

Appendix

Contents

1. Cohort Descriptions	2
2. Calculation of rate advancement periods (RAPs)	8
3. Supplementary tables and figures	9

1. Cohort Descriptions

Further information can be found at:

Kuulasmaa K, Palosaari T (eds). CHANCES cohort descriptions, assessment of the availability and quality of data, and definitions of variables. MORGAM Project e-publications [Internet]. 2015; (6). URN: NBN:fi-fe201501151161. Available from URL:

http://www.thl.fi/publications/morgam/chances_d9/index.html

ELSA (English Longitudinal Study of Ageing)

ELSA is an on-going cohort study that contains a nationally representative sample of the English population living in households. The ELSA cohort consists of men and women born on or before 29 February 1952. The sample was drawn from households that have participated in Health Survey for England (HSE) in 1998, 1999, and 2001 (“wave 0”). HSE recruits participants using multi-stage stratified probability sampling with postcode sectors selected at the first stage and household addresses selected at the second stage. The sample first assessed in 2002 included more than 11,000 participants, and they have been restudied every two years since then. Mortality data is supplied by the National Health Service central data registry.

EPIC-Elderly (European Prospective Investigation into Cancer and Nutrition)

EPIC-Elderly consists of approximately 100,000 participants (aged 60 years and older at recruitment) from the EPIC study. EPIC is an on-going, multi-centre, prospective cohort study aiming to investigate the role of biological, dietary, lifestyle, and environmental factors in the aetiology of cancer and other chronic diseases. The study recruitments took place from 1992 to 2000 via administration of baseline questionnaires and interviews. Mortality was assessed differently in different countries and included record linkages as well as active follow-up procedures. Twenty three research centres from 10 European countries participate in EPIC. In this study, EPIC-Elderly cohorts from Greece, the Netherlands (Bilthoven and Utrecht), Sweden (Umeå) and Spain (Asturias, Granada, Murcia, Navarra and San Sebastian) were used.

ESTHER (Epidemiological Study on the Chances of Prevention, Early Recognition and Optimised Treatment of Chronic Diseases in the Older Population)

The ESTHER study is a population-based cohort of 9949 adults at ages 50-74 recruited in the years 2000-2002 in the entire federal state of Saarland, Germany, with on-going follow-up. Participants were recruited at their general practitioners' office while doing a health check-up (a general health screening examination offered every two years for people older than 35 years in Germany). Participants completed a comprehensive self-administered questionnaire, medical data and biological samples were collected. All baseline participants were re-contacted 2, 5, 8 and 10 years after baseline. Participants completed a standardised questionnaire. The occurrence of selected incident diseases was confirmed by the caring physicians. A comprehensive follow-up with respect to overall and cause-specific mortality was done by record linkage with population registries and death certificates.

HAPIEE (Health, Alcohol and Psychosocial factors in Eastern Europe)

The HAPIEE study comprises four cohorts in the Czech Republic, Poland, Russia, and Lithuania; each consists of a random sample of men and women aged 45-69 years old at baseline. The Czech, Polish and Russian cohorts were recruited in 2002-2005, and the Lithuanian cohort in 2006-2008. Baseline information includes data on health, lifestyle, diet (food frequency), socioeconomic circumstances and psychosocial factors. A short examination included measurement of anthropometric parameters, blood pressure, lung function and cognitive function, and a fasting venous blood sample. The baseline survey included 16,812 men and 19,180 women across the 4 cohorts. Mortality and incidence of mortality and diseases is obtained through linkage to local registers or hospital records. The Russian and Lithuanian cohorts are linked annually to local myocardial infarction, stroke and mortality registers. The Czech cohort is checked annually against hospital records for myocardial infarction and stroke and against mortality records. The Polish cohort is checked annually against mortality records.

MORGAM (MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) Risk, Genetics, Archiving and Monograph Project)

The MORGAM project is a European-wide, prospective, multinational collaborative study of cardiovascular diseases risk. It has harmonized data from about 60 population cohorts from 21 MORGAM Participating Centres in 12 countries, adding up to more than 145,000

participants. Nearly all cohorts consist of the respondents of representative probability samples of geographically defined populations. Most of the cohorts include both men and women. In this project 9 studies were included; FINRISK from Finland, SHIP Greifswald from Germany (federal state Mecklenburg-West Pomerania), Glostrup from Denmark, Kaunas from Lithuania, KORA Augsburg from Germany (federal state Bavaria), Warsaw from Poland, Northern Sweden, Brianza from Italy (Brianza area, Lombardia Region) and Catalonia from Spain. Recruitments took place through baseline examinations in 1980s, 1990s and early 2000s. Participants were followed until death or the end of a pre-defined follow-up period. Follow-up procedures and periods vary between cohorts. For cohort specific information, see www.thl.fi/publications/morgam/cohorts/.

NHANES (National Health and Nutrition Examination Survey)

The National Health and Nutrition Examination Survey (NHANES) is a major program of the National Center for Health Statistics (NCHS) and comprises studies designed to assess the health and nutritional status of adults and children in the United States. NHANES III, which was used in this study, was conducted from 1988-1994 and focused on oversampling many groups within the U.S. population including persons over age 60. The included subjects participated in an interview conducted at home and an extensive physical examination. In total, 30,818 people were interviewed in NHANES III, of which about 6,600 were above the age of 60. The NCHS has updated the mortality linkage of NHANES III to death certificate data obtained in the National Death Index (NDI) such that mortality ascertainment is based on results of a probabilistic match between NHANES III and NDI death certificate records.

NIH-AARP (National Institutes of Health-AARP)

The cohort study was initiated in 1995–1996 when a baseline questionnaire eliciting information on usual dietary intake, physical activity, and other health-related behaviours was sent to 3.5 million AARP members aged 50–71 years who resided in one of six US states (California, Florida, Pennsylvania, New Jersey, North Carolina, and Louisiana) or two US metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). A total of 617,119 men and women returned the baseline questionnaire, a response rate of 17.6 percent. In late 1996, a supplementary questionnaire was mailed to participants who satisfactorily completed the baseline questionnaire, who still lived in the study area, and who did not have prevalent cancer of the colon, breast, or prostate. The supplementary questionnaire inquired about history of hypertension and weight at age 18 years, among other health-related questions. In

total, 334,908 participants responded to the supplementary questionnaire. All-cause mortality was assessed via record linkage to the cancer registries of enrolment states plus those of Arizona, Nevada, and Texas, as well as the National Death Index.

SENECA (Survey in Europe on Nutrition and the Elderly; a Concerted Action)

SENECA is a multi-centre European prospective mixed cross-sectional and longitudinal study that recruited in 1988/89 around 2000 individuals from 12 countries (Belgium, Denmark, France, Italy, the Netherlands, Portugal, Spain, Switzerland, Poland, Hungary, Norway and Greece) born between 1913 and 1918 (70-75 years old at baseline). Information on the dietary intake, nutritional status, physical activity, lifestyle, and health status were collected through standardised interviews, examinations of blood and anthropometric measurements. Two recontacts with 5-year intervals were conducted after the baseline. Vital status of participants was assessed via municipal registries. Assessments were repeated and extended for the survivors at follow-ups.

SHARE (Survey of Health, Ageing and Retirement in Europe)

SHARE is a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks of more than 85,000 individuals (approximately 150,000 interviews) from 19 European countries (Sweden, Denmark, Estonia, Poland, Germany, the Netherlands, Belgium, Czech Republic, Austria, Hungary, Switzerland, France, Luxembourg, Ireland, Portugal, Spain, Italy, Greece) and Israel aged 50 or over. Random nationally representative samples of the non-institutionalised population aged 50 years and over were recruited between 2004-2005 in the first wave of study, between 2006-2007 in the second wave, between 2008-2009 in the third wave (SHARELIFE), and between 2011-2012 in the fourth wave. The recruitment procedure varies among the participating countries. Face-to-face interviews were conducted at baseline and re-contacts, which took place approximately 2 years after the baseline contacts. Follow-up procedures and end-point confirmations are country-specific.

SMC (Swedish Mammography Cohort)

SMC is a large population-based cohort of over 60,000 women. From 1987 to 1990, all women who lived in the Uppsala County of central Sweden and were born between 1914-1948 and all women who lived in the adjacent Västmanland County and were born between 1917-1948 received an invitation by mail to participate in a mammography screening

program. A total of 66,651 women returned a completed questionnaire on diet, weight, height, parity, and education. In 1997, a follow-up questionnaire was sent to all cohort members who were still living in the study area; the follow-up questionnaire was extended to include information on physical activity, medical history, age at menarche, history of oral contraceptive use, age at menopause, postmenopausal hormone use, and lifestyle factors such as, cigarette smoking history, and use of dietary supplements. For this study, a sub-cohort of SMC called SMC Clinical (SMCC) was used. Between November 2003 and October 2009, this randomly selected sub-cohort of the SMC was invited to undergo dual energy x-ray absorptiometry measurements, to provide blood and urine samples, and to have height and weight measurements taken. A third questionnaire on diet and lifestyle factors (similar to the 1997 food frequency questionnaire) was also completed before the clinical examination. Complete follow-up is achieved via record linkages to the nationwide Cancer Register, the In-Patient Register and the Death and Population Register.

Tromsø Study

The Tromsø Study is a prospective study of inhabitants in the municipality of Tromsø, Norway. It is a repeated population-based health survey with examinations in 1974 (Tromsø 1), 1979-80 (Tromsø 2), 1986-87 (Tromsø 3), 1994-95 (Tromsø 4), 2001 (Tromsø 5), 2007-08 (Tromsø 6). Surveys between 1979-80 and 2001 (Tromsø 2 to 5) were available for CHANCES consortium, which include more than 37,000 participants. The examinations included standardized measurements of height, weight, blood pressure, non-fasting serum lipids, and blood cell counts. A self-administered questionnaire handed in at the screening examination covered information about current and previous cigarette smoking, physical activity in leisure time, currently or previously treated hypertension, and a medical history of angina pectoris, diabetes mellitus, asthma, myocardial infarction, and stroke. Mortality was assessed until end of 2010 for this study via record linkage to Statistics Norway.

Zutphen Elderly Study

The Zutphen Elderly Study is a prospective cohort study of men born between 1900 and 1920 who lived in Zutphen, a town in the Eastern part of the Netherlands. A random sample of men aged 65-84 in 1985 were recruited through March-May 1985. Participants were examined again in 1990, 1995 and 2000. The interviews, dietary assessments and medical examinations were conducted at homes and at a study centre. Factors were measured repeatedly with the

same methodology and questions. Municipal registries provided information on vital status and causes of death of deceased participants were obtained at 5-year intervals.

2. Calculation of rate advancement periods (RAPs)

As described in detail in Brenner et al. 1993¹, RAPs are measures of risk factor impact that give the time periods by which the rate of an incident event (such as death) is advanced in exposed compared to unexposed subjects. They are applicable for risk factors of diseases whose rates increase with age. RAPs are calculated from the results of the multivariable regression models as ratio of the regression coefficients of the exposure variable of interest and age. Their 95% confidence intervals are calculated by deriving the variance of the RAP from variances and covariances of the regression coefficients.

