**Evidence relating cigarettes, cigars and pipes to cardiovascular disease and stroke:**

**Meta-analysis of recent data from three regions**

**Supplementary material 1**

Authors                     Peter N Lee, Katharine J Coombs, Jan S Hamling

This supplementary file provides the detailed output from the meta-analyses relating smoking to AMI (acute myocardial infarction), IHD (ischaemic heart disease) and stroke. This relates to cigarette smoking only as the data on pipe and cigar smoking were too limited to make meta-analysis of these smoking products feasible.

Smoking and CVD: Cigarette Smoking analyses

These analyses are restricted to results for current cigarette smokers versus never smokers. Results

for three CVD diseases are presented: acute myocardial infarction (AMI), ischaemic heart disease (IHD) and Stroke.

In the initial analyses, if multiple results are available from a single study, the results to be

included in meta-analysis are selected by applying the following criteria:

1) Exclusive cigarette smoking rather than non-exclusive.

2) A latency rule was applied rather than none being used.

3) The greatest amount of adjustment for possible confounding factors.


In additional analyses,

- The ratio of results for males and females within a single study are reported and meta-analysed;

- The ratios of adjusted to unadjusted results for a single study are reported,

  but, because these are not independent findings, only a sign test is carried out,

- The ratios of multiply-adjusted to (unadjusted or only age-adjusted) results are similarly reported.


Key:

   Study ID: Identifier assigned to the study

   NRR:     Sequence number assigned to the risk estimates within a study

   REFID:   Identifier assigned to the published paper

   Nature of pop: Nature of the population; National, Regional or Other

   YRST:    Year of start of baseline

   NAMI, NIHD, NSTR: Number of CVD cases (AMI, IHD or Stroke) in the study

   Excl:    Exclusive use of the product: 0 = No; x = Yes

   Latent:  A latency rule was applied, such as ignoring CVD cases identified in the first two or five

         years after smoking data were gathered: 0 = No; x = Yes

   Pop analysed: The type of population considered in analysis: Cohort or Nested case control

   Disease: Disease reported; AMI = acute myocardial infarction, IHD = Ischaemic heart disease or Stroke

   Sex:     Gender reported by the risk estimate; b = both sexes combined, m = male, f = female

   LowAge, HighAge: Age range reported by the risk estimate

   YrsFU:   Number of years of follow up reported by the risk estimate

   Endpoint: The way the cases were identified: by diagnosis (inc. reported death) or only by reported death

   Adj:     Number of adjustment factors applied to the risk estimate

   CA1, CA0, CO1, CO0: For estimates derived from numbers, the values used: CA=Cases, CO=At Risk, 1=Exposed, 0=Unexposed

   RR, RRL, RRU: The estimate of relative risk (e.g. hazard ratio) and its 95% confidence interval.

   Derived: How the estimate was obtained. Hamling method: see paper by Hamling et al. Stat Med 2008

   Definition of AMI/IHD/Stroke: how the disease was defined within the study

   Standard AMI/IHD/Stroke definition: The study used the standard definition of the disease: 0 = No; present = Yes

Smoking and CVD: Cigarette Smoking analyses

**CONTENTS**

Smoking and CVD: Cigarette Smoking analyses

Table 1
Smoking and CVD: Cigarette Smoking analyses
Results for AMI
List of study details for all the AMI results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NAMI | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|----------|-----|-------|---------|---------------|------|------|------|--------|--------------|---------|-----|--------|---------|-------|----------|-----|
| BIOBANK | 1 | MILLET2018 | UK | National | 2006 | 5081 | 0 | 0 | Cohort | AMI | f | 40 | 69 | 12 | Diagnosed | 2 |
| BIOBANK | 2 | MILLET2018 | UK | National | 2006 | 5081 | 0 | 0 | Cohort | AMI | m | 40 | 69 | 12 | Diagnosed | 2 |
| CALIBER | 3 | PUJADE2015 | UK | GP records | 1997 | 5628 | 0 | 0 | Cohort | AMI | f | 30 | 999 | 13 | Diagnosed | 1 |
| CaCHS | 1 | NG2020 | Canada | Regional | 2001 | 1133 | 0 | 0 | Cohort | AMI | f | 20 | 999 | 13 | Diagnosed | 15 |
| CaCHS | 3 | NG2020 | Canada | Regional | 2001 | 1133 | 0 | 0 | Cohort | AMI | m | 20 | 999 | 13 | Diagnosed | 15 |
| EPIC-GERM | 1 | WIRTH2015 | Germany | Regional | 1994 | 507 | 0 | 0 | Cohort | AMI | b | 35 | 65 | 14 | Diagnosed | 0 |
| EPIC-GERM | 2 | WIRTH2015 | Germany | Regional | 1994 | 507 | 0 | 0 | Cohort | AMI | b | 35 | 65 | 14 | Diagnosed | 9 |
| ESTONGENOME | 2 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | m | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 5 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | f | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 9 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 12 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | f | 18 | 999 | 13 | Died | 1 |
| KIHD | 1 | MUJAHI2017 | Finland | Regional | 1984 | 205 | 0 | 0 | Cohort | AMI | m | 42 | 60 | 18 | Diagnosed | 0 |
| TROMSO | 1 | ALBREK2017 | Norway | Regional | 1979 | 854 | 0 | 0 | Cohort | AMI | f | 20 | 94 | 33 | Diagnosed | 0 |
| TROMSO | 2 | ALBREK2017 | Norway | Regional | 1979 | 854 | 0 | 0 | Cohort | AMI | f | 20 | 94 | 33 | Diagnosed | 4 |
| VASTERBOTTEN | 1 | WALLER2015 | Sweden | Regional | 1990 | 2062 | 0 | 0 | Cohort | AMI | b | 30 | 60 | 19 | Diagnosed | 2 |
| VASTERBOTTEN | 2 | WALLER2015 | Sweden | Regional | 1990 | 2062 | 0 | 0 | Cohort | AMI | b | 30 | 60 | 19 | Diagnosed | 9 |
| WHILA | 1 | CALLIN2018 | Sweden | Regional | 1995 | 205 | 0 | 0 | Cohort | Non-fatal AMI | f | 50 | 59 | 20 | Diagnosed | 1 |
| WHILA | 2 | CALLIN2018 | Sweden | Regional | 1995 | 205 | 0 | 0 | Cohort | Non-fatal AMI | f | 50 | 59 | 20 | Diagnosed | 7 |
| WHS | 3 | KURTH2020 | USA | National | 1992 | 629 | 0 | 0 | Cohort | AMI | f | 45 | 999 | 26 | Diagnosed | 0 |
| WHS | 4 | KURTH2020 | USA | National | 1992 | 629 | 0 | 0 | Cohort | AMI | f | 45 | 999 | 26 | Diagnosed | 14 |

Table 2
Smoking and CVD: Cigarette Smoking analyses
Results for AMI
List of risk estimates for all the AMI results (not all to be included in any one meta-analysis), Current cigarette smokers versus never smokers

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|----------|-----|-------|-----|-----|-----|-----|-----|-----|-----|---------|
| BIOBANK | 1 | MILLET2018 | - | - | - | - | 3.46 | 3.02 | 3.98 | Given in the paper |
| BIOBANK | 2 | MILLET2018 | - | - | - | - | 2.23 | 2.03 | 2.44 | Given in the paper |
| CALIBER | 3 | PUJADE2015 | - | - | - | - | 2.51 | 2.35 | 2.73 | Given in the paper |
| CaCHS | 1 | NG2020 | - | - | - | - | 3.64 | 2.52 | 5.26 | Hamling method |
| CaCHS | 3 | NG2020 | - | - | - | - | 3.79 | 3.02 | 4.75 | Hamling method |
| EPIC-GERM | 1 | WIRTH2015 | 221 | 144 | 9693 | 21692 | 3.43 | 2.79 | 4.23 | From numbers |
| EPIC-GERM | 2 | WIRTH2015 | - | - | - | - | 3.52 | 2.87 | 4.31 | Hamling method |
| ESTONGENOME | 2 | KOKS2017 | * | * | * | * | 1.32 | 0.63 | 2.79 | Given in the paper |
| ESTONGENOME | 5 | KOKS2017 | * | * | * | * | 0.57 | 0.24 | 1.37 | Given in the paper |
| ESTONGENOME | 9 | KOKS2017 | - | - | - | - | 2.07 | 0.95 | 4.53 | Given in the paper |
| ESTONGENOME | 12 | KOKS2017 | - | - | - | - | 4.72 | 1.83 | 12.17 | Given in the paper |
| KIHD | 1 | MUJAHI2017 | 86 | 55 | 444 | 418 | 1.47 | 1.08 | 2.01 | From numbers |
| TROMSO | 1 | ALBREK2017 | 348 | 333 | 118030 | 112612 | 1.00 | 0.86 | 1.16 | From numbers |
| TROMSO | 2 | ALBREK2017 | - | - | - | - | 2.11 | 1.81 | 2.47 | Given in the paper |
| VASTERBOTTEN | 1 | WALLER2015 | - | - | - | - | 2.65 | 2.37 | 2.95 | Given in the paper |
| VASTERBOTTEN | 2 | WALLER2015 | - | - | - | - | 2.58 | 2.29 | 2.91 | Given in the paper |
| WHILA | 1 | CALLIN2018 | - | - | - | - | 2.84 | 2.09 | 3.86 | Given in the paper |
| WHILA | 2 | CALLIN2018 | - | - | - | - | 2.66 | 1.95 | 3.64 | Given in the paper |
| WHS | 3 | KURTH2020 | 150 | 256 | 61325 | 308857 | 2.95 | 2.41 | 3.61 | From numbers |
| WHS | 4 | KURTH2020 | - | - | - | - | 3.00 | 2.39 | 3.76 | Other calculations |

Table 3
Smoking and CVD: Cigarette Smoking analyses
Results for AMI
List of the disease definitions for all the AMI results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | Definition of AMI | Standard AMI definition |
|---|---|---|---|---|---|---|
| BIOBANK | 1 | MILLET2018 | UK | National | ICD-10 I21, I22, I23, I24.1, I25.2 | 0 |
| BIOBANK | 2 | MILLET2018 | UK | National | ICD-10 I21, I22, I23, I24.1, I25.2 | 0 |
| CALIBER | 3 | PUJADE2015 | UK | GP records | From Read Codes | 0 |
| CaCHS | 1 | NG2020 | Canada | Regional | ICD-9 410, ICD-10 I21 | present |
| CaCHS | 3 | NG2020 | Canada | Regional | ICD-9 410, ICD-10 I21 | present |
| EPIC-GERM | 1 | WIRTH2015 | Germany | Regional | ICD-10 I21 | present |
| EPIC-GERM | 2 | WIRTH2015 | Germany | Regional | ICD-10 I21 | present |
| ESTONGENOME | 2 | KOKS2017 | Estonia | National | ICD-10 I21 | present |
| ESTONGENOME | 5 | KOKS2017 | Estonia | National | ICD-10 I21 | present |
| ESTONGENOME | 9 | KOKS2017 | Estonia | National | ICD-10 I21 | present |
| ESTONGENOME | 12 | KOKS2017 | Estonia | National | ICD-10 I21 | present |
| KIHD | 1 | MUJAHI2017 | Finland | Regional | Non-fatal: WHO MONICA. Fatal: ICD-8 410-414, 795 | 0 |
| TROMSO | 1 | ALBREK2017 | Norway | Regional | WHO-MONICA | 0 |
| TROMSO | 2 | ALBREK2017 | Norway | Regional | WHO-MONICA | 0 |
| VASTERBOTTEN | 1 | WALLER2015 | Sweden | Regional | ICD-9 410, ICD-10 I21 | present |
| VASTERBOTTEN | 2 | WALLER2015 | Sweden | Regional | ICD-9 410, ICD-10 I21 | present |
| WHILA | 1 | CALLIN2018 | Sweden | Regional | ICD-8 410, ICD-10 I21 | present |
| WHILA | 2 | CALLIN2018 | Sweden | Regional | ICD-8 410, ICD-10 I21 | present |
| WHS | 3 | KURTH2020 | USA | National | WHO criteria. | 0 |
| WHS | 4 | KURTH2020 | USA | National | WHO criteria. | 0 |

Table 4
Smoking and CVD: Cigarette Smoking analyses
Results for AMI
List of the study details for the selected results, Current cigarette smokers versus never smokers, no overlapping results for any study

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NAMI | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|----------|-----|-------|---------|---------------|------|------|------|--------|--------------|---------|-----|--------|---------|-------|----------|-----|
| BIOBANK | 1 | MILLET2018 | UK | National | 2006 | 5081 | 0 | 0 | Cohort | AMI | f | 40 | 69 | 12 | Diagnosed | 2 |
| BIOBANK | 2 | MILLET2018 | UK | National | 2006 | 5081 | 0 | 0 | Cohort | AMI | m | 40 | 69 | 12 | Diagnosed | 2 |
| CALIBER | 3 | PUJADE2015 | UK | GP records | 1997 | 5628 | 0 | 0 | Cohort | AMI | f | 30 | 999 | 13 | Diagnosed | 1 |
| CaCHS | 1 | NG2020 | Canada | Regional | 2001 | 1133 | 0 | 0 | Cohort | AMI | f | 20 | 999 | 13 | Diagnosed | 15 |
| CaCHS | 3 | NG2020 | Canada | Regional | 2001 | 1133 | 0 | 0 | Cohort | AMI | m | 20 | 999 | 13 | Diagnosed | 15 |
| EPIC-GERM | 2 | WIRTH2015 | Germany | Regional | 1994 | 507 | 0 | 0 | Cohort | AMI | b | 35 | 65 | 14 | Diagnosed | 9 |
| ESTONGENOME | 9 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 12 | KOKS2017 | Estonia | National | 2002 | 118 | 0 | 0 | Cohort | AMI | f | 18 | 999 | 13 | Died | 1 |
| KIHD | 1 | MUJAHI2017 | Finland | Regional | 1984 | 205 | 0 | 0 | Cohort | AMI | m | 42 | 60 | 18 | Diagnosed | 0 |
| TROMSO | 2 | ALBREK2017 | Norway | Regional | 1979 | 854 | 0 | 0 | Cohort | AMI | f | 20 | 94 | 33 | Diagnosed | 4 |
| VASTERBOTTEN | 2 | WALLER2015 | Sweden | Regional | 1990 | 2062 | 0 | 0 | Cohort | AMI | b | 30 | 60 | 19 | Diagnosed | 9 |
| WHILA | 2 | CALLIN2018 | Sweden | Regional | 1995 | 205 | 0 | 0 | Cohort | Non-fatal AMI | f | 50 | 59 | 20 | Diagnosed | 7 |
| WHS | 4 | KURTH2020 | USA | National | 1992 | 629 | 0 | 0 | Cohort | AMI | f | 45 | 999 | 26 | Diagnosed | 14 |

Table 5
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by sex

**Combined**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *EPIC-GERM | 2 | - | - | - | - | 3.52 ( 2.87- 4.31) |
| *VASTERBOTTEN | 2 | - | - | - | - | 2.58 ( 2.29- 2.91) |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**Male**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 2 | - | - | - | - | 2.23 ( 2.03- 2.44) |
| *CaCHS | 3 | - | - | - | - | 3.79 ( 3.02- 4.75) |
| *ESTONGENOME | 9 | - | - | - | - | 2.07 ( 0.95- 4.53) |
| *KIHD | 1 | 86 | 444 | 55 | 418 | 1.47 ( 1.08- 2.01) |
| Partial Totals | | 86 | 444 | 55 | 418 | | |

*prospective study

**Female**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 1 | - | - | - | - | 3.46 ( 3.02- 3.98) |
| *CALIBER | 3 | - | - | - | - | 2.51 ( 2.35- 2.73) |
| *CaCHS | 1 | - | - | - | - | 3.64 ( 2.52- 5.26) |
| *ESTONGENOME | 12 | - | - | - | - | 4.72 ( 1.83- 12.17) |
| *TROMSO | 2 | - | - | - | - | 2.11 ( 1.81- 2.47) |
| *WHILA | 2 | - | - | - | - | 2.66 ( 1.95- 3.64) |
| *WHS | 4 | - | - | - | - | 3.00 ( 2.39- 3.76) |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

| | | RR Sex | | | |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | |
| | | Combined | Male | Female | Total |

**RR Data**

| | | 1 Combined | 2 Male | 3 Female | Total |
|---|---|---|---|---|---|
| | N | 2 | 4 | 7 | 13 |
| | NS | 2 | 4 | 7 | 13 |
| | Wt | 360.59 | 575.00 | 1191.56 | 2127.14 |
| Het | Chi | 6.66 | 27.06 | 30.05 | 73.50 |
| Het | df | 1 | 3 | 6 | 12 |
| Het | P | ** | *** | *** | *** |
| Fixed | RR | 2.80 | 2.32 | 2.65 | 2.58 |
| | RRl | 2.52 | 2.14 | 2.51 | 2.47 |
| | RRu | 3.10 | 2.52 | 2.81 | 2.69 |
| | P | +++ | +++ | +++ | +++ |
| Random | RR | 2.98 | 2.30 | 2.83 | 2.72 |
| | RRl | 2.20 | 1.57 | 2.40 | 2.40 |
| | RRu | 4.04 | 3.37 | 3.34 | 3.08 |
| | P | +++ | +++ | +++ | +++ |
| Asymm | P | | N.S. | N.S. | N.S. |
| Between | Chi | | 7.69 | 0.75 | 9.72 |
| Between | df | | 1 | 1 | 2 |
| Between | P | | -- | N.S. | ** |
| Btwn(F) | P | | N.S. | N.S. | N.S. |
| Btwn(R) | P | | N.S. | N.S. | N.S. |

Table 6
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by region

**N America**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *CaCHS | 3 | – | – | – | – | 3.79 ( 3.02– 4.75) | |
| *CaCHS | 1 | – | – | – | – | 3.64 ( 2.52– 5.26) | |
| Subtotal CaCHS | | | | | | 3.75 ( 3.09– 4.55) | |
| *WHS | 4 | – | – | – | – | 3.00 ( 2.39– 3.76) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study


**Europe**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 2 | – | – | – | – | 2.23 ( 2.03– 2.44) | |
| *BIOBANK | 1 | – | – | – | – | 3.46 ( 3.02– 3.98) | |
| Subtotal BIOBANK | | | | | | 2.55 ( 2.36– 2.76) | |
| *CALIBER | 3 | – | – | – | – | 2.51 ( 2.35– 2.73) | |
| *EPIC-GERM | 2 | – | – | – | – | 3.52 ( 2.87– 4.31) | |
| *ESTONGENOME | 9 | – | – | – | – | 2.07 ( 0.95– 4.53) | |
| *ESTONGENOME | 12 | – | – | – | – | 4.72 ( 1.83– 12.17) | |
| Subtotal ESTONGENOME | | | | | | 2.89 ( 1.58– 5.28) | |
| *KIHD | 1 | 86 | 444 | 55 | 418 | 1.47 ( 1.08– 2.01) | |
| *TROMSO | 2 | – | – | – | – | 2.11 ( 1.81– 2.47) | |
| *VASTERBOTTEN | 2 | – | – | – | – | 2.58 ( 2.29– 2.91) | |
| *WHILA | 2 | – | – | – | – | 2.66 ( 1.95– 3.64) | |
| Partial Totals | | 86 | 444 | 55 | 418 | | |

*prospective study


| | | Region | | | |
|--|--|--------|--|--|--|
| | | 1 | 2 | 3 | |
| | | N America | Europe | Japan | Total |

**RR Data**

| | | N America | Europe | Japan | Total |
|--|--|-----------|--------|-------|-------|
| | N | 3 | 10 | | 13 |
| | NS | 2 | 8 | | 10 |
| | Wt | 178.13 | 1949.01 | | 2127.14 |
| Het | Chi | 2.19 | 56.13 | | 73.50 |
| Het | df | 2 | 9 | | 12 |
| Het | P | N.S. | *** | | *** |
| Fixed | RR | 3.41 | 2.52 | | 2.58 |
| | RRl | 2.95 | 2.41 | | 2.47 |
| | RRu | 3.95 | 2.63 | | 2.69 |
| | P | +++ | +++ | | +++ |
| Random | RR | 3.42 | 2.54 | | 2.72 |
| | RRl | 2.93 | 2.22 | | 2.40 |
| | RRu | 3.99 | 2.90 | | 3.08 |
| | P | +++ | +++ | | +++ |
| Asymm | P | N.S. | N.S. | | N.S. |
| Between | Chi | | 15.18 | | 15.18 |
| Between | df | | 1 | | 1 |
| Between | P | | --- | N.S. | *** |
| Btwn(F) | P | | N.S. | N.S. | N.S. |
| Btwn(R) | P | | -- | N.S. | ** |

Table 7
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by nature of the population

```
National
                    Numbers exposed Non-exposed
 Study ID      NRR    Case    Cont    Case    Cont      RR        95.00%CI
*BIOBANK       2       -       -       -       -      2.23 ( 2.03-   2.44)
*BIOBANK       1       -       -       -       -      3.46 ( 3.02-   3.98)
 Subtotal BIOBANK                                     2.55 ( 2.36-   2.76)
*ESTONGENOME   9       -       -       -       -      2.07 ( 0.95-   4.53)
*ESTONGENOME  12       -       -       -       -      4.72 ( 1.83-  12.17)
 Subtotal ESTONGENOME                                 2.89 ( 1.58-   5.28)
*WHS           4       -       -       -       -      3.00 ( 2.39-   3.76)
Partial Totals         0       0       0       0
*prospective study


Regional
                    Numbers exposed Non-exposed
 Study ID      NRR    Case    Cont    Case    Cont      RR        95.00%CI
*CaCHS         3       -       -       -       -      3.79 ( 3.02-   4.75)
*CaCHS         1       -       -       -       -      3.64 ( 2.52-   5.26)
 Subtotal CaCHS                                       3.75 ( 3.09-   4.55)
*EPIC-GERM     2       -       -       -       -      3.52 ( 2.87-   4.31)
*KIHD          1      86     444      55     418      1.47 ( 1.08-   2.01)
*TROMSO        2       -       -       -       -      2.11 ( 1.81-   2.47)
*VASTERBOTTEN  2       -       -       -       -      2.58 ( 2.29-   2.91)
*WHILA         2       -       -       -       -      2.66 ( 1.95-   3.64)
Partial Totals        86     444      55     418
*prospective study


Other
                    Numbers exposed Non-exposed
 Study ID      NRR    Case    Cont    Case    Cont      RR        95.00%CI
*CALIBER       3       -       -       -       -      2.51 ( 2.35-   2.73)
Partial Totals         0       0       0       0
*prospective study
```

```
                         Population Type
                          1        2        3
                       National  Regional   Other     Total

RR Data

                  N       5        7        1        13
                  NS      3        6        1        10

                  Wt    741.14   702.04   683.96   2127.14
            Het Chi    30.55    42.09     0.00     73.50
            Het  df       4        6        0        12
            Het  P      ***      ***      N.S.      ***
            Fixed RR    2.60     2.63     2.51      2.58
                  RRl   2.42     2.45     2.33      2.47
                  RRu   2.79     2.84     2.71      2.69
                  P     +++      +++      +++       +++
         Random  RR     2.85     2.69     2.51      2.72
                  RRl   2.16     2.18     2.33      2.40
                  RRu   3.77     3.33     2.71      3.08
                  P     +++      +++      +++       +++
            Asymm P     N.S.     N.S.               N.S.
         Between Chi             0.06     0.43      0.85
         Between  df              1        1         2
         Between  P             N.S.     N.S.      N.S.
         Btwn(F)  P             N.S.     N.S.      N.S.
         Btwn(R)  P             N.S.     N.S.      N.S.
```

Table 8
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by year of start of baseline

**<1988**

```
                Numbers exposed Non-exposed
 Study ID    NRR    Case   Cont   Case   Cont     RR        95.00%CI
*KIHD         1      86    444     55    418    1.47 (  1.08-   2.01)
*TROMSO       2      -      -      -      -     2.11 (  1.81-   2.47)
Partial Totals       86    444     55    418
*prospective study
```

**1988+**

```
                Numbers exposed Non-exposed
 Study ID    NRR    Case   Cont   Case   Cont     RR        95.00%CI
*BIOBANK      2      -      -      -      -     2.23 (  2.03-   2.44)
*BIOBANK      1      -      -      -      -     3.46 (  3.02-   3.98)
 Subtotal BIOBANK                              2.55 (  2.36-   2.76)
*CALIBER      3      -      -      -      -     2.51 (  2.35-   2.73)
*CaCHS        3      -      -      -      -     3.79 (  3.02-   4.75)
*CaCHS        1      -      -      -      -     3.64 (  2.52-   5.26)
 Subtotal CaCHS                                3.75 (  3.09-   4.55)
*EPIC-GERM    2      -      -      -      -     3.52 (  2.87-   4.31)
*ESTONGENOME  9      -      -      -      -     2.07 (  0.95-   4.53)
*ESTONGENOME 12      -      -      -      -     4.72 (  1.83-  12.17)
 Subtotal ESTONGENOME                          2.89 (  1.58-   5.28)
*VASTERBOTTEN 2      -      -      -      -     2.58 (  2.29-   2.91)
*WHILA        2      -      -      -      -     2.66 (  1.95-   3.64)
*WHS          4      -      -      -      -     3.00 (  2.39-   3.76)
Partial Totals        0      0      0      0
*prospective study
```

```
                     YrSt
                      1       2
                    <1988   1988+    Total

 RR Data

             N        2      11       13
             NS       2       8       10

             Wt   198.72  1928.42  2127.14
      Het Chi     4.12    52.97    73.50
      Het  df        1       10       12
      Het  P         *      ***      ***
    Fixed RR      1.96     2.66     2.58
         RRl      1.71     2.54     2.47
         RRu      2.26     2.78     2.69
           P      +++      +++      +++
   Random  RR     1.81     2.93     2.72
          RRl     1.28     2.58     2.40
          RRu     2.56     3.32     3.08
            P     +++      +++      +++
    Asymm  P               (*)     N.S.
  Between Chi             16.41    16.41
  Between df                 1        1
  Between P               +++      ***
  Btwn(F)  P              N.S.     N.S.
  Btwn(R)  P                +        *
```

Table 9
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by number of cases in the study

```
<1000
                  Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR       95.00%CI
*EPIC-GERM    2      -      -      -      -      3.52 ( 2.87-  4.31)
*ESTONGENOME  9      -      -      -      -      2.07 ( 0.95-  4.53)
*ESTONGENOME  12     -      -      -      -      4.72 ( 1.83- 12.17)
 Subtotal ESTONGENOME                           2.89 ( 1.58-  5.28)
*KIHD         1      86     444    55     418    1.47 ( 1.08-  2.01)
*TROMSO       2      -      -      -      -      2.11 ( 1.81-  2.47)
*WHILA        2      -      -      -      -      2.66 ( 1.95-  3.64)
*WHS          4      -      -      -      -      3.00 ( 2.39-  3.76)
Partial Totals       86     444    55     418
*prospective study


1000+
                  Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR       95.00%CI
*BIOBANK      2      -      -      -      -      2.23 ( 2.03-  2.44)
*BIOBANK      1      -      -      -      -      3.46 ( 3.02-  3.98)
 Subtotal BIOBANK                               2.55 ( 2.36-  2.76)
*CALIBER      3      -      -      -      -      2.51 ( 2.35-  2.73)
*CaCHS        3      -      -      -      -      3.79 ( 3.02-  4.75)
*CaCHS        1      -      -      -      -      3.64 ( 2.52-  5.26)
 Subtotal CaCHS                                 3.75 ( 3.09-  4.55)
*VASTERBOTTEN 2      -      -      -      -      2.58 ( 2.29-  2.91)
Partial Totals       0      0      0      0
*prospective study
```

|  | Number of AMI cases | | | |
|---|---|---|---|---|
|  | 1 | 2 | 3 | |
|  | absent | <1000 | 1000+ | Total |

**RR Data**

|  | | | | |
|---|---|---|---|---|
| N | | 7 | 6 | 13 |
| NS | | 6 | 4 | 10 |
| Wt | | 416.51 | 1710.63 | 2127.14 |
| Het Chi | | 31.19 | 41.88 | 73.50 |
| Het df | | 6 | 5 | 12 |
| Het P | | *** | *** | *** |
| Fixed RR | | 2.51 | 2.60 | 2.58 |
| RRl | | 2.28 | 2.48 | 2.47 |
| RRu | | 2.76 | 2.73 | 2.69 |
| P | | +++ | +++ | +++ |
| Random RR | | 2.52 | 2.87 | 2.72 |
| RRl | | 1.96 | 2.46 | 2.40 |
| RRu | | 3.25 | 3.35 | 3.08 |
| P | | +++ | +++ | +++ |
| Asymm P | | N.S. | N.S. | N.S. |
| Between Chi | | | | 0.42 |
| Between df | | | | 1 |
| Between P | | N.S. | N.S. | N.S. |
| Btwn(F) P | | N.S. | N.S. | N.S. |
| Btwn(R) P | | N.S. | N.S. | N.S. |

Table 10
Smoking and CVD: Cigarette Smoking analyses
<ins>Results for AMI</ins>
Analysis by lowest age considered, with trend

**<30**

| | | Numbers exposed | | Non-exposed | | | |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *CaCHS | 3 | - | - | - | - | 3.79 ( 3.02- 4.75) | |
| *CaCHS | 1 | - | - | - | - | 3.64 ( 2.52- 5.26) | |
| Subtotal CaCHS | | | | | | 3.75 ( 3.09- 4.55) | |
| *ESTONGENOME | 9 | - | - | - | - | 2.07 ( 0.95- 4.53) | |
| *ESTONGENOME | 12 | - | - | - | - | 4.72 ( 1.83- 12.17) | |
| Subtotal ESTONGENOME | | | | | | 2.89 ( 1.58- 5.28) | |
| *TROMSO | 2 | - | - | - | - | 2.11 ( 1.81- 2.47) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**30-<45**

| | | Numbers exposed | | Non-exposed | | | |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *BIOBANK | 2 | - | - | - | - | 2.23 ( 2.03- 2.44) | |
| *BIOBANK | 1 | - | - | - | - | 3.46 ( 3.02- 3.98) | |
| Subtotal BIOBANK | | | | | | 2.55 ( 2.36- 2.76) | |
| *CALIBER | 3 | - | - | - | - | 2.51 ( 2.35- 2.73) | |
| *EPIC-GERM | 2 | - | - | - | - | 3.52 ( 2.87- 4.31) | |
| *KIHD | 1 | 86 | 444 | 55 | 418 | 1.47 ( 1.08- 2.01) | |
| *VASTERBOTTEN | 2 | - | - | - | - | 2.58 ( 2.29- 2.91) | |
| Partial Totals | | 86 | 444 | 55 | 418 | | |

*prospective study

**45+**

| | | Numbers exposed | | Non-exposed | | | |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *WHILA | 2 | - | - | - | - | 2.66 ( 1.95- 3.64) | |
| *WHS | 4 | - | - | - | - | 3.00 ( 2.39- 3.76) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

