile of hypertensive patients in Estonia	Org E	BMC Cardiovasc Disord. 2011 Aug 31;11:55	2004-2007	cross-sectional	617 women and 390 men aged 18-85 years	Estonia	Hypertension	Age, Gender, Smoking, BMI, Dyslipidaemia, Thyroid gland diseases, Cardivascular diseases	The distribution of recruited men and women was 39% and 61% respectively. Majority of Estonian hypertension patients (85%) were overweight (BMI ≥ 25 kg/m2) and a total of 79% of patients had additional complications with cardiovascular system. In men, the hypertension started almost 5 years earlier than in women (40.5 ± 14.5 vs 46.1 ± 12.7 years), which led to earlier age of first myocardial infarction (MI) and overall higher incidence rate of MI among male patients (men 21.2%, women 8.9%, P < 0.0001). Heart arrhythmia, thyroid diseases, renal tubulo-intestinal diseases and hyperlipidemia were more prevalent in hypertensive women compared to men (P < 0.0001). An earlier age of HTN onset was significantly associated with smoking (P = 0.00007), obesity (BMI ≥ 30 kg/m2; P = 0.0003), increased stress (P = 0.0003) and alcohol consumption (P = 0.004).

14	Impact of abdominal obesity on the frequency of hypertension and cardiovascular disease in Poland - results from the IDEA study (international day for the evaluation of abdominal obesity)	Chrostowska M	Blood Press. 2011 Jun;20(3):145-52		cross-sectional	5371 patients of general practicioners aged 18-80 years	Poland	Cardivascular diseases, Hipertension	Waist circumference	Increasing Waist circumference (WC) was significantly associated with hypertension (HT) and CVD, after adjustment for age (p<0.001). The frequency of abdominal obesity(WC >102/88 cm) was higher in Poland than in North-West Europe (36% vs 33% in men and 54% vs 45% in women, respectively, p<0.0001). Similarly, the frequency of HT in Poland was higher than in North-West Europe (47 vs 36% in men and 45 vs 30% in women, respectively p<0.001). In Poland CVD was 1.7-fold more frequent in men and 2.5-fold more frequent in women, compared with North-West Europe.
15	Total cardiovascular risk estimation in Romania. Data from the SEPHAR study	Dorobantu M	Rom J Intern Med. 2008;46(1): 29-37	2005	cross-sectional	2017 subjects aged over 18 yrs, a representative sample for the Romanian adult population	Romania	Cardivascular diseases risk	Gender, Dislipidaemia, Blood pressure	Average total risk in Romanian adult population was 3.5%. Male population had a significantly higher risk than females (5.4% vs. 1.7%, p<0.01). About one fifth of subjects (20.7%) had a high risk > or = 5%. Four percent of subjects (all males) had a very high risk > or = 15%. The cardivascular risk risk was relatively homogeneously distributed between Romania's geographic regions. The prevalence of hypercholesterolemia as CV risk factor was high (40%), and also was the prevalence of high systolic blood pressure (36.6%). The prevalence of smoking was similar to other European countries (27%
16	Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study	Yusuf S	Lancet. 2004 Sep 11-17;364(9438):937-52		case control	52 countries, representing every inhabited continent. 15152 cases and 14820 controls enrolled	Croatia, Czech Republic, Hungary, Poland, Russia	Myocardial infraction	Smoking, Diabetes, Hypertension, Apo lipoprotein, Alcohol intake, Dietary pattern	Smoking (odds ratio 2.87 for current vs never, PAR 35.7% for current and former vs never), raised ApoB/ApoA1 ratio (3.25 for top vs lowest quintile, PAR 49.2% for top four quintiles vs lowest quintile), history of hypertension (1.91, PAR 17.9%), diabetes (2.37, PAR 9.9%), abdominal obesity (1.12 for top vs lowest tertile and 1.62 for middle vs lowest tertile, PAR 20.1% for top two tertiles vs lowest tertile), psychosocialfactors (2.67, PAR 32.5%), daily consumption of fruits and vegetables (0.70, PAR 13.7% for lack of daily consumption), regular

										alcohol consumption (0.91, PAR 6.7%), and regular physical activity (0.86, PAR 12.2%), were all significantly related to acute myocardial infarction (p<0.0001 for all risk factors and p=0.03 for alcohol). These associations were noted in men and women, old and young, and in all regions of the world. Collectively, these nine risk factors accounted for 90% of the PAR in men and 94% in women.
17	Visit-to-Visit Blood Pressure Variability and Arterial Stiffness Independently Predict Cardiovascular Risk Category in a General Population: Results from the SEPHAR II Study	Darabont R	Hellenic J Cardiol. 2015 May-Jun;56(3):208-16	2011-2012	cross-sectional	1975 individuals aged 18-80 year	Romania	Hypertension, Cardivascular risk	Dislipidaemia, Obesity, Diabetes, Metabolic syndrome	Mean blood pressure (SBP) was 132.37/82.01 mmHg. Mean systolic pressure variability (BPV) was 6.16 mmHg, with 24.62% of values above the 75th percentile (8.48 mmHg). Factors found to be associated with high systolic BPV were age, SBP, pulse pressure, total and LDL-cholesterol, triglycerides, visceral obesity, diabetes mellitus, metabolic syndrome and increased aortic stiffness. In addition, in the hypertensive group high BPV was associated with the severity of hypertension and a lack of treatment control. Both visit-to-visit systolic BPV and aortic stiffness proved to be positively andindependently correlated with the risk category. Based on these parameters it was possible to predict with 72.6% accuracy the probability of finding subjects in a high and very high cardiovascular risk category.

18	The global risk for cardiovascular death in the adult Polish population: Prospective assessment of the cohorts studied within the Multi-center national Research on the Polish population Health Status (WOBASZ and WOBASZSenior)	Piotrowski W	Kardiol Pol. 2015 Sep 14.	2003–2005 and 2007	cohort cross-sectional	14769 persons examined in the age 20-74 and in 2007 1096 persons examined in the age above 74	Poland	Cardivascular risk, Mortality due to cardivascular diseases	Age, Gender, Smoking, Dislipidaemia	The period the mortality because of CVD constituted 8 years of observation in WOBASZ examining the 38% amongst men and the 31% amongst women of the whole of deaths. At men they were the most frequent causes of the cardiological death: coronary heart disease of the 33% and angiopathies of the brain of the 17%, whereas at women - angiopathies of the brain of the 31% and coronary heart disease of the 23%. They stated essential statistically diversifying curves of the experience both of general mortality ($p < 0.0001$) between men and women, as well as mortalities because of CVD ($p < 0.0001$). For the mortality amongst men and women almost all chosen factors turned out to be the whole essential statistically in analyses univariate, except for the level HDL and the indicator of atherogenics at men and the status of smoking at women. As in multivariate analysis for men turned out to be independent: age, glucose level, pressure level arterial systolic and status of the smoking. At women whereas - independent predictors were: age, status of the smoking and diabetes. In the period the mortality because of CVD constituted 5 years in the WOBASZ Senior examination of the population of the 48% amongst men and the 58% amongst women of the whole of deaths. Both at men, and at women a coronary heart disease was the most frequent causes of the cardiological death, appropriately 29 and 24%, and then angiopathies of the brain, appropriately 16 and 21%. amongst elderly patients they stated essential statistically diversifying curves of surviving for the mortality with the whole between men and women ($p < 0.0001$), however statistical diversifying the caused CVD mortality wasn't stated ($p = 0.0755$).