In a proportional hazards model of the form

$$h_i(t) = h_0(t)\exp(\beta_1 E + \beta_2 A + \sum_i \beta_i F_i),$$

let β_1 and β_2 and β_i be the regression coefficients of the exposure variable E, the age variable A, and the covariates F_i , respectively. The adjusted RAP parameter per one-unit increase in exposure is then given by the ratio of the regression coefficients of the exposure and the age variable, i.e.

$$\text{RAP} = \frac{\beta_1}{\beta_2}.$$

The asymptotic variance of the RAP is derived from the variances and covariances of the parameters as

$$\text{var}(\text{RAP}) = \frac{1}{\beta_2^2} \left[\text{var}(\beta_1) - 2 \times \left(\frac{\beta_1}{\beta_2} \right) \times \text{cov}(\beta_1, \beta_2) + \left(\frac{\beta_1}{\beta_2} \right)^2 \times \text{var}(\beta_2) \right],$$

which can be used to calculate the 95% confidence limits of the RAP as follows

$$\text{RAP} \pm 1.96 \times \sqrt{\text{var}(\text{RAP})}.$$

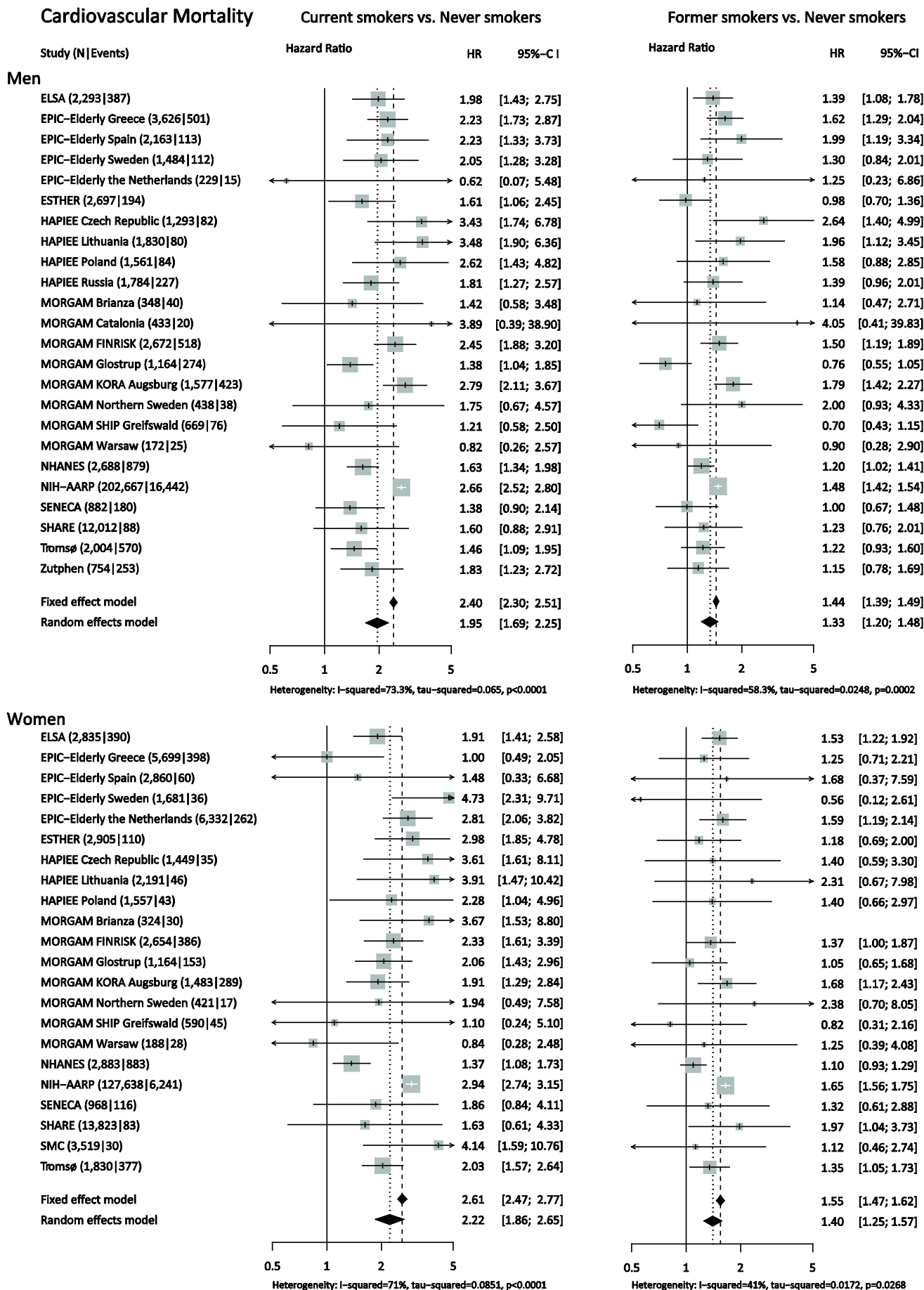
¹ Brenner H, Gefeller O, Greenland S. Risk and rate advancement periods as measures of exposure impact on the occurrence of chronic diseases. *Epidemiology* 1993; 4(3): 229-36.

3. Supplementary tables and figures

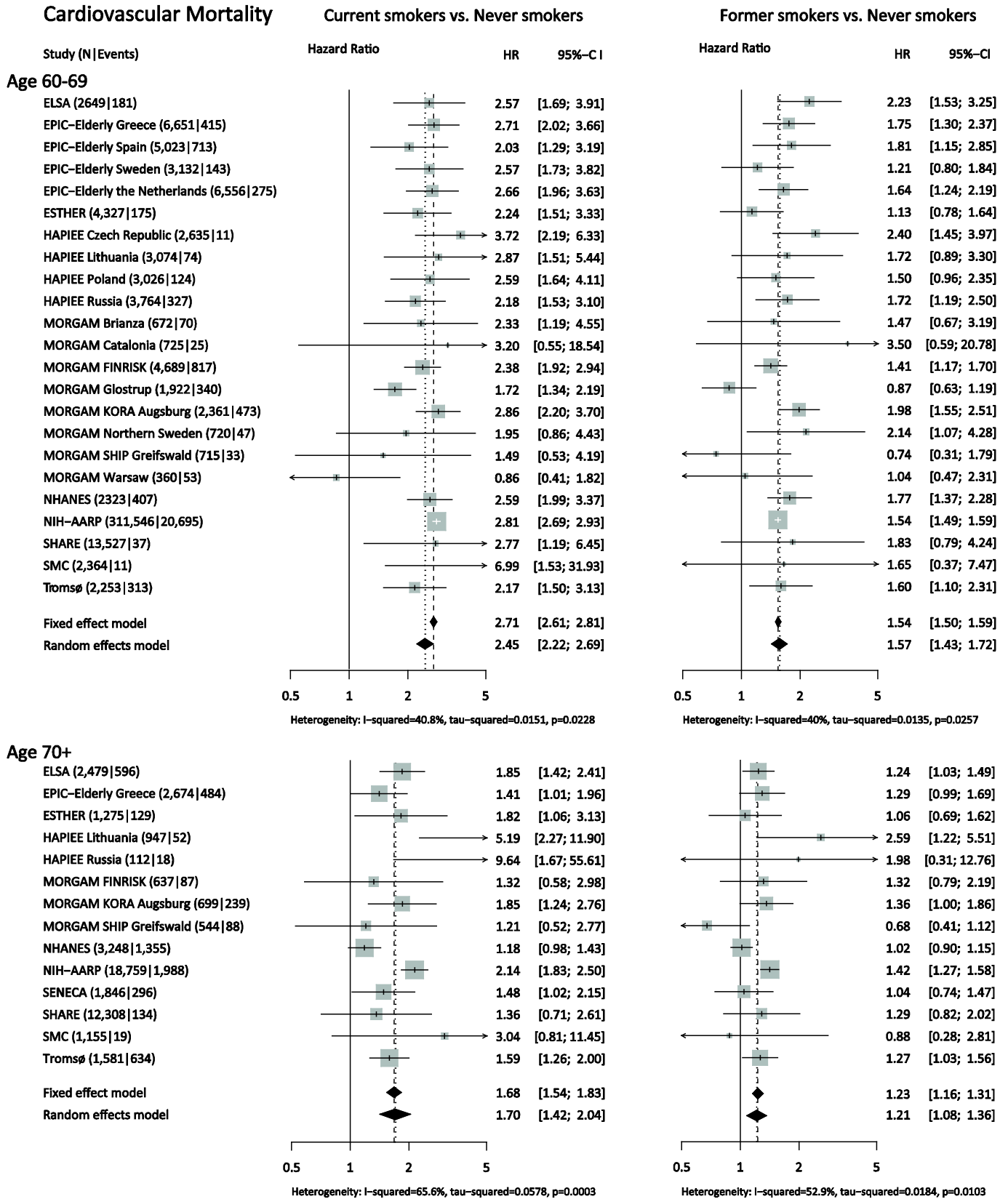
Supplementary Table 1. Availability of variables (predictors and covariates)

Cohort	Smoking status	Cigarette consumption	Age/date of smoking cessation	Age	Sex	Education	Alcohol consumption	Weight and height		Physical activity	History of diabetes		Total cholesterol	Systolic blood pressure
								Measured	Self-reported		Physician-confirmed	Self-reported		
ELSA	X	X	X	X	X	X	X		X	X	X		X	X
EPIC-Elderly Greece	X	X	X	X	X	X	X	X		X		X	X	X
EPIC-Elderly Spain	X	X	X	X	X	X	X	X		X		X	-	X
EPIC-Elderly Sweden	X	-	X	X	X	X	X	X		-		X	-	-
EPIC-Elderly the Netherlands	X	X	X	X	X	X	X	X		X		X	-	-
ESTHER	X	X	X	X	X	X	X	X		X	X		X	X
HAPIEE Czech Republic	X	X	X	X	X	X	X	X		X		X	X	X
HAPIEE Lithuania	X	X	X	X	X	X	X	X		X		X	X	X
HAPIEE Poland	X	X	X	X	X	X	X	X		X		X	X	X
HAPIEE Russia	X	X	X	X	X	X	X	X		X		X	X	X
MORGAM Brianza	X	X	X	X	X	X	X	X		-		X	X	X
MORGAM Catalonia	X	X	X	X	X	X	X	X		-		X	X	X
MORGAM FINRISK	X	X	-	X	X	X	X	X		-		X	X	X
MORGAM Glostrup	X	X	X	X	X	X	X	X		-		X	X	X
MORGAM KORA Augsburg	X	X	X	X	X	X	X	X		-	X		X	X
MORGAM Northern Sweden	X	X	X	X	X	X	-	X		-		X	X	X
MORGAM SHIP Greifswald	X	X	X	X	X	X	X	X		-		X	X	X
MORGAM Warsaw	X	X		X	X	X	X	X		-		X	X	X
NHANES	X	X	X	X	X	X	-		X	X		X	X	X
NIH-AARP	X	X	-	X	X	X	X		X	X		X	-	-
SENECA	X	-	X	X	X	X	X	X		X		X	X	-
SHARE	X	X	X	X	X	X	X		X	X		X	-	-
SMC	X	X	X	X	X	X	X		X	X	X		X	X
Tromsø	X	X	X	X	X	X	X	X		X	X		X	X
Zutphen	X	X	X	X	X	X	X	X		X	X		X	X