Lowest age included, grouped, excluding Missing

| | | 1 | 2 | 3 | | |
|---|---|---|---|---|---|---|
| | | <30 | 30-<45 | 45+ | Total | Trend |
| **RR Data** | | | | | | |
| | N | 5 | 6 | 2 | 13 | |
| | NS | 3 | 5 | 2 | 10 | |
| | Wt | 272.85 | 1740.01 | 114.28 | 2127.14 | |
| Het | Chi | 22.51 | 48.81 | 0.37 | 73.50 | |
| Het | df | 4 | 5 | 1 | 12 | |
| Het | P | *** | *** | N.S. | *** | |
| Fixed | RR | 2.65 | 2.55 | 2.88 | 2.58 | |
| | RRl | 2.36 | 2.43 | 2.40 | 2.47 | |
| | RRu | 2.99 | 2.67 | 3.46 | 2.69 | |
| | P | +++ | +++ | +++ | +++ | |
| Random | RR | 3.02 | 2.58 | 2.88 | 2.72 | |
| | RRl | 2.09 | 2.20 | 2.40 | 2.40 | |
| | RRu | 4.35 | 3.04 | 3.46 | 3.08 | |
| | P | +++ | +++ | +++ | +++ | |
| Asymm | P | N.S. | N.S. | | N.S. | |
| Between | Chi | | 0.37 | 0.52 | 1.80 | 0.06 |
| Between | df | | 1 | 1 | 2 | 1 |
| Between | P | | N.S. | N.S. | N.S. | N.S. |
| Btwn(F) | P | | N.S. | N.S. | N.S. | N.S. |
| Btwn(R) | P | | N.S. | N.S. | N.S. | N.S. |

Table 11
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by years of follow-up

```
10-<20
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*BIOBANK       2      -      -      -      -     2.23 ( 2.03-   2.44)
*BIOBANK       1      -      -      -      -     3.46 ( 3.02-   3.98)
 Subtotal BIOBANK                               2.55 ( 2.36-   2.76)
*CALIBER       3      -      -      -      -     2.51 ( 2.35-   2.73)
*CaCHS         3      -      -      -      -     3.79 ( 3.02-   4.75)
*CaCHS         1      -      -      -      -     3.64 ( 2.52-   5.26)
 Subtotal CaCHS                                 3.75 ( 3.09-   4.55)
*EPIC-GERM     2      -      -      -      -     3.52 ( 2.87-   4.31)
*ESTONGENOME  9      -      -      -      -     2.07 ( 0.95-   4.53)
*ESTONGENOME 12      -      -      -      -     4.72 ( 1.83-  12.17)
 Subtotal ESTONGENOME                           2.89 ( 1.58-   5.28)
*KIHD          1     86    444     55    418    1.47 ( 1.08-   2.01)
*VASTERBOTTEN 2      -      -      -      -     2.58 ( 2.29-   2.91)
Partial Totals       86    444     55    418
*prospective study


20-<30
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*WHILA         2      -      -      -      -     2.66 ( 1.95-   3.64)
*WHS           4      -      -      -      -     3.00 ( 2.39-   3.76)
Partial Totals        0      0      0      0
*prospective study


30+
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*TROMSO        2      -      -      -      -     2.11 ( 1.81-   2.47)
Partial Totals        0      0      0      0
*prospective study
```

```
                      Years follow-up, grouped
                      1        2        3      4
                     <10    10-<20  20-<30    30+      Total     Trend

RR Data

                N              10       2       1       13
                NS              7       2       1       10

                Wt         1853.88  114.28  158.98  2127.14
        Het Chi            65.10     0.37    0.00    73.50
        Het  df                9       1       0       12
        Het  P              ***     N.S.    N.S.     ***
        Fixed  RR           2.61    2.88    2.11     2.58
             RRl            2.49    2.40    1.81     2.47
             RRu            2.73    3.46    2.46     2.69
               P            +++     +++     +++      +++
        Random  RR          2.78    2.88    2.11     2.72
             RRl            2.40    2.40    1.81     2.40
             RRu            3.23    3.46    2.46     3.08
               P            +++     +++     +++      +++
        Asymm  P            N.S.                    N.S.
     Between Chi                                     8.02     4.92
     Between  df                                        2        1
     Between  P             N.S.    N.S.    N.S.       *        -
     Btwn(F)  P             N.S.    N.S.    N.S.     N.S.     N.S.
     Btwn(R)  P             N.S.    N.S.    N.S.       *       --
```

Table 12
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by endpoint

**Died**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ESTONGENOME | 9 | – | – | – | – | 2.07 ( 0.95– | 4.53) |
| *ESTONGENOME | 12 | – | – | – | – | 4.72 ( 1.83– | 12.17) |
| Subtotal ESTONGENOME | | | | | | 2.89 ( 1.58– | 5.28) |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study


**Diagnosed**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 2 | – | – | – | – | 2.23 ( 2.03– | 2.44) |
| *BIOBANK | 1 | – | – | – | – | 3.46 ( 3.02– | 3.98) |
| Subtotal BIOBANK | | | | | | 2.55 ( 2.36– | 2.76) |
| *CALIBER | 3 | – | – | – | – | 2.51 ( 2.35– | 2.73) |
| *CaCHS | 3 | – | – | – | – | 3.79 ( 3.02– | 4.75) |
| *CaCHS | 1 | – | – | – | – | 3.64 ( 2.52– | 5.26) |
| Subtotal CaCHS | | | | | | 3.75 ( 3.09– | 4.55) |
| *EPIC-GERM | 2 | – | – | – | – | 3.52 ( 2.87– | 4.31) |
| *KIHD | 1 | 86 | 444 | 55 | 418 | 1.47 ( 1.08– | 2.01) |
| *TROMSO | 2 | – | – | – | – | 2.11 ( 1.81– | 2.47) |
| *VASTERBOTTEN | 2 | – | – | – | – | 2.58 ( 2.29– | 2.91) |
| *WHILA | 2 | – | – | – | – | 2.66 ( 1.95– | 3.64) |
| *WHS | 4 | – | – | – | – | 3.00 ( 2.39– | 3.76) |
| Partial Totals | | 86 | 444 | 55 | 418 | | |

*prospective study

RR Description:Endpoint reported

| | 1 | 2 | |
|---|---|---|---|
| | Died | Diagnosed | Total |

**RR Data**

| | | 1 | 2 | Total |
|---|---|---|---|---|
| | N | 2 | 11 | 13 |
| | NS | 1 | 9 | 10 |
| | Wt | 10.58 | 2116.56 | 2127.14 |
| Het | Chi | 1.73 | 71.63 | 73.50 |
| Het | df | 1 | 10 | 12 |
| Het | P | N.S. | *** | *** |
| Fixed | RR | 2.89 | 2.58 | 2.58 |
| | RRl | 1.58 | 2.47 | 2.47 |
| | RRu | 5.28 | 2.69 | 2.69 |
| | P | +++ | +++ | +++ |
| Random | RR | 2.99 | 2.71 | 2.72 |
| | RRl | 1.34 | 2.38 | 2.40 |
| | RRu | 6.67 | 3.08 | 3.08 |
| | P | ++ | +++ | +++ |
| Asymm | P | | N.S. | N.S. |
| Between | Chi | | 0.14 | 0.14 |
| Between | df | | 1 | 1 |
| Between | P | | N.S. | N.S. |
| Btwn(F) | P | | N.S. | N.S. |
| Btwn(R) | P | | N.S. | N.S. |

Table 13
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by number of adjustment factors

```
Unadj
                    Numbers exposed Non-exposed
 Study ID      NRR   Case   Cont   Case   Cont     RR        95.00%CI
*KIHD           1     86    444     55    418     1.47 ( 1.08-  2.01)
Totals                86    444     55    418
*prospective study


Age-only
                    Numbers exposed Non-exposed
 Study ID      NRR   Case   Cont   Case   Cont     RR        95.00%CI
*CALIBER        3      -      -      -      -     2.51 ( 2.35-  2.73)
*ESTONGENOME    9      -      -      -      -     2.07 ( 0.95-  4.53)
*ESTONGENOME   12      -      -      -      -     4.72 ( 1.83- 12.17)
 Subtotal ESTONGENOME                            2.89 ( 1.58-  5.28)
Partial Totals         0      0      0      0
*prospective study


More adj
                    Numbers exposed Non-exposed
 Study ID      NRR   Case   Cont   Case   Cont     RR        95.00%CI
*BIOBANK        2      -      -      -      -     2.23 ( 2.03-  2.44)
*BIOBANK        1      -      -      -      -     3.46 ( 3.02-  3.98)
 Subtotal BIOBANK                                2.55 ( 2.36-  2.76)
*CaCHS          3      -      -      -      -     3.79 ( 3.02-  4.75)
*CaCHS          1      -      -      -      -     3.64 ( 2.52-  5.26)
 Subtotal CaCHS                                  3.75 ( 3.09-  4.55)
*EPIC-GERM      2      -      -      -      -     3.52 ( 2.87-  4.31)
*TROMSO         2      -      -      -      -     2.11 ( 1.81-  2.47)
*VASTERBOTTEN 2        -      -      -      -     2.58 ( 2.29-  2.91)
*WHILA          2      -      -      -      -     2.66 ( 1.95-  3.64)
*WHS            4      -      -      -      -     3.00 ( 2.39-  3.76)
Partial Totals         0      0      0      0
*prospective study
```

```
                   Number of adjustment factors, grouped
                        1        2        3
                     Unadj  Age-only  More adj      Total

RR Data

                  N       1        3        9        13
                  NS      1        2        7        10

                  Wt  39.74   694.54  1392.86  2127.14
           Het Chi   0.00     1.94    57.40    73.50
           Het  df      0        2        8        12
           Het  P    N.S.     N.S.      ***      ***
          Fixed RR   1.47     2.52     2.66     2.58
                RRl   1.08     2.34     2.52     2.47
                RRu   2.01     2.71     2.80     2.69
                  P      +      +++      +++      +++
         Random RR   1.47     2.52     2.89     2.72
                RRl   1.08     2.34     2.48     2.40
                RRu   2.01     2.71     3.37     3.08
                  P      +      +++      +++      +++
          Asymm  P            N.S.     N.S.     N.S.
        Between Chi          10.79    13.47    14.16
        Between  df             1        1        2
        Between  P              ++      +++      ***
        Btwn(F)  P             (+)     N.S.     N.S.
        Btwn(R)  P              ++      +++      ***
```

Table 14
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Analysis by disease definition standard or not

**absent**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 2 | – | – | – | – | 2.23 ( 2.03– 2.44) | |
| *BIOBANK | 1 | – | – | – | – | 3.46 ( 3.02– 3.98) | |
| Subtotal BIOBANK | | | | | | 2.55 ( 2.36– 2.76) | |
| *CALIBER | 3 | – | – | – | – | 2.51 ( 2.35– 2.73) | |
| *KIHD | 1 | 86 | 444 | 55 | 418 | 1.47 ( 1.08– 2.01) | |
| *TROMSO | 2 | – | – | – | – | 2.11 ( 1.81– 2.47) | |
| *WHS | 4 | – | – | – | – | 3.00 ( 2.39– 3.76) | |
| Partial Totals | | 86 | 444 | 55 | 418 | | |

*prospective study

**present**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *CaCHS | 3 | – | – | – | – | 3.79 ( 3.02– 4.75) | |
| *CaCHS | 1 | – | – | – | – | 3.64 ( 2.52– 5.26) | |
| Subtotal CaCHS | | | | | | 3.75 ( 3.09– 4.55) | |
| *EPIC-GERM | 2 | – | – | – | – | 3.52 ( 2.87– 4.31) | |
| *ESTONGENOME | 9 | – | – | – | – | 2.07 ( 0.95– 4.53) | |
| *ESTONGENOME | 12 | – | – | – | – | 4.72 ( 1.83– 12.17) | |
| Subtotal ESTONGENOME | | | | | | 2.89 ( 1.58– 5.28) | |
| *VASTERBOTTEN | 2 | – | – | – | – | 2.58 ( 2.29– 2.91) | |
| *WHILA | 2 | – | – | – | – | 2.66 ( 1.95– 3.64) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

Study description:Standard definition

| | | 1 | 2 | |
|---|---|---|---|---|
| | | absent | present | Total |

**RR Data**

| | | 1 absent | 2 present | Total |
|---|---|---|---|---|
| | N | 6 | 7 | 13 |
| | NS | 5 | 5 | 10 |
| | Wt | 1613.24 | 513.90 | 2127.14 |
| Het | Chi | 45.25 | 15.82 | 73.50 |
| Het | df | 5 | 6 | 12 |
| Het | P | *** | * | *** |
| Fixed | RR | 2.47 | 2.96 | 2.58 |
| | RRl | 2.35 | 2.71 | 2.47 |
| | RRu | 2.60 | 3.22 | 2.69 |
| | P | +++ | +++ | +++ |
| Random | RR | 2.43 | 3.14 | 2.72 |
| | RRl | 2.06 | 2.63 | 2.40 |
| | RRu | 2.87 | 3.74 | 3.08 |
| | P | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | N.S. |
| Between | Chi | | 12.43 | 12.43 |
| Between | df | | 1 | 1 |
| Between | P | | +++ | *** |
| Btwn(F) | P | | N.S. | N.S. |
| Btwn(R) | P | | + | * |

Table 15
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of study details for all the IHD results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NIHD | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 1 | MENOTT2016 | Italy | Regional | 1960 | 319 | 0 | 0 | Cohort | IHD | m | 40 | 59 | 50 | Died | 3 |
| ARIC | 1 | DING2019A | USA | National | 1987 | 1798 | 0 | 0 | Cohort | IHD | b | 45 | 64 | 30 | Diagnosed | 0 |
| ARIC | 2 | DING2019A | USA | National | 1987 | 1798 | 0 | 0 | Cohort | IHD | b | 45 | 64 | 30 | Diagnosed | 15 |
| BIOBANK | 3 | ZHANG2021H | UK | National | 2006 | 547 | 0 | 0 | Cohort | IHD | b | 40 | 69 | 12 | Diagnosed | 0 |
| CALIBER | 1 | PUJADE2015 | UK | GP records | 1997 | 16800 | 0 | 0 | Cohort | IHD | f | 30 | 999 | 13 | Diagnosed | 1 |
| CPS-II | 1 | TURNER2017 | USA | National | 1982 | 13478 | 0 | 0 | Cohort | IHD | b | 30 | 999 | 22 | Died | 0 |
| CPS-II | 3 | TURNER2017 | USA | National | 1982 | 13478 | 0 | 0 | Cohort | IHD | b | 30 | 999 | 22 | Died | 23 |
| CoCHS | 1 | SCHNOH2015 | Denmark | Regional | 1991 | 900 | 0 | 0 | Cohort | IHD | f | 20 | 93 | 22 | Diagnosed | 1 |
| ELSA | 1 | JACKSO2019E | UK | National | 2004 | 352 | 0 | 0 | Cohort | Non-fatal IHD | b | 52 | 999 | 13 | Diagnosed | 0 |
| ELSA | 2 | JACKSO2019E | UK | National | 2004 | 352 | 0 | 0 | Cohort | Non-fatal IHD | b | 52 | 999 | 13 | Diagnosed | 7 |
| EPIC-10 | 1 | KEY2019 | Multi | International | 1991 | 7198 | 0 | 0 | Cohort | IHD | m | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-10 | 2 | KEY2019 | Multi | International | 1991 | 7198 | 0 | 0 | Cohort | IHD | f | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-10 | 3 | RICCI2018 | Multi | International | 1991 | 7198 | 0 | 0 | Nested CC | Non-fatal IHD | b | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-UK | 1 | STOEKE2016 | UK | Regional | 1993 | 2332 | 0 | 0 | Cohort | IHD | b | 45 | 79 | 14 | Diagnosed | 0 |
| EPIC-UK | 2 | STOEKE2016 | UK | Regional | 1993 | 2332 | 0 | 0 | Cohort | IHD | b | 45 | 79 | 14 | Diagnosed | 2 |
| EPIC-UK | 3 | STOEKE2016 | UK | Regional | 1993 | 2332 | 0 | 0 | Cohort | IHD | b | 45 | 79 | 14 | Diagnosed | 6 |
| ESTONGENOME | 1 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | m | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 4 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | f | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 7 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 10 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | f | 18 | 999 | 13 | Died | 1 |
| FINRISK | 1 | BARENG2017 | Finland | National | 1982 | * | 0 | 0 | Cohort | IHD | f | 25 | 74 | 25 | Died | 3 |
| FINRISK | 2 | BARENG2017 | Finland | National | 1982 | * | 0 | 0 | Cohort | IHD | f | 25 | 74 | 25 | Died | 8 |
| HAPIEE | 1 | STEFLE2016 | Multi | International | 2002 | 225 | 0 | 0 | Cohort | IHD | b | * | * | 9 | Died | 0 |
| HSE-SHS | 1 | DEMEST2019 | UK | National | 1994 | 1412 | 0 | 0 | Cohort | IHD | b | * | * | 17 | Died | 0 |
| HSE-SHS | 3 | DEMEST2019 | UK | National | 1994 | 1412 | 0 | 0 | Cohort | IHD | b | * | * | 17 | Died | 7 |
| JACC | 1 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | m | 40 | 79 | 21 | Died | 0 |
| JACC | 3 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | f | 40 | 79 | 21 | Died | 0 |
| JACC | 5 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | m | 40 | 79 | 21 | Died | 7 |
| JACC | 7 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | f | 40 | 79 | 21 | Died | 9 |
| MALMO | 2 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | m | 46 | 67 | 22 | Diagnosed | 0 |
| MALMO | 3 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | f | 46 | 67 | 22 | Diagnosed | 0 |
| MALMO | 4 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | m | 46 | 67 | 22 | Diagnosed | 6 |
| MALMO | 5 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | f | 46 | 67 | 22 | Diagnosed | 6 |
| MESA | 1 | MCEVOY2015A | USA | Regional | 2000 | 449 | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 1 |
| MESA | 2 | MCEVOY2015A | USA | Regional | 2000 | 449 | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 14 |
| MESA | 3 | NANCE2017 | USA | Regional | 2000 | 449 | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 0 |
| NAS | 1 | DING2019 | USA | Regional | 1991 | 137 | 0 | 0 | Cohort | IHD | b | * | * | 20 | Diagnosed | 0 |
| NHS | 1 | HART2015A | USA | Medical workers | 1989 | 3874 | 0 | 0 | Cohort | IHD | f | 43 | 68 | 17 | Diagnosed | 0 |
| NHS-II | 1 | CHOMIS2015 | USA | Medical workers | 1991 | 456 | 0 | 0 | Cohort | IHD | f | 25 | 42 | 20 | Diagnosed | 1 |

Table 15
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
<u>List of study details for all the IHD results (not all to be included in any one meta-analysis), Current smokers versus never smokers</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NIHD | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NHS-II | 2 | CHOMIS2015 | USA | Medical workers | 1991 | 456 | 0 | 0 | Cohort | IHD | f | 25 | 42 | 20 | Diagnosed | 15 |
| PREVEND | 1 | KUNUT2018 | Netherlands | Regional | 2001 | 212 | 0 | 0 | Cohort | IHD | b | 32 | 80 | 9 | Diagnosed | 0 |
| PREVEND | 2 | KUNUT2018 | Netherlands | Regional | 2001 | 212 | 0 | 0 | Cohort | IHD | b | 32 | 80 | 9 | Diagnosed | 2 |
| PREVEND | 3 | KUNUT2018 | Netherlands | Regional | 2001 | 212 | 0 | 0 | Cohort | IHD | b | 32 | 80 | 9 | Diagnosed | 10 |
| USA5 | 1 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | f | 55 | 999 | 11 | Died | 0 |
| USA5 | 2 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | m | 55 | 999 | 11 | Died | 0 |
| USA5 | 5 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | f | 55 | 999 | 11 | Died | 5 |
| USA5 | 6 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | m | 55 | 999 | 11 | Died | 5 |
| WHI | 1 | KABAT2017 | USA | National | 1993 | 2975 | 0 | 0 | Cohort | IHD | f | 50 | 79 | 20 | Died | 11 |
| WHITEHALL | 1 | BATTY2015 | UK | Civil servants | 1967 | 3250 | 0 | 0 | Cohort | IHD | m | 40 | 69 | 43 | Died | 1 |

Table 16
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of risk estimates for all the IHD results (not all to be included in any one meta-analysis), Current cigarette smokers versus never smokers

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 1 | MENOTT2016 | - | - | - | - | 1.33 | 1.02 | 1.72 | Other calculations |
| ARIC | 1 | DING2019A | 377 | 610 | 41210 | 125486 | 1.88 | 1.66 | 2.14 | From numbers |
| ARIC | 2 | DING2019A | - | - | - | - | 2.27 | 2.00 | 2.63 | Other calculations |
| BIOBANK | 3 | ZHANG2021H | 60 | 231 | 44435 | 239412 | 1.40 | 1.05 | 1.86 | From numbers |
| CALIBER | 1 | PUJADE2015 | - | - | - | - | 1.28 | 1.14 | 1.44 | Other calculations |
| CPS-II | 1 | TURNER2017 | 4444 | 9034 | 65275 | 149617 | 1.13 | 1.09 | 1.17 | From numbers |
| CPS-II | 3 | TURNER2017 | - | - | - | - | 1.98 | 1.90 | 2.06 | Hamling method |
| CoCHS | 1 | SCHNOH2015 | - | - | - | - | 1.63 | 1.39 | 1.90 | Hamling method |
| ELSA | 1 | JACKSO2019E | 59 | 117 | 897 | 2387 | 1.69 | 1.21 | 2.36 | Given in the paper |
| ELSA | 2 | JACKSO2019E | - | - | - | - | 1.93 | 1.23 | 3.03 | Given in the paper |
| EPIC-10 | 1 | KEY2019 | 1969 | 926 | 33695 | 32986 | 2.08 | 1.93 | 2.25 | From numbers |
| EPIC-10 | 2 | KEY2019 | 937 | 1071 | 58059 | 168240 | 2.54 | 2.32 | 2.77 | From numbers |
| EPIC-10 | 3 | RICCI2018 | 3368 | 3008 | 4315 | 7679 | 1.99 | 1.93 | 2.06 | From numbers |
| EPIC-UK | 1 | STOEKE2016 | 328 | 823 | 28629 | 122077 | 1.71 | 1.51 | 1.95 | Given in the paper |
| EPIC-UK | 2 | STOEKE2016 | - | - | - | - | 1.76 | 1.54 | 2.00 | Given in the paper |
| EPIC-UK | 3 | STOEKE2016 | - | - | - | - | 1.77 | 1.55 | 2.03 | Given in the paper |
| ESTONGENOME | 1 | KOKS2017 | * | * | * | * | 0.94 | 0.72 | 1.22 | Given in the paper |
| ESTONGENOME | 4 | KOKS2017 | * | * | * | * | 0.31 | 0.21 | 0.45 | Given in the paper |
| ESTONGENOME | 7 | KOKS2017 | - | - | - | - | 2.10 | 1.59 | 2.76 | Given in the paper |
| ESTONGENOME | 10 | KOKS2017 | - | - | - | - | 2.44 | 1.62 | 3.68 | Given in the paper |
| FINRISK | 1 | BARENG2017 | - | - | - | - | 2.56 | 1.86 | 3.53 | Hamling method |
| FINRISK | 2 | BARENG2017 | - | - | - | - | 2.89 | 2.08 | 4.02 | Hamling method |
| HAPIEE | 1 | STEFLE2016 | 125 | 51 | 5871 | 9254 | 3.86 | 2.79 | 5.34 | From numbers |
| HSE-SHS | 1 | DEMEST2019 | 398 | 356 | 24704 | 38119 | 1.73 | 1.50 | 1.99 | From numbers |
| HSE-SHS | 3 | DEMEST2019 | - | - | - | - | 2.28 | 1.95 | 2.66 | Other calculations |
| JACC | 1 | MATSUN2017 | 513 | 127 | 375755 | 150359 | 1.62 | 1.33 | 1.96 | From numbers |
| JACC | 3 | MATSUN2017 | 75 | 590 | 52615 | 945625 | 2.28 | 1.80 | 2.90 | From numbers |
| JACC | 5 | MATSUN2017 | - | - | - | - | 1.95 | 1.58 | 2.39 | Given in the paper |
| JACC | 7 | MATSUN2017 | - | - | - | - | 2.45 | 1.89 | 3.18 | Given in the paper |
| MALMO | 2 | HINDY2018 | 669 | 475 | 2686 | 2695 | 1.41 | 1.27 | 1.57 | From numbers |
| MALMO | 3 | HINDY2018 | 419 | 506 | 4191 | 6732 | 1.33 | 1.18 | 1.51 | From numbers |
| MALMO | 4 | HINDY2018 | - | - | - | - | 1.63 | 1.42 | 1.87 | Other calculations |
| MALMO | 5 | HINDY2018 | - | - | - | - | 1.86 | 1.61 | 2.14 | Other calculations |
| MESA | 1 | MCEVOY2015A | - | - | - | - | 1.41 | 1.07 | 1.86 | Given in the paper |
| MESA | 2 | MCEVOY2015A | - | - | - | - | 1.55 | 1.14 | 2.10 | Given in the paper |
| MESA | 3 | NANCE2017 | 69 | 186 | 887 | 3418 | 1.43 | 1.10 | 1.87 | From numbers |
| NAS | 1 | DING2019 | 9 | 37 | 55 | 184 | 0.81 | 0.42 | 1.58 | From numbers |
| NHS | 1 | HART2015A | 876 | 1309 | 262982 | 803757 | 2.05 | 1.88 | 2.23 | From numbers |
| NHS-II | 1 | CHOMIS2015 | - | - | - | - | 5.40 | 3.39 | 8.61 | Hamling method |

Table 16
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of risk estimates for all the IHD results (not all to be included in any one meta-analysis), Current cigarette smokers versus never smokers

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|----------|-----|-------|-----|-----|-----|-----|----|-----|-----|---------|
| NHS-II | 2 | CHOMIS2015 | - | - | - | - | 4.30 | 2.78 | 6.65 | Hamling method |
| PREVEND | 1 | KUNUT2018 | 68 | 46 | 1282 | 1458 | 1.68 | 1.17 | 2.43 | From numbers |
| PREVEND | 2 | KUNUT2018 | - | - | - | - | 1.70 | 1.17 | 2.48 | Hamling method |
| PREVEND | 3 | KUNUT2018 | - | - | - | - | 1.62 | 1.11 | 2.37 | Hamling method |
| USA5 | 1 | CARTER2015 | 1014 | 4119 | 50488 | 259659 | 1.27 | 1.18 | 1.36 | From numbers |
| USA5 | 2 | CARTER2015 | 1522 | 4947 | 38128 | 136613 | 1.10 | 1.04 | 1.17 | From numbers |
| USA5 | 5 | CARTER2015 | - | - | - | - | 3.00 | 2.80 | 3.20 | Given in the paper |
| USA5 | 6 | CARTER2015 | - | - | - | - | 2.60 | 2.40 | 2.70 | Given in the paper |
| WHI | 1 | KABAT2017 | - | - | - | - | 2.06 | 1.78 | 2.38 | Given in the paper |
| WHITEHALL | 1 | BATTY2015 | - | - | - | - | 1.52 | 1.38 | 1.68 | Given in the paper |

Table 17
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of the disease definitions for all the IHD results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | Definition of IHD | Standard IHD definition |
|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 1 | MENOTT2016 | Italy | Regional | CHD NOS | 0 |
| ARIC | 1 | DING2019A | USA | National | Fatal and non-fatal MI or fatal CHD. | 0 |
| ARIC | 2 | DING2019A | USA | National | Fatal and non-fatal MI or fatal CHD. | 0 |
| BIOBANK | 3 | ZHANG2021H | UK | National | ICD-10 I20-I25 | present |
| CALIBER | 1 | PUJADE2015 | UK | GP records | From Read Codes | 0 |
| CPS-II | 1 | TURNER2017 | USA | National | ICD-9 410-414, ICD-10 I20-I25 | present |
| CPS-II | 3 | TURNER2017 | USA | National | ICD-9 410-414, ICD-10 I20-I25 | present |
| CoCHS | 1 | SCHNOH2015 | Denmark | Regional | ICD-8 410-414, ICD-10: I20-I25 | present |
| ELSA | 1 | JACKSO2019E | UK | National | Non-fatal CHD: self-reported | 0 |
| ELSA | 2 | JACKSO2019E | UK | National | Non-fatal CHD: self-reported | 0 |
| EPIC-10 | 1 | KEY2019 | Multi | International | ICD-10 I20-I25 | present |
| EPIC-10 | 2 | KEY2019 | Multi | International | ICD-10 I20-I25 | present |
| EPIC-10 | 3 | RICCI2018 | Multi | International | ICD-10 I20-I25 | present |
| EPIC-UK | 1 | STOEKE2016 | UK | Regional | ICD 10 I20-I25 | present |
| EPIC-UK | 2 | STOEKE2016 | UK | Regional | ICD 10 I20-I25 | present |
| EPIC-UK | 3 | STOEKE2016 | UK | Regional | ICD 10 I20-I25 | present |
| ESTONGENOME | 1 | KOKS2017 | Estonia | National | ICD-10 I20-I25 | present |
| ESTONGENOME | 4 | KOKS2017 | Estonia | National | ICD-10 I20-I25 | present |
| ESTONGENOME | 7 | KOKS2017 | Estonia | National | ICD-10 I20-I25 | present |
| ESTONGENOME | 10 | KOKS2017 | Estonia | National | ICD-10 I20-I25 | present |
| FINRISK | 1 | BARENG2017 | Finland | National | ICD-9 410-414, ICD-10 I20-I25 | present |
| FINRISK | 2 | BARENG2017 | Finland | National | ICD-9 410-414, ICD-10 I20-I25 | present |
| HAPIEE | 1 | STEFLE2016 | Multi | International | ICD-10 I20-I25 | present |
| HSE-SHS | 1 | DEMEST2019 | UK | National | CHD NOS | 0 |
| HSE-SHS | 3 | DEMEST2019 | UK | National | CHD NOS | 0 |
| JACC | 1 | MATSUN2017 | Japan | Regional | ICD-10 I20-I25 | present |
| JACC | 3 | MATSUN2017 | Japan | Regional | ICD-10 I20-I25 | present |
| JACC | 5 | MATSUN2017 | Japan | Regional | ICD-10 I20-I25 | present |
| JACC | 7 | MATSUN2017 | Japan | Regional | ICD-10 I20-I25 | present |
| MALMO | 2 | HINDY2018 | Sweden | Regional | MI, fatal IHD, bypass graft, coronary op. | 0 |
| MALMO | 3 | HINDY2018 | Sweden | Regional | MI, fatal IHD, bypass graft, coronary op. | 0 |
| MALMO | 4 | HINDY2018 | Sweden | Regional | MI, fatal IHD, bypass graft, coronary op. | 0 |
| MALMO | 5 | HINDY2018 | Sweden | Regional | MI, fatal IHD, bypass graft, coronary op. | 0 |
| MESA | 1 | MCEVOY2015A | USA | Regional | MI, CHD, angina, revasc., cardiac arrest | 0 |
| MESA | 2 | MCEVOY2015A | USA | Regional | MI, CHD, angina, revasc., cardiac arrest | 0 |
| MESA | 3 | NANCE2017 | USA | Regional | MI, CHD, angina, revasc., cardiac arrest | 0 |
| NAS | 1 | DING2019 | USA | Regional | MI, angina, CHD death (ICD-9 410-414, 429.2) | 0 |
| NHS | 1 | HART2015A | USA | Medical workers | ICD-8/9 410-412, ICD-10 I21-I22; WHO criteria | 0 |
| NHS-II | 1 | CHOMIS2015 | USA | Medical workers | MI (WHO criteria), fatal CHD (med recs/death cert) | 0 |