19	Factors and estimation of risk for cardivascular diseases among patients in primary health care in Central Serbia	Đokić B	Cent Eur J Public Health. 2015 Sep;23(3):195-9		cross-sectional	505 men and 548 women	Serbia	Cardivascular diseases, Dislipidaemia, Diabetes	Gender, Age, Smoking, BMI	68.8% of people were overweight and obese, arterial hypertension was noted in 72.6%, and diabetes type II in 13.3% of people. 67.6% of people had a high level of total cholesterol in blood serum and 39.6% of people had a high level of triglycerids in blood serum. The metabolic syndrome was noted in 44.3%, and 3 or more risk factors forcardiovascular disease were noted in 65% of the population. We determined a significant statistic difference for age, smoking, nutritional status, dyslipidemia, and diabetes
20	Physical Comorbidities in Depression Co-Occurring with Anxiety: A Cross Sectional Study in the Czech Primary Care System	Winkler P	Int J Environ Res Public Health. 2015 Dec 10;12(12)	2010-2011	cross-sectional	4264 patients aged 18-98	Czech Republic	Comorbidity of depression		There were 51.29% of those who have a physical comorbidity, and 45.5% of those who have a comorbid anxiety disorders among patients treated withdepression in Czech primary care. Results of logistic regressions show that odds of having pain, hypertension or diabetes mellitus are particularly elevated at those who have co-occuring depressive and anxiety disorder. Our findings demonstrate that comorbidities associated with depressive disorders are highly prevalent in primary health care practice, and that physical comorbidities are particularly frequent among those with co-occurringdepressive and anxiety disorders
21	Health factors and risk of all-cause, cardiovascular, and coronary heart disease mortality: findings from the MONICA and HAPIEE studies in Lithuania	Tamosiunas A	PLoS One. 2014 Dec 5;9(12):e114283	1983–2008	cohort cross-sectional	9209 men and women aged 45-64 (7648 were free from coronary heart disease (CHD) and stroke at baseline)	Lithuania	Cardivascular diseases	Gender, Blood pressure, Smoking, Dislipidaemia, Physical activity	Between 1983 and 2008, the proportion of subjects with 6 healthy levels of risk factors was higher in 2006-2008 than in 1983-1984 (0.6% vs. 0.2%; p = 0.09), although there was a significant increase in fasting glucose and a decline in intermediate physical activity. Men and women with normal or intermediate levels of risk factors had significantly lower all-cause, CVD and CHD mortality risk than persons with high levels of riskfactors. Subjects with 5-6 healthy factors had hazard ratio (HR) of CVD mortality 0.35 (95% confidence interval (CI) 0.15-0.83) compared to averagerisk in the whole population. The hazard ratio for CVD mortality risk was significant in men (HR 0.34,

										95% CI 0.12-0.97) but not in women (HR 0.38, 95% CI 0.09-1.67).
22	Inclusion of hazardous drinking does not improve the SCORE performance in men from Central and Eastern Europe: the findings from the HAPIEE cohorts	Vikhireva O	BMC Public Health. 2014 Nov 20;14:1187.	2002-2005	cohort	8927 men participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)	Czech Republic, Poland, Russia	Mortality due to cardivascular diseases	Alcohol, Drinking pattern	In HAPIEE men, the baseline levels of the high-risk SCORE ≥5% significantly predicted fatal CVD. After controlling for the high-risk SCORE, binge drinking (drinking ≥100 g of ethanol at least once a month) and problem drinking (≥2 positive answers to CAGE questionnaire) were inconsistently associated with fatal CVD. No marked improvement in calibration and discrimination was observed for the high-risk SCORE extended by these hazardous drinking indicators, and all values of integrated discrimination improvement were <0.5%.
23	Healthy diet indicator and mortality in Eastern European populations: prospective evidence from the HAPIEE cohort	Stefler D	Eur J Clin Nutr. 2014 Dec;68(12):1346-52. doi: 10.1038/ejcn.2014.134. Epub 2014 Jul 16	2002-2005	cohort	18 559 adults aged: 45-69 years participants of the Health Alcohol and Psychosocial factors in Eastern Europe (HAPIEE)	Czech Republic, Poland, Russia	Mortality due to cardivascular diseases	Diet patterns	After adjusting for covariates, healthy diet indicator was inversely and statistically significantly associated with cardiovascular disease (CVD) and coronary heart disease (CHD) mortality, but not with other cause-specific and all-cause mortality in the pooled sample. Hazard ratios per one standard deviation (s.d.) increase in HDI score were 0.95 (95% confidence interval=0.89-1.00, P=0.068), 0.90 (0.81-0.99, P=0.030) and 0.85 (0.74-0.97, P=0.018) for all-cause, CVD and CHD mortality, respectively. Population attributable risk fractions for low HDI were 2.9% for all-cause, 14.2% for CVD and 10.7% for CHD mortality

24	Trends in prevalence of dyslipidaemias and the risk of mortality in Lithuanian urban population aged 45-64 in relation to the presence of the dyslipidaemias and the other cardiovascular risk factors	Luksiene D	PLoS One. 2014 Jun 23;9(6):e100158. doi: 10.1371/journal.pone.0100158. eCollection 2014	1983–2008	cohort cross-sectional	9209 subjects aged 45-64	Lithuania	Mortality due to cardivascular diseases	Dislipidaemia	During 25 year period the prevalence of normal total cholesterol level (<5.2 mmol/L) significantly increased only in women; triglycerides and high density lipoprotein (HDL) cholesterol did not change in men and women. Findings in our longitudinal study showed that in men and women mixed dyslipidaemias (HDL cholesterol <1.03 mmol/L plus triglycerides ≥1.70 mmol/L) significantly increased the risk for all-cause and CVD mortality(respectively in men HR = 1.30; HR = 1.15, in women HR = 1.83; HR = 2.13). These mixed dyslipidaemia combinations combination with the other riskfactors such as arterial hypertension, high fasting glucose level increased all-cause and CVD mortality risk in men and women; while, these mixeddyslipidaemias plus smoking increased all-cause and CVD mortality risk only in men compared to never smokers without these dyslipidaemias(respectively HR = 1.89; HR = 1.92); and these dyslipidaemias plus obesity increased all-cause and CVD mortality risk in women (respectively HR = 2.25; HR = 2.39) and CVD mortality risk in men (HR = 1.72), as compared to responders without obesity and these dyslipidaemias.
25	The contribution of educational class in improving accuracy of cardiovascular risk prediction across European regions: The MORGAM Project Cohort Component	Ferrario MM	Heart. 2014 Aug;100(15):1179-87		systematic review	68455 40-64-year-old men and womenfrom 47 prospective cohorts	Lithuania, Poland, Russia	Mortality due to cardivascular diseases	SCORE risk, Education	The lowest educational class was associated with higher CVD mortality in men (pooled age-adjusted HR=1.64, 95% CI 1.42 to 1.90) and women (HR=1.31, 1.02 to 1.68). In men, the HRs ranged from 1.3 (Central Europe) to 2.1 (Eastern Europe and Russia). After adjustment for the SCORE risk, the association remained statistically significant overall, in the UK and Eastern Europe and Russia. Education significantly improved discrimination in all European regions and classification in Nordic countries (clinical NRI=5.3%) and in Eastern Europe and Russia (NRI=24.7%). In women, after SCORE risk adjustment, the association was not statistically significant, but the reduced number of deaths plays a major role, and the addition of education led to improvements in discrimination

										and classification in the Nordic countries only
26	Does inclusion of education and marital status improve SCORE performance in central and eastern europe and former soviet union? findings from MONICA and HAPIEE cohorts	Vikhireva O	PLoS One. 2014 Apr 8;9(4):e94344.	1985-1995 2002-2005	cohort	14969 participants from MONICA study (MONItoring of trends and determinants in CArdiovascular disease) and 19900 participants of HAPIEE study (Health, Alcohol, and Psychosocial factors In Eastern Europe)	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	SCORE risk	In MONICA and HAPIEE, the high-risk SCORE ≥5% at baseline strongly and significantly predicted fatal CVD both before and after adjustment for education and marital status. After controlling for SCORE, lower education and non-married status were significantly associated with CVD mortality in some samples. SCORE extension by these additional risk factors only slightly improved indices of calibration and discrimination (integrated discrimination improvement <5% in men and ≤1% in women).
27	Is there an association between depressive symptoms and coronary artery disease in the Polish adult population?	Piwoński J	Kardiol Pol. 2014;72(1):50-5	2003-2005	cohort cross-sectional	A random sample of the Polish population (6392 men and 7153 women), aged 20-74 years from Multicenter Polish Population Health Status Study-WOBASZ	Poland	Coronary Heart Disease	Depression	In the examined population, coronary arterial disease (CAD) was found in 12.1% of men and 11.0% of women. Persons with CAD were older, more often finished their education at the level of primary school and lived in large communes, and more often had obesity, hypertension, diabetes and hyperlipidaemia compared to those without CAD. DS were found twice more often in persons with CAD compared to those without CAD, both in men and women. Subjects with DS were twice more likely to have CAD (men: odds ratio [OR] 2.14, 95% confidence interval [CI] 1.78-2.56; women: OR 2.03, 95% CI 1.70-2.43) and arrhythmia (women), and 1.5-fold more likely to report myocardial infarction and arrhythmia