Supplementary Figure 1. Meta-analysis of the association of current smoking status with cardiovascular mortality by sex



Supplementary Figure 2. Meta-analysis of the association of current smoking status with cardiovascular mortality by age group



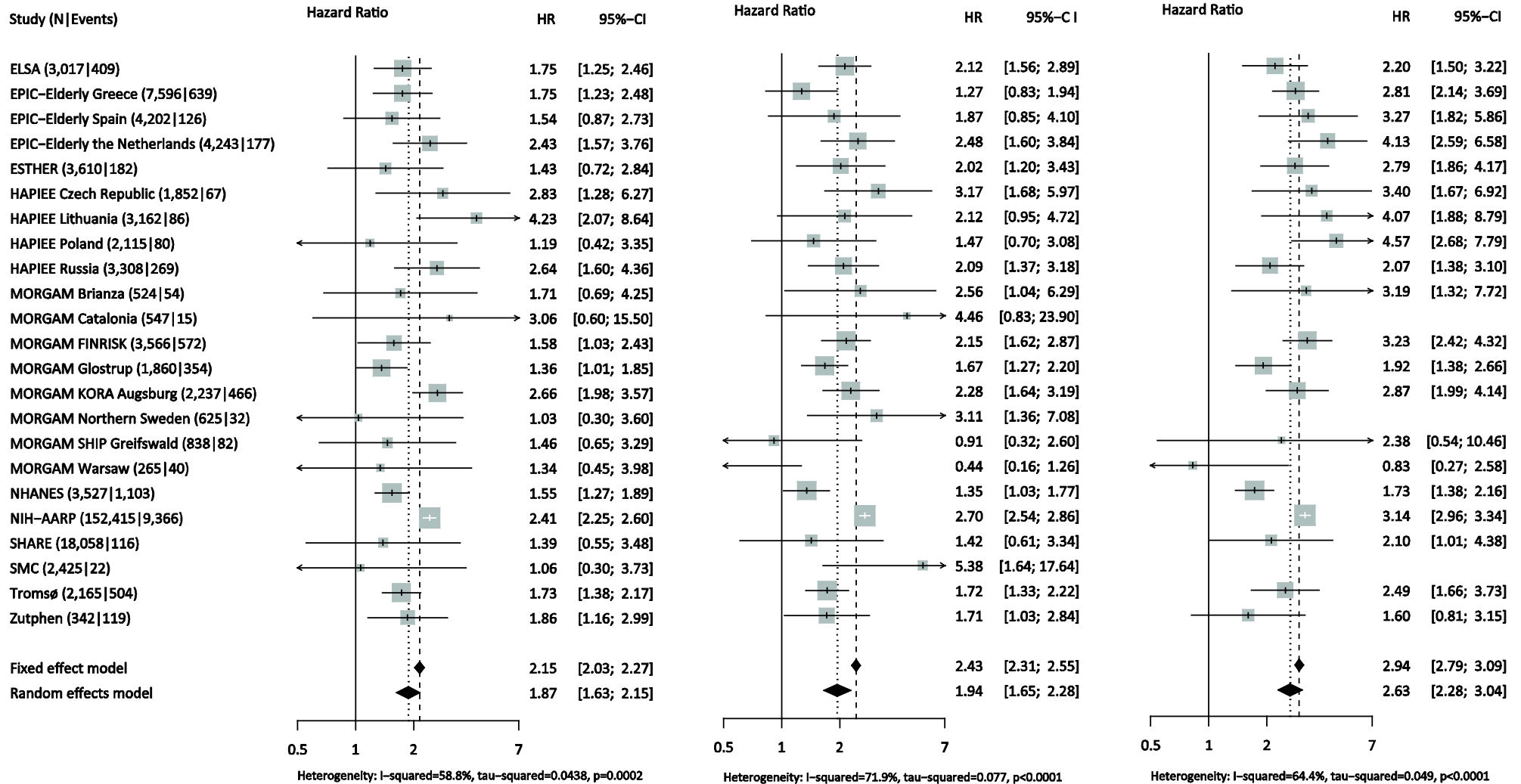
Supplementary Figure 3. Meta-analysis of the association of categories of cigarette consumption with cardiovascular mortality

Cardiovascular Mortality

Smoking < 10 cigs/day vs. Never smokers

Smoking 10 to 19 cigs/day vs. Never smokers

Smoking ≥ 20 cigs/day vs. Never smokers



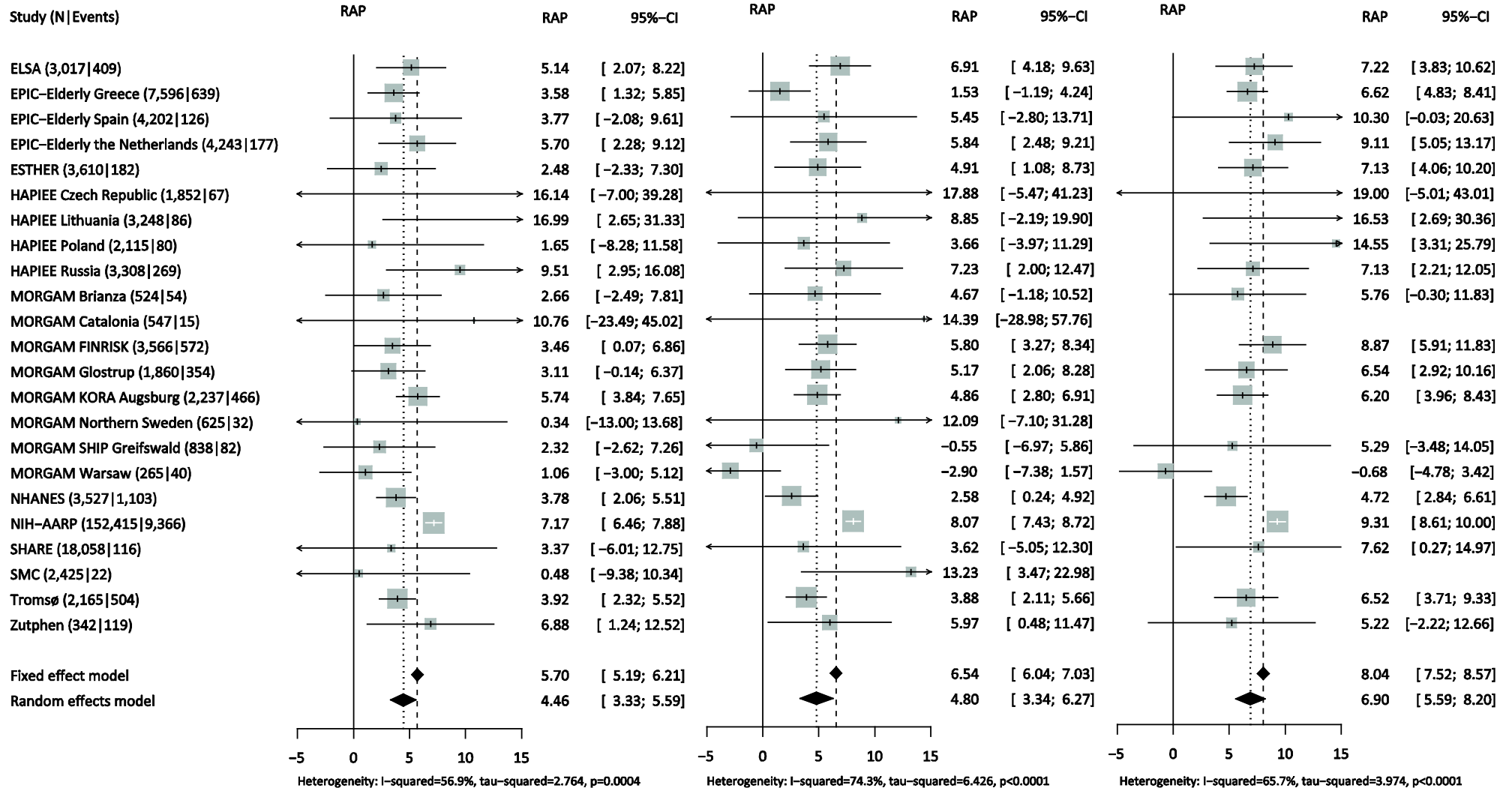
Supplementary Figure 4. Meta-analysis of risk advancement periods (RAPs) for categories of cigarette consumption and cardiovascular mortality

Cardiovascular Mortality

Smoking < 10 cigs/day vs. Never smokers

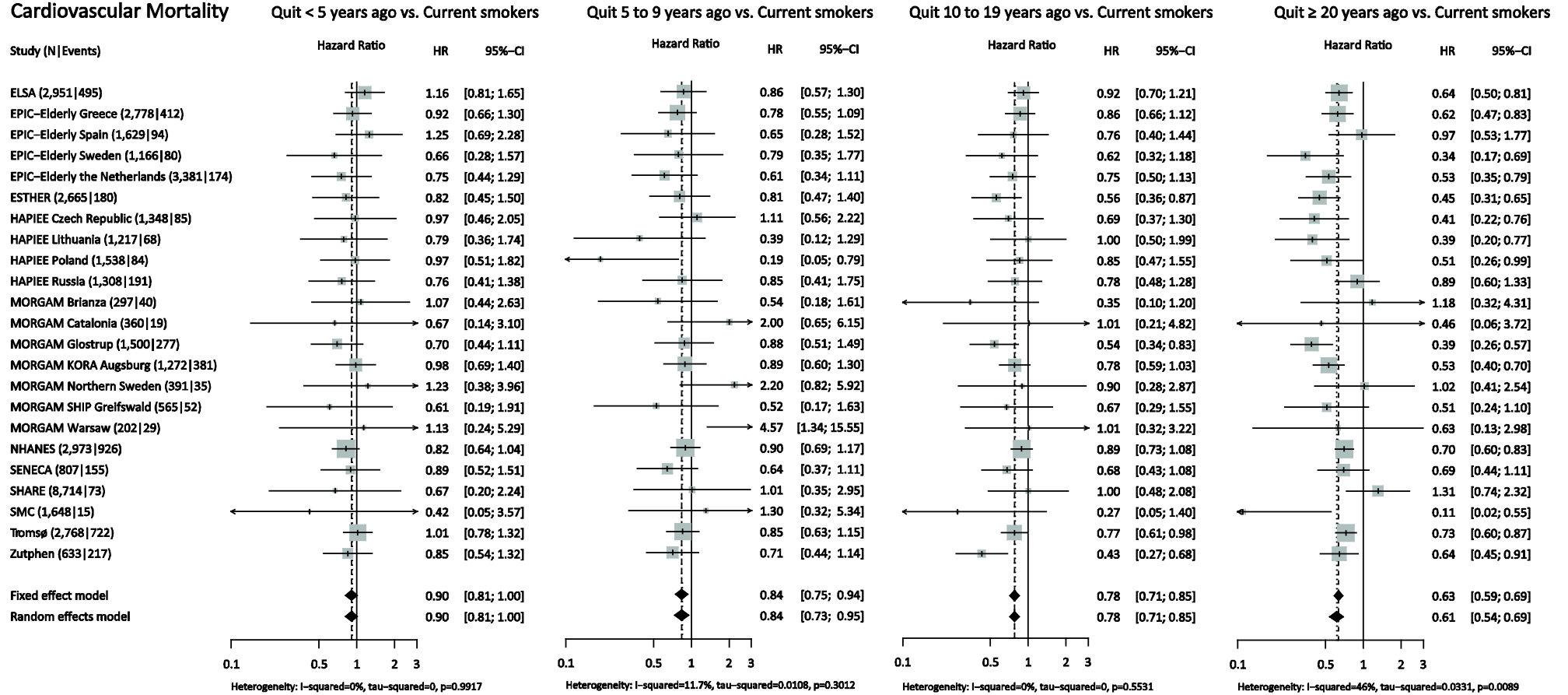
Smoking 10 to 19 cigs/day vs. Never smokers