_____

Table 17
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of the disease definitions for all the IHD results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | Definition of IHD | Standard IHD definition |
|----------|-----|-------|---------|---------------|-------------------|-------------------------|
| NHS-II | 2 | CHOMIS2015 | USA | Medical workers | MI (WHO criteria), fatal CHD (med recs/death cert) | 0 |
| PREVEND | 1 | KUNUT2018 | Netherlands | Regional | IHD, MI, bypass graft, coronary angioplasty | 0 |
| PREVEND | 2 | KUNUT2018 | Netherlands | Regional | IHD, MI, bypass graft, coronary angioplasty | 0 |
| PREVEND | 3 | KUNUT2018 | Netherlands | Regional | IHD, MI, bypass graft, coronary angioplasty | 0 |
| USA5 | 1 | CARTER2015 | USA | Regional | ICD-10 I20-I25 | present |
| USA5 | 2 | CARTER2015 | USA | Regional | ICD-10 I20-I25 | present |
| USA5 | 5 | CARTER2015 | USA | Regional | ICD-10 I20-I25 | present |
| USA5 | 6 | CARTER2015 | USA | Regional | ICD-10 I20-I25 | present |
| WHI | 1 | KABAT2017 | USA | National | Review of medical records and death certificates | 0 |
| WHITEHALL | 1 | BATTY2015 | UK | Civil servants | ICD-8,9 410-414, ICD-10 I20-I25 | present |

Table 18
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
<u>List of the study details for the selected results, Current cigarette smokers versus never smokers, no overlapping results for any study</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NIHD | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 1 | MENOTT2016 | Italy | Regional | 1960 | 319 | 0 | 0 | Cohort | IHD | m | 40 | 59 | 50 | Died | 3 |
| ARIC | 2 | DING2019A | USA | National | 1987 | 1798 | 0 | 0 | Cohort | IHD | b | 45 | 64 | 30 | Diagnosed | 15 |
| BIOBANK | 3 | ZHANG2021H | UK | National | 2006 | 547 | 0 | 0 | Cohort | IHD | b | 40 | 69 | 12 | Diagnosed | 0 |
| CALIBER | 1 | PUJADE2015 | UK | GP records | 1997 | 16800 | 0 | 0 | Cohort | IHD | f | 30 | 999 | 13 | Diagnosed | 1 |
| CPS-II | 3 | TURNER2017 | USA | National | 1982 | 13478 | 0 | 0 | Cohort | IHD | b | 30 | 999 | 22 | Died | 23 |
| CoCHS | 1 | SCHNOH2015 | Denmark | Regional | 1991 | 900 | 0 | 0 | Cohort | IHD | f | 20 | 93 | 22 | Diagnosed | 1 |
| ELSA | 2 | JACKSO2019E | UK | National | 2004 | 352 | 0 | 0 | Cohort | Non-fatal IHD | b | 52 | 999 | 13 | Diagnosed | 7 |
| EPIC-10 | 1 | KEY2019 | Multi | International | 1991 | 7198 | 0 | 0 | Cohort | IHD | m | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-10 | 2 | KEY2019 | Multi | International | 1991 | 7198 | 0 | 0 | Cohort | IHD | f | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-UK | 3 | STOEKE2016 | UK | Regional | 1993 | 2332 | 0 | 0 | Cohort | IHD | b | 45 | 79 | 14 | Diagnosed | 6 |
| ESTONGENOME | 7 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 10 | KOKS2017 | Estonia | National | 2002 | 696 | 0 | 0 | Cohort | IHD | f | 18 | 999 | 13 | Died | 1 |
| FINRISK | 2 | BARENG2017 | Finland | National | 1982 | * | 0 | 0 | Cohort | IHD | f | 25 | 74 | 25 | Died | 8 |
| HAPIEE | 1 | STEFLE2016 | Multi | International | 2002 | 225 | 0 | 0 | Cohort | IHD | b | * | * | 9 | Died | 0 |
| HSE-SHS | 3 | DEMEST2019 | UK | National | 1994 | 1412 | 0 | 0 | Cohort | IHD | b | * | * | 17 | Died | 7 |
| JACC | 5 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | m | 40 | 79 | 21 | Died | 7 |
| JACC | 7 | MATSUN2017 | Japan | Regional | 1988 | 1554 | x | 0 | Cohort | IHD | f | 40 | 79 | 21 | Died | 9 |
| MALMO | 4 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | m | 46 | 67 | 22 | Diagnosed | 6 |
| MALMO | 5 | HINDY2018 | Sweden | Regional | 1991 | 3217 | 0 | 0 | Cohort | IHD | f | 46 | 67 | 22 | Diagnosed | 6 |
| MESA | 2 | MCEVOY2015A | USA | Regional | 2000 | 449 | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 14 |
| NAS | 1 | DING2019 | USA | Regional | 1991 | 137 | 0 | 0 | Cohort | IHD | b | * | * | 20 | Diagnosed | 0 |
| NHS | 1 | HART2015A | USA | Medical workers | 1989 | 3874 | 0 | 0 | Cohort | IHD | f | 43 | 68 | 17 | Diagnosed | 0 |
| NHS-II | 2 | CHOMIS2015 | USA | Medical workers | 1991 | 456 | 0 | 0 | Cohort | IHD | f | 25 | 42 | 20 | Diagnosed | 15 |
| PREVEND | 3 | KUNUT2018 | Netherlands | Regional | 2001 | 212 | 0 | 0 | Cohort | IHD | b | 32 | 80 | 9 | Diagnosed | 10 |
| USA5 | 5 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | f | 55 | 999 | 11 | Died | 5 |
| USA5 | 6 | CARTER2015 | USA | Regional | 2000 | 29931 | 0 | 0 | Cohort | IHD | m | 55 | 999 | 11 | Died | 5 |
| WHI | 1 | KABAT2017 | USA | National | 1993 | 2975 | 0 | 0 | Cohort | IHD | f | 50 | 79 | 20 | Died | 11 |
| WHITEHALL | 1 | BATTY2015 | UK | Civil servants | 1967 | 3250 | 0 | 0 | Cohort | IHD | m | 40 | 69 | 43 | Died | 1 |

_____

Table 19
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by sex

```
Combined

                  Numbers exposed Non-exposed
 Study ID     NRR   Case    Cont   Case    Cont      RR        95.00%CI
*ARIC          2     -       -      -       -      2.27 ( 2.00-  2.63)
*BIOBANK       3    60    44435    231  239412     1.40 ( 1.05-  1.86)
*CPS-II        3     -       -      -       -      1.98 ( 1.90-  2.06)
*ELSA          2     -       -      -       -      1.93 ( 1.23-  3.03)
*EPIC-UK       3     -       -      -       -      1.77 ( 1.55-  2.03)
*HAPIEE        1   125     5871     51    9254     3.86 ( 2.79-  5.34)
*HSE-SHS       3     -       -      -       -      2.28 ( 1.95-  2.66)
*MESA          2     -       -      -       -      1.55 ( 1.14-  2.10)
*NAS           1     9       55     37     184     0.81 ( 0.42-  1.58)
*PREVEND       3     -       -      -       -      1.62 ( 1.11-  2.37)
Partial Totals     194    50361    319  248850
*prospective study


Male

                  Numbers exposed Non-exposed
 Study ID     NRR   Case    Cont   Case    Cont      RR        95.00%CI
*7CNTRY-ITALY 1     -       -      -       -      1.33 ( 1.02-  1.72)
*EPIC-10       1  1969    33695    926   32986     2.08 ( 1.93-  2.25)
*ESTONGENOME   7     -       -      -       -      2.10 ( 1.59-  2.76)
*JACC          5     -       -      -       -      1.95 ( 1.58-  2.39)
 MALMO         4     -       -      -       -      1.63 ( 1.42-  1.87)
*USA5          6     -       -      -       -      2.60 ( 2.40-  2.70)
*WHITEHALL     1     -       -      -       -      1.52 ( 1.38-  1.68)
Partial Totals    1969    33695    926   32986
*prospective study


Female

                  Numbers exposed Non-exposed
 Study ID     NRR   Case    Cont   Case    Cont      RR        95.00%CI
*CALIBER       1     -       -      -       -      1.28 ( 1.14-  1.44)
*CoCHS         1     -       -      -       -      1.63 ( 1.39-  1.90)
*EPIC-10       2   937    58059   1071  168240     2.54 ( 2.32-  2.77)
*ESTONGENOME  10     -       -      -       -      2.44 ( 1.62-  3.68)
*FINRISK       2     -       -      -       -      2.89 ( 2.08-  4.02)
*JACC          7     -       -      -       -      2.45 ( 1.89-  3.18)
 MALMO         5     -       -      -       -      1.86 ( 1.61-  2.14)
*NHS           1   876   262982   1309  803757     2.05 ( 1.88-  2.23)
*NHS-II        2     -       -      -       -      4.30 ( 2.78-  6.65)
*USA5          5     -       -      -       -      3.00 ( 2.80-  3.20)
*WHI           1     -       -      -       -      2.06 ( 1.78-  2.38)
Partial Totals    1813   321041   2380  971997
*prospective study
```

|  |  | RR Sex |  |  |
|---|---|---|---|---|
|  |  | 1 | 2 | 3 |
|  |  | Combined | Male | Female | Total |

```
RR Data


              N      10        7       11       28
             NS      10        7       11       28

             Wt  3105.78  2558.54  2839.44  8503.76
        Het Chi   42.17   117.17   208.56   394.17
        Het  df       9        6       10       27
        Het  P       ***      ***      ***      ***
      Fixed  RR     1.99     2.12     2.27     2.12
             RRl    1.92     2.04     2.19     2.07
             RRu    2.06     2.20     2.35     2.16
             P      +++      +++      +++      +++
     Random  RR     1.94     1.86     2.23     2.01
             RRl    1.71     1.53     1.86     1.84
             RRu    2.21     2.26     2.69     2.21
             P      +++      +++      +++      +++
      Asymm  P      N.S.     N.S.     N.S.     N.S.
    Between Chi               5.50    26.27    26.27
    Between  df                  1        1        2
    Between  P                   +      +++      ***
    Btwn(F)  P                N.S.     N.S.     N.S.
    Btwn(R)  P                N.S.     N.S.     N.S.
```

Table 20
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by region

**N America**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 2 | – | – | – | – | 2.27 ( 2.00– 2.63) | |
| *CPS-II | 3 | – | – | – | – | 1.98 ( 1.90– 2.06) | |
| *MESA | 2 | – | – | – | – | 1.55 ( 1.14– 2.10) | |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42– 1.58) | |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88– 2.23) | |
| *NHS-II | 2 | – | – | – | – | 4.30 ( 2.78– 6.65) | |
| *USA5 | 6 | – | – | – | – | 2.60 ( 2.40– 2.70) | |
| *USA5 | 5 | – | – | – | – | 3.00 ( 2.80– 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65– 2.89) | |
| *WHI | 1 | – | – | – | – | 2.06 ( 1.78– 2.38) | |
| Partial Totals | | 885 | 263037 | 1346 | 803941 | | |

*prospective study

**Europe**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 1 | – | – | – | – | 1.33 ( 1.02– 1.72) | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05– 1.86) | |
| *CALIBER | 1 | – | – | – | – | 1.28 ( 1.14– 1.44) | |
| *CoCHS | 1 | – | – | – | – | 1.63 ( 1.39– 1.90) | |
| *ELSA | 2 | – | – | – | – | 1.93 ( 1.23– 3.03) | |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93– 2.25) | |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32– 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14– 2.40) | |
| *EPIC-UK | 3 | – | – | – | – | 1.77 ( 1.55– 2.03) | |
| *ESTONGENOME | 7 | – | – | – | – | 2.10 ( 1.59– 2.76) | |
| *ESTONGENOME | 10 | – | – | – | – | 2.44 ( 1.62– 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75– 2.77) | |
| *FINRISK | 2 | – | – | – | – | 2.89 ( 2.08– 4.02) | |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79– 5.34) | |
| *HSE-SHS | 3 | – | – | – | – | 2.28 ( 1.95– 2.66) | |
| MALMO | 4 | – | – | – | – | 1.63 ( 1.42– 1.87) | |
| MALMO | 5 | – | – | – | – | 1.86 ( 1.61– 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57– 1.92) | |
| *PREVEND | 3 | – | – | – | – | 1.62 ( 1.11– 2.37) | |
| *WHITEHALL | 1 | – | – | – | – | 1.52 ( 1.38– 1.68) | |
| Partial Totals | | 3091 | 142060 | 2279 | 449892 | | |

*prospective study

**Japan**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *JACC | 5 | – | – | – | – | 1.95 ( 1.58– 2.39) | |
| *JACC | 7 | – | – | – | – | 2.45 ( 1.89– 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81– 2.50) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

| | | Region | | | |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | |
| | | N America | Europe | Japan | Total |

**RR Data**

| | | N America | Europe | Japan | Total |
|---|---|---|---|---|---|
| | N | 9 | 17 | 2 | 28 |
| | NS | 8 | 14 | 1 | 23 |
| | Wt | 5303.26 | 3054.03 | 146.47 | 8503.76 |
| Het | Chi | 162.14 | 164.78 | 1.81 | 394.17 |
| Het | df | 8 | 16 | 1 | 27 |
| Het | P | *** | *** | N.S. | *** |
| Fixed | RR | 2.26 | 1.88 | 2.13 | 2.12 |
| | RRl | 2.20 | 1.82 | 1.81 | 2.07 |
| | RRu | 2.33 | 1.95 | 2.50 | 2.16 |
| | P | +++ | +++ | +++ | +++ |
| Random | RR | 2.23 | 1.90 | 2.15 | 2.01 |
| | RRl | 1.92 | 1.67 | 1.73 | 1.84 |
| | RRu | 2.58 | 2.15 | 2.69 | 2.21 |
| | P | +++ | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | | N.S. |
| Between | Chi | | 65.44 | 0.52 | 65.45 |
| Between | df | | 1 | 1 | 2 |

Table 20
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by region

| | | **Region** | | | |
|---|---|---|---|---|---|
| | | **1** | **2** | **3** | |
| | | **N America** | **Europe** | **Japan** | **Total** |

**RR Data**

| | | N America | Europe | Japan | Total |
|---|---|---|---|---|---|
| **Between** | **P** | | --- | N.S. | *** |
| **Btwn(F)** | **P** | | - | N.S. | N.S. |
| **Btwn(R)** | **P** | | N.S. | N.S. | N.S. |

Table 21
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by nature of the population

**National**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|-----|----------|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 2 | – | – | – | – | 2.27 ( 2.00- 2.63) | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- 1.86) | |
| *CPS-II | 3 | – | – | – | – | 1.98 ( 1.90- 2.06) | |
| *ELSA | 2 | – | – | – | – | 1.93 ( 1.23- 3.03) | |
| *ESTONGENOME | 7 | – | – | – | – | 2.10 ( 1.59- 2.76) | |
| *ESTONGENOME | 10 | – | – | – | – | 2.44 ( 1.62- 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- 2.77) | |
| *FINRISK | 2 | – | – | – | – | 2.89 ( 2.08- 4.02) | |
| *HSE-SHS | 3 | – | – | – | – | 2.28 ( 1.95- 2.66) | |
| *WHI | 1 | – | – | – | – | 2.06 ( 1.78- 2.38) | |
| Partial Totals | | 60 | 44435 | 231 | 239412 | | |

*prospective study

**Regional**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|-----|----------|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 1 | – | – | – | – | 1.33 ( 1.02- 1.72) | |
| *CoCHS | 1 | – | – | – | – | 1.63 ( 1.39- 1.90) | |
| *EPIC-UK | 3 | – | – | – | – | 1.77 ( 1.55- 2.03) | |
| *JACC | 5 | – | – | – | – | 1.95 ( 1.58- 2.39) | |
| *JACC | 7 | – | – | – | – | 2.45 ( 1.89- 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81- 2.50) | |
| MALMO | 4 | – | – | – | – | 1.63 ( 1.42- 1.87) | |
| MALMO | 5 | – | – | – | – | 1.86 ( 1.61- 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- 1.92) | |
| *MESA | 2 | – | – | – | – | 1.55 ( 1.14- 2.10) | |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- 1.58) | |
| *PREVEND | 3 | – | – | – | – | 1.62 ( 1.11- 2.37) | |
| *USA5 | 6 | – | – | – | – | 2.60 ( 2.40- 2.70) | |
| *USA5 | 5 | – | – | – | – | 3.00 ( 2.80- 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- 2.89) | |
| Partial Totals | | 9 | 55 | 37 | 184 | | |

*prospective study

**Other**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|-----|----------|
| | | Case | Cont | Case | Cont | | |
| *CALIBER | 1 | – | – | – | – | 1.28 ( 1.14- 1.44) | |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- 2.25) | |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- 2.40) | |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- 5.34) | |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- 2.23) | |
| *NHS-II | 2 | – | – | – | – | 4.30 ( 2.78- 6.65) | |
| *WHITEHALL | 1 | – | – | – | – | 1.52 ( 1.38- 1.68) | |
| Partial Totals | | 3907 | 360607 | 3357 | 1014237 | | |

*prospective study

| | Population Type | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | |
| | National | Regional | Other | Total |

**RR Data**

| | 1 National | 2 Regional | 3 Other | Total |
|---|---|---|---|---|
| N | 9 | 12 | 7 | 28 |
| NS | 8 | 9 | 6 | 23 |
| Wt | 3072.30 | 3009.67 | 2421.79 | 8503.76 |
| Het Chi | 18.03 | 180.33 | 142.85 | 394.17 |
| Het df | 8 | 11 | 6 | 27 |
| Het P | * | *** | *** | *** |
| Fixed RR | 2.02 | 2.35 | 1.97 | 2.12 |
| RRl | 1.95 | 2.27 | 1.89 | 2.07 |
| RRu | 2.09 | 2.44 | 2.05 | 2.16 |
| P | +++ | +++ | +++ | +++ |
| Random RR | 2.10 | 1.85 | 2.18 | 2.01 |
| RRl | 1.92 | 1.56 | 1.77 | 1.84 |
| RRu | 2.30 | 2.19 | 2.69 | 2.21 |
| P | +++ | +++ | +++ | +++ |
| Asymm P | N.S. | ** | N.S. | N.S. |
| Between Chi | | 35.33 | 0.88 | 52.96 |
| Between df | | 1 | 1 | 2 |

Table 21
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by nature of the population

|  | | Population Type | | |  |
|---|---|---|---|---|---|
|  | | **1** | **2** | **3** |  |
|  | | **National** | **Regional** | **Other** | **Total** |

**RR Data**

| | | National | Regional | Other | Total |
|---|---|---|---|---|---|
| **Between** | **P** | | **+++** | **N.S.** | **\*\*\*** |
| **Btwn(F)** | **P** | | **(+)** | **N.S.** | **N.S.** |
| **Btwn(R)** | **P** | | **N.S.** | **N.S.** | **N.S.** |

Table 22
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by year of start of baseline

**<1988**

| Study ID | NRR | Numbers exposed Case | Cont | Non-exposed Case | Cont | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( 1.02- | 1.72) |
| *ARIC | 2 | - | - | - | - | 2.27 ( 2.00- | 2.63) |
| *CPS-II | 3 | - | - | - | - | 1.98 ( 1.90- | 2.06) |
| *FINRISK | 2 | - | - | - | - | 2.89 ( 2.08- | 4.02) |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( 1.38- | 1.68) |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**1988+**

| Study ID | NRR | Numbers exposed Case | Cont | Non-exposed Case | Cont | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- | 1.86) |
| *CALIBER | 1 | - | - | - | - | 1.28 ( 1.14- | 1.44) |
| *CoCHS | 1 | - | - | - | - | 1.63 ( 1.39- | 1.90) |
| *ELSA | 2 | - | - | - | - | 1.93 ( 1.23- | 3.03) |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- | 2.25) |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- | 2.77) |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- | 2.40) |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( 1.55- | 2.03) |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( 1.59- | 2.76) |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( 1.62- | 3.68) |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- | 2.77) |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- | 5.34) |
| *HSE-SHS | 3 | - | - | - | - | 2.28 ( 1.95- | 2.66) |
| *JACC | 5 | - | - | - | - | 1.95 ( 1.58- | 2.39) |
| *JACC | 7 | - | - | - | - | 2.45 ( 1.89- | 3.18) |
| Subtotal JACC | | | | | | 2.13 ( 1.81- | 2.50) |
| MALMO | 4 | - | - | - | - | 1.63 ( 1.42- | 1.87) |
| MALMO | 5 | - | - | - | - | 1.86 ( 1.61- | 2.14) |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- | 1.92) |
| *MESA | 2 | - | - | - | - | 1.55 ( 1.14- | 2.10) |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- | 1.58) |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- | 2.23) |
| *NHS-II | 2 | - | - | - | - | 4.30 ( 2.78- | 6.65) |
| *PREVEND | 3 | - | - | - | - | 1.62 ( 1.11- | 2.37) |
| *USA5 | 6 | - | - | - | - | 2.60 ( 2.40- | 2.70) |
| *USA5 | 5 | - | - | - | - | 3.00 ( 2.80- | 3.20) |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- | 2.89) |
| *WHI | 1 | - | - | - | - | 2.06 ( 1.78- | 2.38) |
| Partial Totals | | 3976 | 405097 | 3625 | 1253833 | | |

*prospective study

| | YrSt 1 <1988 | 2 1988+ | Total |
|---|---|---|---|

**RR Data**

| | | 1 <1988 | 2 1988+ | Total |
|---|---|---|---|---|
| | N | 5 | 23 | 28 |
| | NS | 5 | 18 | 23 |
| | Wt | 3044.26 | 5459.50 | 8503.76 |
| Het | Chi | 43.13 | 308.18 | 394.17 |
| Het | df | 4 | 22 | 27 |
| Het | P | *** | *** | *** |
| Fixed | RR | 1.92 | 2.23 | 2.12 |
| | RRl | 1.86 | 2.17 | 2.07 |
| | RRu | 1.99 | 2.29 | 2.16 |
| | P | +++ | +++ | +++ |
| Random | RR | 1.89 | 2.04 | 2.01 |
| | RRl | 1.58 | 1.83 | 1.84 |
| | RRu | 2.27 | 2.28 | 2.21 |
| | P | +++ | +++ | +++ |
| Asymm | P | N.S. | (*) | N.S. |
| Between | Chi | | 42.86 | 42.86 |
| Between | df | | 1 | 1 |
| Between | P | | +++ | *** |
| Btwn(F) | P | | (+) | (*) |
| Btwn(R) | P | | N.S. | N.S. |

Table 23
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by number of cases in the study

```
<1000
                  Numbers exposed Non-exposed
 Study ID      NRR   Case   Cont   Case   Cont      RR        95.00%CI
*7CNTRY-ITALY 1        -      -      -      -     1.33 ( 1.02-  1.72)
*BIOBANK       3      60  44435    231 239412     1.40 ( 1.05-  1.86)
*CoCHS         1        -      -      -      -     1.63 ( 1.39-  1.90)
*ELSA          2        -      -      -      -     1.93 ( 1.23-  3.03)
*ESTONGENOME   7        -      -      -      -     2.10 ( 1.59-  2.76)
*ESTONGENOME  10        -      -      -      -     2.44 ( 1.62-  3.68)
 Subtotal ESTONGENOME                             2.20 ( 1.75-  2.77)
*FINRISK       2        -      -      -      -     2.89 ( 2.08-  4.02)
*HAPIEE        1      125   5871     51   9254     3.86 ( 2.79-  5.34)
*MESA          2        -      -      -      -     1.55 ( 1.14-  2.10)
*NAS           1        9     55     37    184     0.81 ( 0.42-  1.58)
*NHS-II        2        -      -      -      -     4.30 ( 2.78-  6.65)
*PREVEND       3        -      -      -      -     1.62 ( 1.11-  2.37)
Partial Totals       194  50361    319 248850
*prospective study


1000+
                  Numbers exposed Non-exposed
 Study ID      NRR   Case   Cont   Case   Cont      RR        95.00%CI
*ARIC          2        -      -      -      -     2.27 ( 2.00-  2.63)
*CALIBER       1        -      -      -      -     1.28 ( 1.14-  1.44)
*CPS-II        3        -      -      -      -     1.98 ( 1.90-  2.06)
*EPIC-10       1     1969  33695    926  32986     2.08 ( 1.93-  2.25)
*EPIC-10       2      937  58059   1071 168240     2.54 ( 2.32-  2.77)
 Subtotal EPIC-10                                 2.27 ( 2.14-  2.40)
*EPIC-UK       3        -      -      -      -     1.77 ( 1.55-  2.03)
*HSE-SHS       3        -      -      -      -     2.28 ( 1.95-  2.66)
*JACC          5        -      -      -      -     1.95 ( 1.58-  2.39)
*JACC          7        -      -      -      -     2.45 ( 1.89-  3.18)
 Subtotal JACC                                    2.13 ( 1.81-  2.50)
 MALMO         4        -      -      -      -     1.63 ( 1.42-  1.87)
 MALMO         5        -      -      -      -     1.86 ( 1.61-  2.14)
 Subtotal MALMO                                   1.74 ( 1.57-  1.92)
*NHS           1      876 262982   1309 803757     2.05 ( 1.88-  2.23)
*USA5          6        -      -      -      -     2.60 ( 2.40-  2.70)
*USA5          5        -      -      -      -     3.00 ( 2.80-  3.20)
 Subtotal USA5                                    2.77 ( 2.65-  2.89)
*WHI           1        -      -      -      -     2.06 ( 1.78-  2.38)
*WHITEHALL     1        -      -      -      -     1.52 ( 1.38-  1.68)
Partial Totals      3782 354736   3306 1004983
*prospective study
```

```
                    Number of IHD cases
                      1        2        3
                    absent   <1000    1000+     Total

 RR Data

                 N            12       16       28
                 NS          11       12       23

                 Wt       522.31  7981.45  8503.76
         Het Chi           63.84   321.21   394.17
         Het  df              11       15       27
         Het  P             ***      ***      ***
         Fixed  RR          1.86     2.13     2.12
               RRl          1.71     2.09     2.07
               RRu          2.03     2.18     2.16
                 P          +++      +++      +++
         Random  RR         1.97     2.04     2.01
               RRl          1.58     1.83     1.84
               RRu          2.45     2.27     2.21
                 P          +++      +++      +++
         Asymm  P          N.S.     N.S.     N.S.
       Between Chi                            9.13
       Between  df                               1
       Between  P          N.S.     N.S.      **
       Btwn(F)  P          N.S.     N.S.     N.S.
       Btwn(R)  P          N.S.     N.S.     N.S.
```

Table 24
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by cigarette smoking exclusively

**absent**

|  |  | Numbers exposed | | Non-exposed | | | |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( 1.02- 1.72) | |
| *ARIC | 2 | - | - | - | - | 2.27 ( 2.00- 2.63) | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- 1.86) | |
| *CALIBER | 1 | - | - | - | - | 1.28 ( 1.14- 1.44) | |
| *CPS-II | 3 | - | - | - | - | 1.98 ( 1.90- 2.06) | |
| *CoCHS | 1 | - | - | - | - | 1.63 ( 1.39- 1.90) | |
| *ELSA | 2 | - | - | - | - | 1.93 ( 1.23- 3.03) | |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- 2.25) | |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- 2.40) | |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( 1.55- 2.03) | |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( 1.59- 2.76) | |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( 1.62- 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- 2.77) | |
| *FINRISK | 2 | - | - | - | - | 2.89 ( 2.08- 4.02) | |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- 5.34) | |
| *HSE-SHS | 3 | - | - | - | - | 2.28 ( 1.95- 2.66) | |
| MALMO | 4 | - | - | - | - | 1.63 ( 1.42- 1.87) | |
| MALMO | 5 | - | - | - | - | 1.86 ( 1.61- 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- 1.92) | |
| *MESA | 2 | - | - | - | - | 1.55 ( 1.14- 2.10) | |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- 1.58) | |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- 2.23) | |
| *NHS-II | 2 | - | - | - | - | 4.30 ( 2.78- 6.65) | |
| *PREVEND | 3 | - | - | - | - | 1.62 ( 1.11- 2.37) | |
| *USA5 | 6 | - | - | - | - | 2.60 ( 2.40- 2.70) | |
| *USA5 | 5 | - | - | - | - | 3.00 ( 2.80- 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- 2.89) | |
| *WHI | 1 | - | - | - | - | 2.06 ( 1.78- 2.38) | |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( 1.38- 1.68) | |
| Partial Totals | | 3976 | 405097 | 3625 | 1253833 | | |

*prospective study

**present**

|  |  | Numbers exposed | | Non-exposed | | | |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *JACC | 5 | - | - | - | - | 1.95 ( 1.58- 2.39) | |
| *JACC | 7 | - | - | - | - | 2.45 ( 1.89- 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81- 2.50) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

RR Description:Exclusive use of the product

|  | 1 | 2 |  |
|---|---|---|---|
|  | absent | present | Total |

**RR Data**

|  |  | 1 | 2 |  |
|---|---|---|---|---|
|  | N | 26 | 2 | 28 |
|  | NS | 22 | 1 | 23 |
|  | Wt | 8357.29 | 146.47 | 8503.76 |
| Het | Chi | 392.35 | 1.81 | 394.17 |
| Het | df | 25 | 1 | 27 |
| Het | P | *** | N.S. | *** |
| Fixed | RR | 2.12 | 2.13 | 2.12 |
|  | RRl | 2.07 | 1.81 | 2.07 |
|  | RRu | 2.16 | 2.50 | 2.16 |
|  | P | +++ | +++ | +++ |
| Random | RR | 2.00 | 2.15 | 2.01 |
|  | RRl | 1.82 | 1.73 | 1.84 |
|  | RRu | 2.21 | 2.69 | 2.21 |
|  | P | +++ | +++ | +++ |
| Asymm | P | N.S. |  | N.S. |
| Between | Chi |  | 0.01 | 0.01 |
| Between | df |  | 1 | 1 |
| Between | P |  | N.S. | N.S. |
| Btwn(F) | P |  | N.S. | N.S. |
| Btwn(R) | P |  | N.S. | N.S. |

Table 25
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by lowest age considered in the study

**<30**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *CoCHS | 1 | - | - | - | - | 1.63 ( 1.39- 1.90) | |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( 1.59- 2.76) | |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( 1.62- 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- 2.77) | |
| *FINRISK | 2 | - | - | - | - | 2.89 ( 2.08- 4.02) | |
| *NHS-II | 2 | - | - | - | - | 4.30 ( 2.78- 6.65) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**30-<45**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( 1.02- 1.72) | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- 1.86) | |
| *CALIBER | 1 | - | - | - | - | 1.28 ( 1.14- 1.44) | |
| *CPS-II | 3 | - | - | - | - | 1.98 ( 1.90- 2.06) | |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- 2.25) | |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- 2.40) | |
| *JACC | 5 | - | - | - | - | 1.95 ( 1.58- 2.39) | |
| *JACC | 7 | - | - | - | - | 2.45 ( 1.89- 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81- 2.50) | |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- 2.23) | |
| *PREVEND | 3 | - | - | - | - | 1.62 ( 1.11- 2.37) | |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( 1.38- 1.68) | |
| Partial Totals | | 3842 | 399171 | 3537 | 1244395 | | |