28	SCORE performance in Central and Eastern Europe and former Soviet Union: MONICA and HAPIEE results	Vikhireva O	Eur Heart J. 2014 Mar;35(9):571-7	1985-1995 2002-2005	cohort	14969 participants from MONICA study (MONItoring of trends and determinants in CArdiovascular disease) and 19900 participants of HAPIEE study (Health, Alcohol, and Psychosocial factors In Eastern Europe)	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	SCORE risk	The cohorts based on the World Health Organization MONitoring of trends and determinants in CArdiovascular disease (MONICA) surveys in the Czech Republic, Poland (Warsaw and Tarnobrzeg), Lithuania (Kaunas), and Russia (Novosibirsk) were followed from the mid-1980s. The Health, Alcohol, and Psychosocial factors in Eastern Europe (HAPIEE) study follows Czech, Polish (Krakow), and Russian (Novosibirsk) cohorts from 2002-05. In Cox regression analyses, the high-risk SCORE ≥5% at baseline significantly predicted CVD mortality in both MONICA [n = 15 027; hazard ratios (HR), 1.7-6.3] and HAPIEE (n = 20 517; HR, 2.6-10.5) samples. While SCORE calibration was good in most MONICA samples (predicted and observed mortality were close), the risk was underestimated in Russia. In HAPIEE, the high-risk SCORE overpredicted the estimated 10 year mortality for Czech and Polish samples and adequately predicted it for Russia. SCORE discrimination was satisfactory in both MONICA and HAPIEE
29	New cardiovascular risk factors and their use for an accurate cardiovascular risk assessment in hypertensive patients	Tautu OF	Maedica (Buchar). 2014 Jun;9(2):127-34	2011-2012	cross-sectional	424 adult hypertensive subjects identified in the national representative SEPHAR II	Romania	Hypertension	SCORE risk	The mean blood pressure (BP) value of the study group was 148.46±19.61 mmHg. Over forty percent of hypertensives had a high and very high cardivascular (CV) risk. Predictors of high/very high CV risk category validated by regression analysis were: increased visit-to-visit BP variability (OR: 2.49; 95%CI: 1.67-3.73), aortic pulse wave velocity (OR: 1.12; 95%CI: 1.02-1.22), RT (OR: 0.95; 95% CI: 0.93-0.98), systolic blood pressure (OR: 1.01; 95%CI: 1.01-1.03) and atherogenic index of plasma (OR: 7.08; 95%CI: 3.91-12.82)

30	Socioeconomic inequalities in all-cause mortality in the Czech Republic, Russia, Poland and Lithuania in the 2000s: findings from the HAPIEE Study	Vanden heede H	J Epidemiol Community Health. 2014 Apr;68(4):297-303	2002-2005	cohort	16 812 men and 19 180 women aged 45-69 years participants of HAPIEE study	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	Gender, Age,Education	Mortality inequalities by the three SEP indicators were observed in all samples. The magnitude of inequalities varied according to gender, country and SEP measure. As expected, given the high mortality rates in Russian men, largest absolute inequalities were found among Russian men (educational slope index of inequality was 19.4 per 1000 person-years). Largest relative inequalities were observed in Czech men and Lithuanian subjects. Disadvantage by all three SEP measures remained strongly associated with increased mortality after adjusting for the other SEP indicators.
31	Cardiovascular disease risk factors associated with low level of physical activity in postmenopausal Polish women	Lwow F	Gynecol Endocrinol. 2013 Jul;29(7):683-6.		cross-sectional	343 postmenopausal Polish women selected from an urban population, aged 50-60	Poland	Cardivascular risk	Physical activity	In the tested sample, a low level of physical activity significantly increased odds ratios for CVD risk factors such as BMI ≥ 30 kg/m(2), total body fat (TBF) > 75 th percentile, gynoid fat deposit (GFD) > 75 th percentile, total cholesterol (TC) ≥ 5 mM, low-density lipoprotein cholesterol (LDL-C) > 3 mM and HOMA ≥ 1.95
32	Trends in prevalence, awareness, treatment, and control of hypertension, and the risk of mortality among middle-aged Lithuanian urban population in 1983-2009	Reklaitiene R	BMC Cardiovasc Disord. 2012 Aug 31;12:68.	1983-2002	cross-sectional	4709 subjects from from MONICA study and HAPIEE studies	Lithuania	Hypertension	Age, Gender	In men during 1983–2002 period hypertension prevalence was 52.1–58.7% and did not significantly change whereas in women decreased from 61.0 to 51.0%. There was a significant increase in hypertension awareness among hypertensive men and women (45.0 to 64.4% and 47.7 to 72.3%, respectively) and in treated hypertensives (55.4 to 68.3% in men and 65.6 to 86.2% in women). Adjusted Cox proportional hazard regression analyses revealed a strong dose–response association between blood-pressure level and all-cause, CVD, CHD and stroke-mortality risk in both men and women groups

33	Is level of social support associated with health behaviours modifying cardiovascular risk? Results of theWOBASZ study	Piwońska i J	Kardiol Pol. 2012;70(8):803-9	2003-2005	cross-sectional	The random sample of Polish population of 6164 men and 6915 women, aged 20-74 from National Multicenter Health Survey (WOBASZ)	Poland	Cardivascular risk	Measured social support level, Gender	31% of men and 39% of women had low social support level (SSL) and they more often had high cardiovascular risk, depressive symptoms andcardiovascular disease risk factors, especially women. Men and women with low SSL more often smoked cigarettes than those with high SSL, rarely try to quit smoking, made regular physical activity, and rarely self-measured their blood pressure. Additionally men more often drank alcohol ≥ 30.0 g/day. They also more often did not take the prescribed medication, although they bought them. Out of unhealthy elements, lack of regular physical activity and blood pressure self-measuring were significantly and independently associated with SSL in both genders and additionally smoking habit and lack of quit smoking in the past in women
34	Associations between risk factors in childhood (12-13 years) and adulthood (48-49 years) and subclinical atherosclerosis: the Kaunas Cardiovascular Risk Cohort Study	Ceponiene I	BMC Cardiovasc Disord. 2015 Aug 18;15:89	1977-2012	cohort	380 adults aged 48-49 from Kaunas Cardiovascular Risk Cohort study	Lithuania	Atherosclerosis, Arterial stiffness	Childhood and adulthood cardiavascular risk factors	In linear regression model with childhood variables childhood systolic blood pressure (BP) (β = 0.014; p = 0.016) and BMI (β = 0.006; p = 0.003) were directly associated with intima-media thickness (IMT) only in women. When adulthood variables were included into regression model, the association between childhoodsystolic BP and IMT remained significant (β = 0.013; p = 0.021), while childhood BMI was not associated with IMT (β = 0.003; p = 0.143). Additionally, association of adult smoking and IMT was found in women (β = 0.033; p = 0.018). IMT of men was directly related to adult systolic BP (β = 0.022; p = 0.018) and inversely to HDL cholesterol level (β = -0.044; p = 0.021). Pulse wave velocity (PWV) was directly associated only with adult systolic BP in both genders (β = 0.729 for men and β = 0.476 for women; p = 0.001)