Smoking ≥ 20 cigs/day vs. Never smokers



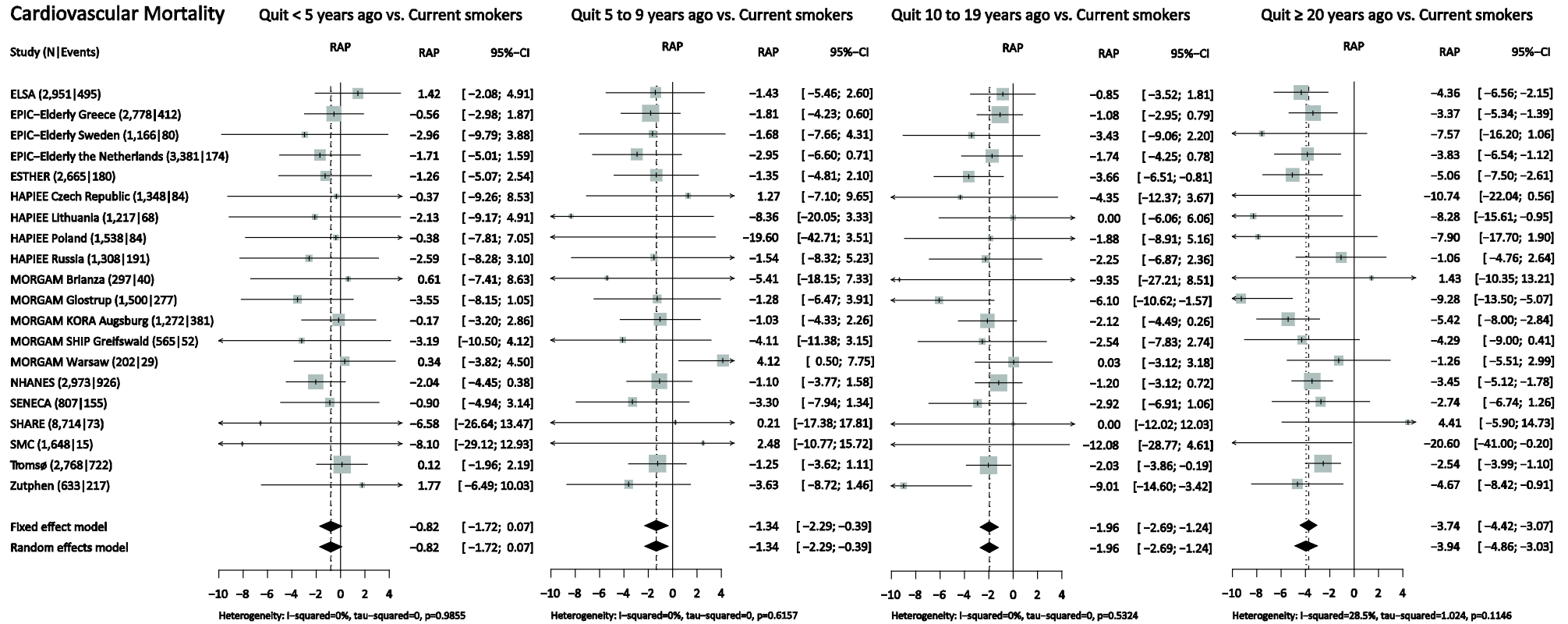
Supplementary Figure 5. Meta-analysis of the association of categories of time since smoking cessation with cardiovascular mortality

Cardiovascular Mortality

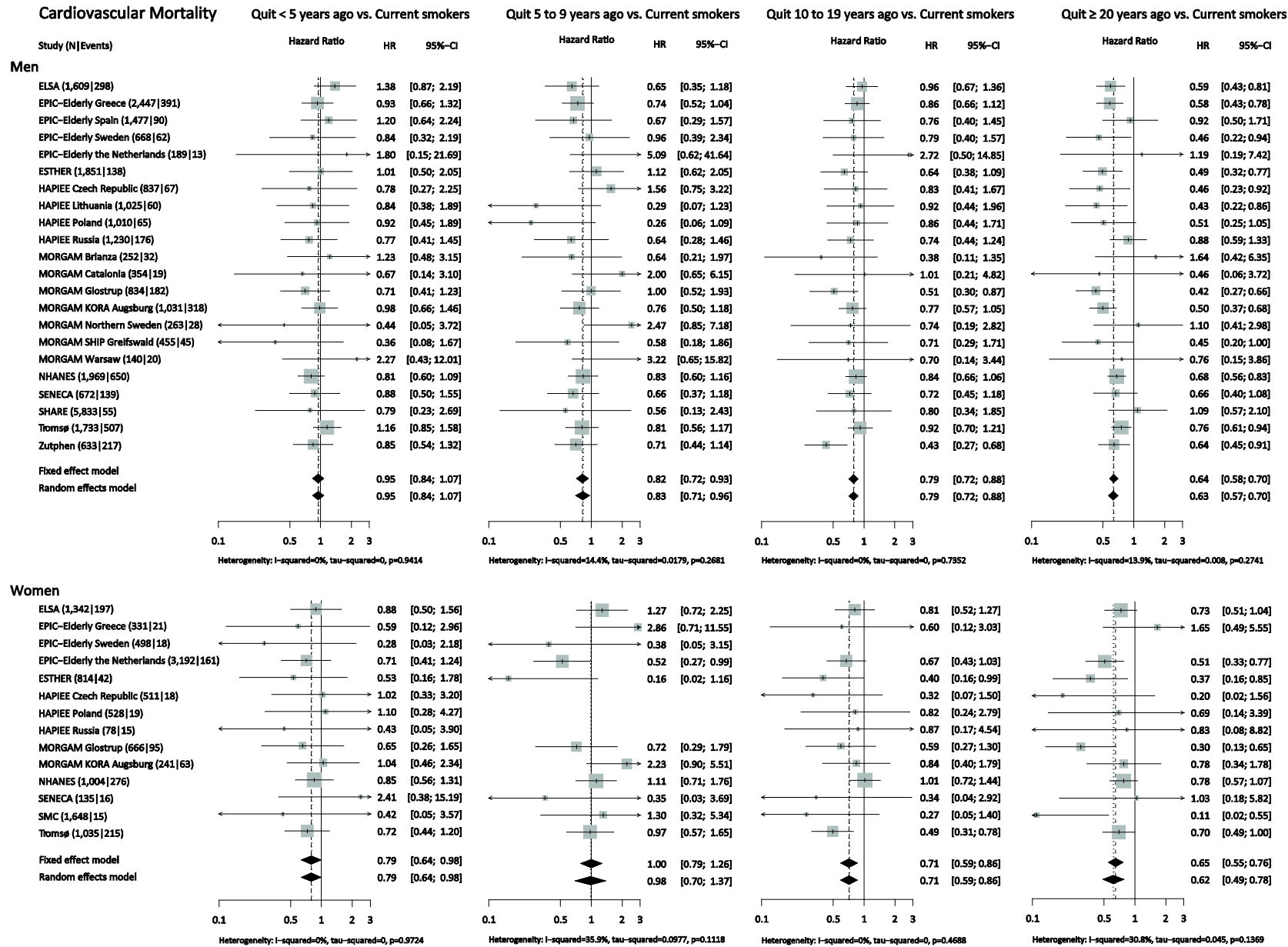


Supplementary Figure 6. Meta-analysis of risk advancement periods (RAPs) for categories of time since smoking cessation and cardiovascular mortality

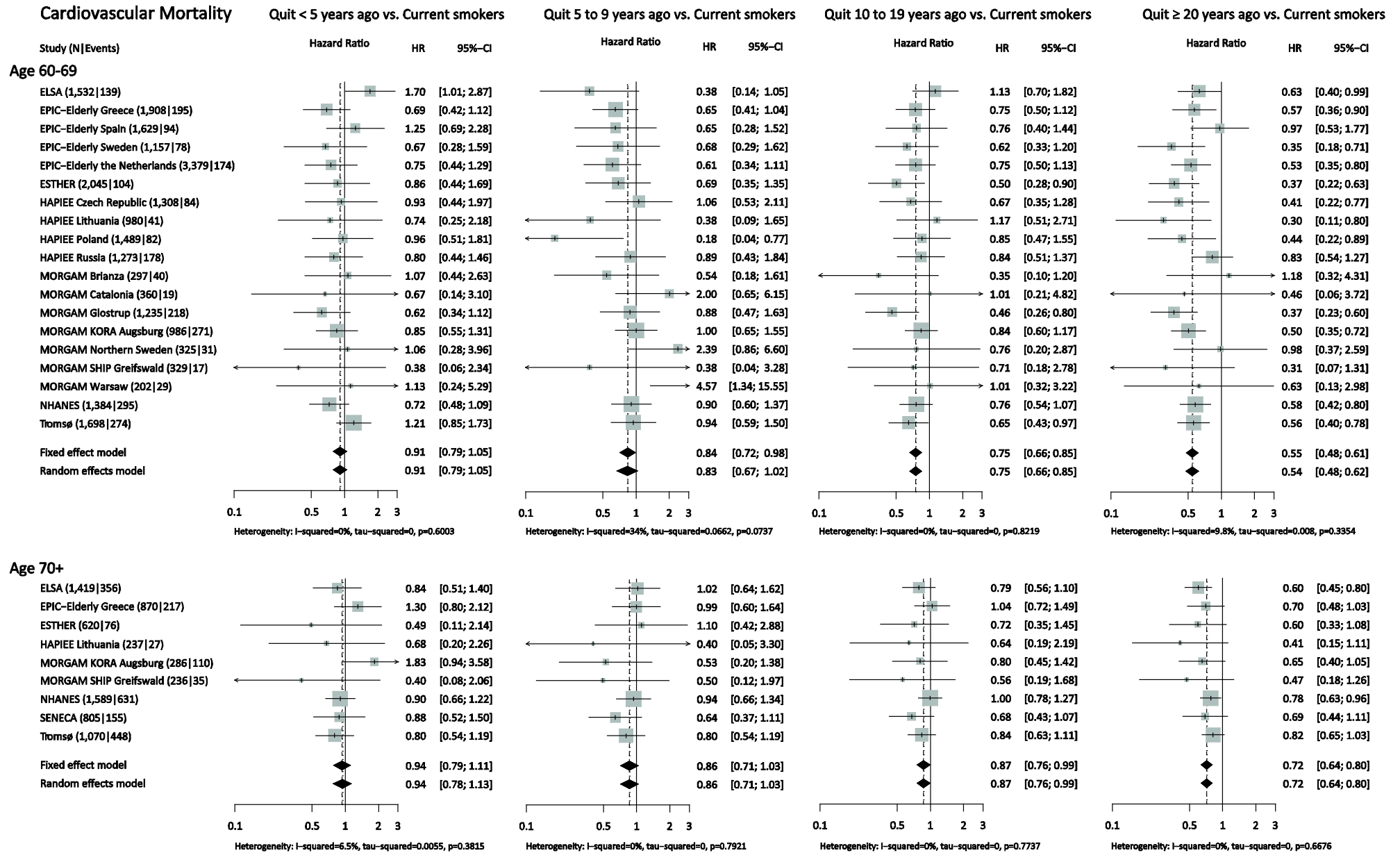
Cardiovascular Mortality



Supplementary Figure 7. Meta-analysis of the association of categories of time since smoking cessation with cardiovascular mortality by sex