*prospective study

**45+**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 2 | - | - | - | - | 2.27 ( 2.00- 2.63) | |
| *ELSA | 2 | - | - | - | - | 1.93 ( 1.23- 3.03) | |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( 1.55- 2.03) | |
| MALMO | 4 | - | - | - | - | 1.63 ( 1.42- 1.87) | |
| MALMO | 5 | - | - | - | - | 1.86 ( 1.61- 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- 1.92) | |
| *MESA | 2 | - | - | - | - | 1.55 ( 1.14- 2.10) | |
| *USA5 | 6 | - | - | - | - | 2.60 ( 2.40- 2.70) | |
| *USA5 | 5 | - | - | - | - | 3.00 ( 2.80- 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- 2.89) | |
| *WHI | 1 | - | - | - | - | 2.06 ( 1.78- 2.38) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**Missing**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- 5.34) | |
| *HSE-SHS | 3 | - | - | - | - | 2.28 ( 1.95- 2.66) | |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- 1.58) | |
| Partial Totals | | 134 | 5926 | 88 | 9438 | | |

*prospective study

Table 25
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by lowest age considered in the study

**RR Data**

| | | **Lowest age included, grouped** | | | | |
|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | |
| | | **<30** | **30-<45** | **45+** | **Missing** | **Total** |
| | N | 5 | 11 | 9 | 3 | 28 |
| | NS | 4 | 9 | 7 | 3 | 23 |
| | Wt | 286.23 | 4992.71 | 3020.11 | 204.71 | 8503.76 |
| Het | Chi | 24.20 | 131.24 | 125.64 | 18.93 | 394.17 |
| Het | df | 4 | 10 | 8 | 2 | 27 |
| Het | P | *** | *** | *** | *** | *** |
| Fixed | RR | 2.02 | 1.95 | 2.42 | 2.40 | 2.12 |
| | RRl | 1.80 | 1.89 | 2.34 | 2.09 | 2.07 |
| | RRu | 2.27 | 2.00 | 2.51 | 2.75 | 2.16 |
| | P | +++ | +++ | +++ | +++ | +++ |
| Random | RR | 2.45 | 1.81 | 2.06 | 2.09 | 2.01 |
| | RRl | 1.77 | 1.61 | 1.76 | 1.16 | 1.84 |
| | RRu | 3.39 | 2.05 | 2.42 | 3.78 | 2.21 |
| | P | +++ | +++ | +++ | + | +++ |
| Asymm | P | * | N.S. | * | N.S. | N.S. |
| Between | Chi | | 0.41 | 8.49 | 3.44 | 94.16 |
| Between | df | | 1 | 1 | 1 | 3 |
| Between | P | | N.S. | ++ | (+) | *** |
| Btwn(F) | P | | N.S. | N.S. | N.S. | (*) |
| Btwn(R) | P | | (-) | N.S. | N.S. | N.S. |

---

Table 26
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by lowest age considered, with trend

**<30**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *CoCHS | 1 | - | - | - | - | 1.63 ( 1.39- 1.90) | |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( 1.59- 2.76) | |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( 1.62- 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- 2.77) | |
| *FINRISK | 2 | - | - | - | - | 2.89 ( 2.08- 4.02) | |
| *NHS-II | 2 | - | - | - | - | 4.30 ( 2.78- 6.65) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

**30-<45**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( 1.02- 1.72) | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- 1.86) | |
| *CALIBER | 1 | - | - | - | - | 1.28 ( 1.14- 1.44) | |
| *CPS-II | 3 | - | - | - | - | 1.98 ( 1.90- 2.06) | |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- 2.25) | |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- 2.40) | |
| *JACC | 5 | - | - | - | - | 1.95 ( 1.58- 2.39) | |
| *JACC | 7 | - | - | - | - | 2.45 ( 1.89- 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81- 2.50) | |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- 2.23) | |
| *PREVEND | 3 | - | - | - | - | 1.62 ( 1.11- 2.37) | |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( 1.38- 1.68) | |
| Partial Totals | | 3842 | 399171 | 3537 | 1244395 | | |

*prospective study

**45+**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 2 | - | - | - | - | 2.27 ( 2.00- 2.63) | |
| *ELSA | 2 | - | - | - | - | 1.93 ( 1.23- 3.03) | |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( 1.55- 2.03) | |
| MALMO | 4 | - | - | - | - | 1.63 ( 1.42- 1.87) | |
| MALMO | 5 | - | - | - | - | 1.86 ( 1.61- 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- 1.92) | |
| *MESA | 2 | - | - | - | - | 1.55 ( 1.14- 2.10) | |
| *USA5 | 6 | - | - | - | - | 2.60 ( 2.40- 2.70) | |
| *USA5 | 5 | - | - | - | - | 3.00 ( 2.80- 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- 2.89) | |
| *WHI | 1 | - | - | - | - | 2.06 ( 1.78- 2.38) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

| | | Lowest age included, grouped, excluding Missing | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | | |
| | | <30 | 30-<45 | 45+ | Total | Trend |
| **RR Data** | | | | | | |
| | N | 5 | 11 | 9 | 25 | |
| | NS | 4 | 9 | 7 | 20 | |
| | Wt | 286.23 | 4992.71 | 3020.11 | 8299.05 | |
| | Het Chi | 24.20 | 131.24 | 125.64 | 371.99 | |
| | Het df | 4 | 10 | 8 | 24 | |
| | Het P | *** | *** | *** | *** | |
| | Fixed RR | 2.02 | 1.95 | 2.42 | 2.11 | |
| | RRl | 1.80 | 1.89 | 2.34 | 2.07 | |
| | RRu | 2.27 | 2.00 | 2.51 | 2.16 | |
| | P | +++ | +++ | +++ | +++ | |
| | Random RR | 2.45 | 1.81 | 2.06 | 1.99 | |
| | RRl | 1.77 | 1.61 | 1.76 | 1.81 | |
| | RRu | 3.39 | 2.05 | 2.42 | 2.19 | |
| | P | +++ | +++ | +++ | +++ | |
| | Asymm P | * | N.S. | * | N.S. | |
| | Between Chi | | 0.41 | 8.49 | 90.90 | 76.50 |
| | Between df | | 1 | 1 | 2 | 1 |
| | Between P | | N.S. | ++ | *** | +++ |
| | Btwn(F) P | | N.S. | N.S. | * | + |
| | Btwn(R) P | | (-) | N.S. | N.S. | N.S. |

Table 27
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by years of follow-up

**<10**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| **\*HAPIEE** | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- 5.34) | |
| **\*PREVEND** | 3 | - | - | - | - | 1.62 ( 1.11- 2.37) | |
| **Partial Totals** | | 125 | 5871 | 51 | 9254 | | |

**\*prospective study**

**10-<20**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| **\*BIOBANK** | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- 1.86) | |
| **\*CALIBER** | 1 | - | - | - | - | 1.28 ( 1.14- 1.44) | |
| **\*ELSA** | 2 | - | - | - | - | 1.93 ( 1.23- 3.03) | |
| **\*EPIC-10** | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- 2.25) | |
| **\*EPIC-10** | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- 2.77) | |
| Subtotal EPIC-10 | | | | | | 2.27 ( 2.14- 2.40) | |
| **\*EPIC-UK** | 3 | - | - | - | - | 1.77 ( 1.55- 2.03) | |
| **\*ESTONGENOME** | 7 | - | - | - | - | 2.10 ( 1.59- 2.76) | |
| **\*ESTONGENOME** | 10 | - | - | - | - | 2.44 ( 1.62- 3.68) | |
| Subtotal ESTONGENOME | | | | | | 2.20 ( 1.75- 2.77) | |
| **\*HSE-SHS** | 3 | - | - | - | - | 2.28 ( 1.95- 2.66) | |
| **\*MESA** | 2 | - | - | - | - | 1.55 ( 1.14- 2.10) | |
| **\*NHS** | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- 2.23) | |
| **\*USA5** | 6 | - | - | - | - | 2.60 ( 2.40- 2.70) | |
| **\*USA5** | 5 | - | - | - | - | 3.00 ( 2.80- 3.20) | |
| Subtotal USA5 | | | | | | 2.77 ( 2.65- 2.89) | |
| **Partial Totals** | | 3842 | 399171 | 3537 | 1244395 | | |

**\*prospective study**

**20-<30**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| **\*CPS-II** | 3 | - | - | - | - | 1.98 ( 1.90- 2.06) | |
| **\*CoCHS** | 1 | - | - | - | - | 1.63 ( 1.39- 1.90) | |
| **\*FINRISK** | 2 | - | - | - | - | 2.89 ( 2.08- 4.02) | |
| **\*JACC** | 5 | - | - | - | - | 1.95 ( 1.58- 2.39) | |
| **\*JACC** | 7 | - | - | - | - | 2.45 ( 1.89- 3.18) | |
| Subtotal JACC | | | | | | 2.13 ( 1.81- 2.50) | |
| **MALMO** | 4 | - | - | - | - | 1.63 ( 1.42- 1.87) | |
| **MALMO** | 5 | - | - | - | - | 1.86 ( 1.61- 2.14) | |
| Subtotal MALMO | | | | | | 1.74 ( 1.57- 1.92) | |
| **\*NAS** | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- 1.58) | |
| **\*NHS-II** | 2 | - | - | - | - | 4.30 ( 2.78- 6.65) | |
| **\*WHI** | 1 | - | - | - | - | 2.06 ( 1.78- 2.38) | |
| **Partial Totals** | | 9 | 55 | 37 | 184 | | |

**\*prospective study**

**30+**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| **\*7CNTRY-ITALY** | 1 | - | - | - | - | 1.33 ( 1.02- 1.72) | |
| **\*ARIC** | 2 | - | - | - | - | 2.27 ( 2.00- 2.63) | |
| **\*WHITEHALL** | 1 | - | - | - | - | 1.52 ( 1.38- 1.68) | |
| **Partial Totals** | | 0 | 0 | 0 | 0 | | |

**\*prospective study**

Table 27
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by years of follow-up

| | | Years follow-up, grouped | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | | |
| | | <10 | 10-<20 | 20-<30 | 30+ | Total | Trend |

**RR Data**

| | | <10 | 10-<20 | 20-<30 | 30+ | Total | Trend |
|---|---|---|---|---|---|---|---|
| | N | 2 | 13 | 10 | 3 | 28 | |
| | NS | 2 | 10 | 8 | 3 | 23 | |
| | Wt | 63.30 | 4488.90 | 3293.27 | 658.29 | 8503.76 | |
| Het | Chi | 11.66 | 226.42 | 40.81 | 25.50 | 394.17 | |
| Het | df | 1 | 12 | 9 | 2 | 27 | |
| Het | P | *** | *** | *** | *** | *** | |
| Fixed | RR | 2.68 | 2.31 | 1.95 | 1.70 | 2.12 | |
| | RRl | 2.09 | 2.24 | 1.89 | 1.58 | 2.07 | |
| | RRu | 3.43 | 2.38 | 2.02 | 1.84 | 2.16 | |
| | P | +++ | +++ | +++ | +++ | +++ | |
| Random | RR | 2.52 | 2.04 | 1.99 | 1.68 | 2.01 | |
| | RRl | 1.07 | 1.77 | 1.78 | 1.23 | 1.84 | |
| | RRu | 5.90 | 2.35 | 2.23 | 2.29 | 2.21 | |
| | P | + | +++ | +++ | ++ | +++ | |
| Asymm | P | | N.S. | N.S. | N.S. | N.S. | |
| Between | Chi | | 1.36 | 6.15 | 11.83 | 89.78 | 83.98 |
| Between | df | | 1 | 1 | 1 | 3 | 1 |
| Between | P | | N.S. | – | --- | *** | --- |
| Btwn(F) | P | | N.S. | N.S. | N.S. | (*) | – |
| Btwn(R) | P | | N.S. | N.S. | N.S. | N.S. | N.S. |

Table 28
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by endpoint

```
Died
                Numbers exposed Non-exposed
 Study ID      NRR   Case    Cont   Case    Cont     RR        95.00%CI
*7CNTRY-ITALY 1       -       -      -       -     1.33 ( 1.02-  1.72)
*CPS-II        3      -       -      -       -     1.98 ( 1.90-  2.06)
*ESTONGENOME   7      -       -      -       -     2.10 ( 1.59-  2.76)
*ESTONGENOME  10      -       -      -       -     2.44 ( 1.62-  3.68)
 Subtotal ESTONGENOME                             2.20 ( 1.75-  2.77)
*FINRISK       2      -       -      -       -     2.89 ( 2.08-  4.02)
*HAPIEE        1     125    5871     51    9254    3.86 ( 2.79-  5.34)
*HSE-SHS       3      -       -      -       -     2.28 ( 1.95-  2.66)
*JACC          5      -       -      -       -     1.95 ( 1.58-  2.39)
*JACC          7      -       -      -       -     2.45 ( 1.89-  3.18)
 Subtotal JACC                                    2.13 ( 1.81-  2.50)
*USA5          6      -       -      -       -     2.60 ( 2.40-  2.70)
*USA5          5      -       -      -       -     3.00 ( 2.80-  3.20)
 Subtotal USA5                                    2.77 ( 2.65-  2.89)
*WHI           1      -       -      -       -     2.06 ( 1.78-  2.38)
*WHITEHALL     1      -       -      -       -     1.52 ( 1.38-  1.68)
Partial Totals      125    5871     51    9254
*prospective study


Diagnosed
                Numbers exposed Non-exposed
 Study ID      NRR   Case    Cont   Case    Cont     RR        95.00%CI
*ARIC          2      -       -      -       -     2.27 ( 2.00-  2.63)
*BIOBANK       3      60   44435    231  239412    1.40 ( 1.05-  1.86)
*CALIBER       1      -       -      -       -     1.28 ( 1.14-  1.44)
*CoCHS         1      -       -      -       -     1.63 ( 1.39-  1.90)
*ELSA          2      -       -      -       -     1.93 ( 1.23-  3.03)
*EPIC-10       1    1969   33695    926   32986    2.08 ( 1.93-  2.25)
*EPIC-10       2     937   58059   1071  168240    2.54 ( 2.32-  2.77)
 Subtotal EPIC-10                                 2.27 ( 2.14-  2.40)
*EPIC-UK       3      -       -      -       -     1.77 ( 1.55-  2.03)
 MALMO         4      -       -      -       -     1.63 ( 1.42-  1.87)
 MALMO         5      -       -      -       -     1.86 ( 1.61-  2.14)
 Subtotal MALMO                                   1.74 ( 1.57-  1.92)
*MESA          2      -       -      -       -     1.55 ( 1.14-  2.10)
*NAS           1      9      55     37     184     0.81 ( 0.42-  1.58)
*NHS           1     876  262982   1309  803757    2.05 ( 1.88-  2.23)
*NHS-II        2      -       -      -       -     4.30 ( 2.78-  6.65)
*PREVEND       3      -       -      -       -     1.62 ( 1.11-  2.37)
Partial Totals     3851  399226   3574 1244579
*prospective study
```

```
                  RR Description:Endpoint reported
                        1          2
                      Died   Diagnosed    Total

RR Data

                N       13        15        28
                NS      10        13        23

               Wt   5406.61   3097.15   8503.76
        Het Chi      225.55    135.05    394.17
        Het  df          12        14        27
        Het   P         ***       ***       ***
       Fixed RR        2.22      1.95      2.12
             RRl       2.16      1.88      2.07
             RRu       2.28      2.02      2.16
               P       +++       +++       +++
      Random RR        2.23      1.83      2.01
             RRl       1.94      1.62      1.84
             RRu       2.57      2.08      2.21
               P       +++       +++       +++
       Asymm  P       N.S.      N.S.      N.S.
     Between Chi                 33.57     33.57
     Between  df                     1         1
     Between   P                   ---       ***
      Btwn(F)  P                  N.S.      N.S.
      Btwn(R)  P                     -         *
```

Table 29
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by number of adjustment factors

**Unadj**

|  |  | Numbers exposed | | Non-exposed | |  |  |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( 1.05- | 1.86) |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( 1.93- | 2.25) |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( 2.32- | 2.77) |
| Subtotal EPIC-10 |  |  |  |  |  | 2.27 ( 2.14- | 2.40) |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( 2.79- | 5.34) |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( 0.42- | 1.58) |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( 1.88- | 2.23) |
| Totals |  | 3976 | 405097 | 3625 | 1253833 |  |  |

*prospective study

**Age-only**

|  |  | Numbers exposed | | Non-exposed | |  |  |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *CALIBER | 1 | - | - | - | - | 1.28 ( 1.14- | 1.44) |
| *CoCHS | 1 | - | - | - | - | 1.63 ( 1.39- | 1.90) |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( 1.59- | 2.76) |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( 1.62- | 3.68) |
| Subtotal ESTONGENOME |  |  |  |  |  | 2.20 ( 1.75- | 2.77) |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( 1.38- | 1.68) |
| Partial Totals |  | 0 | 0 | 0 | 0 |  |  |

*prospective study

**More adj**

|  |  | Numbers exposed | | Non-exposed | |  |  |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( 1.02- | 1.72) |
| *ARIC | 2 | - | - | - | - | 2.27 ( 2.00- | 2.63) |
| *CPS-II | 3 | - | - | - | - | 1.98 ( 1.90- | 2.06) |
| *ELSA | 2 | - | - | - | - | 1.93 ( 1.23- | 3.03) |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( 1.55- | 2.03) |
| *FINRISK | 2 | - | - | - | - | 2.89 ( 2.08- | 4.02) |
| *HSE-SHS | 3 | - | - | - | - | 2.28 ( 1.95- | 2.66) |
| *JACC | 5 | - | - | - | - | 1.95 ( 1.58- | 2.39) |
| *JACC | 7 | - | - | - | - | 2.45 ( 1.89- | 3.18) |
| Subtotal JACC |  |  |  |  |  | 2.13 ( 1.81- | 2.50) |
| MALMO | 4 | - | - | - | - | 1.63 ( 1.42- | 1.87) |
| MALMO | 5 | - | - | - | - | 1.86 ( 1.61- | 2.14) |
| Subtotal MALMO |  |  |  |  |  | 1.74 ( 1.57- | 1.92) |
| *MESA | 2 | - | - | - | - | 1.55 ( 1.14- | 2.10) |
| *NHS-II | 2 | - | - | - | - | 4.30 ( 2.78- | 6.65) |
| *PREVEND | 3 | - | - | - | - | 1.62 ( 1.11- | 2.37) |
| *USA5 | 6 | - | - | - | - | 2.60 ( 2.40- | 2.70) |
| *USA5 | 5 | - | - | - | - | 3.00 ( 2.80- | 3.20) |
| Subtotal USA5 |  |  |  |  |  | 2.77 ( 2.65- | 2.89) |
| *WHI | 1 | - | - | - | - | 2.06 ( 1.78- | 2.38) |
| Partial Totals |  | 0 | 0 | 0 | 0 |  |  |

*prospective study

**Number of adjustment factors, grouped**

|  | 1 | 2 | 3 |  |
|---|---|---|---|---|
|  | Unadj | Age-only | More adj | Total |

**RR Data**

|  | 1 | 2 | 3 | Total |
|---|---|---|---|---|
| N | 6 | 5 | 17 | 28 |
| NS | 5 | 4 | 14 | 23 |
| Wt | 1779.36 | 909.29 | 5815.11 | 8503.76 |
| Het Chi | 44.88 | 19.36 | 210.29 | 394.17 |
| Het df | 5 | 4 | 16 | 27 |
| Het P | *** | *** | *** | *** |
| Fixed RR | 2.18 | 1.50 | 2.21 | 2.12 |
| RRl | 2.09 | 1.41 | 2.16 | 2.07 |
| RRu | 2.29 | 1.60 | 2.27 | 2.16 |
| P | +++ | +++ | +++ | +++ |
| Random RR | 2.11 | 1.64 | 2.10 | 2.01 |
| RRl | 1.78 | 1.39 | 1.88 | 1.84 |
| RRu | 2.50 | 1.93 | 2.35 | 2.21 |
| P | +++ | +++ | +++ | +++ |
| Asymm P | N.S. | N.S. | N.S. | N.S. |
| Between Chi |  | 84.17 | 0.21 | 119.65 |
| Between df |  | 1 | 1 | 2 |

Table 29
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Analysis by number of adjustment factors

| | | Number of adjustment factors, grouped | | | |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | |
| | | Unadj | Age-only | More adj | Total |

**RR Data**

| | | 1 Unadj | 2 Age-only | 3 More adj | Total |
|---|---|---|---|---|---|
| **Between** | **P** | | --- | N.S. | *** |
| **Btwn(F)** | **P** | | -- | N.S. | * |
| **Btwn(R)** | **P** | | - | N.S. | * |

Table 30
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
Analysis by disease definition standard or not

**absent**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI | |
|---|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | | |
| *7CNTRY-ITALY | 1 | - | - | - | - | 1.33 ( | 1.02- | 1.72) |
| *ARIC | 2 | - | - | - | - | 2.27 ( | 2.00- | 2.63) |
| *CALIBER | 1 | - | - | - | - | 1.28 ( | 1.14- | 1.44) |
| *ELSA | 2 | - | - | - | - | 1.93 ( | 1.23- | 3.03) |
| *HSE-SHS | 3 | - | - | - | - | 2.28 ( | 1.95- | 2.66) |
| MALMO | 4 | - | - | - | - | 1.63 ( | 1.42- | 1.87) |
| MALMO | 5 | - | - | - | - | 1.86 ( | 1.61- | 2.14) |
| Subtotal MALMO | | | | | | 1.74 ( | 1.57- | 1.92) |
| *MESA | 2 | - | - | - | - | 1.55 ( | 1.14- | 2.10) |
| *NAS | 1 | 9 | 55 | 37 | 184 | 0.81 ( | 0.42- | 1.58) |
| *NHS | 1 | 876 | 262982 | 1309 | 803757 | 2.05 ( | 1.88- | 2.23) |
| *NHS-II | 2 | - | - | - | - | 4.30 ( | 2.78- | 6.65) |
| *PREVEND | 3 | - | - | - | - | 1.62 ( | 1.11- | 2.37) |
| *WHI | 1 | - | - | - | - | 2.06 ( | 1.78- | 2.38) |
| Partial Totals | | 885 | 263037 | 1346 | 803941 | | | |

*prospective study

**present**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI | |
|---|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | | |
| *BIOBANK | 3 | 60 | 44435 | 231 | 239412 | 1.40 ( | 1.05- | 1.86) |
| *CPS-II | 3 | - | - | - | - | 1.98 ( | 1.90- | 2.06) |
| *CoCHS | 1 | - | - | - | - | 1.63 ( | 1.39- | 1.90) |
| *EPIC-10 | 1 | 1969 | 33695 | 926 | 32986 | 2.08 ( | 1.93- | 2.25) |
| *EPIC-10 | 2 | 937 | 58059 | 1071 | 168240 | 2.54 ( | 2.32- | 2.77) |
| Subtotal EPIC-10 | | | | | | 2.27 ( | 2.14- | 2.40) |
| *EPIC-UK | 3 | - | - | - | - | 1.77 ( | 1.55- | 2.03) |
| *ESTONGENOME | 7 | - | - | - | - | 2.10 ( | 1.59- | 2.76) |
| *ESTONGENOME | 10 | - | - | - | - | 2.44 ( | 1.62- | 3.68) |
| Subtotal ESTONGENOME | | | | | | 2.20 ( | 1.75- | 2.77) |
| *FINRISK | 2 | - | - | - | - | 2.89 ( | 2.08- | 4.02) |
| *HAPIEE | 1 | 125 | 5871 | 51 | 9254 | 3.86 ( | 2.79- | 5.34) |
| *JACC | 5 | - | - | - | - | 1.95 ( | 1.58- | 2.39) |
| *JACC | 7 | - | - | - | - | 2.45 ( | 1.89- | 3.18) |
| Subtotal JACC | | | | | | 2.13 ( | 1.81- | 2.50) |
| *USA5 | 6 | - | - | - | - | 2.60 ( | 2.40- | 2.70) |
| *USA5 | 5 | - | - | - | - | 3.00 ( | 2.80- | 3.20) |
| Subtotal USA5 | | | | | | 2.77 ( | 2.65- | 2.89) |
| *WHITEHALL | 1 | - | - | - | - | 1.52 ( | 1.38- | 1.68) |
| Partial Totals | | 3091 | 142060 | 2279 | 449892 | | | |

*prospective study

| | Study description:Standard definition | | |
|---|---|---|---|
| | 1 | 2 | |
| | absent | present | Total |

**RR Data**

| | | 1 absent | 2 present | Total |
|---|---|---|---|---|
| | N | 13 | 15 | 28 |
| | NS | 12 | 11 | 23 |
| | Wt | 1918.64 | 6585.12 | 8503.76 |
| Het | Chi | 92.58 | 256.80 | 394.17 |
| Het | df | 12 | 14 | 27 |
| Het | P | *** | *** | *** |
| Fixed | RR | 1.85 | 2.20 | 2.12 |
| | RRl | 1.77 | 2.15 | 2.07 |
| | RRu | 1.94 | 2.26 | 2.16 |
| | P | +++ | +++ | +++ |
| Random | RR | 1.83 | 2.17 | 2.01 |
| | RRl | 1.59 | 1.93 | 1.84 |
| | RRu | 2.10 | 2.45 | 2.21 |
| | P | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | N.S. |
| Between | Chi | | 44.79 | 44.79 |
| Between | df | | 1 | 1 |
| Between | P | | +++ | *** |
| Btwn(F) | P | | (+) | (*) |
| Btwn(R) | P | | (+) | (*) |

Table 31
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of study details for all the Stroke results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NSTR | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 2 | MENOTT2016 | Italy | Regional | 1960 | 225 | 0 | 0 | Cohort | Stroke | m | 40 | 59 | 50 | Died | 3 |
| ARIC | 3 | DING2019A | USA | National | 1987 | 1106 | 0 | 0 | Cohort | Stroke | b | 45 | 64 | 30 | Diagnosed | 0 |
| ARIC | 4 | DING2019A | USA | National | 1987 | 1106 | 0 | 0 | Cohort | Stroke | b | 45 | 64 | 30 | Diagnosed | 14 |
| BIOBANK | 4 | PETERS2020 | UK | National | 2006 | 4662 | 0 | 0 | Cohort | Stroke | f | 40 | 69 | 12 | Diagnosed | 2 |
| BIOBANK | 5 | PETERS2020 | UK | National | 2006 | 4662 | 0 | 0 | Cohort | Stroke | m | 40 | 69 | 12 | Diagnosed | 2 |
| CALIBER | 2 | PUJADE2015 | UK | GP records | 1997 | 11842 | 0 | 0 | Cohort | Stroke | f | 30 | 999 | 13 | Diagnosed | 1 |
| CPS-II | 2 | TURNER2017 | USA | National | 1982 | 5582 | 0 | 0 | Cohort | Stroke | b | 30 | 999 | 22 | Died | 0 |
| CPS-II | 4 | TURNER2017 | USA | National | 1982 | 5582 | 0 | 0 | Cohort | Stroke | b | 30 | 999 | 22 | Died | 23 |
| CaCHS | 2 | NG2020 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | f | 20 | 999 | 13 | Diagnosed | 15 |
| CaCHS | 4 | NG2020 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | m | 20 | 999 | 13 | Diagnosed | 15 |
| CaCHS | 5 | MANUEL2015 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | m | 20 | 999 | 11 | Diagnosed | 0 |
| CaCHS | 6 | MANUEL2015 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | f | 20 | 999 | 11 | Diagnosed | 0 |
| ELSA | 3 | JACKSO2019E | UK | National | 2004 | 326 | 0 | 0 | Cohort | Non-fatal Stroke | b | 52 | 999 | 13 | Diagnosed | 0 |
| ELSA | 4 | JACKSO2019E | UK | National | 2004 | 326 | 0 | 0 | Cohort | Non-fatal Stroke | b | 52 | 999 | 13 | Diagnosed | 7 |
| EPIC-10 | 4 | RICCI2018 | Multi | International | 1991 | 2187 | 0 | 0 | Nested CC | Non-fatal Stroke | b | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-ITALY | 1 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | m | 35 | 74 | 15 | Diagnosed | 0 |
| EPIC-ITALY | 2 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | f | 35 | 74 | 15 | Diagnosed | 0 |
| EPIC-ITALY | 3 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | m | 35 | 74 | 15 | Diagnosed | 2 |
| EPIC-ITALY | 4 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | m | 35 | 74 | 15 | Diagnosed | 10 |
| EPIC-ITALY | 5 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | f | 35 | 74 | 15 | Diagnosed | 2 |
| EPIC-ITALY | 6 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | f | 35 | 74 | 15 | Diagnosed | 10 |
| EPIC-SPAIN | 1 | AMIANO2016 | Spain | Regional | 1992 | 301 | 0 | 0 | Cohort | Stroke | f | 29 | 69 | 16 | Diagnosed | 0 |
| EPIC-UK | 4 | STOEKE2016 | UK | Regional | 1993 | 385 | 0 | 0 | Cohort | Stroke | b | 45 | 79 | 14 | Diagnosed | 0 |
| EPIC-UK | 5 | STOEKE2016 | UK | Regional | 1993 | 385 | 0 | 0 | Cohort | Stroke | b | 45 | 79 | 14 | Diagnosed | 2 |
| EPIC-UK | 6 | STOEKE2016 | UK | Regional | 1993 | 385 | 0 | 0 | Cohort | Stroke | b | 45 | 79 | 14 | Diagnosed | 6 |
| ESTONGENOME | 3 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | m | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 6 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | f | 18 | 999 | 13 | Died | 0 |
| ESTONGENOME | 8 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 11 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | f | 18 | 999 | 13 | Died | 1 |
| HAPIEE | 2 | STEFLE2016 | Multi | International | 2002 | 109 | 0 | 0 | Cohort | Stroke | b | * | * | 9 | Died | 0 |
| HSE-SHS | 2 | DEMEST2019 | UK | National | 1994 | 690 | 0 | 0 | Cohort | Stroke | b | * | * | 17 | Died | 0 |
| HSE-SHS | 4 | DEMEST2019 | UK | National | 1994 | 690 | 0 | 0 | Cohort | Stroke | b | * | * | 17 | Died | 7 |
| JACC | 2 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | m | 40 | 79 | 21 | Died | 0 |
| JACC | 4 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | f | 40 | 79 | 21 | Died | 0 |
| JACC | 6 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | m | 40 | 79 | 21 | Died | 7 |
| JACC | 8 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | f | 40 | 79 | 21 | Died | 9 |
| JHS | 1 | OSHUNB2020 | USA | Regional | 2000 | 183 | 0 | 0 | Cohort | Stroke | b | 21 | 84 | 15 | Diagnosed | 0 |
| JHS | 2 | OSHUNB2020 | USA | Regional | 2000 | 183 | 0 | 0 | Cohort | Stroke | b | 21 | 84 | 15 | Diagnosed | 11 |
| JP8 | 1 | ABE2019 | Japan | National | 1983 | 3487 | 0 | 0 | Cohort | Stroke | m | 40 | 999 | 30 | Died | 0 |