35	The impact of early menopause on risk of coronary artery disease (PREmature Coronary Artery Disease In Women-PRECADIW case-control study	Lubiszewska B	Eur J Prev Cardiol. 2012 Feb;19(1):95-101	2005-2008 2003-2005	case-control	Case: 323 women (less than 55 years) with established crooronary artery disease Control: 347 age-matched healthy women selected from National Multicenter Health Survey (WOBASZ)	Poland	Coronary artery disease in women	Hypertension, Diabetes, Menopause	In multivariate analysis smoking, parental history of premature CVD, diabetes, menopause and hypertension were the strongest riskmarkers for premature CAD with ORs (95% CI): 3.83 (2.52-5.82); 3.08 (1.85-5.14); 2.89 (1.59-5.23); 2.82 (1.91-4.19); 2.39 (1.16-3.54). The most significant association was found for early postmenopause in a model including the early and late stage of postmenopause (≤ and >3 years of its onset), with OR 4.55 (95% CI 2.82-7.35), higher than other risk factors. The receiver operating characteristic (ROC) curves area revealed a significant increase from 0.81 in that model that included traditional risk factors and parental premature CVD to 0.85 after addition of the early and late stage of postmenopause
36	A cross-sectional study of cardiovascular disease and associated factors	Islami F	Ann Agric Environ Med. 2011 Dec;18(2):255-9	2010-2011	cross-sectional cohort	3853 participants, aged 45-64 from PONS study	Poland	Self-reported cardivascular disease	Gender, Hypertension, Diabetes, Alcohol paterrns	Prevalence of chronic diseases among participants was as follows: hypertension, 38.4%; diabetes, 5.9%; and CVD, 11.0%. There was no association between CVD and gender and place of residence. CVD was associated with ever-smoking (OR= 1.25; 95% CI: 1.00-1.55), whereas there was an inverse association with alcohol drinking in the year preceding enrolment in the study (OR= 0.50; 95% CI: 0.39-0.63). CVD wasassociated with body mass index (BMI), as well as with measures of abdominal adiposity, in the following order: waist to height ratio>waist circumference>waist to hip ratio; however, none of these measures showed a stronger association with CVD than BMI. Both hypertension (OR= 1.33; 95% CI: 1.05-1.68) and diabetes (OR= 1.33; 95% CI: 1.05-1.68) were associated with CVD in adjusted models

37	Awareness of cardiovascular prevention methods among residents of post-communist Polish provinces with highest mortality rates	Pikala M	Cent Eur J Public Health. 2011 Dec;19(4):183-9		cross-sectional	2211 (51.9% women) aged 20-74 years from Łódź and Lublin voivodeships participating in the National Polish Health Survey WOBASZ	Poland	Awareness of healthy lifestyle behaviours	Gender, Age	Approximately 68% of participants, had poor awareness of preventive methods and majority of them were not able to name any specific approach. Most often mentioned method of cardivascular disease (CVD) prevention was relaxing/avoiding stress (51.2%). The least known healthy behaviour was a reduction of salt intake and adequate fruit/vegetables consumption, mentioned by 18.2% and 23%, respectively. About 16.4% of women and 23% of men with risk factors of CVD were not aware of any non-pharmacological preventive method. Poor knowledge of CVD prevention was significantly more prevalent among persons aged > or = 65 years, with elementary education level, lower income, living in the rural settings, declaring poor self-rated health. Dietary and physical activity advice given by a primary care physician was significantly related to better knowledge among men with CVD risk factors
38	Is the cardiovascular risk profile of people living in Roma settlements worse in comparison with the majority population in Slovakia?	Babinska I	Int J Public Health. 2013 Jun;58(3):417-25		cross-sectional	452 Roma people (mean age = 34.7, 35.2 % men) and 403 non-Roma (mean age = 33.5, 45.9 % men)	Slovakia	Cardivascular risk	Gender, Ethnic status	Roma were more likely to have obesity, low HDL cholesterol, normal total cholesterol, and to smoke than non-Roma. Moreover, Romawomen were more likely to have abdominal obesity and Roma men to have normal LDL cholesterol than non-Roma. No significant differences by ethnicity were found regarding hypertriglyceridaemia, hyperglycaemia and hypertension.

39	Predictive impact of coronary risk factors in southern Croatia: a case control study.	Carević V	Coll Antropol. 2010 Dec;34(4)		case-control	Croatian arm of INTERHEART study	Croatia	Myocardial infraction	Gender, Age, Smoking, BMI, Hypertension	The main identified MI risk factors in Southern Croatia were heavy smoking (>20 cig/day; OR 3.86; 95% CI 2.31-6.46), diabetes mellitus (OR 2.83; 95% CI 1.58-5.23), abnormal ratio of B-100 and A-1 apolipoproteins (OR 2.23; 95% CI 1.28-3.89), elevated waist to hip ratio (OR 1.96; 95% CI 1.21-3.18), and arterial hypertension (OR 1.68; 95% CI 1.15-2.45). Protective was moderate alcohol consumption (OR 0.63; 95% CI 0.40-0.99). The prevalence of major MI risk factors in Croatia is similar to that in the surrounding countries and in the world, accounting for over 90% of the population attributable risk. However, physical activity, dietary and psychosocial factors are seemingly less important in this country, while moderate alcohol consumption is more protective than regionally or globally.
40	Neighbourhood socioeconomic status and cardiovascular risk factors: a multilevel analysis of nine cities in the Czech Republic and Germany	Dragano N	BMC Public Health. 2007 Sep 21;7:255	2000-2003 2002-2005	cohort	11 554 men and women from nine German and one Czech towns (combined Heinz Nixdorf Recall (HNR) Study and HAPIEE	Czech Republic	Mortality due to cardivascular diseases	Gender, Education, Smoking, Income	Smoking, obesity and low physical activity were more common in deprived neighbourhoods in Germany, even when personal characteristics including individual education were controlled for. For hypertension associations were weak. In the Czech Republic associations were observed for smoking and physical inactivity, but not for obesity and hypertension when individual-level covariates were adjusted for. The strongest association was found for smoking in both countries: in the fully adjusted model the odds ratio for 'high unemployment rate' was 1.30 [95% CI 1.02-1.66] in the Czech Republic and 1.60 [95% CI 1.29-1.98] in Germany
41	Characteristics of patients with coronary artery disease managed on an outpatient basis in the population of Poland. Results of the	Banasiak W	Kardiol Pol. 2007 Feb;65(2):132-40		cross-sectional	2593 patients with coronary artery disease	Poland	Coronary Arterial Disease	Age, Dyslipidaemia, Blood pressure	Coronary artery disease (CAD) was confirmed predominantly based on a history of myocardial infarction (50.1%), followed by positive electrocardiographic stress test (38.8%), history of typical angina in subjects at the age of >60 years (36.4%), history of previous acute coronarysyndrome (29.0%), PCI (22.1%) or CABG (14.3%) or positive coronary angiography (17.6%). In patients with diagnosed stable CAD, 44.6% were women and the mean age was

	multicentre RECENT trial									65.0+/-9.8 years. Among patients with a history of hypertension (78.0%), only 34.0% had blood pressure within the normal range. History of dyslipidaemia was positive in 57.6% of patients. Normal LDL cholesterol concentrations (<3.36 mmol/L) were found in 56.7% of patients. A family history of CAD had 17.3% of subjects, 23.5% had previously detected diabetes mellitus and 11.0% were active smokers at the time of study enrolment. Overweight or obesity both in men and women was found in 79.3% of patients while metabolic syndrome (diagnosed according to NCEP ATP III criteria) was found in 31.3%. The following comorbidities were detected: 34.3% presented symptoms of congestive heart failure, 32.1% had rhythm or conduction disturbances (most commonly atrial fibrillation--in 19.0% of cases). Previous stroke was noted in 4.7% ofpatients with CAD and transient ischaemic attack in 5.5%. Peripheral artery disease was observed in 9.9% of CAD patients, whereas asthma or COPD--in 9.0%
42	Do lipids contribute to the lack of cardio-protective effect of binge drinking: alcohol consumption and lipids in three eastern European countries	Peasey A	Alcohol Alcohol. 2005 Sep-Oct;40(5):431-5. Epub 2005 Jun 6	2002-2005	cohort cross-sectional	282 men aged 45-64 years from HAPIEE study	Czech Republic, Lithuania, Poland, Russia,	Dislipidaemia	Alcohol, Drinking pattern	Annual intake of alcohol was positively associated with total and HDL cholesterol. After controlling for annual intake, the frequency of heavy binge drinking was associated with increased concentrations of total and HDL cholesterol. By combining annual intake and drinking pattern, we found that men consuming >8 l of alcohol per year who had a heavy binge at least once a month had the mean total, HDL and LDL cholesterol 1.69 (SE 0.35), 0.61 (0.11) and 0.97 (0.34) mmol/l, respectively, higher than non-drinkers; this resulted in more favourable ratios of total and LDL cholesterol relative to HDL cholesterol in frequent heavy bingers. Triglycerides were not related to alcohol intake or binge drinking.