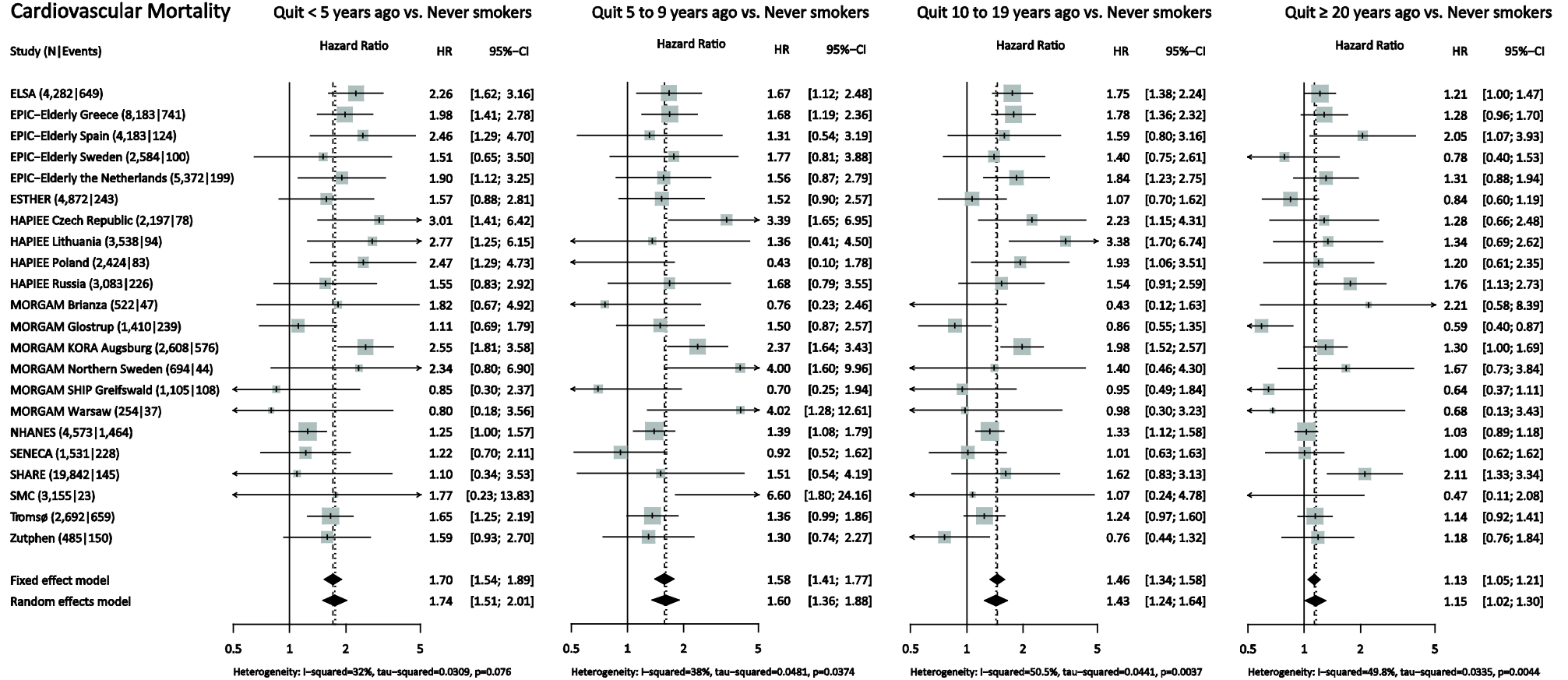


Supplementary Figure 8. Meta-analysis of the association of categories of time since smoking cessation with cardiovascular mortality by age group



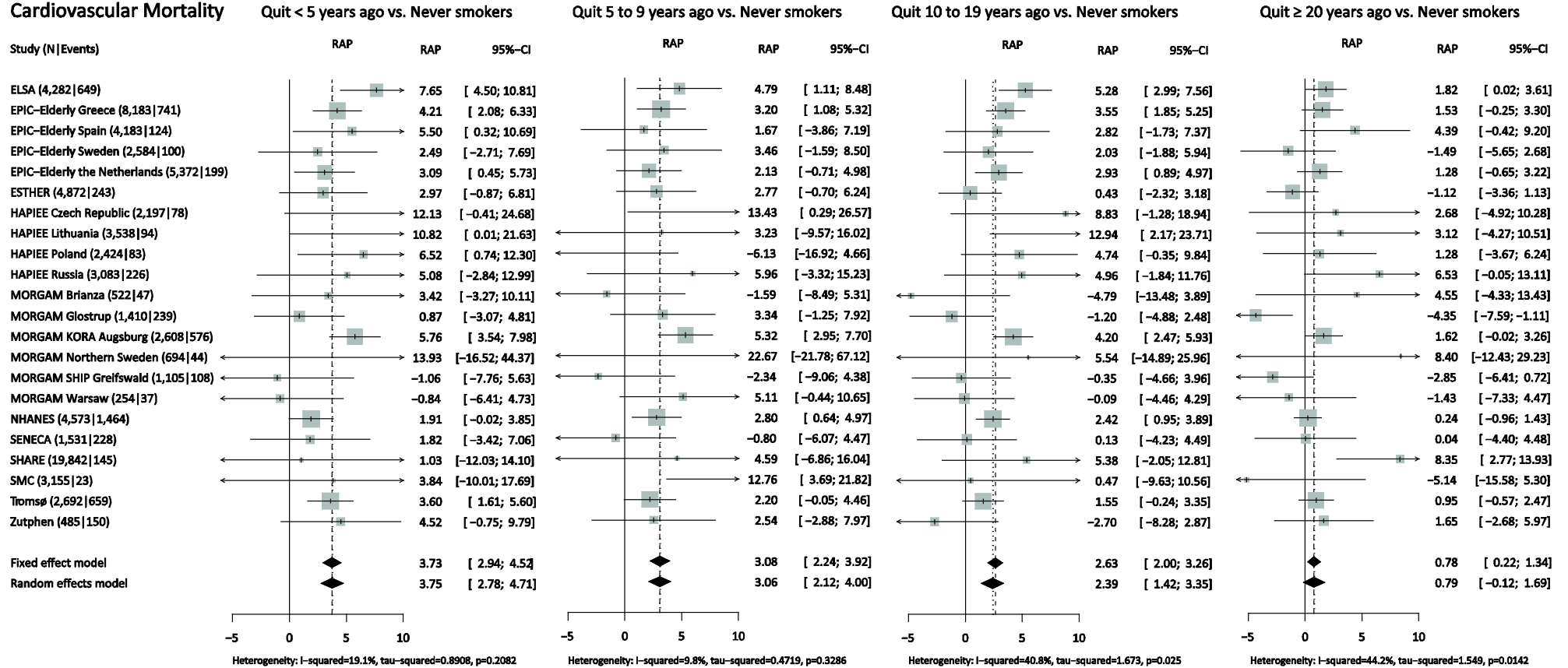
Supplementary Figure 9. Meta-analysis of the association of categories of time since smoking cessation with cardiovascular mortality in reference to never smokers

Cardiovascular Mortality



Supplementary Figure 10. Meta-analysis of risk advancement periods (RAPs) for categories of time since smoking cessation and cardiovascular mortality in reference to never smokers

Cardiovascular Mortality

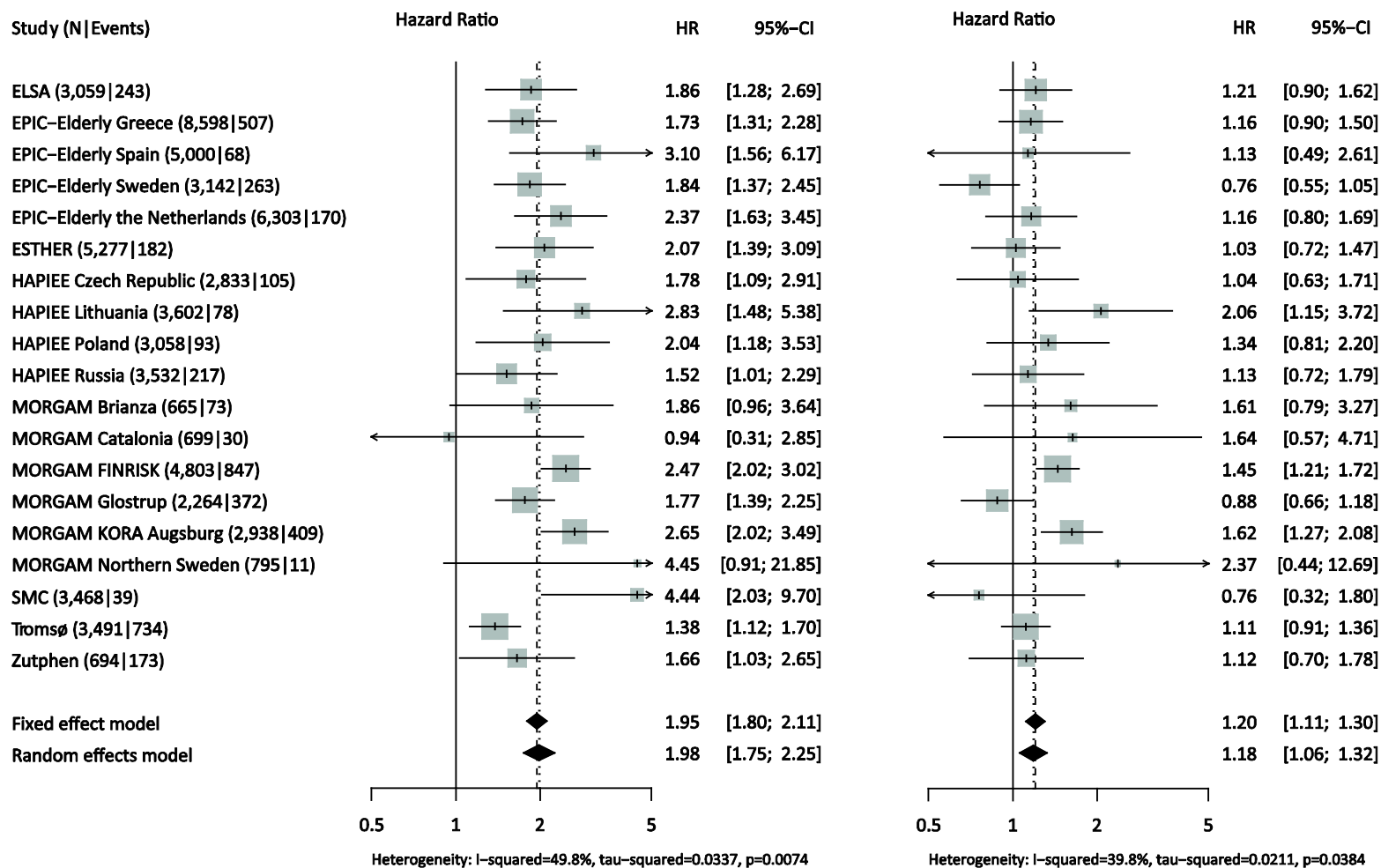


Supplementary Figure 11. Meta-analysis of the association of current smoking status with acute coronary events