Table 31
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of study details for all the Stroke results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NSTR | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MALMO | 1 | LI2019A | Sweden | Regional | 1991 | 305 | 0 | 0 | Cohort | Stroke | b | 46 | 67 | 22 | Diagnosed | 0 |
| MESA | 4 | NANCE2017 | USA | Regional | 2000 | 180 | 0 | 0 | Cohort | Stroke | b | 45 | 84 | 11 | Diagnosed | 0 |
| MILLION | 1 | PRICE2018 | UK | National | 1996 | 8103 | 0 | 0 | Cohort | Stroke | f | 46 | 66 | 19 | Diagnosed | 8 |
| NFBC | 1 | RISSAN2019 | Finland | Regional | 1966 | 352 | 0 | 0 | Cohort | Stroke | b | 14 | 46 | 49 | Diagnosed | 0 |
| NFBC | 2 | RISSAN2019 | Finland | Regional | 1966 | 352 | 0 | 0 | Cohort | Stroke | b | 14 | 46 | 49 | Diagnosed | 10 |
| NHIS | 1 | INOUEC2020 | USA | National | 1987 | 2046 | x | 0 | Cohort | Stroke | b | 18 | 95 | 24 | Died | 0 |
| NHIS | 3 | INOUEC2020 | USA | National | 1987 | 2046 | x | 0 | Cohort | Stroke | b | 18 | 95 | 24 | Died | 5 |
| NHIS | 5 | QIN2020A | USA | National | 1987 | 2046 | 0 | 0 | Cohort | Stroke | b | 18 | 95 | 14 | Died | 0 |
| NHIS | 6 | QIN2020A | USA | National | 1987 | 2046 | 0 | 0 | Cohort | Stroke | b | 18 | 95 | 14 | Died | 8 |
| NHIS | 7 | QIN2020A | USA | National | 1987 | 2046 | 0 | x | Cohort | Stroke | b | 18 | 95 | 14 | Died | 9 |
| NHIS | 8 | RODU2019 | USA | National | 1987 | 2046 | 0 | x | Cohort | Stroke | m | 40 | 79 | 28 | Died | 0 |
| NHIS | 9 | RODU2019 | USA | National | 1987 | 2046 | 0 | x | Cohort | Stroke | m | 40 | 79 | 28 | Died | 1 |
| NHIS | 10 | RODU2019 | USA | National | 1987 | 2046 | 0 | x | Cohort | Stroke | m | 40 | 79 | 28 | Died | 9 |
| NHS | 2 | HART2015A | USA | Medical workers | 1989 | 3288 | 0 | 0 | Cohort | Stroke | f | 43 | 68 | 17 | Diagnosed | 0 |
| NIH-AARP | 1 | NASH2017 | USA | Regional | 2004 | 1369 | 0 | 0 | Cohort | Stroke | b | 70 | 999 | 7 | Died | 0 |
| NIH-AARP | 2 | NASH2017 | USA | Regional | 2004 | 1369 | 0 | 0 | Cohort | Stroke | b | 70 | 999 | 7 | Died | 4 |
| NLMS | 1 | CHRIST2018 | USA | National | 1985 | 3083 | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 0 |
| NLMS | 2 | CHRIST2018 | USA | National | 1985 | 3083 | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 1 |
| NLMS | 3 | CHRIST2018 | USA | National | 1985 | 3083 | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 5 |
| OHASAMA | 1 | MURAKA2017 | Japan | Regional | 1998 | 293 | x | 0 | Cohort | Stroke | b | 60 | 999 | 12 | Diagnosed | 2 |
| PREVEND | 4 | KUNUT2018 | Netherlands | Regional | 2001 | 83 | 0 | 0 | Cohort | Stroke | b | 32 | 80 | 9 | Diagnosed | 0 |
| PREVEND | 5 | KUNUT2018 | Netherlands | Regional | 2001 | 83 | 0 | 0 | Cohort | Stroke | b | 32 | 80 | 9 | Diagnosed | 2 |
| PREVEND | 6 | KUNUT2018 | Netherlands | Regional | 2001 | 83 | 0 | 0 | Cohort | Stroke | b | 32 | 80 | 9 | Diagnosed | 10 |
| SCCS | 1 | MUNRO2016 | USA | Regional | 2002 | 389 | 0 | 0 | Cohort | Stroke | b | 40 | 79 | 11 | Died | 7 |
| USA5 | 3 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | f | 55 | 999 | 11 | Died | 0 |
| USA5 | 4 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | m | 55 | 999 | 11 | Died | 0 |
| USA5 | 7 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | f | 55 | 999 | 11 | Died | 5 |
| USA5 | 8 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | m | 55 | 999 | 11 | Died | 5 |
| WHITEHALL | 2 | BATTY2015 | UK | Civil servants | 1967 | 1061 | 0 | 0 | Cohort | Stroke | m | 40 | 69 | 43 | Died | 1 |
| WHS | 1 | KURTH2020 | USA | National | 1992 | 887 | 0 | 0 | Cohort | Stroke | f | 45 | 999 | 26 | Diagnosed | 0 |
| WHS | 2 | KURTH2020 | USA | National | 1992 | 887 | 0 | 0 | Cohort | Stroke | f | 45 | 999 | 26 | Diagnosed | 14 |

Table 32
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of risk estimates for all the Stroke results (not all to be included in any one meta-analysis). Current cigarette smokers versus never smokers

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 2 | MENOTT2016 | - | - | - | - | 1.43 | 1.04 | 1.96 | Other calculations |
| ARIC | 3 | DING2019A | 195 | 434 | 42035 | 126807 | 1.36 | 1.15 | 1.60 | From numbers |
| ARIC | 4 | DING2019A | - | - | - | - | 2.00 | 1.64 | 2.38 | Other calculations |
| BIOBANK | 4 | PETERS2020 | - | - | - | - | 1.94 | 1.71 | 2.19 | Hamling method |
| BIOBANK | 5 | PETERS2020 | - | - | - | - | 1.82 | 1.66 | 2.00 | Hamling method |
| CALIBER | 2 | PUJADE2015 | - | - | - | - | 1.46 | 1.29 | 1.66 | Other calculations |
| CPS-II | 2 | TURNER2017 | 1461 | 4121 | 65275 | 149617 | 0.81 | 0.77 | 0.86 | From numbers |
| CPS-II | 4 | TURNER2017 | - | - | - | - | 1.55 | 1.45 | 1.66 | Hamling method |
| CaCHS | 2 | NG2020 | - | - | - | - | 1.55 | 1.20 | 1.99 | Hamling method |
| CaCHS | 4 | NG2020 | - | - | - | - | 1.08 | 0.85 | 1.38 | Hamling method |
| CaCHS | 5 | MANUEL2015 | 146 | 196 | 88312 | 125398 | 1.06 | 0.85 | 1.31 | From numbers |
| CaCHS | 6 | MANUEL2015 | 189 | 433 | 89702 | 197336 | 0.96 | 0.81 | 1.14 | From numbers |
| ELSA | 3 | JACKSO2019E | 54 | 113 | 897 | 2387 | 1.58 | 1.12 | 2.22 | Given in the paper |
| ELSA | 4 | JACKSO2019E | - | - | - | - | 1.74 | 1.06 | 2.85 | Given in the paper |
| EPIC-10 | 4 | RICCI2018 | 2004 | 2187 | 4315 | 7679 | 1.63 | 1.55 | 1.71 | From numbers |
| EPIC-ITALY | 1 | TRAJKO2017 | 61 | 39 | 3708 | 4028 | 1.70 | 1.14 | 2.53 | From numbers |
| EPIC-ITALY | 2 | TRAJKO2017 | 71 | 126 | 7995 | 16475 | 1.16 | 0.87 | 1.55 | From numbers |
| EPIC-ITALY | 3 | TRAJKO2017 | - | - | - | - | 1.99 | 1.33 | 2.98 | Given in the paper |
| EPIC-ITALY | 4 | TRAJKO2017 | - | - | - | - | 1.80 | 1.19 | 2.72 | Given in the paper |
| EPIC-ITALY | 5 | TRAJKO2017 | - | - | - | - | 1.84 | 1.36 | 2.48 | Given in the paper |
| EPIC-ITALY | 6 | TRAJKO2017 | - | - | - | - | 1.96 | 1.44 | 2.66 | Given in the paper |
| EPIC-SPAIN | 1 | AMIANO2016 | 42 | 241 | 4798 | 18190 | 0.66 | 0.48 | 0.92 | From numbers |
| EPIC-UK | 4 | STOEKE2016 | 57 | 156 | 28629 | 122077 | 1.64 | 1.22 | 2.20 | Hamling method |
| EPIC-UK | 5 | STOEKE2016 | - | - | - | - | 1.91 | 1.41 | 2.58 | Hamling method |
| EPIC-UK | 6 | STOEKE2016 | - | - | - | - | 1.89 | 1.40 | 2.55 | Hamling method |
| ESTONGENOME | 3 | KOKS2017 | * | * | * | * | 1.20 | 0.70 | 2.06 | Given in the paper |
| ESTONGENOME | 6 | KOKS2017 | * | * | * | * | 0.44 | 0.26 | 0.74 | Given in the paper |
| ESTONGENOME | 8 | KOKS2017 | - | - | - | - | 2.91 | 1.65 | 5.12 | Given in the paper |
| ESTONGENOME | 11 | KOKS2017 | - | - | - | - | 2.88 | 1.60 | 5.15 | Given in the paper |
| HAPIEE | 2 | STEFLE2016 | 50 | 41 | 5871 | 9254 | 1.92 | 1.27 | 2.90 | From numbers |
| HSE-SHS | 2 | DEMEST2019 | 161 | 239 | 25045 | 38581 | 1.04 | 0.85 | 1.27 | From numbers |
| HSE-SHS | 4 | DEMEST2019 | - | - | - | - | 1.86 | 1.49 | 2.32 | Other calculations |
| JACC | 2 | MATSUN2017 | 850 | 314 | 375755 | 150359 | 1.08 | 0.95 | 1.23 | From numbers |
| JACC | 4 | MATSUN2017 | 105 | 1439 | 52615 | 945625 | 1.31 | 1.08 | 1.60 | From numbers |
| JACC | 6 | MATSUN2017 | - | - | - | - | 1.23 | 1.07 | 1.42 | Given in the paper |
| JACC | 8 | MATSUN2017 | - | - | - | - | 1.35 | 1.08 | 1.68 | Given in the paper |
| JHS | 1 | OSHUNB2020 | 37 | 105 | 546 | 3089 | 1.99 | 1.39 | 2.87 | From numbers |
| JHS | 2 | OSHUNB2020 | - | - | - | - | 2.48 | 1.60 | 3.83 | Given in the paper |
| JP8 | 1 | ABE2019 | 1737 | 616 | 78235 | 29255 | 1.05 | 0.96 | 1.15 | From numbers |

Table 32
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of risk estimates for all the Stroke results (not all to be included in any one meta-analysis). Current cigarette smokers versus never smokers

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|----------|-----|-------|-----|-----|-----|-----|-----|-----|-----|---------|
| MALMO | 1 | LI2019A | 79 | 128 | 12672 | 32087 | 1.56 | 1.18 | 2.07 | From numbers |
| MESA | 4 | NANCE2017 | 31 | 88 | 887 | 3418 | 1.36 | 0.91 | 2.03 | From numbers |
| MILLION | 1 | PRICE2018 | - | - | - | - | 2.41 | 2.29 | 2.54 | Hamling method |
| NFBC | 1 | RISSAN2019 | 57 | 76 | 63123 | 153226 | 1.82 | 1.29 | 2.57 | From numbers |
| NFBC | 2 | RISSAN2019 | - | - | - | - | 1.69 | 1.10 | 2.60 | Given in the paper |
| NHIS | 1 | INOUEC2020 | 317 | 989 | 32038 | 83972 | 0.84 | 0.74 | 0.95 | From numbers |
| NHIS | 3 | INOUEC2020 | - | - | - | - | 1.59 | 1.33 | 1.90 | Given in the paper |
| NHIS | 5 | QIN2020A | 308 | 1067 | 73186 | 183269 | 0.72 | 0.64 | 0.82 | From numbers |
| NHIS | 6 | QIN2020A | - | - | - | - | 2.10 | 1.81 | 2.43 | Hamling method |
| NHIS | 7 | QIN2020A | - | - | - | - | 1.94 | 1.65 | 2.28 | Hamling method |
| NHIS | 8 | RODU2019 | 182 | 199 | 11949 | 16650 | 1.27 | 1.04 | 1.56 | From numbers |
| NHIS | 9 | RODU2019 | - | - | - | - | 1.76 | 1.41 | 2.18 | Hamling method |
| NHIS | 10 | RODU2019 | - | - | - | - | 1.43 | 1.13 | 1.82 | Hamling method |
| NHS | 2 | HART2015A | 616 | 1266 | 262982 | 803757 | 1.49 | 1.35 | 1.64 | From numbers |
| NIH-AARP | 1 | NASH2017 | 132 | 455 | 9591 | 60973 | 1.84 | 1.52 | 2.24 | From numbers |
| NIH-AARP | 2 | NASH2017 | - | - | - | - | 2.22 | 1.82 | 2.70 | Other calculations |
| NLMS | 1 | CHRIST2018 | 569 | 1595 | 66665 | 203071 | 1.09 | 0.99 | 1.20 | From numbers |
| NLMS | 2 | CHRIST2018 | - | - | - | - | 1.26 | 1.14 | 1.38 | Given in the paper |
| NLMS | 3 | CHRIST2018 | - | - | - | - | 1.24 | 1.12 | 1.36 | Given in the paper |
| OHASAMA | 1 | MURAKA2017 | - | - | - | - | 1.25 | 0.87 | 1.80 | Given in the paper |
| PREVEND | 4 | KUNUT2018 | 29 | 23 | 1282 | 1458 | 1.43 | 0.83 | 2.47 | From numbers |
| PREVEND | 5 | KUNUT2018 | - | - | - | - | 1.69 | 0.97 | 2.95 | Hamling method |
| PREVEND | 6 | KUNUT2018 | - | - | - | - | 1.85 | 1.05 | 3.27 | Hamling method |
| SCCS | 1 | MUNRO2016 | - | - | - | - | 1.45 | 1.14 | 1.84 | Hamling method |
| USA5 | 3 | CARTER2015 | 385 | 2435 | 50488 | 259659 | 0.81 | 0.73 | 0.91 | From numbers |
| USA5 | 4 | CARTER2015 | 279 | 1399 | 38128 | 136613 | 0.71 | 0.63 | 0.81 | From numbers |
| USA5 | 7 | CARTER2015 | - | - | - | - | 2.10 | 1.80 | 2.30 | Given in the paper |
| USA5 | 8 | CARTER2015 | - | - | - | - | 1.90 | 1.70 | 2.20 | Given in the paper |
| WHITEHALL | 2 | BATTY2015 | - | - | - | - | 1.31 | 1.12 | 1.54 | Given in the paper |
| WHS | 1 | KURTH2020 | 138 | 442 | 61724 | 308040 | 1.56 | 1.29 | 1.89 | From numbers |
| WHS | 2 | KURTH2020 | - | - | - | - | 1.71 | 1.39 | 2.09 | Other calculations |

Table 33
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of the disease definitions for all the Stroke results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | Definition of stroke | Standard Stroke definition |
|----------|-----|-------|---------|---------------|----------------------|----------------------------|
| 7CNTRY-ITALY | 2 | MENOTT2016 | Italy | Regional | Stroke NOS | 0 |
| ARIC | 3 | DING2019A | USA | National | ICD-9 430-438, ICD-10 G45, I60-I63, I65-I67 | 0 |
| ARIC | 4 | DING2019A | USA | National | ICD-9 430-438, ICD-10 G45, I60-I63, I65-I67 | 0 |
| BIOBANK | 4 | PETERS2020 | UK | National | ICD-10 I60, I61, I63, I64 | 0 |
| BIOBANK | 5 | PETERS2020 | UK | National | ICD-10 I60, I61, I63, I64 | 0 |
| CALIBER | 2 | PUJADE2015 | UK | GP records | From Read Codes | 0 |
| CPS-II | 2 | TURNER2017 | USA | National | ICD-9 430-438, ICD-10 I60-I69 | present |
| CPS-II | 4 | TURNER2017 | USA | National | ICD-9 430-438, ICD-10 I60-I69 | present |
| CaCHS | 2 | NG2020 | Canada | Regional | Canadian Stroke Network definition | 0 |
| CaCHS | 4 | NG2020 | Canada | Regional | Canadian Stroke Network definition | 0 |
| CaCHS | 5 | MANUEL2015 | Canada | Regional | Canadian Stroke Network definition | 0 |
| CaCHS | 6 | MANUEL2015 | Canada | Regional | Canadian Stroke Network definition | 0 |
| ELSA | 3 | JACKSO2019E | UK | National | Self-reported | 0 |
| ELSA | 4 | JACKSO2019E | UK | National | Self-reported | 0 |
| EPIC-10 | 4 | RICCI2018 | Multi | International | ICD-10 I60-I69, F01 | 0 |
| EPIC-ITALY | 1 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-ITALY | 2 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-ITALY | 3 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-ITALY | 4 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-ITALY | 5 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-ITALY | 6 | TRAJKO2017 | Italy | Regional | ICD-10 I60-I69 | present |
| EPIC-SPAIN | 1 | AMIANO2016 | Spain | Regional | ICD-9 430-438; ICD-10 I60-I69 | present |
| EPIC-UK | 4 | STOEKE2016 | UK | Regional | ICD-10 I60-I63, I65, I66 | 0 |
| EPIC-UK | 5 | STOEKE2016 | UK | Regional | ICD-10 I60-I63, I65, I66 | 0 |
| EPIC-UK | 6 | STOEKE2016 | UK | Regional | ICD-10 I60-I63, I65, I66 | 0 |
| ESTONGENOME | 3 | KOKS2017 | Estonia | National | ICD-10 I60-I69 | present |
| ESTONGENOME | 6 | KOKS2017 | Estonia | National | ICD-10 I60-I69 | present |
| ESTONGENOME | 8 | KOKS2017 | Estonia | National | ICD-10 I60-I69 | present |
| ESTONGENOME | 11 | KOKS2017 | Estonia | National | ICD-10 I60-I69 | present |
| HAPIEE | 2 | STEFLE2016 | Multi | International | ICD 10 I60-I69 | present |
| HSE-SHS | 2 | DEMEST2019 | UK | National | Stroke NOS | 0 |
| HSE-SHS | 4 | DEMEST2019 | UK | National | Stroke NOS | 0 |
| JACC | 2 | MATSUN2017 | Japan | Regional | ICD-10 I60-69 | present |
| JACC | 4 | MATSUN2017 | Japan | Regional | ICD-10 I60-69 | present |
| JACC | 6 | MATSUN2017 | Japan | Regional | ICD-10 I60-69 | present |
| JACC | 8 | MATSUN2017 | Japan | Regional | ICD-10 I60-69 | present |
| JHS | 1 | OSHUNB2020 | USA | Regional | Carotid endarterectomy/angioplasty, stroke events. | 0 |
| JHS | 2 | OSHUNB2020 | USA | Regional | Carotid endarterectomy/angioplasty, stroke events. | 0 |
| JP8 | 1 | ABE2019 | Japan | National | ICD-10 I60-I69 | present |

Table 33
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of the disease definitions for all the Stroke results (not all to be included in any one meta-analysis), Current smokers versus never smokers

| Study ID | NRR | REFID | Country | Nature of pop | Definition of stroke | Standard Stroke definition |
|---|---|---|---|---|---|---|
| MALMO | 1 | LI2019A | Sweden | Regional | ICD-9 430,431,434,436; ICD-10 I60, I61, I63, I64 | 0 |
| MESA | 4 | NANCE2017 | USA | Regional | Adjudicated, NOS | 0 |
| MILLION | 1 | PRICE2018 | UK | National | ICD-10 I60, I61, I63 | 0 |
| NFBC | 1 | RISSAN2019 | Finland | Regional | ICD-8/9 430-438, ICD-10 I60,I61,I63-I69,G45,G46 | 0 |
| NFBC | 2 | RISSAN2019 | Finland | Regional | ICD-8/9 430-438, ICD-10 I60,I61,I63-I69,G45,G46 | 0 |
| NHIS | 1 | INOUEC2020 | USA | National | ICD-10 I60-I69 | present |
| NHIS | 3 | INOUEC2020 | USA | National | ICD-10 I60-I69 | present |
| NHIS | 5 | QIN2020A | USA | National | ICD-10 I60-I69 | present |
| NHIS | 6 | QIN2020A | USA | National | ICD-10 I60-I69 | present |
| NHIS | 7 | QIN2020A | USA | National | ICD-10 I60-I69 | present |
| NHIS | 8 | RODU2019 | USA | National | ICD-10 I60-I69 | present |
| NHIS | 9 | RODU2019 | USA | National | ICD-10 I60-I69 | present |
| NHIS | 10 | RODU2019 | USA | National | ICD-10 I60-I69 | present |
| NHS | 2 | HART2015A | USA | Medical workers | By symptoms | 0 |
| NIH-AARP | 1 | NASH2017 | USA | Regional | ICD-9 430-438, ICD-10 I60-I69 | present |
| NIH-AARP | 2 | NASH2017 | USA | Regional | ICD-9 430-438, ICD-10 I60-I69 | present |
| NLMS | 1 | CHRIST2018 | USA | National | ICD-10 I60-I69 | present |
| NLMS | 2 | CHRIST2018 | USA | National | ICD-10 I60-I69 | present |
| NLMS | 3 | CHRIST2018 | USA | National | ICD-10 I60-I69 | present |
| OHASAMA | 1 | MURAKA2017 | Japan | Regional | NINDS special report: see ref 20 | 0 |
| PREVEND | 4 | KUNUT2018 | Netherlands | Regional | ICD-10 I60-I66 | 0 |
| PREVEND | 5 | KUNUT2018 | Netherlands | Regional | ICD-10 I60-I66 | 0 |
| PREVEND | 6 | KUNUT2018 | Netherlands | Regional | ICD-10 I60-I66 | 0 |
| SCCS | 1 | MUNRO2016 | USA | Regional | ICD-10 I60-I69 | present |
| USA5 | 3 | CARTER2015 | USA | Regional | ICD-10 I60-I69 | present |
| USA5 | 4 | CARTER2015 | USA | Regional | ICD-10 I60-I69 | present |
| USA5 | 7 | CARTER2015 | USA | Regional | ICD-10 I60-I69 | present |
| USA5 | 8 | CARTER2015 | USA | Regional | ICD-10 I60-I69 | present |
| WHITEHALL | 2 | BATTY2015 | UK | Civil servants | ICD-8,9 430-438, ICD-10 I60-I69 | present |
| WHS | 1 | KURTH2020 | USA | National | Review of medical records. | 0 |
| WHS | 2 | KURTH2020 | USA | National | Review of medical records. | 0 |

Table 34
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of the study details for the selected results, Current cigarette smokers versus never smokers, no overlapping results for any study

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NSTR | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7CNTRY-ITALY | 2 | MENOTT2016 | Italy | Regional | 1960 | 225 | 0 | 0 | Cohort | Stroke | m | 40 | 59 | 50 | Died | 3 |
| ARIC | 4 | DING2019A | USA | National | 1987 | 1106 | 0 | 0 | Cohort | Stroke | b | 45 | 64 | 30 | Diagnosed | 14 |
| BIOBANK | 4 | PETERS2020 | UK | National | 2006 | 4662 | 0 | 0 | Cohort | Stroke | f | 40 | 69 | 12 | Diagnosed | 2 |
| BIOBANK | 5 | PETERS2020 | UK | National | 2006 | 4662 | 0 | 0 | Cohort | Stroke | m | 40 | 69 | 12 | Diagnosed | 2 |
| CALIBER | 2 | PUJADE2015 | UK | GP records | 1997 | 11842 | 0 | 0 | Cohort | Stroke | f | 30 | 999 | 13 | Diagnosed | 1 |
| CPS-II | 4 | TURNER2017 | USA | National | 1982 | 5582 | 0 | 0 | Cohort | Stroke | b | 30 | 999 | 22 | Died | 23 |
| CaCHS | 2 | NG2020 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | f | 20 | 999 | 13 | Diagnosed | 15 |
| CaCHS | 4 | NG2020 | Canada | Regional | 2001 | 1636 | 0 | 0 | Cohort | Stroke | m | 20 | 999 | 13 | Diagnosed | 15 |
| ELSA | 4 | JACKSO2019E | UK | National | 2004 | 326 | 0 | 0 | Cohort | Non-fatal Stroke | b | 52 | 999 | 13 | Diagnosed | 7 |
| EPIC-10 | 4 | RICCI2018 | Multi | International | 1991 | 2187 | 0 | 0 | Nested CC | Non-fatal Stroke | b | 35 | 70 | 19 | Diagnosed | 0 |
| EPIC-ITALY | 4 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | m | 35 | 74 | 15 | Diagnosed | 10 |
| EPIC-ITALY | 6 | TRAJKO2017 | Italy | Regional | 1993 | 386 | 0 | 0 | Cohort | Stroke | f | 35 | 74 | 15 | Diagnosed | 10 |
| EPIC-SPAIN | 1 | AMIANO2016 | Spain | Regional | 1992 | 301 | 0 | 0 | Cohort | Stroke | f | 29 | 69 | 16 | Diagnosed | 0 |
| EPIC-UK | 6 | STOEKE2016 | UK | Regional | 1993 | 385 | 0 | 0 | Cohort | Stroke | b | 45 | 79 | 14 | Diagnosed | 6 |
| ESTONGENOME | 8 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | m | 18 | 999 | 13 | Died | 1 |
| ESTONGENOME | 11 | KOKS2017 | Estonia | National | 2002 | 156 | 0 | 0 | Cohort | Stroke | f | 18 | 999 | 13 | Died | 1 |
| HAPIEE | 2 | STEFLE2016 | Multi | International | 2002 | 109 | 0 | 0 | Cohort | Stroke | b | * | * | 9 | Died | 0 |
| HSE-SHS | 4 | DEMEST2019 | UK | National | 1994 | 690 | 0 | 0 | Cohort | Stroke | b | * | * | 17 | Died | 7 |
| JACC | 6 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | m | 40 | 79 | 21 | Died | 7 |
| JACC | 8 | MATSUN2017 | Japan | Regional | 1988 | 3163 | x | 0 | Cohort | Stroke | f | 40 | 79 | 21 | Died | 9 |
| JHS | 2 | OSHUNB2020 | USA | Regional | 2000 | 183 | 0 | 0 | Cohort | Stroke | b | 21 | 84 | 15 | Diagnosed | 11 |
| JP8 | 1 | ABE2019 | Japan | National | 1983 | 3487 | 0 | 0 | Cohort | Stroke | m | 40 | 999 | 30 | Died | 0 |
| MALMO | 1 | LI2019A | Sweden | Regional | 1991 | 305 | 0 | 0 | Cohort | Stroke | b | 46 | 67 | 22 | Diagnosed | 0 |
| MESA | 4 | NANCE2017 | USA | Regional | 2000 | 180 | 0 | 0 | Cohort | Stroke | b | 45 | 84 | 11 | Diagnosed | 0 |
| MILLION | 1 | PRICE2018 | UK | National | 1996 | 8103 | 0 | 0 | Cohort | Stroke | f | 46 | 66 | 19 | Diagnosed | 8 |
| NFBC | 2 | RISSAN2019 | Finland | Regional | 1966 | 352 | 0 | 0 | Cohort | Stroke | b | 14 | 46 | 49 | Diagnosed | 10 |
| NHIS | 3 | INOUEC2020 | USA | National | 1987 | 2046 | x | 0 | Cohort | Stroke | b | 18 | 95 | 24 | Died | 5 |
| NHS | 2 | HART2015A | USA | Medical workers | 1989 | 3288 | 0 | 0 | Cohort | Stroke | f | 43 | 68 | 17 | Diagnosed | 0 |
| NIH-AARP | 2 | NASH2017 | USA | Regional | 2004 | 1369 | 0 | 0 | Cohort | Stroke | b | 70 | 999 | 7 | Died | 4 |
| NLMS | 3 | CHRIST2018 | USA | National | 1985 | 3083 | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 5 |
| OHASAMA | 1 | MURAKA2017 | Japan | Regional | 1998 | 293 | x | 0 | Cohort | Stroke | b | 60 | 999 | 12 | Diagnosed | 2 |
| PREVEND | 6 | KUNUT2018 | Netherlands | Regional | 2001 | 83 | 0 | 0 | Cohort | Stroke | b | 32 | 80 | 9 | Diagnosed | 10 |
| SCCS | 1 | MUNRO2016 | USA | Regional | 2002 | 389 | 0 | 0 | Cohort | Stroke | b | 40 | 79 | 11 | Died | 7 |
| USA5 | 7 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | f | 55 | 999 | 11 | Died | 5 |
| USA5 | 8 | CARTER2015 | USA | Regional | 2000 | 9821 | 0 | 0 | Cohort | Stroke | m | 55 | 999 | 11 | Died | 5 |
| WHITEHALL | 2 | BATTY2015 | UK | Civil servants | 1967 | 1061 | 0 | 0 | Cohort | Stroke | m | 40 | 69 | 43 | Died | 1 |
| WHS | 2 | KURTH2020 | USA | National | 1992 | 887 | 0 | 0 | Cohort | Stroke | f | 45 | 999 | 26 | Diagnosed | 14 |

Table 35
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by sex

**Combined**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 4 | - | - | - | - | 2.00 ( 1.64- 2.38) | |
| *CPS-II | 4 | - | - | - | - | 1.55 ( 1.45- 1.66) | |
| *ELSA | 4 | - | - | - | - | 1.74 ( 1.06- 2.85) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *EPIC-UK | 6 | - | - | - | - | 1.89 ( 1.40- 2.55) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27- 2.90) | |
| *HSE-SHS | 4 | - | - | - | - | 1.86 ( 1.49- 2.32) | |
| *JHS | 2 | - | - | - | - | 2.48 ( 1.60- 3.83) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *NFBC | 2 | - | - | - | - | 1.69 ( 1.10- 2.60) | |
| *NHIS | 3 | - | - | - | - | 1.59 ( 1.33- 1.90) | |
| *NIH-AARP | 2 | - | - | - | - | 2.22 ( 1.82- 2.70) | |
| *NLMS | 3 | - | - | - | - | 1.24 ( 1.12- 1.36) | |
| *OHASAMA | 1 | - | - | - | - | 1.25 ( 0.87- 1.80) | |
| *PREVEND | 6 | - | - | - | - | 1.85 ( 1.05- 3.27) | |
| *SCCS | 1 | - | - | - | - | 1.45 ( 1.14- 1.84) | |
| Partial Totals | | 2164 | 23745 | 2444 | 52438 | | |

*prospective study

**Male**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 2 | - | - | - | - | 1.43 ( 1.04- 1.96) | |
| *BIOBANK | 5 | - | - | - | - | 1.82 ( 1.66- 2.00) | |
| *CaCHS | 4 | - | - | - | - | 1.08 ( 0.85- 1.38) | |
| *EPIC-ITALY | 4 | - | - | - | - | 1.80 ( 1.19- 2.72) | |
| *ESTONGENOME | 8 | - | - | - | - | 2.91 ( 1.65- 5.12) | |
| *JACC | 6 | - | - | - | - | 1.23 ( 1.07- 1.42) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *USA5 | 8 | - | - | - | - | 1.90 ( 1.70- 2.20) | |
| *WHITEHALL | 2 | - | - | - | - | 1.31 ( 1.12- 1.54) | |
| Partial Totals | | 1737 | 78235 | 616 | 29255 | | |