43	Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study	Rosengren A	Lancet. 2004 Sep 11-17;364(9438)		case control	11119 patients with a first myocardial infarction and 13648 age-matched (up to 5 years older or younger) and sex-matched controls from 262 centres	Croatia, Czech Republic, Hungary, Poland, Russia	Myocardial infraction	Gender, Age, Mental health, Smoking	People with myocardial infarction (cases) reported higher prevalence of all four stress factors (p<0.0001). Of those cases still working, 23.0% (n=1249) experienced several periods of work stress compared with 17.9% (1324) of controls, and 10.0% (540) experienced permanent work stress during the previous year versus 5.0% (372) of controls. Odds ratios were 1.38 (99% CI 1.19-1.61) for several periods of work stress and 2.14 (1.73-2.64) for permanent stress at work, adjusted for age, sex, geographic region, and smoking. 11.6% (1288) of cases had several periods of stress at home compared with 8.6% (1179) of controls (odds ratio 1.52 [99% CI 1.34-1.72]), and 3.5% (384) of cases reported permanent stress at home versus 1.9% (253) of controls (2.12 [1.68-2.65]). General stress (work, home, or both) was associated with an odds ratio of 1.45 (99% CI 1.30-1.61) for several periods and 2.17 (1.84-2.55) for permanent stress. Severe financial stress was more typical in cases than controls (14.6% [1622] vs 12.2% [1659]; odds ratio 1.33 [99% CI 1.19-1.48]). Stressful life events in the past year were also more frequent in cases than controls (16.1% [1790] vs 13.0% [1771]; 1.48 [1.33-1.64]), as was depression (24.0% [2673] vs 17.6% [2404]; odds ratio 1.55 [1.42-1.69]). These differences were consistent across regions, in different ethnic groups, and in men and women.
44	Epidemiology of physical activity in adult Polish population in the second decade of the 21st century. Results of the NATPOL 2011 study	Drygas W	Int J Occup Med Environ Health. 2013 Dec;26(6)	2011	cross-sectional	2413 randomly selected individuals (51.5% women) aged 18-79 years, who participated in the Nationwide Study of Occurrence of Risk Factors of	Poland	Physical activity	Gender, Age	About 48.2% of adults do exercise for at least 30 minutes on most days of a week. About 11% of the respondents declare a sedentary lifestyle. About 26.5% of working population report hard physical work, while sedentary work is reported by 47.6% of the employed participants. Active commuting is declared by 27.3% of working/studying population. About 47.2%, 36.6%, and 15.3% spend < 15, 15-30, and > 30 min per day, respectively, on this kind of PA

						Cardiovascular Diseases NATPOL 2011				
45	Homocysteine concentration and the risk of death in the adult Polish population	Waśkiewicz A	Kardiol Pol. 2012;70(9):897-902	2003-2009	cohort	7165 men and women aged 20-74 - participants of WOBASZ study (Polish Multi-centre Population Health Survey)	Poland	Mortality due to cardivascular diseases	Homocysteine concentration, Gender, Smoking, BMI, Diabetes, Dyslipidaemia	During the 38,818.9 person-years of follow-up there were 270 deaths including 108 due to cardivascular disease (CVD), 37 due to coronary heart disease and 21 due to stroke. The relative risk of all-cause and CVD mortality was significantly higher in the highest (> 10.51 µmol/L) compared to the lowest (< 8.20 µmol/L) Hcy tercile in crude and multivariable proportional hazards models adjusted for sex, age, smoking status, hypertension, body mass index, total cholesterol, glucose and high sensitivity-C-reactive protein. Hazards ratios (95% confidence intervals) were as follows: all-cause mortality HR (95% CI): crude = 4.528 (2.947-6.154), multivariable-adjusted = 1.766 (1.197-2.605), CVD mortality crude = 4.322 (2.426-7.700), multivariable- -adjusted = 1.937 (1.051-3.569)
46	Prevalence of classical risk factors in Polish women with premature coronary artery disease	Lubiszewska B	Kardiol Pol. 2010 Sep;68(9):1032-7	2008	case-control	330 female 〈 55 years with acute coronary syndrome and control of 347 age-matched healthy women from WOBASZ study (Polish Multi-centre Population Health Survey)	Poland	Coronary artery disease	Hypertension, Dislipidaemia, Diabetes, Smoking	Compared to age-matched healthy controls, women with premature cronary disease (CAD) had a very high prevalence of traditional risk factors - hypercholesterolaemia (82% vs 68%), smoking (current and former) (81% vs 48%), and hypertension (68% vs 42%). Women with premature CAD had 4.3 times more often diabetes, 1.68 times smoking and 1.63 times hypertension compared to controls. At least one of five classical risk factorswas present in 98.8% of patients, compared to 89% in controls, while 10% of patients vs 1.4% of controls had all five of them.

47	Cardiovascular disease (CVD) risk factors in older adults – Perception and reality	Mazalin Protulip ac J	Arch Gerontol Geriatr. 2015 Jul-Aug;61(1)	2011	cross-sectional	969 subjects aged >70 years	Croatia	Cardivascular risk		The actual presence of cardivascular disease (CVD) risk factors in participants did not appear to alter their perceptions of risk compared to participants withoutCVD risk factors (the percentage of participants who think that they have moderate/high CVD risk is almost the same: 75.5% among participants with actual CVD risk factors; 75.7% among those without CVD risk factors). Accordingly, 24.5% of participants with actual CVD risk factors failed to recognize that risk. Only 23.4% of participants correctly recognized blood pressure (BP) target values, while 49.8% participants successfully recognized TC target levels. The knowledge of target BP and/or cholesterol (TC) levels did not influence participants' ability to assess their own CVD risk. Surprisingly, 41.8% of participants reported that they have not discussed CVD risk factors with their physicians.
48	Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium.	Mons U	BMJ. 2015 Apr 20;350:h1551		systematic review	503905 participants >60 years	Czech Republic, Lithuania, Poland, Russia,	Mortality due to cardivascular diseases	Smoking	Random effects meta-analysis of the association of smoking status with cardiovascular mortality yielded a summary hazard ratio of 2.07 (95% CI 1.82 to 2.36) for current smokers and 1.37 (1.25 to 1.49) for former smokers compared with never smokers. Corresponding summary estimates for risk advancement periods were 5.50 years (4.25 to 6.75) for current smokers and 2.16 years (1.38 to 2.39) for former smokers. The excess risk in smokers increased with cigarette consumption in a dose-response manner, and decreased continuously with time since smoking cessation in former smokers. Relative risk estimates for acute coronary events and for stroke events were somewhat lower than for cardiovascular mortality, but patterns were similar.