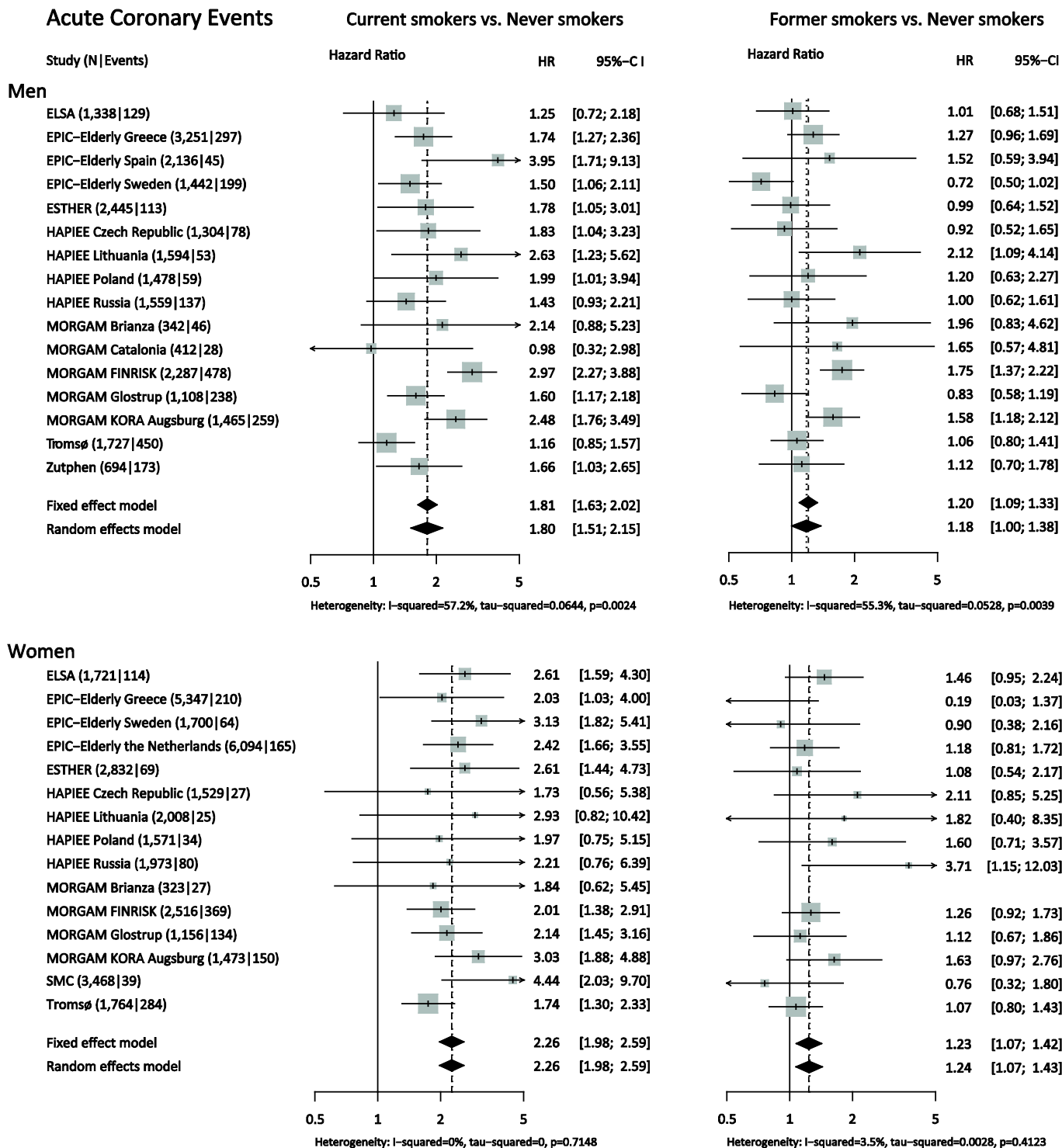
Acute Coronary Events

Current smokers vs. Never smokers

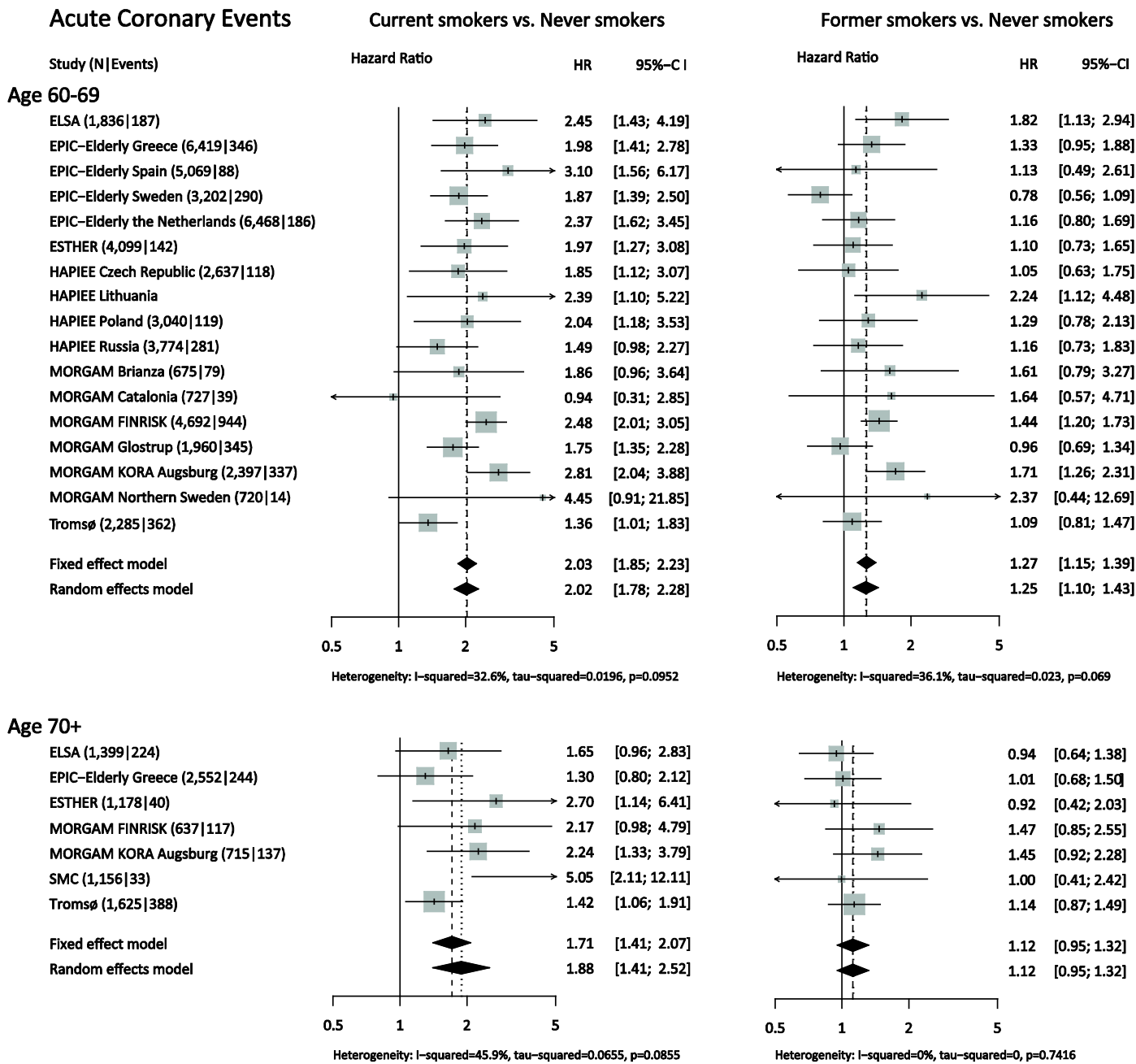
Former smokers vs. Never smokers



Supplementary Figure 12. Meta-analysis of the association of current smoking status with acute coronary events by sex



Supplementary Figure 13. Meta-analysis of the association of current smoking status with acute coronary events by age