*prospective study

**Female**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *BIOBANK | 4 | - | - | - | - | 1.94 ( 1.71- 2.19) | |
| *CALIBER | 2 | - | - | - | - | 1.46 ( 1.29- 1.66) | |
| *CaCHS | 2 | - | - | - | - | 1.55 ( 1.20- 1.99) | |
| *EPIC-ITALY | 6 | - | - | - | - | 1.96 ( 1.44- 2.66) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *ESTONGENOME | 11 | - | - | - | - | 2.88 ( 1.60- 5.15) | |
| *JACC | 8 | - | - | - | - | 1.35 ( 1.08- 1.68) | |
| *MILLION | 1 | - | - | - | - | 2.41 ( 2.29- 2.54) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *USA5 | 7 | - | - | - | - | 2.10 ( 1.80- 2.30) | |
| *WHS | 2 | - | - | - | - | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 658 | 267780 | 1507 | 821947 | | |

*prospective study

| | RR Sex | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | |
| | Combined | Male | Female | Total |

**RR Data**

| | | 1 Combined | 2 Male | 3 Female | Total |
|---|---|---|---|---|---|
| | N | 17 | 9 | 11 | 37 |
| | NS | 17 | 9 | 11 | 37 |
| | Wt | 3641.90 | 1619.93 | 2914.24 | 8176.07 |
| Het | Chi | 54.99 | 105.30 | 174.93 | 474.03 |
| Het | df | 16 | 8 | 10 | 36 |
| Het | P | *** | *** | *** | *** |
| Fixed | RR | 1.59 | 1.42 | 1.98 | 1.68 |
| | RRl | 1.54 | 1.35 | 1.91 | 1.64 |
| | RRu | 1.64 | 1.49 | 2.06 | 1.72 |
| | P | +++ | +++ | +++ | +++ |
| Random | RR | 1.65 | 1.48 | 1.66 | 1.62 |
| | RRl | 1.52 | 1.21 | 1.39 | 1.48 |
| | RRu | 1.80 | 1.80 | 1.99 | 1.77 |

Table 35
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by sex

|  |  | **RR Sex** |  |  |  |
|---|---|---|---|---|---|
|  |  | **1** | **2** | **3** |  |
|  |  | **Combined** | **Male** | **Female** | **Total** |

**RR Data**

|  |  | | | | |
|---|---|---|---|---|---|
| | **P** | **+++** | **+++** | **+++** | **+++** |
| **Asymm** | **P** | **N.S.** | **N.S.** | **(\*)** | **N.S.** |
| **Between** | **Chi** | | **14.92** | **79.43** | **138.81** |
| **Between** | **df** | | **1** | **1** | **2** |
| **Between** | **P** | | **---** | **+++** | **\*\*\*** |
| **Btwn(F)** | **P** | | **N.S.** | **++** | **\*\*** |
| **Btwn(R)** | **P** | | **N.S.** | **N.S.** | **N.S.** |

_____

Table 36
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by region

**N America**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 4 | - | - | - | - | 2.00 ( 1.64- 2.38) | |
| *CPS-II | 4 | - | - | - | - | 1.55 ( 1.45- 1.66) | |
| *CaCHS | 4 | - | - | - | - | 1.08 ( 0.85- 1.38) | |
| *CaCHS | 2 | - | - | - | - | 1.55 ( 1.20- 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08- 1.53) | |
| *JHS | 2 | - | - | - | - | 2.48 ( 1.60- 3.83) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *NHIS | 3 | - | - | - | - | 1.59 ( 1.33- 1.90) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *NIH-AARP | 2 | - | - | - | - | 2.22 ( 1.82- 2.70) | |
| *NLMS | 3 | - | - | - | - | 1.24 ( 1.12- 1.36) | |
| *SCCS | 1 | - | - | - | - | 1.45 ( 1.14- 1.84) | |
| *USA5 | 8 | - | - | - | - | 1.90 ( 1.70- 2.20) | |
| *USA5 | 7 | - | - | - | - | 2.10 ( 1.80- 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83- 2.19) | |
| *WHS | 2 | - | - | - | - | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 647 | 263869 | 1354 | 807175 | | |

*prospective study

**Europe**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 2 | - | - | - | - | 1.43 ( 1.04- 1.96) | |
| *BIOBANK | 5 | - | - | - | - | 1.82 ( 1.66- 2.00) | |
| *BIOBANK | 4 | - | - | - | - | 1.94 ( 1.71- 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73- 2.01) | |
| *CALIBER | 2 | - | - | - | - | 1.46 ( 1.29- 1.66) | |
| *ELSA | 4 | - | - | - | - | 1.74 ( 1.06- 2.85) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *EPIC-ITALY | 4 | - | - | - | - | 1.80 ( 1.19- 2.72) | |
| *EPIC-ITALY | 6 | - | - | - | - | 1.96 ( 1.44- 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49- 2.43) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *EPIC-UK | 6 | - | - | - | - | 1.89 ( 1.40- 2.55) | |
| *ESTONGENOME | 8 | - | - | - | - | 2.91 ( 1.65- 5.12) | |
| *ESTONGENOME | 11 | - | - | - | - | 2.88 ( 1.60- 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93- 4.35) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27- 2.90) | |
| *HSE-SHS | 4 | - | - | - | - | 1.86 ( 1.49- 2.32) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MILLION | 1 | - | - | - | - | 2.41 ( 2.29- 2.54) | |
| *NFBC | 2 | - | - | - | - | 1.69 ( 1.10- 2.60) | |
| *PREVEND | 6 | - | - | - | - | 1.85 ( 1.05- 3.27) | |
| *WHITEHALL | 2 | - | - | - | - | 1.31 ( 1.12- 1.54) | |
| Partial Totals | | 2175 | 27656 | 2597 | 67210 | | |

*prospective study

**Japan**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *JACC | 6 | - | - | - | - | 1.23 ( 1.07- 1.42) | |
| *JACC | 8 | - | - | - | - | 1.35 ( 1.08- 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12- 1.42) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *OHASAMA | 1 | - | - | - | - | 1.25 ( 0.87- 1.80) | |
| Partial Totals | | 1737 | 78235 | 616 | 29255 | | |

*prospective study

Table 36
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by region

| | | Region | | | |
|---|---|---|---|---|---|
| | | **1** | **2** | **3** | |
| | **N** | **America** | **Europe** | **Japan** | **Total** |

**RR Data**

| | | **1** America | **2** Europe | **3** Japan | **Total** |
|---|---|---|---|---|---|
| | **N** | 14 | 19 | 4 | 37 |
| | **NS** | 12 | 16 | 3 | 31 |
| | **Wt** | 2808.82 | 4602.95 | 764.30 | 8176.07 |
| **Het** | **Chi** | 87.02 | 206.41 | 6.39 | 474.03 |
| **Het** | **df** | 13 | 18 | 3 | 36 |
| **Het** | **P** | *** | *** | (*) | *** |
| **Fixed** | **RR** | 1.59 | 1.86 | 1.13 | 1.68 |
| | **RRl** | 1.53 | 1.80 | 1.05 | 1.64 |
| | **RRu** | 1.65 | 1.91 | 1.21 | 1.72 |
| | **P** | +++ | +++ | +++ | +++ |
| **Random** | **RR** | 1.64 | 1.71 | 1.18 | 1.62 |
| | **RRl** | 1.48 | 1.51 | 1.04 | 1.48 |
| | **RRu** | 1.83 | 1.94 | 1.34 | 1.77 |
| | **P** | +++ | +++ | ++ | +++ |
| **Asymm** | **P** | N.S. | N.S. | N.S. | N.S. |
| **Between** | **Chi** | | 42.22 | 69.39 | 174.21 |
| **Between** | **df** | | 1 | 1 | 2 |
| **Between** | **P** | | +++ | --- | *** |
| **Btwn(F)** | **P** | | + | -- | *** |
| **Btwn(R)** | **P** | | N.S. | --- | *** |

Table 37
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
Analysis by nature of the population

**National**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 4 | – | – | – | – | 2.00 ( 1.64- 2.38) | |
| *BIOBANK | 5 | – | – | – | – | 1.82 ( 1.66- 2.00) | |
| *BIOBANK | 4 | – | – | – | – | 1.94 ( 1.71- 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73- 2.01) | |
| *CPS-II | 4 | – | – | – | – | 1.55 ( 1.45- 1.66) | |
| *ELSA | 4 | – | – | – | – | 1.74 ( 1.06- 2.85) | |
| *ESTONGENOME | 8 | – | – | – | – | 2.91 ( 1.65- 5.12) | |
| *ESTONGENOME | 11 | – | – | – | – | 2.88 ( 1.60- 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93- 4.35) | |
| *HSE-SHS | 4 | – | – | – | – | 1.86 ( 1.49- 2.32) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *MILLION | 1 | – | – | – | – | 2.41 ( 2.29- 2.54) | |
| *NHIS | 3 | – | – | – | – | 1.59 ( 1.33- 1.90) | |
| *NLMS | 3 | – | – | – | – | 1.24 ( 1.12- 1.36) | |
| *WHS | 2 | – | – | – | – | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 1737 | 78235 | 616 | 29255 | | |

*prospective study

**Regional**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 2 | – | – | – | – | 1.43 ( 1.04- 1.96) | |
| *CaCHS | 4 | – | – | – | – | 1.08 ( 0.85- 1.38) | |
| *CaCHS | 2 | – | – | – | – | 1.55 ( 1.20- 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08- 1.53) | |
| *EPIC-ITALY | 4 | – | – | – | – | 1.80 ( 1.19- 2.72) | |
| *EPIC-ITALY | 6 | – | – | – | – | 1.96 ( 1.44- 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49- 2.43) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *EPIC-UK | 6 | – | – | – | – | 1.89 ( 1.40- 2.55) | |
| *JACC | 6 | – | – | – | – | 1.23 ( 1.07- 1.42) | |
| *JACC | 8 | – | – | – | – | 1.35 ( 1.08- 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12- 1.42) | |
| *JHS | 2 | – | – | – | – | 2.48 ( 1.60- 3.83) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *NFBC | 2 | – | – | – | – | 1.69 ( 1.10- 2.60) | |
| *NIH-AARP | 2 | – | – | – | – | 2.22 ( 1.82- 2.70) | |
| *OHASAMA | 1 | – | – | – | – | 1.25 ( 0.87- 1.80) | |
| *PREVEND | 6 | – | – | – | – | 1.85 ( 1.05- 3.27) | |
| *SCCS | 1 | – | – | – | – | 1.45 ( 1.14- 1.84) | |
| *USA5 | 8 | – | – | – | – | 1.90 ( 1.70- 2.20) | |
| *USA5 | 7 | – | – | – | – | 2.10 ( 1.80- 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83- 2.19) | |
| Partial Totals | | 152 | 18357 | 457 | 53695 | | |

*prospective study

**Other**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|------|----------|
| | | Case | Cont | Case | Cont | | |
| *CALIBER | 2 | – | – | – | – | 1.46 ( 1.29- 1.66) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27- 2.90) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *WHITEHALL | 2 | – | – | – | – | 1.31 ( 1.12- 1.54) | |
| Partial Totals | | 2670 | 273168 | 3494 | 820690 | | |

*prospective study

Table 37
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by nature of the population

| | | Population Type | | | |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | |
| | | National | Regional | Other | Total |

**RR Data**

| | | National | Regional | Other | Total |
|---|---|---|---|---|---|
| | N | 13 | 19 | 5 | 37 |
| | NS | 11 | 15 | 5 | 31 |
| | Wt | 4278.41 | 1383.88 | 2513.79 | 8176.07 |
| Het | Chi | 338.86 | 100.78 | 10.81 | 474.03 |
| Het | df | 12 | 18 | 4 | 36 |
| Het | P | *** | *** | * | *** |
| Fixed | RR | 1.77 | 1.63 | 1.57 | 1.68 |
| | RRl | 1.71 | 1.55 | 1.51 | 1.64 |
| | RRu | 1.82 | 1.72 | 1.63 | 1.72 |
| | P | +++ | +++ | +++ | +++ |
| Random | RR | 1.76 | 1.55 | 1.51 | 1.62 |
| | RRl | 1.47 | 1.36 | 1.39 | 1.48 |
| | RRu | 2.11 | 1.78 | 1.65 | 1.77 |
| | P | +++ | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | N.S. | N.S. |
| Between | Chi | | 6.90 | 21.96 | 23.58 |
| Between | df | | 1 | 1 | 2 |
| Between | P | | -- | --- | *** |
| Btwn(F) | P | | N.S. | N.S. | N.S. |
| Btwn(R) | P | | N.S. | N.S. | N.S. |

Table 38
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by year of start of baseline

```
<1988

                 Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont      RR        95.00%CI
*7CNTRY-ITALY 2      -      -      -      -      1.43 ( 1.04-   1.96)
*ARIC         4      -      -      -      -      2.00 ( 1.64-   2.38)
*CPS-II       4      -      -      -      -      1.55 ( 1.45-   1.66)
*JP8          1    1737  78235    616  29255    1.05 ( 0.96-   1.15)
*NFBC         2      -      -      -      -      1.69 ( 1.10-   2.60)
*NHIS         3      -      -      -      -      1.59 ( 1.33-   1.90)
*NLMS         3      -      -      -      -      1.24 ( 1.12-   1.36)
*WHITEHALL    2      -      -      -      -      1.31 ( 1.12-   1.54)
Partial Totals     1737  78235    616  29255
*prospective study


1988+

                 Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont      RR        95.00%CI
*BIOBANK      5      -      -      -      -      1.82 ( 1.66-   2.00)
*BIOBANK      4      -      -      -      -      1.94 ( 1.71-   2.19)
 Subtotal BIOBANK                              1.86 ( 1.73-   2.01)
*CALIBER      2      -      -      -      -      1.46 ( 1.29-   1.66)
*CaCHS        4      -      -      -      -      1.08 ( 0.85-   1.38)
*CaCHS        2      -      -      -      -      1.55 ( 1.20-   1.99)
 Subtotal CaCHS                                1.28 ( 1.08-   1.53)
*ELSA         4      -      -      -      -      1.74 ( 1.06-   2.85)
*EPIC-10      4    2004   4315   2187   7679    1.63 ( 1.55-   1.71)
*EPIC-ITALY   4      -      -      -      -      1.80 ( 1.19-   2.72)
*EPIC-ITALY   6      -      -      -      -      1.96 ( 1.44-   2.66)
 Subtotal EPIC-ITALY                           1.90 ( 1.49-   2.43)
*EPIC-SPAIN   1     42   4798    241  18190    0.66 ( 0.48-   0.92)
*EPIC-UK      6      -      -      -      -      1.89 ( 1.40-   2.55)
*ESTONGENOME  8      -      -      -      -      2.91 ( 1.65-   5.12)
*ESTONGENOME 11      -      -      -      -      2.88 ( 1.60-   5.15)
 Subtotal ESTONGENOME                          2.90 ( 1.93-   4.35)
*HAPIEE       2     50   5871     41   9254    1.92 ( 1.27-   2.90)
*HSE-SHS      4      -      -      -      -      1.86 ( 1.49-   2.32)
*JACC         6      -      -      -      -      1.23 ( 1.07-   1.42)
*JACC         8      -      -      -      -      1.35 ( 1.08-   1.68)
 Subtotal JACC                                 1.26 ( 1.12-   1.42)
*JHS          2      -      -      -      -      2.48 ( 1.60-   3.83)
*MALMO        1     79  12672    128  32087    1.56 ( 1.18-   2.07)
*MESA         4     31    887     88   3418    1.36 ( 0.91-   2.03)
*MILLION      1      -      -      -      -      2.41 ( 2.29-   2.54)
*NHS          2    616 262982   1266 803757    1.49 ( 1.35-   1.64)
*NIH-AARP     2      -      -      -      -      2.22 ( 1.82-   2.70)
*OHASAMA      1      -      -      -      -      1.25 ( 0.87-   1.80)
*PREVEND      6      -      -      -      -      1.85 ( 1.05-   3.27)
*SCCS         1      -      -      -      -      1.45 ( 1.14-   1.84)
*USA5         8      -      -      -      -      1.90 ( 1.70-   2.20)
*USA5         7      -      -      -      -      2.10 ( 1.80-   2.30)
 Subtotal USA5                                 2.00 ( 1.83-   2.19)
*WHS          2      -      -      -      -      1.71 ( 1.39-   2.09)
Partial Totals     2822 291525   3951 874385
*prospective study


                      YrSt
                       1      2
                     <1988   1988+   Total

RR Data


              N        8      29      37
              NS       8      23      31

              Wt    2154.36 6021.71 8176.07
         Het Chi    68.53  283.55  474.03
         Het  df       7      28      36
         Het   P      ***     ***     ***
        Fixed  RR    1.37    1.81    1.68
               RRl   1.31    1.76    1.64
               RRu   1.43    1.85    1.72
                 P   +++     +++     +++
       Random  RR    1.43    1.68    1.62
               RRl   1.23    1.52    1.48
               RRu   1.67    1.85    1.77
```

Table 38
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by year of start of baseline

|  |  | YrSt | | |
|---|---|---|---|---|
|  |  | 1 | 2 |  |
|  |  | <1988 | 1988+ | Total |

**RR Data**

|  |  | <1988 | 1988+ | Total |
|---|---|---|---|---|
|  | P | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | N.S. |
| Between | Chi |  | 121.96 | 121.96 |
| Between | df |  | 1 | 1 |
| Between | P |  | +++ | *** |
| Btwn(F) | P |  | ++ | ** |
| Btwn(R) | P |  | (+) | (*) |

Table 39
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by number of cases in the study

```
<1000
                  Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont    RR        95.00%CI
*7CNTRY-ITALY 2      -      -      -      -     1.43 ( 1.04-   1.96)
*ELSA         4      -      -      -      -     1.74 ( 1.06-   2.85)
*EPIC-ITALY   4      -      -      -      -     1.80 ( 1.19-   2.72)
*EPIC-ITALY   6      -      -      -      -     1.96 ( 1.44-   2.66)
 Subtotal EPIC-ITALY                           1.90 ( 1.49-   2.43)
*EPIC-SPAIN   1     42   4798    241  18190     0.66 ( 0.48-   0.92)
*EPIC-UK      6      -      -      -      -     1.89 ( 1.40-   2.55)
*ESTONGENOME  8      -      -      -      -     2.91 ( 1.65-   5.12)
*ESTONGENOME  11     -      -      -      -     2.88 ( 1.60-   5.15)
 Subtotal ESTONGENOME                          2.90 ( 1.93-   4.35)
*HAPIEE       2     50   5871     41   9254    1.92 ( 1.27-   2.90)
*HSE-SHS      4      -      -      -      -     1.86 ( 1.49-   2.32)
*JHS          2      -      -      -      -     2.48 ( 1.60-   3.83)
*MALMO        1     79  12672    128  32087    1.56 ( 1.18-   2.07)
*MESA         4     31    887     88   3418    1.36 ( 0.91-   2.03)
*NFBC         2      -      -      -      -     1.69 ( 1.10-   2.60)
*OHASAMA      1      -      -      -      -     1.25 ( 0.87-   1.80)
*PREVEND      6      -      -      -      -     1.85 ( 1.05-   3.27)
*SCCS         1      -      -      -      -     1.45 ( 1.14-   1.84)
*WHS          2      -      -      -      -     1.71 ( 1.39-   2.09)
Partial Totals     202  24228    498  62949
*prospective study


1000+
                  Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont    RR        95.00%CI
*ARIC         4      -      -      -      -     2.00 ( 1.64-   2.38)
*BIOBANK      5      -      -      -      -     1.82 ( 1.66-   2.00)
*BIOBANK      4      -      -      -      -     1.94 ( 1.71-   2.19)
 Subtotal BIOBANK                              1.86 ( 1.73-   2.01)
*CALIBER      2      -      -      -      -     1.46 ( 1.29-   1.66)
*CPS-II       4      -      -      -      -     1.55 ( 1.45-   1.66)
*CaCHS        4      -      -      -      -     1.08 ( 0.85-   1.38)
*CaCHS        2      -      -      -      -     1.55 ( 1.20-   1.99)
 Subtotal CaCHS                                1.28 ( 1.08-   1.53)
*EPIC-10      4   2004   4315   2187   7679    1.63 ( 1.55-   1.71)
*JACC         6      -      -      -      -     1.23 ( 1.07-   1.42)
*JACC         8      -      -      -      -     1.35 ( 1.08-   1.68)
 Subtotal JACC                                 1.26 ( 1.12-   1.42)
*JP8          1   1737  78235    616  29255    1.05 ( 0.96-   1.15)
*MILLION      1      -      -      -      -     2.41 ( 2.29-   2.54)
*NHIS         3      -      -      -      -     1.59 ( 1.33-   1.90)
*NHS          2    616 262982   1266 803757    1.49 ( 1.35-   1.64)
*NIH-AARP     2      -      -      -      -     2.22 ( 1.82-   2.70)
*NLMS         3      -      -      -      -     1.24 ( 1.12-   1.36)
*USA5         8      -      -      -      -     1.90 ( 1.70-   2.20)
*USA5         7      -      -      -      -     2.10 ( 1.80-   2.30)
 Subtotal USA5                                 2.00 ( 1.83-   2.19)
*WHITEHALL    2      -      -      -      -     1.31 ( 1.12-   1.54)
Partial Totals    4357 345532   4069 840691
*prospective study


                   Number of Stroke cases
                     1      2      3
                   absent  <1000  1000+    Total

RR Data


               N            18     19     37
               NS           16     15     31

               Wt       634.50 7541.57 8176.07
         Het Chi          50.19 423.20 474.03
         Het  df             17     18     36
         Het  P            ***    ***    ***
         Fixed RR         1.63   1.69   1.68
              RRl         1.51   1.65   1.64
              RRu         1.76   1.72   1.72
               P          +++    +++    +++
       Random  RR         1.66   1.59   1.62
              RRl         1.44   1.41   1.48
              RRu         1.91   1.78   1.77
```

Table 39
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by number of cases in the study

| | **Number of Stroke cases** | | | |
|---|---|---|---|---|
| | **1** | **2** | **3** | |
| | **absent** | **<1000** | **1000+** | **Total** |

**RR Data**

| | | | | |
|---|---|---|---|---|
| **P** | | **+++** | **+++** | **+++** |
| **Asymm P** | | **N.S.** | **N.S.** | **N.S.** |
| **Between Chi** | | | | **0.64** |
| **Between df** | | | | **1** |
| **Between P** | | **N.S.** | **N.S.** | **N.S.** |
| **Btwn(F) P** | | **N.S.** | **N.S.** | **N.S.** |
| **Btwn(R) P** | | **N.S.** | **N.S.** | **N.S.** |

Table 40
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by cigarette smoking exclusively

**absent**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
| | | Case | Cont | Case | Cont | | |
|---|---|---|---|---|---|---|---|
| *7CNTRY-ITALY | 2 | - | - | - | - | 1.43 ( 1.04- 1.96) | |
| *ARIC | 4 | - | - | - | - | 2.00 ( 1.64- 2.38) | |
| *BIOBANK | 5 | - | - | - | - | 1.82 ( 1.66- 2.00) | |
| *BIOBANK | 4 | - | - | - | - | 1.94 ( 1.71- 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73- 2.01) | |
| *CALIBER | 2 | - | - | - | - | 1.46 ( 1.29- 1.66) | |
| *CPS-II | 4 | - | - | - | - | 1.55 ( 1.45- 1.66) | |
| *CaCHS | 4 | - | - | - | - | 1.08 ( 0.85- 1.38) | |
| *CaCHS | 2 | - | - | - | - | 1.55 ( 1.20- 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08- 1.53) | |
| *ELSA | 4 | - | - | - | - | 1.74 ( 1.06- 2.85) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *EPIC-ITALY | 4 | - | - | - | - | 1.80 ( 1.19- 2.72) | |
| *EPIC-ITALY | 6 | - | - | - | - | 1.96 ( 1.44- 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49- 2.43) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *EPIC-UK | 6 | - | - | - | - | 1.89 ( 1.40- 2.55) | |
| *ESTONGENOME | 8 | - | - | - | - | 2.91 ( 1.65- 5.12) | |
| *ESTONGENOME | 11 | - | - | - | - | 2.88 ( 1.60- 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93- 4.35) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27- 2.90) | |
| *HSE-SHS | 4 | - | - | - | - | 1.86 ( 1.49- 2.32) | |
| *JHS | 2 | - | - | - | - | 2.48 ( 1.60- 3.83) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *MILLION | 1 | - | - | - | - | 2.41 ( 2.29- 2.54) | |
| *NFBC | 2 | - | - | - | - | 1.69 ( 1.10- 2.60) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *NIH-AARP | 2 | - | - | - | - | 2.22 ( 1.82- 2.70) | |
| *PREVEND | 6 | - | - | - | - | 1.85 ( 1.05- 3.27) | |
| *SCCS | 1 | - | - | - | - | 1.45 ( 1.14- 1.84) | |
| *USA5 | 8 | - | - | - | - | 1.90 ( 1.70- 2.20) | |
| *USA5 | 7 | - | - | - | - | 2.10 ( 1.80- 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83- 2.19) | |
| *WHITEHALL | 2 | - | - | - | - | 1.31 ( 1.12- 1.54) | |
| *WHS | 2 | - | - | - | - | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 4559 | 369760 | 4567 | 903640 | | |

*prospective study

**present**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
| | | Case | Cont | Case | Cont | | |
|---|---|---|---|---|---|---|---|
| *JACC | 6 | - | - | - | - | 1.23 ( 1.07- 1.42) | |
| *JACC | 8 | - | - | - | - | 1.35 ( 1.08- 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12- 1.42) | |
| *NHIS | 3 | - | - | - | - | 1.59 ( 1.33- 1.90) | |
| *NLMS | 3 | - | - | - | - | 1.24 ( 1.12- 1.36) | |
| *OHASAMA | 1 | - | - | - | - | 1.25 ( 0.87- 1.80) | |
| Partial Totals | | 0 | 0 | 0 | 0 | | |

*prospective study

RR Description:Exclusive use of the product

|  | 1 | 2 |  |
|---|---|---|---|
|  | absent | present | Total |

RR Data

|  |  | 1 | 2 |  |
|---|---|---|---|---|
|  | N | 32 | 5 | 37 |
|  | NS | 27 | 4 | 31 |
|  | Wt | 7348.03 | 828.05 | 8176.07 |
| Het | Chi | 404.55 | 6.54 | 474.03 |
| Het | df | 31 | 4 | 36 |
| Het | P | *** | N.S. | *** |
| Fixed | RR | 1.73 | 1.29 | 1.68 |
|  | RRl | 1.69 | 1.21 | 1.64 |
|  | RRu | 1.77 | 1.39 | 1.72 |
|  | P | +++ | +++ | +++ |
| Random | RR | 1.67 | 1.31 | 1.62 |
|  | RRl | 1.52 | 1.19 | 1.48 |
|  | RRu | 1.84 | 1.45 | 1.77 |

Table 40
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by cigarette smoking exclusively

**RR Description:Exclusive use of the product**

|  | | 1 | 2 | |
|---|---|---|---|---|
|  | | absent | present | Total |

**RR Data**

|  | P | +++ | +++ | +++ |
|---|---|---|---|---|
| Asymm | P | N.S. | N.S. | N.S. |
| Between | Chi | | 62.94 | 62.94 |
| Between | df | | 1 | 1 |
| Between | P | | --- | *** |
| Btwn(F) | P | | – | * |
| Btwn(R) | P | | --- | *** |

Table 41
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by lowest age considered in the study

```
<30
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*CaCHS         4     -      -      -      -      1.08 ( 0.85-   1.38)
*CaCHS         2     -      -      -      -      1.55 ( 1.20-   1.99)
 Subtotal CaCHS                                  1.28 ( 1.08-   1.53)
*EPIC-SPAIN    1     42    4798   241   18190    0.66 ( 0.48-   0.92)
*ESTONGENOME   8     -      -      -      -      2.91 ( 1.65-   5.12)
*ESTONGENOME  11     -      -      -      -      2.88 ( 1.60-   5.15)
 Subtotal ESTONGENOME                            2.90 ( 1.93-   4.35)
*JHS           2     -      -      -      -      2.48 ( 1.60-   3.83)
*NFBC          2     -      -      -      -      1.69 ( 1.10-   2.60)
*NHIS          3     -      -      -      -      1.59 ( 1.33-   1.90)
Partial Totals      42    4798   241   18190
*prospective study


30-<45
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*7CNTRY-ITALY 2      -      -      -      -      1.43 ( 1.04-   1.96)
*BIOBANK       5     -      -      -      -      1.82 ( 1.66-   2.00)
*BIOBANK       4     -      -      -      -      1.94 ( 1.71-   2.19)
 Subtotal BIOBANK                                1.86 ( 1.73-   2.01)
*CALIBER       2     -      -      -      -      1.46 ( 1.29-   1.66)
*CPS-II        4     -      -      -      -      1.55 ( 1.45-   1.66)
*EPIC-10       4    2004   4315   2187   7679    1.63 ( 1.55-   1.71)
*EPIC-ITALY    4     -      -      -      -      1.80 ( 1.19-   2.72)
*EPIC-ITALY    6     -      -      -      -      1.96 ( 1.44-   2.66)
 Subtotal EPIC-ITALY                             1.90 ( 1.49-   2.43)
*JACC          6     -      -      -      -      1.23 ( 1.07-   1.42)
*JACC          8     -      -      -      -      1.35 ( 1.08-   1.68)
 Subtotal JACC                                   1.26 ( 1.12-   1.42)
*JP8           1    1737  78235   616   29255    1.05 ( 0.96-   1.15)
*NHS           2     616 262982  1266  803757    1.49 ( 1.35-   1.64)
*NLMS          3     -      -      -      -      1.24 ( 1.12-   1.36)
*PREVEND       6     -      -      -      -      1.85 ( 1.05-   3.27)
*SCCS          1     -      -      -      -      1.45 ( 1.14-   1.84)
*WHITEHALL     2     -      -      -      -      1.31 ( 1.12-   1.54)
Partial Totals     4357 345532  4069 840691
*prospective study


45+
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*ARIC          4     -      -      -      -      2.00 ( 1.64-   2.38)
*ELSA          4     -      -      -      -      1.74 ( 1.06-   2.85)
*EPIC-UK       6     -      -      -      -      1.89 ( 1.40-   2.55)
*MALMO         1     79   12672   128   32087    1.56 ( 1.18-   2.07)
*MESA          4     31    887    88    3418     1.36 ( 0.91-   2.03)
*MILLION       1     -      -      -      -      2.41 ( 2.29-   2.54)
*NIH-AARP      2     -      -      -      -      2.22 ( 1.82-   2.70)
*OHASAMA       1     -      -      -      -      1.25 ( 0.87-   1.80)
*USA5          8     -      -      -      -      1.90 ( 1.70-   2.20)
*USA5          7     -      -      -      -      2.10 ( 1.80-   2.30)
 Subtotal USA5                                   2.00 ( 1.83-   2.19)
*WHS           2     -      -      -      -      1.71 ( 1.39-   2.09)
Partial Totals     110   13559   216   35505
*prospective study


Missing
                Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont     RR        95.00%CI
*HAPIEE        2     50    5871   41    9254     1.92 ( 1.27-   2.90)
*HSE-SHS       4     -      -      -      -      1.86 ( 1.49-   2.32)
Partial Totals      50    5871   41    9254
*prospective study
```

Table 41
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by lowest age considered in the study

| | | Lowest age included, grouped | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | |
| | | <30 | 30-<45 | 45+ | Missing | Total |