49	The Rise and Fall of Hypertension: Lessons Learned from Eastern Europe	Bielecka-Dabrowa A	Curr Cardiovasc Risk Rep. 2011 Apr;5(2):174-179		case study		Poland, Russia	Hypertension	Gender, Age	Hypertension is a progressive cardiovascular syndrome that arises from many differing, but interrelated, etiologies. Hypertension is the most prevalent cardiovascular disorder, affecting 20% to 50% of the adult population in developed countries. Arterial hypertension is a major risk factor for cardiovascular diseases and death. Epidemiologic data have shown that control of hypertension is achieved in only a small percentage of hypertensive patients. Findings from the World Health Organization project Monitoring Trends and Determinants in Cardiovascular Diseases (MONICA) showed a remarkably high prevalence (about 65%) of hypertension in Eastern Europeans. There is virtually no difference however, between the success rate in controlling hypertension when comparing Eastern and Western European populations. Diagnosing hypertension depends on both population awareness of the dangers of hypertension and medical interventions aimed at the detecting elevated blood pressure, even in asymptomatic patients. Medical compliance with guidelines for the treatment of hypertension is variable throughout Eastern Europe. Prevalence ofhypertension increases with age, and the management of hypertension in elderly is a significant problem. The treatment of hypertension demands a comprehensive approach to the patient with regard to cardiovascular risk and individualization of hypertensive therapy

50	Metabolic syndrome in Russian adults: associated factors and mortality from cardiovascular diseases and all causes	Sidorenkov O	BMC Public Health. 2010 Sep 29;10:582	2000-20009	cross-sectional cohort	3555 adults aged 18-90 years	Russia	Mortality due to cardivascular diseases	Age, Metabolic syndrome, BMI, Smoking	After adjustment for all studied factors except BMI, age, serum GGT, C-reactive protein and AST-to-ALT ratio were associated with metabolic syndrome (MetS) in both genders. Additionally, MetS was associated with sedentary lifestyle in women and with smoking in men. In the same regression model drinking alcohol 2-4 times a month and consumption of five or more alcohol units at one occasion in men, and drinking alcohol 5 times or more a month in women were inversely associated with MetS. After a 9-year follow-up, MetS was associated with higher risk of death from stroke (RR = 3.76, 95% CI:1.35-10.46) and from either stroke or myocardial infarction (MI, RR = 2.87, 95% CI:1.32-6.23) in men. No associations between MetS and any of the studied causes of death were observed in women.
51	Perceived control as a predictor of cardiovascular disease mortality in Poland. The HAPIEE study.	Kozela M	Cardiol J. 2015;22(4):404-12	2002-2005	cohort	Random sample of 10 728 permanent residents of Krakow aged 45-69 from HAPIEE study	Poland	Mortality due to cardivascular diseases	Perceived control	Low perceived control was strongly associated with a higher CVD mortality, independently of age, education, marital status, history of CVD, hypertension, hypercholesterolemia, smoking, body mass index, physical activity or diabetes in both men and women (HR 2.68, 95% CI 1.36-5.31 and HR 5.18, 95% CI 1.17-22.96, respectively). After adjustment for age, both in men and women, the highest risk of death from all causes was observed in persons with low perceived control. Further adjustment for covariates attenuated the relationshi
52	Prevalence of lipid abnormalities in Poland. The NATPOL 2011 survey.	Zdrojewski T	Kardiol Pol. 2016;74(3):213-23	2011	cross-sectional	1168 males and 1245 females, aged 18-79 years from NATPOL 2011 study	Poland	Dislipidaemia	Age, Gender	Mean serum total cholesterol (TC) concentration was 197.1 mg/dL (95% CI 193.8-200.4) in males (M) and 198.6 mg/dL (95% CI 195.7-201.5) in females (F). Levels of LDL-C were 123.6 mg/dL (120.9-126.2) and 123.7 mg/dL (121.4-126.1), HDL-C - 45.8 mg/dL (44.7-47.0) and 54.1 mg/dL (53.1-55.1), TG - 140.9 mg/dL (133.0-148.8) and 104.0 mg/dL (99.8-108.2) for males and females, respectively. TC ≥ 190 mg/dL was found in 54.3% subjects (M 54.3%; F 54.4%). After adding patients on lipid-lowering treatment, hypercholesterolemia was present in 61.1% of adults (M 60.8%; F 61.3%). LDL-C ≥ 115 mg/dL was

										detected in 57.8% of all subjects (M 58.3%; F 57.3%), while HDL-C < 40 mg/dL in 35.2% of males and < 45 mg/dL in 22% of females TG ≥ 150 mg/dL was found in 21.1% of subjects (M 28.4%; F 14.0%). The highest prevalence of elevated TC and LDL-C levels was present in the age group of 40-59-year-olds. Of those with hypercholesterolemia 58.7% (M 61.5%, F 56.0%) were not aware of the condition; 22.0% (M 21.0%, F 24.5%) were aware but were not being treated; 8.1% (M 7.7%, F 8.5%) were treated but with TC ≥ 190 mg/dL; and only 10.9% (M 10.7%, F 11.0%) were being treated with TC < 190 mg/dL

Table 2. Outcomes of literature review in the area of metabolic diseases epidemiology in Eastern European countries

No.	Title	First author	Bibliographical informations	Years of study	Type of study	Population	Countries from Eastern Europe involved in study	Health problems	Main risk factors	Main outcomes
1	Does abdominal obesity have a similar impact on cardiovascular disease and diabetes? A study of 91,246 ambulant patients in 27 European countries.	Fox KA	Eur Heart J. 2009 Dec;30(24):3055-63	2005	cross-sectional	37 437 men and 53 809 women from 27 countries (IDEA study) including 30375 subjects from Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Russia, Slovakia, Slovenia, and Ukraine	Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Russia, Slovakia, Slovenia, and Ukraine	Diabetes, Overweight and obesity, Dyslipidaemia	Age, Gender, Waist circumference, BMI	Abdominal obesity predicted increased diabetes risk, despite socio-economic, demographic, and risk factor differences. Cardiovascular disease was at least two-fold more frequent in Eastern Europe vs. Northwest Europe ($P < 0.0001$) and 2.5-fold more vs. Southern Europe ($P < 0.0001$). Waist circumference (WC) predicted increased ($P < 0.0001$) age- and BMI-adjusted risks of CVD and diabetes. In women, odds ratios (95% confidence intervals) for CVD per 1 SD increase in WC were: Northwest Europe 1.28 (1.18-1.40); Southern Europe 1.26 (1.16-1.37); and Eastern Europe 1.10 (1.03-1.18). Values for diabeteswere 1.72 (1.58-1.88), 1.45 (1.35-1.56), and 1.59 (1.46-1.73), with similar findings in men.
2	Obesity and education in three countries of the Central and Eastern Europe: the HAPIEE study	Pikhart H	Cent Eur J Public Health. 2007 Dec	2002–2005	cross-sectional and cohort	25 482 men and women in aged 45-69 from Poland, Czech Rep and Russia	Poland, Czech Rep,Russia	Overweight and obesity	Age, Gender, Education	The prevalence of obesity (body-mass index > 30 kg/m2) was extremely high It ranged from 21% (Russia) to 30% (the Czech Republic) in men and from 32% (the Czech Republic) to 47% (Russia) in women. More than 70% of study subjects were overweight (body-mass index > 25 kg/m2)
3	Fitness, fatness and clustering of cardiovascular risk factors in children from Denmark, Estonia and Portugal: the European Youth Heart Study	Andersen LB	Int J Pediatr Obes. 2008;3 Suppl 1:58-66		cross-sectional	1769 children from Denmark, Estonia and Portugal	Estonia	Cardivascular diseases, Metabolic syndrome	Fitness, High blood presure, Lipids in blood	Both waist circumference and skinfolds were associated with clustered CVD risk. Odds ratios for clustered CVD risk for the upper quartiles compared with the lowest quartile were 9.13 (95% CI: 5.78-14.43) and 11.62 (95% CI: 7.11-18.99) when systolic blood pressure, triglyceride, insulin resistance homeostasis assessment model (HOMA) score, cholesterol:HDL, and fitness were included in the score. When fitness was removed from the clustered risk variable, the association for fatness attenuated and after further adjustment for fitness, only the highest quartiles of the fatness parameters were significant. Fitness showed