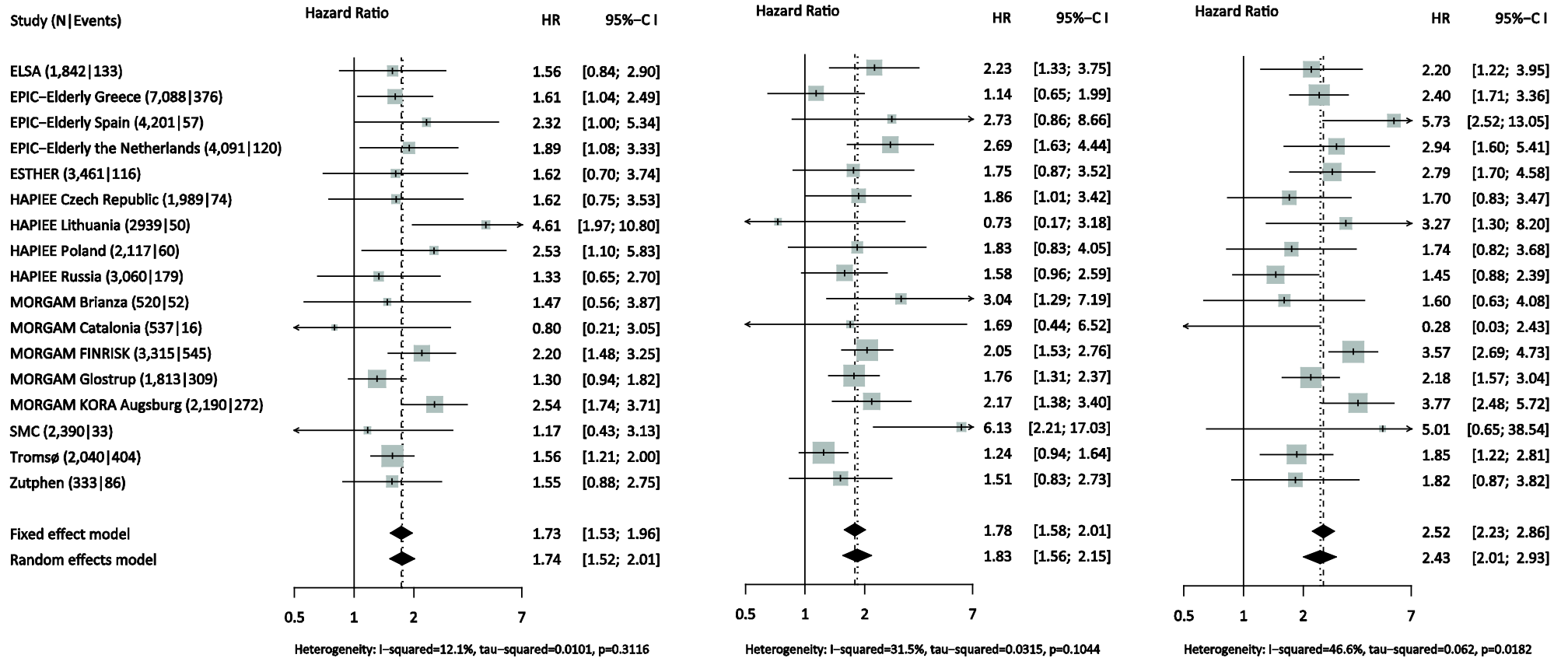
Supplementary Figure 14. Meta-analysis of the association of categories of cigarette consumption with acute coronary events

Acute Coronary Events

Smoking < 10 cigs/day vs. Never smokers

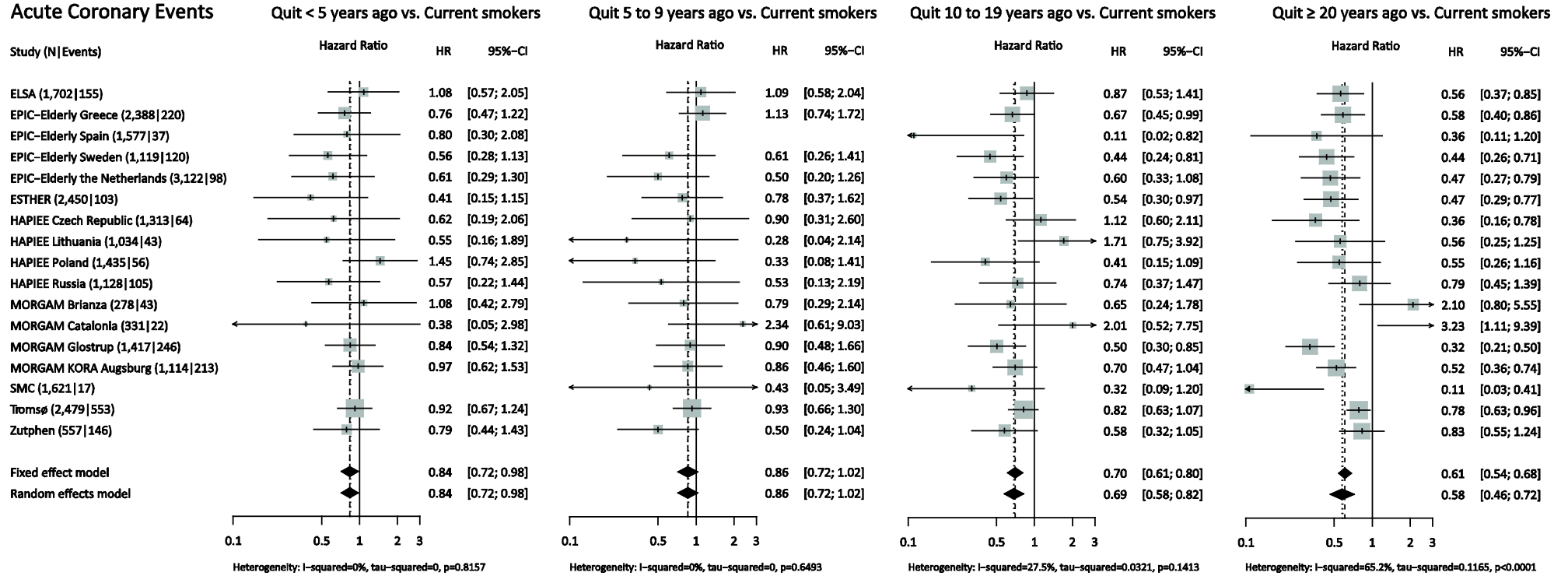
Smoking 10 to 19 cigs/day vs. Never smokers

Smoking ≥ 20 cigs/day vs. Never smokers



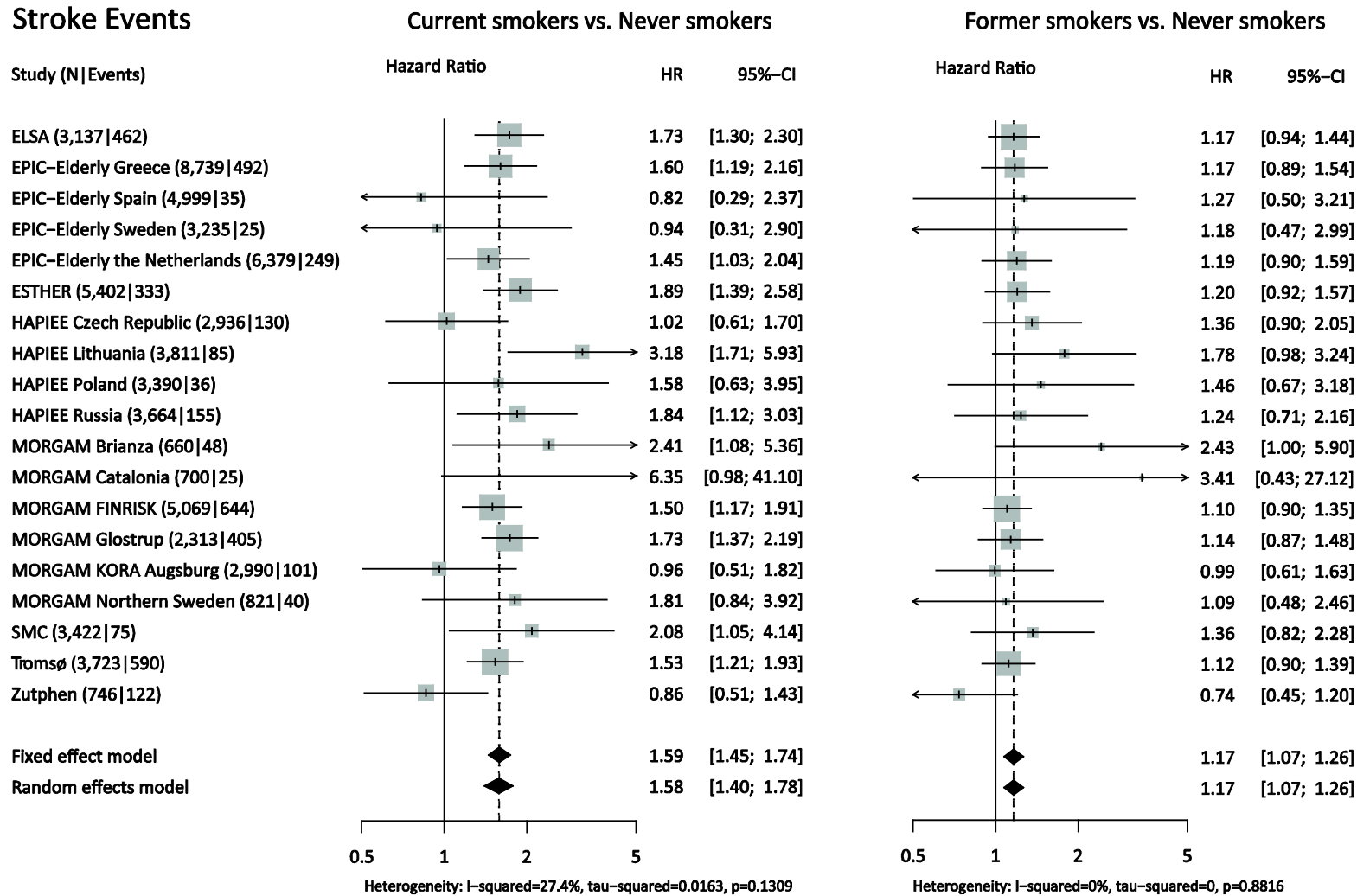
Supplementary Figure 15. Meta-analysis of the association of categories of time since smoking cessation with acute coronary events

Acute Coronary Events



Supplementary Figure 16. Meta-analysis of the association of current smoking status with stroke events

Stroke Events



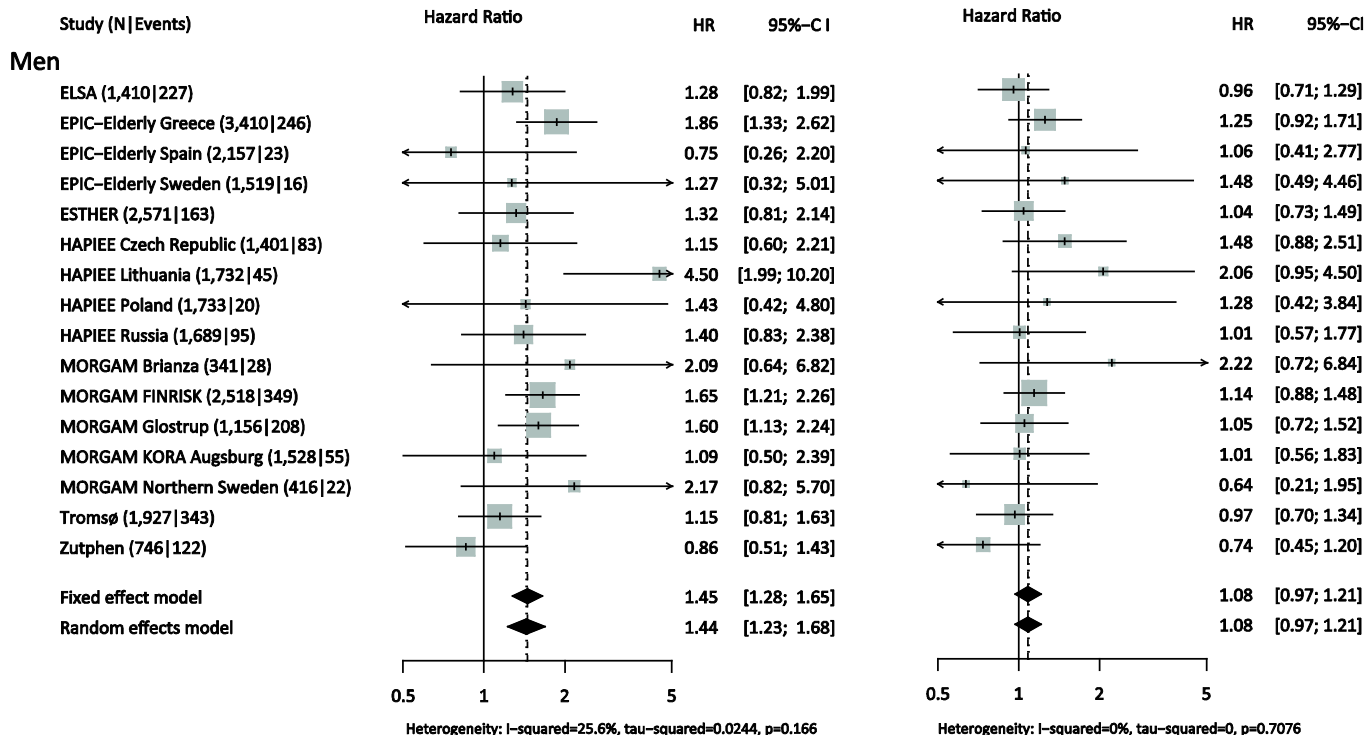
Supplementary Figure 17. Meta-analysis of the association of current smoking status with stroke events by sex