**RR Data**

| | | 1 <br> <30 | 2 <br> 30-<45 | 3 <br> 45+ | 4 <br> Missing | Total |
|---|---|---|---|---|---|---|
| | N | 8 | 16 | 11 | 2 | 37 |
| | NS | 6 | 13 | 10 | 2 | 31 |
| | Wt | 346.54 | 5348.03 | 2380.46 | 101.04 | 8176.07 |
| Het | Chi | 46.67 | 134.04 | 46.70 | 0.02 | 474.03 |
| Het | df | 7 | 15 | 10 | 1 | 36 |
| Het | P | *** | *** | *** | N.S. | *** |
| Fixed | RR | 1.44 | 1.50 | 2.20 | 1.87 | 1.68 |
| | RRl | 1.30 | 1.46 | 2.11 | 1.54 | 1.64 |
| | RRu | 1.60 | 1.54 | 2.29 | 2.28 | 1.72 |
| | P | +++ | +++ | +++ | +++ | +++ |
| Random | RR | 1.59 | 1.48 | 1.89 | 1.87 | 1.62 |
| | RRl | 1.19 | 1.35 | 1.68 | 1.54 | 1.48 |
| | RRu | 2.14 | 1.62 | 2.12 | 2.28 | 1.77 |
| | P | ++ | +++ | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | *** | | N.S. |
| Between | Chi | | 0.61 | 54.04 | 5.43 | 246.60 |
| Between | df | | 1 | 1 | 1 | 3 |
| Between | P | | N.S. | +++ | + | *** |
| Btwn(F) | P | | N.S. | ++ | N.S. | *** |
| Btwn(R) | P | | N.S. | N.S. | N.S. | ** |

Table 42
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by lowest age considered, with trend

**<30**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *CaCHS | 4 | – | – | – | – | 1.08 ( 0.85- 1.38) | |
| *CaCHS | 2 | – | – | – | – | 1.55 ( 1.20- 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08- 1.53) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *ESTONGENOME | 8 | – | – | – | – | 2.91 ( 1.65- 5.12) | |
| *ESTONGENOME | 11 | – | – | – | – | 2.88 ( 1.60- 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93- 4.35) | |
| *JHS | 2 | – | – | – | – | 2.48 ( 1.60- 3.83) | |
| *NFBC | 2 | – | – | – | – | 1.69 ( 1.10- 2.60) | |
| *NHIS | 3 | – | – | – | – | 1.59 ( 1.33- 1.90) | |
| Partial Totals | | 42 | 4798 | 241 | 18190 | | |

*prospective study

**30-<45**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *7CNTRY-ITALY | 2 | – | – | – | – | 1.43 ( 1.04- 1.96) | |
| *BIOBANK | 5 | – | – | – | – | 1.82 ( 1.66- 2.00) | |
| *BIOBANK | 4 | – | – | – | – | 1.94 ( 1.71- 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73- 2.01) | |
| *CALIBER | 2 | – | – | – | – | 1.46 ( 1.29- 1.66) | |
| *CPS-II | 4 | – | – | – | – | 1.55 ( 1.45- 1.66) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *EPIC-ITALY | 4 | – | – | – | – | 1.80 ( 1.19- 2.72) | |
| *EPIC-ITALY | 6 | – | – | – | – | 1.96 ( 1.44- 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49- 2.43) | |
| *JACC | 6 | – | – | – | – | 1.23 ( 1.07- 1.42) | |
| *JACC | 8 | – | – | – | – | 1.35 ( 1.08- 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12- 1.42) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *NLMS | 3 | – | – | – | – | 1.24 ( 1.12- 1.36) | |
| *PREVEND | 6 | – | – | – | – | 1.85 ( 1.05- 3.27) | |
| *SCCS | 1 | – | – | – | – | 1.45 ( 1.14- 1.84) | |
| *WHITEHALL | 2 | – | – | – | – | 1.31 ( 1.12- 1.54) | |
| Partial Totals | | 4357 | 345532 | 4069 | 840691 | | |

*prospective study

**45+**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | Case | Cont | Case | Cont | | |
| *ARIC | 4 | – | – | – | – | 2.00 ( 1.64- 2.38) | |
| *ELSA | 4 | – | – | – | – | 1.74 ( 1.06- 2.85) | |
| *EPIC-UK | 6 | – | – | – | – | 1.89 ( 1.40- 2.55) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *MILLION | 1 | – | – | – | – | 2.41 ( 2.29- 2.54) | |
| *NIH-AARP | 2 | – | – | – | – | 2.22 ( 1.82- 2.70) | |
| *OHASAMA | 1 | – | – | – | – | 1.25 ( 0.87- 1.80) | |
| *USA5 | 8 | – | – | – | – | 1.90 ( 1.70- 2.20) | |
| *USA5 | 7 | – | – | – | – | 2.10 ( 1.80- 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83- 2.19) | |
| *WHS | 2 | – | – | – | – | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 110 | 13559 | 216 | 35505 | | |

*prospective study

Table 42
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by lowest age considered, with trend

**Lowest age included, grouped, excluding Missing**

| | | 1 | 2 | 3 | | |
|---|---|---|---|---|---|---|
| | | **<30** | **30-<45** | **45+** | **Total** | **Trend** |

**RR Data**

| | 1 (<30) | 2 (30-<45) | 3 (45+) | Total | Trend |
|---|---|---|---|---|---|
| **N** | 8 | 16 | 11 | 35 | |
| **NS** | 6 | 13 | 10 | 29 | |
| **Wt** | 346.54 | 5348.03 | 2380.46 | 8075.03 | |
| **Het Chi** | 46.67 | 134.04 | 46.70 | 472.80 | |
| **Het df** | 7 | 15 | 10 | 34 | |
| **Het P** | *** | *** | *** | *** | |
| **Fixed RR** | 1.44 | 1.50 | 2.20 | 1.68 | |
| **RRl** | 1.30 | 1.46 | 2.11 | 1.64 | |
| **RRu** | 1.60 | 1.54 | 2.29 | 1.72 | |
| **P** | +++ | +++ | +++ | +++ | |
| **Random RR** | 1.59 | 1.48 | 1.89 | 1.61 | |
| **RRl** | 1.19 | 1.35 | 1.68 | 1.46 | |
| **RRu** | 2.14 | 1.62 | 2.12 | 1.76 | |
| **P** | ++ | +++ | +++ | +++ | |
| **Asymm P** | N.S. | N.S. | *** | N.S. | |
| **Between Chi** | | 0.61 | 54.04 | 245.39 | 217.58 |
| **Between df** | | 1 | 1 | 2 | 1 |
| **Between P** | | N.S. | +++ | *** | +++ |
| **Btwn(F) P** | | N.S. | ++ | *** | +++ |
| **Btwn(R) P** | | N.S. | N.S. | ** | ++ |

Table 43
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by years of follow-up

**<10**

| Study ID | NRR | **Numbers exposed** | | **Non-exposed** | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | **Case** | **Cont** | **Case** | **Cont** | | |
| **\*HAPIEE** | **2** | **50** | **5871** | **41** | **9254** | **1.92 (  1.27-   2.90)** |
| **\*NIH-AARP** | **2** | **-** | **-** | **-** | **-** | **2.22 (  1.82-   2.70)** |
| **\*PREVEND** | **6** | **-** | **-** | **-** | **-** | **1.85 (  1.05-   3.27)** |
| **Partial Totals** | | **50** | **5871** | **41** | **9254** | |

**\*prospective study**

**10-<20**

| Study ID | NRR | **Numbers exposed** | | **Non-exposed** | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | **Case** | **Cont** | **Case** | **Cont** | | |
| **\*BIOBANK** | **5** | **-** | **-** | **-** | **-** | **1.82 (  1.66-   2.00)** |
| **\*BIOBANK** | **4** | **-** | **-** | **-** | **-** | **1.94 (  1.71-   2.19)** |
|  Subtotal BIOBANK | | | | | | 1.86 (  1.73-   2.01) |
| **\*CALIBER** | **2** | **-** | **-** | **-** | **-** | **1.46 (  1.29-   1.66)** |
| **\*CaCHS** | **4** | **-** | **-** | **-** | **-** | **1.08 (  0.85-   1.38)** |
| **\*CaCHS** | **2** | **-** | **-** | **-** | **-** | **1.55 (  1.20-   1.99)** |
|  Subtotal CaCHS | | | | | | 1.28 (  1.08-   1.53) |
| **\*ELSA** | **4** | **-** | **-** | **-** | **-** | **1.74 (  1.06-   2.85)** |
| **\*EPIC-10** | **4** | **2004** | **4315** | **2187** | **7679** | **1.63 (  1.55-   1.71)** |
| **\*EPIC-ITALY** | **4** | **-** | **-** | **-** | **-** | **1.80 (  1.19-   2.72)** |
| **\*EPIC-ITALY** | **6** | **-** | **-** | **-** | **-** | **1.96 (  1.44-   2.66)** |
|  Subtotal EPIC-ITALY | | | | | | 1.90 (  1.49-   2.43) |
| **\*EPIC-SPAIN** | **1** | **42** | **4798** | **241** | **18190** | **0.66 (  0.48-   0.92)** |
| **\*EPIC-UK** | **6** | **-** | **-** | **-** | **-** | **1.89 (  1.40-   2.55)** |
| **\*ESTONGENOME** | **8** | **-** | **-** | **-** | **-** | **2.91 (  1.65-   5.12)** |
| **\*ESTONGENOME** | **11** | **-** | **-** | **-** | **-** | **2.88 (  1.60-   5.15)** |
|  Subtotal ESTONGENOME | | | | | | 2.90 (  1.93-   4.35) |
| **\*HSE-SHS** | **4** | **-** | **-** | **-** | **-** | **1.86 (  1.49-   2.32)** |
| **\*JHS** | **2** | **-** | **-** | **-** | **-** | **2.48 (  1.60-   3.83)** |
| **\*MESA** | **4** | **31** | **887** | **88** | **3418** | **1.36 (  0.91-   2.03)** |
| **\*MILLION** | **1** | **-** | **-** | **-** | **-** | **2.41 (  2.29-   2.54)** |
| **\*NHS** | **2** | **616** | **262982** | **1266** | **803757** | **1.49 (  1.35-   1.64)** |
| **\*OHASAMA** | **1** | **-** | **-** | **-** | **-** | **1.25 (  0.87-   1.80)** |
| **\*SCCS** | **1** | **-** | **-** | **-** | **-** | **1.45 (  1.14-   1.84)** |
| **\*USA5** | **8** | **-** | **-** | **-** | **-** | **1.90 (  1.70-   2.20)** |
| **\*USA5** | **7** | **-** | **-** | **-** | **-** | **2.10 (  1.80-   2.30)** |
|  Subtotal USA5 | | | | | | 2.00 (  1.83-   2.19) |
| **Partial Totals** | | **2693** | **272982** | **3782** | **833044** | |

**\*prospective study**

**20-<30**

| Study ID | NRR | **Numbers exposed** | | **Non-exposed** | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | **Case** | **Cont** | **Case** | **Cont** | | |
| **\*CPS-II** | **4** | **-** | **-** | **-** | **-** | **1.55 (  1.45-   1.66)** |
| **\*JACC** | **6** | **-** | **-** | **-** | **-** | **1.23 (  1.07-   1.42)** |
| **\*JACC** | **8** | **-** | **-** | **-** | **-** | **1.35 (  1.08-   1.68)** |
|  Subtotal JACC | | | | | | 1.26 (  1.12-   1.42) |
| **\*MALMO** | **1** | **79** | **12672** | **128** | **32087** | **1.56 (  1.18-   2.07)** |
| **\*NHIS** | **3** | **-** | **-** | **-** | **-** | **1.59 (  1.33-   1.90)** |
| **\*NLMS** | **3** | **-** | **-** | **-** | **-** | **1.24 (  1.12-   1.36)** |
| **\*WHS** | **2** | **-** | **-** | **-** | **-** | **1.71 (  1.39-   2.09)** |
| **Partial Totals** | | **79** | **12672** | **128** | **32087** | |

**\*prospective study**

**30+**

| Study ID | NRR | **Numbers exposed** | | **Non-exposed** | | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| | | **Case** | **Cont** | **Case** | **Cont** | | |
| **\*7CNTRY-ITALY** | **2** | **-** | **-** | **-** | **-** | **1.43 (  1.04-   1.96)** |
| **\*ARIC** | **4** | **-** | **-** | **-** | **-** | **2.00 (  1.64-   2.38)** |
| **\*JP8** | **1** | **1737** | **78235** | **616** | **29255** | **1.05 (  0.96-   1.15)** |
| **\*NFBC** | **2** | **-** | **-** | **-** | **-** | **1.69 (  1.10-   2.60)** |
| **\*WHITEHALL** | **2** | **-** | **-** | **-** | **-** | **1.31 (  1.12-   1.54)** |
| **Partial Totals** | | **1737** | **78235** | **616** | **29255** | |

**\*prospective study**

Table 43
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by years of follow-up

**Years follow-up, grouped**

| | | 1 | 2 | 3 | 4 | | |
|---|---|---|---|---|---|---|---|
| | | <10 | 10-<20 | 20-<30 | 30+ | Total | Trend |

**RR Data**

| | 1 <10 | 2 10-<20 | 3 20-<30 | 4 30+ | Total | Trend |
|---|---|---|---|---|---|---|
| N | 3 | 22 | 7 | 5 | 37 | |
| NS | 3 | 17 | 6 | 5 | 31 | |
| Wt | 133.35 | 5476.30 | 1780.41 | 786.00 | 8176.07 | |
| Het Chi | 0.64 | 241.37 | 23.00 | 40.75 | 474.03 | |
| Het df | 2 | 21 | 6 | 4 | 36 | |
| Het P | N.S. | *** | *** | *** | *** | |
| Fixed RR | 2.13 | 1.84 | 1.44 | 1.24 | 1.68 | |
| RRl | 1.80 | 1.79 | 1.37 | 1.15 | 1.64 | |
| RRu | 2.53 | 1.89 | 1.51 | 1.33 | 1.72 | |
| P | +++ | +++ | +++ | +++ | +++ | |
| Random RR | 2.13 | 1.69 | 1.43 | 1.44 | 1.62 | |
| RRl | 1.80 | 1.52 | 1.29 | 1.10 | 1.48 | |
| RRu | 2.53 | 1.89 | 1.60 | 1.89 | 1.77 | |
| P | +++ | +++ | +++ | ++ | +++ | |
| Asymm P | N.S. | N.S. | N.S. | N.S. | N.S. | |
| Between Chi | | 2.87 | 19.21 | 33.79 | 168.26 | 154.82 |
| Between df | | 1 | 1 | 1 | 3 | 1 |
| Between P | | (-) | --- | --- | *** | --- |
| Btwn(F) P | | N.S. | - | (-) | ** | --- |
| Btwn(R) P | | - | --- | - | *** | --- |

Table 44
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by endpoint

**Died**

| Study ID | NRR | Numbers exposed Case | Cont | Non-exposed Case | Cont | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| *7CNTRY-ITALY | 2 | – | – | – | – | 1.43 ( 1.04– 1.96) | |
| *CPS-II | 4 | – | – | – | – | 1.55 ( 1.45– 1.66) | |
| *ESTONGENOME | 8 | – | – | – | – | 2.91 ( 1.65– 5.12) | |
| *ESTONGENOME | 11 | – | – | – | – | 2.88 ( 1.60– 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93– 4.35) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27– 2.90) | |
| *HSE-SHS | 4 | – | – | – | – | 1.86 ( 1.49– 2.32) | |
| *JACC | 6 | – | – | – | – | 1.23 ( 1.07– 1.42) | |
| *JACC | 8 | – | – | – | – | 1.35 ( 1.08– 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12– 1.42) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96– 1.15) | |
| *NHIS | 3 | – | – | – | – | 1.59 ( 1.33– 1.90) | |
| *NIH-AARP | 2 | – | – | – | – | 2.22 ( 1.82– 2.70) | |
| *NLMS | 3 | – | – | – | – | 1.24 ( 1.12– 1.36) | |
| *SCCS | 1 | – | – | – | – | 1.45 ( 1.14– 1.84) | |
| *USA5 | 8 | – | – | – | – | 1.90 ( 1.70– 2.20) | |
| *USA5 | 7 | – | – | – | – | 2.10 ( 1.80– 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83– 2.19) | |
| *WHITEHALL | 2 | – | – | – | – | 1.31 ( 1.12– 1.54) | |
| Partial Totals | | 1787 | 84106 | 657 | 38509 | | |

*prospective study

**Diagnosed**

| Study ID | NRR | Numbers exposed Case | Cont | Non-exposed Case | Cont | RR | 95.00%CI |
|---|---|---|---|---|---|---|---|
| *ARIC | 4 | – | – | – | – | 2.00 ( 1.64– 2.38) | |
| *BIOBANK | 5 | – | – | – | – | 1.82 ( 1.66– 2.00) | |
| *BIOBANK | 4 | – | – | – | – | 1.94 ( 1.71– 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73– 2.01) | |
| *CALIBER | 2 | – | – | – | – | 1.46 ( 1.29– 1.66) | |
| *CaCHS | 4 | – | – | – | – | 1.08 ( 0.85– 1.38) | |
| *CaCHS | 2 | – | – | – | – | 1.55 ( 1.20– 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08– 1.53) | |
| *ELSA | 4 | – | – | – | – | 1.74 ( 1.06– 2.85) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55– 1.71) | |
| *EPIC-ITALY | 4 | – | – | – | – | 1.80 ( 1.19– 2.72) | |
| *EPIC-ITALY | 6 | – | – | – | – | 1.96 ( 1.44– 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49– 2.43) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48– 0.92) | |
| *EPIC-UK | 6 | – | – | – | – | 1.89 ( 1.40– 2.55) | |
| *JHS | 2 | – | – | – | – | 2.48 ( 1.60– 3.83) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18– 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91– 2.03) | |
| *MILLION | 1 | – | – | – | – | 2.41 ( 2.29– 2.54) | |
| *NFBC | 2 | – | – | – | – | 1.69 ( 1.10– 2.60) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35– 1.64) | |
| *OHASAMA | 1 | – | – | – | – | 1.25 ( 0.87– 1.80) | |
| *PREVEND | 6 | – | – | – | – | 1.85 ( 1.05– 3.27) | |
| *WHS | 2 | – | – | – | – | 1.71 ( 1.39– 2.09) | |
| Partial Totals | | 2772 | 285654 | 3910 | 865131 | | |

*prospective study

| | RR Description:Endpoint reported | | |
|---|---|---|---|
| | 1 | 2 | |
| | Died | Diagnosed | Total |

**RR Data**

| | | 1 | 2 | Total |
|---|---|---|---|---|
| | N | 16 | 21 | 37 |
| | NS | 13 | 18 | 31 |
| | Wt | 3070.34 | 5105.73 | 8176.07 |
| | Het Chi | 156.10 | 230.28 | 474.03 |
| | Het df | 15 | 20 | 36 |
| | Het P | *** | *** | *** |
| | Fixed RR | 1.47 | 1.82 | 1.68 |
| | RRl | 1.42 | 1.77 | 1.64 |
| | RRu | 1.52 | 1.87 | 1.72 |
| | P | +++ | +++ | +++ |
| | Random RR | 1.60 | 1.63 | 1.62 |
| | RRl | 1.41 | 1.46 | 1.48 |
| | RRu | 1.81 | 1.83 | 1.77 |

Table 44
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by endpoint

**RR Description:Endpoint reported**

|  |  | 1 | 2 |  |
|---|---|---|---|---|
|  |  | **Died** | **Diagnosed** | **Total** |

**RR Data**

|  |  |  |  |  |
|---|---|---|---|---|
|  | **P** | **+++** | **+++** | **+++** |
| **Asymm** | **P** | **N.S.** | **N.S.** | **N.S.** |
| **Between** | **Chi** |  | **87.64** | **87.64** |
| **Between** | **df** |  | **1** | **1** |
| **Between** | **P** |  | **+++** | **\*\*\*** |
| **Btwn(F)** | **P** |  | **++** | **\*\*** |
| **Btwn(R)** | **P** |  | **N.S.** | **N.S.** |

Table 45
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by number of adjustment factors

```
Unadj
                  Numbers exposed Non-exposed
 Study ID    NRR    Case    Cont    Case    Cont      RR        95.00%CI
*EPIC-10      4     2004    4315    2187    7679    1.63 (  1.55-   1.71)
*EPIC-SPAIN   1       42    4798     241   18190    0.66 (  0.48-   0.92)
*HAPIEE       2       50    5871      41    9254    1.92 (  1.27-   2.90)
*JP8          1     1737   78235     616   29255    1.05 (  0.96-   1.15)
*MALMO        1       79   12672     128   32087    1.56 (  1.18-   2.07)
*MESA         4       31     887      88    3418    1.36 (  0.91-   2.03)
*NHS          2      616  262982    1266  803757    1.49 (  1.35-   1.64)
Totals             4559  369760    4567  903640
*prospective study


Age-only
                  Numbers exposed Non-exposed
 Study ID    NRR    Case    Cont    Case    Cont      RR        95.00%CI
*CALIBER      2       -       -       -       -     1.46 (  1.29-   1.66)
*ESTONGENOME  8       -       -       -       -     2.91 (  1.65-   5.12)
*ESTONGENOME 11       -       -       -       -     2.88 (  1.60-   5.15)
 Subtotal ESTONGENOME                              2.90 (  1.93-   4.35)
*WHITEHALL    2       -       -       -       -     1.31 (  1.12-   1.54)
Partial Totals        0       0       0       0
*prospective study


More adj
                  Numbers exposed Non-exposed
 Study ID    NRR    Case    Cont    Case    Cont      RR        95.00%CI
*7CNTRY-ITALY 2       -       -       -       -     1.43 (  1.04-   1.96)
*ARIC         4       -       -       -       -     2.00 (  1.64-   2.38)
*BIOBANK      5       -       -       -       -     1.82 (  1.66-   2.00)
*BIOBANK      4       -       -       -       -     1.94 (  1.71-   2.19)
 Subtotal BIOBANK                                  1.86 (  1.73-   2.01)
*CPS-II       4       -       -       -       -     1.55 (  1.45-   1.66)
*CaCHS        4       -       -       -       -     1.08 (  0.85-   1.38)
*CaCHS        2       -       -       -       -     1.55 (  1.20-   1.99)
 Subtotal CaCHS                                    1.28 (  1.08-   1.53)
*ELSA         4       -       -       -       -     1.74 (  1.06-   2.85)
*EPIC-ITALY   4       -       -       -       -     1.80 (  1.19-   2.72)
*EPIC-ITALY   6       -       -       -       -     1.96 (  1.44-   2.66)
 Subtotal EPIC-ITALY                               1.90 (  1.49-   2.43)
*EPIC-UK      6       -       -       -       -     1.89 (  1.40-   2.55)
*HSE-SHS      4       -       -       -       -     1.86 (  1.49-   2.32)
*JACC         6       -       -       -       -     1.23 (  1.07-   1.42)
*JACC         8       -       -       -       -     1.35 (  1.08-   1.68)
 Subtotal JACC                                     1.26 (  1.12-   1.42)
*JHS          2       -       -       -       -     2.48 (  1.60-   3.83)
*MILLION      1       -       -       -       -     2.41 (  2.29-   2.54)
*NFBC         2       -       -       -       -     1.69 (  1.10-   2.60)
*NHIS         3       -       -       -       -     1.59 (  1.33-   1.90)
*NIH-AARP     2       -       -       -       -     2.22 (  1.82-   2.70)
*NLMS         3       -       -       -       -     1.24 (  1.12-   1.36)
*OHASAMA      1       -       -       -       -     1.25 (  0.87-   1.80)
*PREVEND      6       -       -       -       -     1.85 (  1.05-   3.27)
*SCCS         1       -       -       -       -     1.45 (  1.14-   1.84)
*USA5         8       -       -       -       -     1.90 (  1.70-   2.20)
*USA5         7       -       -       -       -     2.10 (  1.80-   2.30)
 Subtotal USA5                                     2.00 (  1.83-   2.19)
*WHS          2       -       -       -       -     1.71 (  1.39-   2.09)
Partial Totals        0       0       0       0
*prospective study
```

Table 45
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by number of adjustment factors

**Number of adjustment factors, grouped**

| | | 1 | 2 | 3 | |
|---|---|---|---|---|---|
| | | Unadj | Age-only | More adj | Total |

**RR Data**

| | | 1 | 2 | 3 | Total |
|---|---|---|---|---|---|
| | N | 7 | 4 | 26 | 37 |
| | NS | 7 | 3 | 21 | 31 |
| | Wt | 2694.21 | 416.37 | 5065.48 | 8176.07 |
| Het | Chi | 94.52 | 12.67 | 276.67 | 474.03 |
| Het | df | 6 | 3 | 25 | 36 |
| Het | P | *** | ** | *** | *** |
| Fixed | RR | 1.47 | 1.46 | 1.82 | 1.68 |
| | RRl | 1.42 | 1.32 | 1.78 | 1.64 |
| | RRu | 1.53 | 1.61 | 1.88 | 1.72 |
| | P | +++ | +++ | +++ | +++ |
| Random | RR | 1.32 | 1.70 | 1.69 | 1.62 |
| | RRl | 1.08 | 1.31 | 1.53 | 1.48 |
| | RRu | 1.62 | 2.20 | 1.88 | 1.77 |
| | P | ++ | +++ | +++ | +++ |
| Asymm | P | N.S. | N.S. | N.S. | N.S. |
| Between | Chi | | 0.03 | 81.32 | 90.17 |
| Between | df | | 1 | 1 | 2 |
| Between | P | | N.S. | +++ | *** |
| Btwn(F) | P | | N.S. | + | * |
| Btwn(R) | P | | N.S. | + | (*) |

_____

Table 46
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by disease definition standard or not

**absent**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
| | | Case | Cont | Case | Cont | | |
|---|---|---|---|---|---|---|---|
| *7CNTRY-ITALY | 2 | – | – | – | – | 1.43 ( 1.04- 1.96) | |
| *ARIC | 4 | – | – | – | – | 2.00 ( 1.64- 2.38) | |
| *BIOBANK | 5 | – | – | – | – | 1.82 ( 1.66- 2.00) | |
| *BIOBANK | 4 | – | – | – | – | 1.94 ( 1.71- 2.19) | |
| Subtotal BIOBANK | | | | | | 1.86 ( 1.73- 2.01) | |
| *CALIBER | 2 | – | – | – | – | 1.46 ( 1.29- 1.66) | |
| *CaCHS | 4 | – | – | – | – | 1.08 ( 0.85- 1.38) | |
| *CaCHS | 2 | – | – | – | – | 1.55 ( 1.20- 1.99) | |
| Subtotal CaCHS | | | | | | 1.28 ( 1.08- 1.53) | |
| *ELSA | 4 | – | – | – | – | 1.74 ( 1.06- 2.85) | |
| *EPIC-10 | 4 | 2004 | 4315 | 2187 | 7679 | 1.63 ( 1.55- 1.71) | |
| *EPIC-UK | 6 | – | – | – | – | 1.89 ( 1.40- 2.55) | |
| *HSE-SHS | 4 | – | – | – | – | 1.86 ( 1.49- 2.32) | |
| *JHS | 2 | – | – | – | – | 2.48 ( 1.60- 3.83) | |
| *MALMO | 1 | 79 | 12672 | 128 | 32087 | 1.56 ( 1.18- 2.07) | |
| *MESA | 4 | 31 | 887 | 88 | 3418 | 1.36 ( 0.91- 2.03) | |
| *MILLION | 1 | – | – | – | – | 2.41 ( 2.29- 2.54) | |
| *NFBC | 2 | – | – | – | – | 1.69 ( 1.10- 2.60) | |
| *NHS | 2 | 616 | 262982 | 1266 | 803757 | 1.49 ( 1.35- 1.64) | |
| *OHASAMA | 1 | – | – | – | – | 1.25 ( 0.87- 1.80) | |
| *PREVEND | 6 | – | – | – | – | 1.85 ( 1.05- 3.27) | |
| *WHS | 2 | – | – | – | – | 1.71 ( 1.39- 2.09) | |
| Partial Totals | | 2730 | 280856 | 3669 | 846941 | | |

*prospective study

**present**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
| | | Case | Cont | Case | Cont | | |
|---|---|---|---|---|---|---|---|
| *CPS-II | 4 | – | – | – | – | 1.55 ( 1.45- 1.66) | |
| *EPIC-ITALY | 4 | – | – | – | – | 1.80 ( 1.19- 2.72) | |
| *EPIC-ITALY | 6 | – | – | – | – | 1.96 ( 1.44- 2.66) | |
| Subtotal EPIC-ITALY | | | | | | 1.90 ( 1.49- 2.43) | |
| *EPIC-SPAIN | 1 | 42 | 4798 | 241 | 18190 | 0.66 ( 0.48- 0.92) | |
| *ESTONGENOME | 8 | – | – | – | – | 2.91 ( 1.65- 5.12) | |
| *ESTONGENOME | 11 | – | – | – | – | 2.88 ( 1.60- 5.15) | |
| Subtotal ESTONGENOME | | | | | | 2.90 ( 1.93- 4.35) | |
| *HAPIEE | 2 | 50 | 5871 | 41 | 9254 | 1.92 ( 1.27- 2.90) | |
| *JACC | 6 | – | – | – | – | 1.23 ( 1.07- 1.42) | |
| *JACC | 8 | – | – | – | – | 1.35 ( 1.08- 1.68) | |
| Subtotal JACC | | | | | | 1.26 ( 1.12- 1.42) | |
| *JP8 | 1 | 1737 | 78235 | 616 | 29255 | 1.05 ( 0.96- 1.15) | |
| *NHIS | 3 | – | – | – | – | 1.59 ( 1.33- 1.90) | |
| *NIH-AARP | 2 | – | – | – | – | 2.22 ( 1.82- 2.70) | |
| *NLMS | 3 | – | – | – | – | 1.24 ( 1.12- 1.36) | |
| *SCCS | 1 | – | – | – | – | 1.45 ( 1.14- 1.84) | |
| *USA5 | 8 | – | – | – | – | 1.90 ( 1.70- 2.20) | |
| *USA5 | 7 | – | – | – | – | 2.10 ( 1.80- 2.30) | |
| Subtotal USA5 | | | | | | 2.00 ( 1.83- 2.19) | |
| *WHITEHALL | 2 | – | – | – | – | 1.31 ( 1.12- 1.54) | |
| Partial Totals | | 1829 | 88904 | 898 | 56699 | | |

*prospective study

Study description:Standard definition

| | | 1 | 2 | |
| | | absent | present | Total |
|---|---|---|---|---|
| **RR Data** | | | | |
| | N | 20 | 17 | 37 |
| | NS | 18 | 13 | 31 |
| | Wt | 5122.97 | 3053.10 | 8176.07 |
| | Het Chi | 195.07 | 178.86 | 474.03 |
| | Het df | 19 | 16 | 36 |
| | Het P | *** | *** | *** |
| | Fixed RR | 1.83 | 1.46 | 1.68 |
| | RRl | 1.78 | 1.41 | 1.64 |
| | RRu | 1.88 | 1.51 | 1.72 |
| | P | +++ | +++ | +++ |
| | Random RR | 1.68 | 1.55 | 1.62 |
| | RRl | 1.51 | 1.36 | 1.48 |
| | RRu | 1.88 | 1.77 | 1.77 |

Table 46
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Analysis by disease definition standard or not