										the same strength of association with the clustered risk score including systolic blood pressure, triglyceride, HOMA score, and cholesterol:HDL with odds ratio for the upper quartile of 4.97 (95% CI: 3.20-7.73). Physical activity was associated with clustered risk even after adjustment for fitness and fatness with an odds ratio for the upper quartile of 1.81 (95% CI: 1.18-2.76).
4	The FTO gene and obesity in a large Eastern European population sample: the HAPIEE study	Hubacek JA	Obesity (Silver Spring). 2008 Dec;16(12)	2000-2005	cross-sectional and cohort	3079 males and 3602 females 45-69 years oldandomly selected from population registers of seven Czech cities	Czech Rep.	Obesity, Dyslipidaemia	FTO gene variant	The FTO rs17817449 variant was significantly associated with BMI both in males and females. The associations were not affected by adjustment for age, smoking, socioeconomic status, and physical activity. The FTO variant was also associated with waist circumference (difference between GG and TT was 1.1 cm (P = 0.043) in men and 2.4 cm (P < 0.001) in women) but this relationship disappeared after adjustment for BMI. Similarly, BMI explained the weak association of FTO with WHR and C-reactive protein. FTO was not associated with plasma total and high-density lipoprotein cholesterol, triglycerides, blood glucose, and blood pressure. These results confirm that in a Slavic population the FTO variant is strongly associated with BMI but not with other risk factors
5	Incidence of diabetes in the Polish population: results of the Multicenter Polish Population Health Status Study-WOBASZ	Polakowska M	Pol Arch Med Wewn. 2011 May;121(5)	2003-2005	cross-sectional and cohort	12567 randomly selected men and women aged 20 to 74 years who are participating in the WOBASZ (Polish National Multicentre Health Survey)	Poland	Metabolic syndrome	Socioeconomic characteristic, BMI, Smoking, Physical acitivity, Self-rated health	Metabolic Syndrome (MetS) was identified in 26.0% of men and 23.9% of women according to the AHA/NHLBI definition, and in 30.7% of men and 26.8% of women according to the IDF definition. In both genders older age, higher body mass index and current smoking increased the risk of developing MetS, whereas higher physical activity and good self-rated health decreased the risk. Moreover, women with higher education and in the higher quartile of alcohol intake were associated with a lower risk of having MetS. Household per-capita income did not affect the risk of having MetS in either gender
6	National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic	Danaei G	Lancet. 2011 Jul 2;378(9785):31-40	1980-2008	systematic review	Adults aged 25 years and more (370 country-years and 2·7 million participants) including		Diabetes	Age, Gender	In 2008, global age-standardised mean FPG was 5·50 mmol/L (95% uncertainty interval 5·37-5·63) for men and 5·42 mmol/L (5·29-5·54) for women, having risen by 0·07 mmol/L and 0·09 mmol/L per decade, respectively. Age-standardised adult diabetes prevalence was 9·8% (8·6-11·2) in men and 9·2% (8·0-10·5) in women in 2008, up from 8·3% (6·5-10·4) and 7·5% (5·8-9·6) in 1980. The number of people with diabetes increased from 153

	analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants.									(127-182) million in 1980, to 347 (314-382) million in 2008. We recorded almost no change in mean FPG in east and southeast Asia and central and eastern Europe. Oceania had the largest rise, and the highest mean FPG (6·09 mmol/L, 5·73-6·49 for men; 6·08 mmol/L, 5·72-6·46 for women) and diabetes prevalence (15·5%, 11·6-20·1 for men; and 15·9%, 12·1-20·5 for women) in 2008. Mean FPG and diabetes prevalence in 2008 were also high in south Asia, Latin America and the Caribbean, and central Asia, north Africa, and the Middle East. Mean FPG in 2008 was lowest in sub-Saharan Africa, east and southeast Asia, and high-income Asia-Pacific. In high-income subregions, western Europe had the smallest rise, 0·07 mmol/L per decade for men and 0·03 mmol/L per decade for women; North America had the largest rise, 0·18 mmol/L per decade for men and 0·14 mmol/L per decade for women
7	Metabolic syndrome in Poland - the PONS Study	Janszky I	Ann Agric Environ Med. 2011	2010-2011	cross-sectional and cohort	3862 adult males nad females from świętokrzyskie voivodhip in Poland	Poland	Metabolic sydrome, Abdominal obesity, High blood pressure, Glucose intolerance	Age, Gender	Overall, 1 518 participants (39.5%) had metabolic syndrome. The prevalence among females was 34.3% (877 females) vs. 49.9% (641 males) among males, and increased with age in both genders. Abdominal obesity was the most common abnormality (2,897 participants, 75.1%), followed by high blood pressure (2,741 participants, 71%), glucose intolerance (1,437 participants, 37.3%), elevated triglycerides (817 participants, 21.2%) and low HDL (615 participants, 15.9%)
8	Smoking status, the menopausal transition, and metabolic syndrome in women.	Kwaśniewska M	Menopause. 2012 Feb;19(2):194-201	2003-2005	cross-sectional and cohort	7462 randomly selected women aged 20 to 74 years who are participating in the WOBASZ (Polish National Multicentre Health Survey)	Poland	Metabolic syndrome	Smoking, Blood pressure, Fasting plasma glucose, Menopause status	The prevalence of MetS was 3.3-fold higher among postmenopausal than premenopausal women. Regardless of menopause status, the prevalence of central obesity was significantly higher among never and past smokers versus current smokers ($P < 0.001$). Past smoking was associated with a significantly higher probability of elevated blood pressure, fasting plasma glucose, and MetS ($P < 0.05$). However, premenopausal never and past smokers had a substantially lower prevalence of decreased HDL-C than did current smokers. Among postmenopausal nonsmokingwomen, high levels of leisure time and commuting physical activity were associated with a reduced likelihood of MetS ($P < 0.01$). Making an additional adjustment for calorie consumption did not substantially influence the

										result
9	Epidemiological st udy of metabolic syndrome and risk of diabetes mellitus in a rural family medicine practice in Bacau County	Diaa A	Rev Med Chir Soc Med Nat Iasi. 2014 Jul-Sep;118(3):772-9	2011-2102	cross-sectiona l	615 subjects investigated by their family doc tor in Romania	Romania	Diabetes and metabolic syndrome	Waist circumference, Age, Gender, BMI	There was a Gaussian distribution of waist circumference (WC) with a maximum in age-group 70-80 years (46.3%), followed by age- groups 50-60 years (37.8%) and 60-70 years (41.6%). Waist circumference measurement showed an average of 100.76 +/- 11.59 cm, ranges 72 cm - 134 cm, without statistical significance. Mean body mass index (BMI) was 28.25 +/- 4.72 kg/m2 vs. 27.79 +/- 4.48 kg/m2. The difference is statistically significant (p = 0.05)
10	Improved Metabolic Control in Pediatric Patients with Type 1 Diabetes: A Nationwide Prospective 12-Year Time Trends Analysis	Klemen Dovc	Diabetes Technol Ther. 2014 Jan 1; 16(1): 33–40	2000-2011	cohort	886 case subjects in Croatia from 0 to 17.99 years of age at diagnosis and at least 1 year of follow-up until the age of 22.99 years	Croatia	Childhood obesity	Age,Gender, Duration of diabetes, Treatment modality	Hemoglobin A1c (HbA1c) significantly decreased over 12 years, from 78 mmol/mol (interquartile range [IQR], 68-88 mmol/mol) (9.26% [IQR, 8.41-10.24%]) in the year 2000 to 61 mmol/mol (IQR, 55-67 mmol/mol) (7.75% [IQR, 7.20-8.30%]) in the year 2011 (P<0.001). HbA1c was significantly associated with age, treatment modality, and duration of diabetes (P<0.001), with females having on average 1.02% higher HbA1c (P=0.01; 95% confidence interval [CI] 1.005-1.035). The overall use of insulin pumps was 74%. The incidence rate of severe acute complications was low: 1.07 per 100 patient-years for severe diabetic ketoacidosis (95% CI 0.81-1.40) and 1.21 per 100 patient-years for severe (requiring intravenous or intramuscular therapy) hypoglycemia (95% CI 0.81-1.40)