Stroke Events

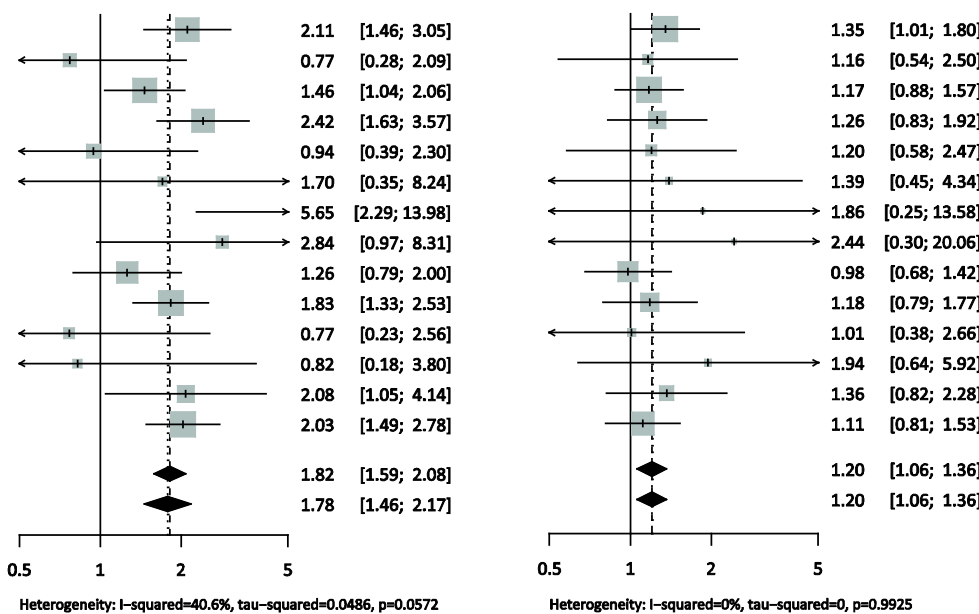
Men

Current smokers vs. Never smokers

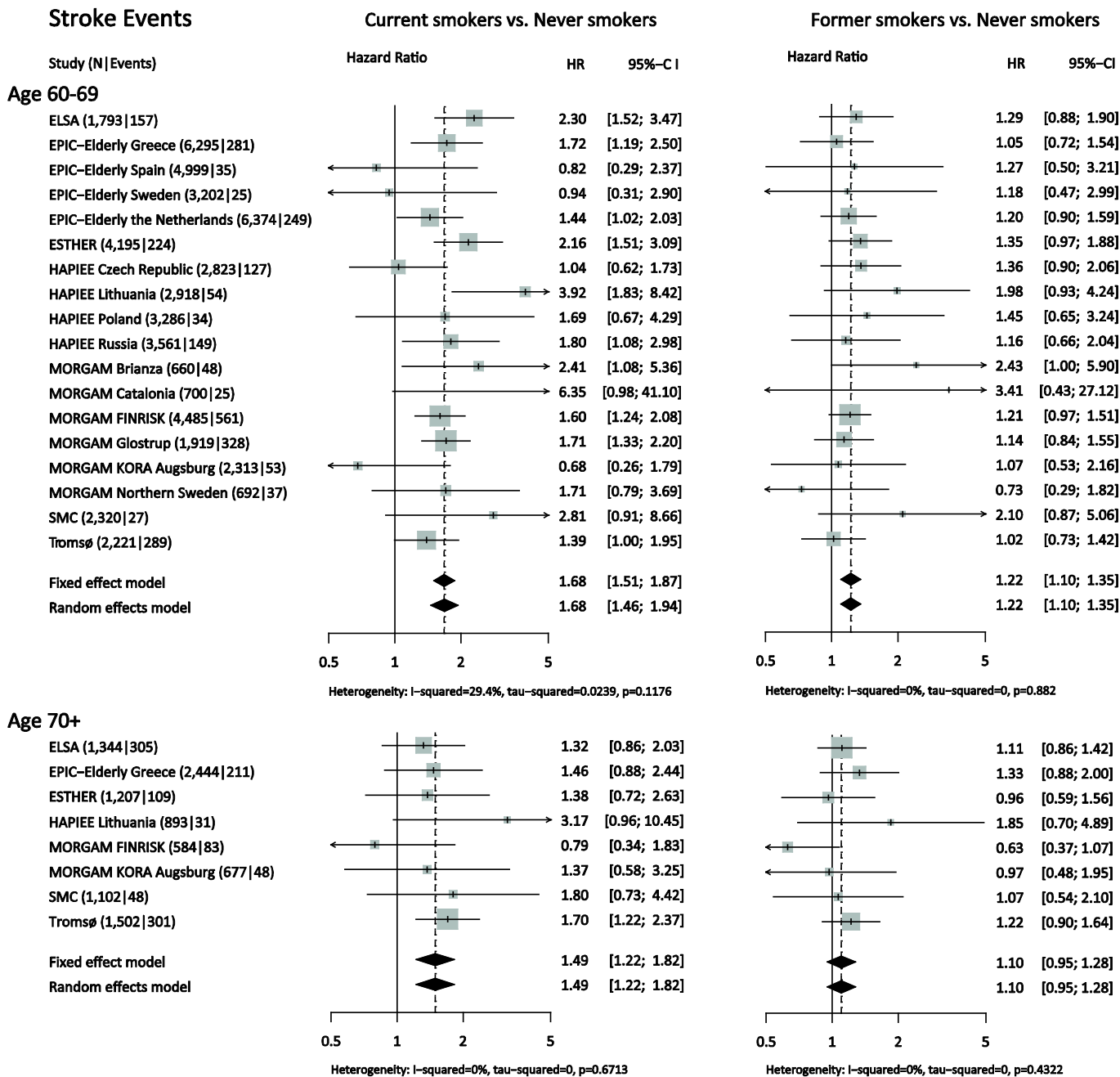
Former smokers vs. Never smokers



Women

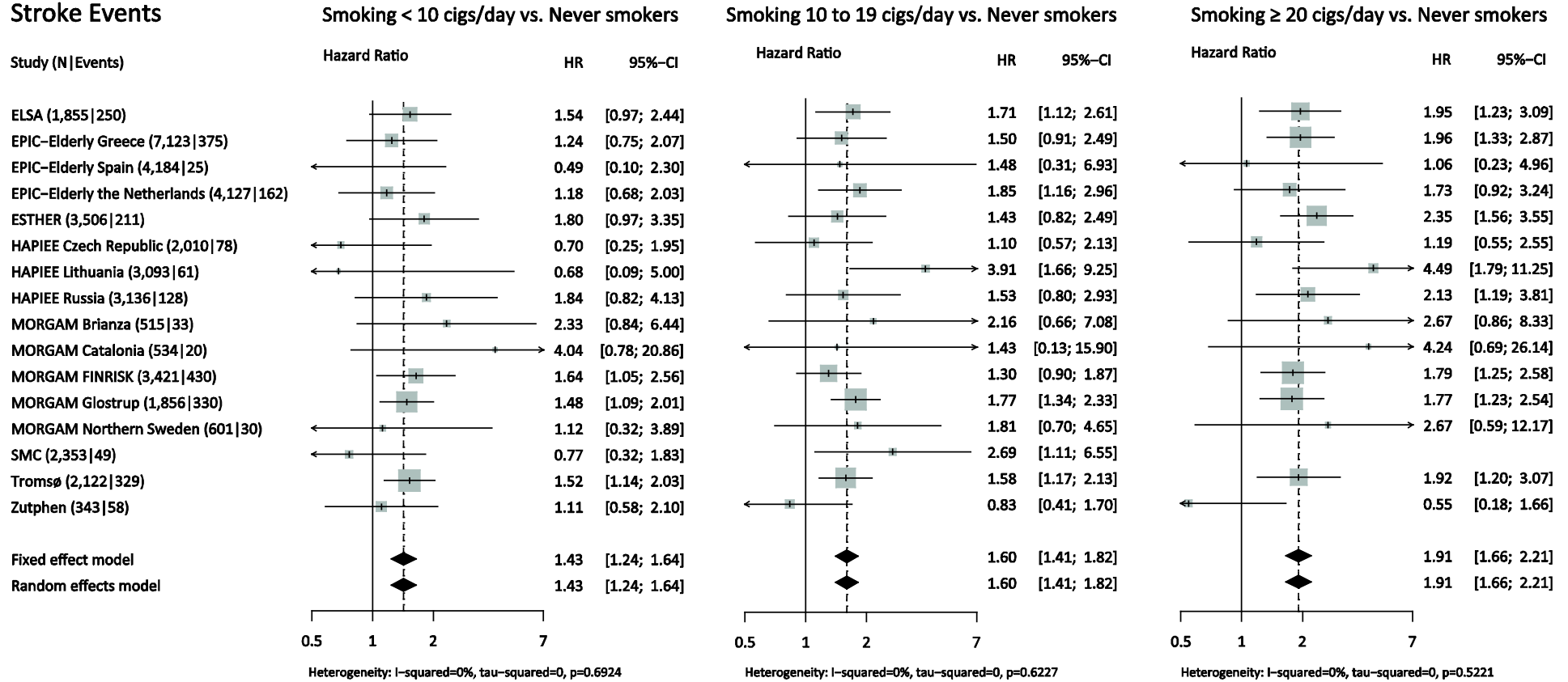


Supplementary Figure 18. Meta-analysis of the association of current smoking status with stroke events by age group



Supplementary Figure 19. Meta-analysis of the association of categories of cigarette consumption with stroke events

Stroke Events



Supplementary Figure 20. Meta-analysis of the association of categories of time since smoking cessation with stroke events

Stroke Events