11	Early life course risk factors for childhood obesity: the IDEFICS case-control study	Ahrens W	PLoS One. 2014 Feb 13;9(2):e86914	2007-2008	case-control	1,024 1:1-matched case-control pairs was nested in the baseline survey of the IDEFICS study, a population-based intervention stu dy on childhood obesity carried out in 8 European countries including Hungary and Estonia	Hungary, Estonia	Childhood obesity	Birth weight, Smoking in pregnancy, Gestational weight gain, Breastfeeding ,Gestational diabetes, Early introduction of solid foods	Gestational weight gain (adjusted OR = 1.02; 95%CI 1.00–1.04), smoking during pregnancy (adjusted OR = 1.48; 95%CI 1.08–2.01), Caesarian section (adjusted OR = 1.38; 95%CI 1.10–1.74), and breastfeeding 4 to 11 months (adjusted OR = 0.77; 95%CI 0.62–0.96). Birth weight was related to lean mass rather than to fat mass, the effect of smoking was found only in boys, but not in girls. After additional adjustment for parental BMI and parental educational status, only gestational weight gain remained statistically significant. Both, maternal as well as paternal BMI were the strongest risk factors in our study, and they confounded several of the investigated associations
12	Prevalence of diabetes and impaired fasting glucose in Poland-- the NATPOL 2011 Study	Rutkowski M	Diabet Med. 2014 Dec;31(12	2011	cross-sectional	2411 adults aged 18-76 years from Poland	Poland	Blood pressure, Overweight Obesity, Diabetes, Dyslipidaemia	Age, Gender	Total prevalence of diabetes in 2011 was 6.7% (95% CI 5.6-7.9); 6.4% (95% CI 5.0-8.0) in women and 7.0% (95% CI 5.4-8.8) in men and did not change from 2002 (6.8%, 95% CI 95% CI 5.8-7.9). Over one quarter of individuals with diabetes were not aware of having the condition. Obesity, arterial hypertension and male gender were strong predictors of screened diabetes. Total prevalence of impaired fasting glucose in the surveyed population was 15.6% (95% CI 14.0-17.2)
13	Association between dietary patterns and metabolic syndrome in individuals with normal weight: a cross-sectional study	Suliga E	Nutr J. 2015; 14: 55	2010-2012	cross-sectional	2479 subjects with a normal weight (BMI = 18.5-24.9 kg/m(2)), aged between 37-66 in Poland	Poland	Metabolic syndrome	Dietary pattern	After controlling for potential confounders, subjects in the highest tertile of prudent dietary pattern scores had a lower odds ratio for the metabolic obesity normal weight) (odds ratio: 0.69; 95% CI: 0.53-0.89; $p < 0.01$) and low HDL cholesterol (odds ratio: 0.77; 95% CI: 0.59-0.99; $p < 0.05$), in comparison to those from the lowest tertile, whereas the individuals in the second tertile had a higher odds ratio for the increased blood glucose concentration than those in the lowest tertile (odds ratio: 0.74; 95% CI: 0.57-0.96; $p < 0.05$)

14	A Mediterranean-type diet is associated with better metabolic profile in urban Polish adults: Results from the HAPIEE study	Grosso G	Metabolism. 2015 Jun;64(6):738-46	2002–2005	cross-sectional and cohort	8821 adult males and females from Kraków	Poland	Metabolic syndrome	Dietary pattern	Significant associations between Mediterranean-type diet score and waist circumference (β=-0.307±0.239cm), systolic blood pressure (β=-0.440±0.428mmHg), and triglycerides (β=-0.021±0.016mmol/L) were observed. After multivariable adjustment, individuals in the highest quartile of the score were less likely to have Metabolic syndrome (MetS), central obesity, high triglycerides, and hypertension. Increase of one standard deviation of the score was associated with 7% less odds of having MetS (OR 0.93, 95% CI: 0.88, 0.97). When analyzing the relation of single components of the MedTypeDiet score, wine, dairy products, and the total unsaturated:saturated fatty acids ratio were associated with MetS
15	Association of daily coffee and tea consumption and metabolic syndrome: results from the Polish arm of the HAPIEE study	Grosso G	Eur J Nutr. 2015 Oct;54(7):1129-37	2002–2005	cross-sectional and cohort	9050 adult males and females from Kraków	Poland	Metabolic syndrome	Dietary pattern	Among high coffee and tea consumers (3 or more cups/day), high prevalence of female gender, young age, medium-high educational and occupational level, high total energy intake, and smoking habit were found. High coffee drinkers had lower BMI, waist circumference, systolic and diastolic blood pressure, triglycerides, and higher HDL cholesterol than those drinking less than 1 cup/day. In contrast, high tea consumers had lower BMI, waist circumference, but not diastolic blood pressure, which was higher than low drinkers. After adjusting for potential confounding factors, both higher coffee and tea consumption were negatively associated with MetS (OR 0.75, 95% CI 0.66, 0.86 and OR 0.79, 95% CI 0.67, 0.92, respectively). Among specific components of MetS, high coffee consumption was negatively associated with waist circumference, hypertension, and triglycerides, whereas tea consumption with central obesity and fasting plasma glucose in women, but not in men
16	Comparison of four definitions of the metabolic syn drome and odds of ischemic heart disease in the Lithuanianurban population	Luksiene DI	Int J Public Health. 2012 Jun;57(3):543-50	2006-2008	cohort	7087 individuals aged 45-72 years from Kaunas	Lithuania	Metabolic syndrome	Blood pressure, Education, Smoking	In Kaunas city, Lithuania, the highest prevalence of metabolic syndrome, in the urban population aged 45–72 years, was determined according to the new Joint Interim Societies (JIS) definition (44.1% of men and 48.7% of women). After adjusting for age, education, and smoking habits, the metabolic syndrome (irrespective of definition) was associated with a significantly higher risk of ischemic heart disease

17	Prevalence of lipid abnormalities in Poland. The NATPOL 2011 survey.	Zdrojewski T	Kardiol Pol. 2016;74(3): 213-23	2011	cross-sectional	1168 males and 1245 females, aged 18-79 years from NATPOL 2011 study	Poland	Dyslipidaemia, Metabolic syndrome	Age, Gender	Mean serum cholesterol TC concentration was 197.1 mg/dL (95% CI 193.8-200.4) in males (M) and 198.6 mg/dL (95% CI 195.7-201.5) in females (F). Levels of LDL-C were 123.6 mg/dL (120.9-126.2) and 123.7 mg/dL (121.4-126.1), HDL-C - 45.8 mg/dL (44.7-47.0) and 54.1 mg/dL (53.1-55.1), TG - 140.9 mg/dL (133.0-148.8) and 104.0 mg/dL (99.8-108.2) for males and females, respectively. TC ≥ 190 mg/dL was found in 54.3% subjects (M 54.3%; F 54.4%). After adding patients on lipid-lowering treatment, hypercholesterolaemia was present in 61.1% of adults (M 60.8%; F 61.3%). LDL-C ≥ 115 mg/dL was detected in 57.8% of all subjects (M 58.3%; F 57.3%), while HDL-C < 40 mg/dL in 35.2% of males and < 45 mg/dL in 22% of females TG ≥ 150 mg/dL was found in 21.1% of subjects (M 28.4%; F 14.0%). The highest prevalence of elevated TC and LDL-C levels was present in the age group of 40-59-year-olds. Of those with hypercholesterolaemia 58.7% (M 61.5%, F 56.0%) were not aware of the condition; 22.0% (M 21.0%, F 24.5%) were aware but were not being treated; 8.1% (M 7.7%, F 8.5%) were treated but with TC ≥ 190 mg/dL; and only 10.9% (M 10.7%, F 11.0%) were being treated with TC < 190 mg/dL