**Study description:Standard definition**

|  |  | 1<br>absent | 2<br>present | Total |
|---|---|---|---|---|
| **RR Data** |  |  |  |  |
|  | P | +++ | +++ | +++ |
| **Asymm** | P | N.S. | N.S. | N.S. |
| **Between** | Chi |  | 100.10 | 100.10 |
| **Between** | df |  | 1 | 1 |
| **Between** | P |  | --- | *** |
| **Btwn(F)** | P |  | -- | ** |
| **Btwn(R)** | P |  | N.S. | N.S. |

Table 47
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
<u>List of the selected results with RR values for male/female (M/F) ratio - Current cigarette smokers versus never smokers</u>

| Study ID | NRR M | RR Male | RRL M | RRU M | NRR F | RR Female | RRL F | RRU F | RR M/F | RRL M/F | RRU M/F |
|---|---|---|---|---|---|---|---|---|---|---|---|
| BIOBANK | 2 | 2.23 | 2.03 | 2.44 | 1 | 3.46 | 3.02 | 3.98 | 0.64 | 0.55 | 0.76 |
| CaCHS | 3 | 3.79 | 3.02 | 4.75 | 1 | 3.64 | 2.52 | 5.26 | 1.04 | 0.68 | 1.60 |
| ESTONGENOME | 9 | 2.07 | 0.95 | 4.53 | 12 | 4.72 | 1.83 | 12.17 | 0.44 | 0.13 | 1.50 |

_____

Smoking and CVD, Analysis run on 15-JUN-2023

Table 48
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
Meta-analysis of M/F ratio

**1**

| Study ID | NRR | Numbers exposed | | Non-exposed | | RR | 95.00%CI |
|----------|-----|------|------|------|------|-----|----------|
| | | Case | Cont | Case | Cont | | |
| **\*BIOBANK** | 1 | - | - | - | - | 0.64 ( | 0.55- 0.76) |
| **\*CaCHS** | 1 | - | - | - | - | 1.04 ( | 0.68- 1.60) |
| **\*ESTONGENOME** | 12 | - | - | - | - | 0.44 ( | 0.13- 1.50) |
| **Partial Totals** | | 0.00 | 0.00 | 0.00 | 0.00 | | |

**\*prospective study**

|  | Group |
|--|-------|
|  | 1 |
|  | 1 |

**M/F ratio**

| | |
|-----------|--------|
| **N** | 3 |
| **NS** | 3 |
| | |
| **Wt** | 162.78 |
| **Het Chi** | 4.63 |
| **Het df** | 2 |
| **Het P** | (\*) |
| **Fixed RR** | 0.68 |
| **RRl** | 0.58 |
| **RRu** | 0.79 |
| **P** | --- |
| **Random RR** | 0.74 |
| **RRl** | 0.50 |
| **RRu** | 1.09 |
| **P** | N.S. |
| **Asymm P** | N.S. |
| **Between Chi** | |
| **Between df** | |
| **Between P** | |
| **Btwn(F) P** | |
| **Btwn(R) P** | |

Table 49
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
<u>List of the selected results with RR values for male/female (M/F) ratio - Current cigarette smokers versus never smokers</u>

| Study ID | NRR M | RR Male | RRL M | RRU M | NRR F | RR Female | RRL F | RRU F | RR M/F | RRL M/F | RRU M/F |
|----------|-------|---------|-------|-------|-------|-----------|-------|-------|--------|---------|---------|
| EPIC-10 | 1 | 2.08 | 1.93 | 2.25 | 2 | 2.54 | 2.32 | 2.77 | 0.82 | 0.73 | 0.92 |
| ESTONGENOME | 7 | 2.10 | 1.59 | 2.76 | 10 | 2.44 | 1.62 | 3.68 | 0.86 | 0.52 | 1.41 |
| JACC | 5 | 1.95 | 1.58 | 2.39 | 7 | 2.45 | 1.89 | 3.18 | 0.80 | 0.57 | 1.11 |
| MALMO | 4 | 1.63 | 1.42 | 1.87 | 5 | 1.86 | 1.61 | 2.14 | 0.88 | 0.72 | 1.07 |
| USA5 | 6 | 2.60 | 2.40 | 2.70 | 5 | 3.00 | 2.80 | 3.20 | 0.87 | 0.79 | 0.95 |

Table 50
Smoking and CVD: Cigarette Smoking analyses
<u>Results for IHD</u>
Meta-analysis of M/F ratio

```
1
                 Numbers exposed Non-exposed
 Study ID     NRR   Case   Cont   Case   Cont    RR        95.00%CI
*EPIC-10      2      -      -      -      -     0.82 ( 0.73-  0.92)
*ESTONGENOME  10     -      -      -      -     0.86 ( 0.52-  1.41)
*JACC         7      -      -      -      -     0.80 ( 0.57-  1.11)
 MALMO        5      -      -      -      -     0.88 ( 0.72-  1.07)
*USA5         5      -      -      -      -     0.87 ( 0.79-  0.95)
Partial Totals      0.00   0.00   0.00   0.00
*prospective study
```

```
                        Group
                          1
                          1


M/F ratio


                  N        5
                  NS       5

                  Wt    918.44
            Het Chi     0.77
            Het df         4
            Het  P      N.S.
          Fixed  RR     0.85
                 RRl     0.80
                 RRu     0.91
                 P       ---
         Random  RR     0.85
                 RRl     0.80
                 RRu     0.91
                 P       ---
          Asymm  P      N.S.
         Between Chi
         Between df
         Between  P
         Btwn(F)  P
         Btwn(R)  P
```

Table 51
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of the selected results with RR values for male/female (M/F) ratio - Current cigarette smokers versus never smokers

| Study ID | NRR M | RR Male | RRL M | RRU M | NRR F | RR Female | RRL F | RRU F | RR M/F | RRL M/F | RRU M/F |
|---|---|---|---|---|---|---|---|---|---|---|---|
| BIOBANK | 5 | 1.82 | 1.66 | 2.00 | 4 | 1.94 | 1.71 | 2.19 | 0.94 | 0.80 | 1.10 |
| CaCHS | 4 | 1.08 | 0.85 | 1.38 | 2 | 1.55 | 1.20 | 1.99 | 0.70 | 0.49 | 0.99 |
| EPIC-ITALY | 4 | 1.80 | 1.19 | 2.72 | 6 | 1.96 | 1.44 | 2.66 | 0.92 | 0.55 | 1.54 |
| ESTONGENOME | 8 | 2.91 | 1.65 | 5.12 | 11 | 2.88 | 1.60 | 5.15 | 1.01 | 0.45 | 2.28 |
| JACC | 6 | 1.23 | 1.07 | 1.42 | 8 | 1.35 | 1.08 | 1.68 | 0.91 | 0.70 | 1.18 |
| USA5 | 8 | 1.90 | 1.70 | 2.20 | 7 | 2.10 | 1.80 | 2.30 | 0.90 | 0.76 | 1.08 |

Table 52
Smoking and CVD: Cigarette Smoking analyses
<u>Results for Stroke</u>
Meta-analysis of M/F ratio

**1**

|  |  | Numbers exposed |  | Non-exposed |  |  |  |
|---|---|---|---|---|---|---|---|
| Study ID | NRR | Case | Cont | Case | Cont | RR | 95.00%CI |
| *BIOBANK | 4 | - | - | - | - | 0.94 ( 0.80- | 1.10) |
| *CaCHS | 2 | - | - | - | - | 0.70 ( 0.49- | 0.99) |
| *EPIC-ITALY | 6 | - | - | - | - | 0.92 ( 0.55- | 1.54) |
| *ESTONGENOME | 11 | - | - | - | - | 1.01 ( 0.45- | 2.28) |
| *JACC | 8 | - | - | - | - | 0.91 ( 0.70- | 1.18) |
| *USA5 | 7 | - | - | - | - | 0.90 ( 0.76- | 1.08) |
| Partial Totals |  | 0.00 | 0.00 | 0.00 | 0.00 |  |  |

**\*prospective study**

|  | Group |
|---|---|
|  | 1 |
|  | 1 |

**M/F ratio**

|  |  |
|---|---|
| N | 6 |
| NS | 6 |
| Wt | 389.01 |
| Het Chi | 2.42 |
| Het df | 5 |
| Het P | N.S. |
| Fixed RR | 0.90 |
| RRl | 0.82 |
| RRu | 1.00 |
| P | - |
| Random RR | 0.90 |
| RRl | 0.82 |
| RRu | 1.00 |
| P | - |
| Asymm P | N.S. |
| Between Chi | |
| Between df | |
| Between P | |
| Btwn(F) P | |
| Btwn(R) P | |

Table 53
Smoking and CVD: Cigarette Smoking analyses
<u>Results for AMI</u>
<u>List of selected results with ratio of multiply-adjusted/unadjusted RRs - Current cigarette smokers versus never smokers</u>

| Study ID | Sex | NRR adjust | Adj | RR adjust | NRR unadj | RR unadj | adj/unadj RR ratio | Ratio >1 | Ratio <1 |
|----------|-----|-----------|-----|-----------|-----------|----------|--------------------|----------|----------|
| EPIC-GERM | b | 2 | 9 | 3.5200 | 1 | 3.4346 | 1.0249 | 1 | 0 |
| TROMSO | f | 2 | 4 | 2.1100 | 1 | 0.9971 | 2.1162 | 1 | 0 |
| WHS | f | 4 | 14 | 3.0000 | 3 | 2.9510 | 1.0166 | 1 | 0 |

<u>Test of significance of the numbers of ratios >1 and <1</u>

**Group**
**1**
**1**
**compared with Ratio greater than 1**
**{Ratio >1}**
**Ratio less than 1**

| | | |
|---|---|---|
| | n | 0 |
| | N | 3 |

_____

Table 54
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of selected results with ratio of multiply-adjusted/unadjusted RRs - Current cigarette smokers versus never smokers

| Study ID | Sex | NRR adjust | Adj | RR adjust | NRR unadj | RR unadj | adj/unadj RR ratio | Ratio >1 | Ratio <1 |
|----------|-----|------------|-----|-----------|-----------|----------|--------------------|---------|---------|
| ARIC | b | 2 | 15 | 2.2700 | 1 | 1.8819 | 1.2062 | 1 | 0 |
| CPS-II | b | 3 | 23 | 1.9800 | 1 | 1.1275 | 1.7561 | 1 | 0 |
| ELSA | b | 2 | 7 | 1.9300 | 1 | 1.6900 | 1.1420 | 1 | 0 |
| EPIC-UK | b | 3 | 6 | 1.7700 | 1 | 1.7100 | 1.0351 | 1 | 0 |
| HSE-SHS | b | 3 | 7 | 2.2800 | 1 | 1.7251 | 1.3217 | 1 | 0 |
| JACC | m | 5 | 7 | 1.9500 | 1 | 1.6164 | 1.2064 | 1 | 0 |
| JACC | f | 7 | 9 | 2.4500 | 3 | 2.2846 | 1.0724 | 1 | 0 |
| MALMO | m | 4 | 6 | 1.6300 | 2 | 1.4131 | 1.1535 | 1 | 0 |
| MALMO | f | 5 | 6 | 1.8600 | 3 | 1.3301 | 1.3984 | 1 | 0 |
| PREVEND | b | 3 | 10 | 1.6200 | 1 | 1.6812 | 0.9636 | 0 | 1 |
| USA5 | f | 5 | 5 | 3.0000 | 1 | 1.2661 | 2.3695 | 1 | 0 |
| USA5 | m | 6 | 5 | 2.6000 | 2 | 1.1024 | 2.3586 | 1 | 0 |

Test of significance of the numbers of ratios >1 and <1

| | Group |
|---|---|
| | 1 |
| | 1 |
| **compared with Ratio greater than 1 {Ratio >1} Ratio less than 1** | |
| n | 1 |
| N | 12 |
| % | 8.33 |
| P | |
| N <1 | 1 |
| N >1 | 11 |
| % <1 | 8.33 |
| % >1 | 91.67 |
| Test P Chi | 0.0063 -- |
| HeterP | N.S. |

Table 55
Smoking and CVD: Cigarette Smoking analyses
Results for Stroke
List of selected results with ratio of multiply-adjusted/unadjusted RRs - Current cigarette smokers versus never smokers

| Study ID | Sex | NRR adjust | Adj | RR adjust | NRR unadj | RR unadj | adj/unadj RR ratio | Ratio >1 | Ratio <1 |
|---|---|---|---|---|---|---|---|---|---|
| ARIC | b | 4 | 14 | 2.0000 | 3 | 1.3554 | 1.4755 | 1 | 0 |
| CPS-II | b | 4 | 23 | 1.5500 | 2 | 0.8126 | 1.9074 | 1 | 0 |
| ELSA | b | 4 | 7 | 1.7400 | 3 | 1.5800 | 1.1013 | 1 | 0 |
| EPIC-ITALY | m | 4 | 10 | 1.8000 | 1 | 1.6991 | 1.0594 | 1 | 0 |
| EPIC-ITALY | f | 6 | 10 | 1.9600 | 2 | 1.1612 | 1.6880 | 1 | 0 |
| EPIC-UK | b | 6 | 6 | 1.8900 | 4 | 1.6400 | 1.1524 | 1 | 0 |
| HSE-SHS | b | 4 | 7 | 1.8600 | 2 | 1.0377 | 1.7924 | 1 | 0 |
| JACC | m | 6 | 7 | 1.2300 | 2 | 1.0832 | 1.1355 | 1 | 0 |
| JACC | f | 8 | 9 | 1.3500 | 4 | 1.3114 | 1.0294 | 1 | 0 |
| JHS | b | 2 | 11 | 2.4800 | 1 | 1.9936 | 1.2440 | 1 | 0 |
| NFBC | b | 2 | 10 | 1.6900 | 1 | 1.8206 | 0.9283 | 0 | 1 |
| NHIS | b | 3 | 5 | 1.5900 | 1 | 0.8401 | 1.8926 | 1 | 0 |
| NIH-AARP | b | 2 | 4 | 2.2200 | 1 | 1.8443 | 1.2037 | 1 | 0 |
| NLMS | b | 3 | 5 | 1.2400 | 1 | 1.0867 | 1.1411 | 1 | 0 |
| PREVEND | b | 6 | 10 | 1.8500 | 4 | 1.4340 | 1.2901 | 1 | 0 |
| USA5 | f | 7 | 5 | 2.1000 | 3 | 0.8132 | 2.5825 | 1 | 0 |
| USA5 | m | 8 | 5 | 1.9000 | 4 | 0.7146 | 2.6590 | 1 | 0 |
| WHS | f | 2 | 14 | 1.7100 | 1 | 1.5582 | 1.0975 | 1 | 0 |

Test of significance of the numbers of ratios >1 and <1

| | Group |
|---|---|
| | 1 |
| | 1 |
| compared with Ratio greater than 1 {Ratio >1} Ratio less than 1 | |
| n | 1 |
| N | 18 |
| % | 5.56 |
| P | |
| N <1 | 1 |
| N >1 | 17 |
| % <1 | 5.56 |
| % >1 | 94.44 |
| Test P | 0.0001 --- |
| Chi | |
| HeterP | N.S. |

Table 56
Smoking and CVD: Cigarette Smoking analyses
Results for AMI
List of selected results with ratio of multiply-adjusted/(unadj or age-adj) RRs - Current cigarette smokers versus never

| Study ID | Sex | NRR adjust | Adj | RR adjust | NRR unadj | RR unadj | adj/unadj RR ratio | Ratio >1 | Ratio <1 |
|----------|-----|------------|-----|-----------|-----------|----------|--------------------|----------|----------|
| EPIC-GERM | b | 2 | 9 | 3.5200 | 1 | 3.4346 | 1.0249 | 1 | 0 |
| TROMSO | f | 2 | 4 | 2.1100 | 1 | 0.9971 | 2.1162 | 1 | 0 |
| WHILA | f | 2 | 7 | 2.6600 | 1 | 2.8400 | 0.9366 | 0 | 1 |
| WHS | f | 4 | 14 | 3.0000 | 3 | 2.9510 | 1.0166 | 1 | 0 |

Test of significance of the numbers of ratios >1 and <1

|  |  | Group 1 1 |
|--|--|-----------|
| **compared with Ratio greater than 1 {Ratio >1} Ratio less than 1** | | |
| | n | 1 |
| | N | 4 |
| | % | 25.00 |
| | P | |
| | N <1 | 1 |
| | N >1 | 3 |
| | % <1 | 25.00 |
| | % >1 | 75.00 |
| | Test P | 0.6250 |
| | Chi | |
| | HeterP | N.S. |

Table 57
Smoking and CVD: Cigarette Smoking analyses
Results for IHD
List of selected results with ratio of multiply-adjusted/(unadj or age-adj) RRs - Current cigarette smokers versus never

| Study ID | Sex | NRR adjust | Adj | RR adjust | NRR unadj | RR unadj | adj/unadj RR ratio | Ratio >1 | Ratio <1 |
|----------|-----|------------|-----|-----------|-----------|----------|--------------------|----------|----------|
| ARIC | b | 2 | 15 | 2.2700 | 1 | 1.8819 | 1.2062 | 1 | 0 |
| CPS-II | b | 3 | 23 | 1.9800 | 1 | 1.1275 | 1.7561 | 1 | 0 |
| ELSA | b | 2 | 7 | 1.9300 | 1 | 1.6900 | 1.1420 | 1 | 0 |
| EPIC-UK | b | 3 | 6 | 1.7700 | 1 | 1.7100 | 1.0351 | 1 | 0 |
| HSE-SHS | b | 3 | 7 | 2.2800 | 1 | 1.7251 | 1.3217 | 1 | 0 |
| JACC | m | 5 | 7 | 1.9500 | 1 | 1.6164 | 1.2064 | 1 | 0 |
| JACC | f | 7 | 9 | 2.4500 | 3 | 2.2846 | 1.0724 | 1 | 0 |
| MALMO | m | 4 | 6 | 1.6300 | 2 | 1.4131 | 1.1535 | 1 | 0 |
| MALMO | f | 5 | 6 | 1.8600 | 3 | 1.3301 | 1.3984 | 1 | 0 |
| MESA | b | 2 | 14 | 1.5500 | 1 | 1.4100 | 1.0993 | 1 | 0 |
| NHS-II | f | 2 | 15 | 4.3000 | 1 | 5.4000 | 0.7963 | 0 | 1 |
| PREVEND | b | 3 | 10 | 1.6200 | 1 | 1.6812 | 0.9636 | 0 | 1 |
| USA5 | f | 5 | 5 | 3.0000 | 1 | 1.2661 | 2.3695 | 1 | 0 |
| USA5 | m | 6 | 5 | 2.6000 | 2 | 1.1024 | 2.3586 | 1 | 0 |

Test of significance of the numbers of ratios >1 and <1

| | **Group** |
|---|---|
| | **1** |
| | **1** |
| **compared with Ratio greater than 1 {Ratio >1} Ratio less than 1** | |
| n | 2 |
| N | 14 |
| % | 14.29 |
| P | |
| N <1 | 2 |
| N >1 | 12 |
| % <1 | 14.29 |
| % >1 | 85.71 |
| Test P | 0.0129 - |
| Chi | |
| HeterP | N.S. |

_____

**Evidence relating cigarettes, cigars and pipes to cardiovascular disease and stroke:**

**Meta-analysis of recent data from three regions**

**Supplementary material 2**

Authors                               Peter N Lee, Katharine J Coombs, Jan S Hamling

This supplementary file gives details of the results available relating cigar and pipe smoking to acute myocardial infarction (AMI), ischaemic heart disease (IHD) and stroke.   The data were too limited to make meta-analysis of these smoking products feasible.

Smoking and CVD: Cigar and Pipe Smoking data

**These listings show results for current cigar or pipe smokers versus never smokers.**


**Key:**

  **Study ID: Identifier assigned to the study**

  **NRR:      Sequence number assigned to the risk estimates within a study**

  **REFID:    Identifier assigned to the published paper**

  **Nature of pop: Nature of the population; National, Regional or Other**

  **YRST:     Year of start of baseline**

  **NAMI, NIHD, NSTR: Number of CVD cases (AMI, IHD or Stroke) in the study**

  **ProductSm: Product smoked**

  **Excl:     Exclusive use of the product: 0 = No; x = Yes**

  **Latent:   A latency rule was applied, such as ignoring CVD cases identified in the first two or five**

        **years after smoking data were gathered: 0 = No; x = Yes**

  **Pop analysed: The type of population considered in analysis: Cohort or Nested case control**

  **Disease:  Disease reported; AMI = myocardial infarction, IHD = Coronary heart disease or Stroke**

  **Sex:      Gender reported by the risk estimate; b = both sexes combined, m = male, f = female**

  **LowAge, HighAge: Age range reported by the risk estimate**

  **YrsFU:    Number of years of follow up reported by the risk estimate**

  **Endpoint: The way the cases were identified: by diagnosis (inc. reported death) or only by reported death**

  **Adj:      Number of adjustment factors applied to the risk estimate**

  **CA1, CA0, CO1, CO0: For estimates derived from numbers, the values used: CA=Cases, CO=At Risk, 1=Exposed, 0=Unexposed**

  **RR, RRL, RRU: The estimate of relative risk (e.g. hazard ratio) and its 95% confidence interval.**

  **Derived:  How the estimate was obtained. Hamling method: see paper by Hamling et al. Stat Med 2008**


**CONTENTS**

Table 1
Smoking and CVD: Cigar and Pipe Smoking data
<u>Results for Cigar smoking</u>
<u>List of all the results for AMI - Current cigar smokers versus never smokers</u>

**There are no results for AMI in current cigar smokers**

<u>List of all the results for IHD - Current cigar smokers versus never smokers</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NIHD | Product Sm | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|----------|-----|-------|---------|---------------|------|------|-----------|------|--------|--------------|---------|-----|--------|---------|-------|----------|-----|
| MESA | 5 | NANCE2017 | USA | Regional | 2000 | 449 | Cigars | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 9 |

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|----------|-----|-------|-----|-----|-----|-----|-----|-----|-----|---------|
| MESA | 5 | NANCE2017 | - | - | - | - | 0.71 | 0.35 | 1.45 | Given in the paper |

<u>List of all the results for Stroke - Current cigar smokers versus never smokers</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NSTR | Product Sm | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|----------|-----|-------|---------|---------------|------|------|-----------|------|--------|--------------|---------|-----|--------|---------|-------|----------|-----|
| NHIS | 2 | INOUEC2020 | USA | National | 1987 | 2046 | Cigars | x | 0 | Cohort | Stroke | b | 18 | 95 | 24 | Died | 0 |
| NHIS | 4 | INOUEC2020 | USA | National | 1987 | 2046 | Cigars | x | 0 | Cohort | Stroke | b | 18 | 95 | 24 | Died | 5 |
| NLMS | 4 | CHRIST2018 | USA | National | 1985 | 3083 | Cigars | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 1 |
| NLMS | 5 | CHRIST2018 | USA | National | 1985 | 3083 | Cigars | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 5 |

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|----------|-----|-------|-----|-----|-----|-----|-----|-----|-----|---------|
| NHIS | 2 | INOUEC2020 | 7 | 989 | 578 | 83972 | 1.03 | 0.49 | 2.15 | From numbers |
| NHIS | 4 | INOUEC2020 | - | - | - | - | 1.60 | 0.72 | 3.57 | Given in the paper |
| NLMS | 4 | CHRIST2018 | - | - | - | - | 0.53 | 0.22 | 1.27 | Given in the paper |
| NLMS | 5 | CHRIST2018 | - | - | - | - | 0.50 | 0.21 | 1.22 | Given in the paper |

Table 2
Smoking and CVD: Cigar and Pipe Smoking data
<u>Results for Pipe smoking</u>
<u>List of all the results for AMI - Current pipe smokers versus never smokers</u>

**There are no results for AMI in current pipe smokers**

<u>List of all the results for IHD - Current pipe smokers versus never smokers</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NIHD | Product Sm | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MESA | 6 | NANCE2017 | USA | Regional | 2000 | 449 | Pipes | 0 | 0 | Cohort | IHD | b | 45 | 84 | 11 | Diagnosed | 9 |

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|---|---|---|---|---|---|---|---|---|---|---|
| MESA | 6 | NANCE2017 | - | - | - | - | 0.81 | 0.26 | 2.55 | Given in the paper |

<u>List of all the results for Stroke - Current pipe smokers versus never smokers</u>

| Study ID | NRR | REFID | Country | Nature of pop | YRST | NSTR | Product Sm | Excl | Latent | Pop analysed | Disease | Sex | LowAge | HighAge | YrsFU | Endpoint | Adj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NLMS | 6 | CHRIST2018 | USA | National | 1985 | 3083 | Pipes | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 1 |
| NLMS | 7 | CHRIST2018 | USA | National | 1985 | 3083 | Pipes | x | 0 | Cohort | Stroke | b | 35 | 80 | 26 | Died | 5 |

| Study ID | NRR | REFID | CA1 | CA0 | CO1 | CO0 | RR | RRL | RRU | Derived |
|---|---|---|---|---|---|---|---|---|---|---|
| NLMS | 6 | CHRIST2018 | - | - | - | - | 0.25 | 0.07 | 0.95 | Given in the paper |
| NLMS | 7 | CHRIST2018 | - | - | - | - | 0.24 | 0.06 | 0.91 | Given in the paper |

**Evidence relating cigarettes, cigars and pipes to cardiovascular disease and stroke: Meta-analysis of recent data from three regions**

**Supplementary material 3**

Authors                    Peter N Lee, Katharine J Coombs, Jan S Hamling

This supplementary file gives details of the results available relating number of cigarettes smoked to risk of acute myocardial infarction (AMI), ischaemic heart disease (IHD) and stroke.

| Disease | Study ID | Source paper | Country | Cigs/day groupings | Gender | RR (95% CI) by cigs/day grouping Group 1 | Group 2 | Group 3 | Variables adjusted for[a] | Footnote |
|---------|----------|--------------|---------|--------------------|--------|---------|---------|---------|---------------------|----------|
| AMI | BIOBANK | [1] | UK | 1-9, 10-19, 20+ | Female | 2.18 (1.55-3.06) | 3.76 (3.07-4.60) | 5.83 (4.76-7.15) | age + 6 | |
| | | | | | Male | 1.77 (1.35-2.31) | 2.64 (2.28-3.06) | 2.90 (2.53-3.32) | age + 6 | |
| | CaCHS | [2] | Canada | <20, 20+ | Female | 3.15 (2.11-4.71) | 6.80 (3.73-12.4) | | age + 14 | |
| | | | | | Male | 3.37 (2.36-4.31) | 5.29 (3.84-7.28) | | age + 14 | |
| | EPIC-GERM | [3] | Germany | 1-15, 16+ | Both | 2.70 (2.10-3.50) | 4.18 (3.25-5.50) | | sex, age + 7 | b |
| | KIHD | [4] | Finland | Low, medium, high | Male | 0.73 (0.43-1.24) | 1.87 (1.29-2.69) | 1.91 (1.29-2.83) | none | c |
| | | | | | | | | | | |
| IHD | ARIC | [5] | USA | <20, 20+ | Both | 1.65 (1.39-1.94) | 1.83 (1.59-2.10) | | sex, age + 13 | |
| | CoCHS | [6] | Denmark | 1-4, 5-14, 15+[d] | Female | 0.94 (0.60-1.47) | 1.57 (1.31-1.88) | 1.84 (1.54-2.21) | age | |
| | | | | | Male | 1.51 (0.84-2.72) | 1.65 (1.25-2.19) | 1.91 (1.49-2.46) | age | |
| | EPIC-10 | [7] | 9 European | 1-9, 10-19, 20+ | Female | 1.84 (1.58-2.14) | 2.87 (2.57-3.20) | 2.74 (2.42-3.11) | none | e |
| | | | | | Male | 1.81 (1.64-2.00) | 2.22 (2.00-2.47) | 2.24 (2.04-2.45) | none | |
| | MESA | [8] | USA | Per pack/day | Both | 1.83 (1.23-2.73) | | | sex, age + 3 | |
| | NHS-II | [9] | USA | 1-14, 15-24, 25+ | Female | 3.26 (1.68-6.33) | 4.43 (2.31-8.52) | 4.35 (2.81-6.74) | age + 14 | f |
| | PREVEND | [10] | Netherlands | 1-9, 10+ | Both | 1.54 (1.02-2.32) | 1.90 (1.28-1.81) | | sex, age + 9 | |
| | | | | | | | | | | |
| Stroke | ARIC | [5] | USA | 1-19, 20+ | Both | 1.36 (1.11-1.68) | 1.34 (1.11-1.62) | | sex, age + 13 | |
| | BIOBANK | [11] | UK | 1-9, 10-19, 20+ | Female | 1.21 (0.80-1.82) | 2.03 (1.62-2.55) | 3.03 (2.41-3.81) | age + others | g |
| | | | | 1-9, 10-19, 20+ | Female | 1.24 (0.56-2.76) | 1.74 (1.06-2.83) | 1.68 (0.90-3.12) | age + others | h |
| | | | | 1-9, 10-19, 20+ | Male | 1.52 (1.05-2.18) | 1.83 (1.49-2.25) | 2.92 (2.50-3.41) | age + others | g |
| | | | | 1-9, 10-19, 20+ | Male | 1.35 (0.56-3.25) | 1.37 (0.80-2.36) | 1.42 (0.86-2.36) | age + others | h |
| | CaCHS | [2] | Canada | 1-19, 20+ | Female | 1.51 (1.15-1.97) | 1.75 (1.03-2.97) | | age + 14 | |
| | | | | | Male | 1.03 (0.79-1.35) | 1.27 (0.84-1.93) | | age + 14 | |
| | | [12] | Canada | 1-19, 20+ | Female | 1.52 (1.24-1.86) | 1.85 (1.44-2.38) | | age | f |
| | | | | | Male | 1.41 (1.08-1.84) | 1.51 (1.15-1.98) | | age | f |
| | EPIC-ITALY | [13] | Italy | 1-8, 9-18, 19+ | Female | 1.24 (0.75-2.05) | 2.18 (1.41-3.37) | 2.96 (1.91-4.58) | age + 8 | i |
| | | | | 1-8, 9-18, 19+ | Male | 0.91 (0.43-1.97) | 1.46 (0.82-2.59) | 2.86 (1.78-4.59) | age + 8 | i |
| | JHS | [14] | USA | 1-19, 20+ | Both | 2.30 (1.37-2.90) | 2.62 (1.37-5.01) | | sex, age + 9 | |
| | MESA | [8] | USA | Per pack/day | Both | 1.92 (1.33-2.76) | | | sex, age + 3 | |
| | NHIS | [15] | USA | 1-10, 11-20, 21+ | Both | 2.18 (1.78-2.67) | 1.98 (1.59-2.46) | 2.16 (1.56-2.99) | sex, age + 6 | e |
| | NIH-AARP | [16] | USA | ≤10, 11-20, 21+ | Both | 1.86 (1.40-2.47) | 1.68 (1.22-2.31) | 2.03 (1.46-2.82) | none | e |
| | PREVEND | [10] | Netherlands | 1-9, 10+ | Both | 1.02 (0.43-2.41) | 2.15 (1.16-4.00) | | sex, age + 9 | |
| | SCCS | [17] | USA | 1-9, 10-19, 20+ | Both | 1.35 (0.98-1.86) | 1.62 (1.19-2.21) | 1.37 (0.98-1.91) | sex, age +4 | e |

a   The number shown is the number of additional variables adjusted for
b   CIs estimated, data are for those with no gallstones
c   CIs estimated, tertiles of packs/year

d  Groupings are by grams/day
e  RRs and CIs estimated
f  CIs estimated
g  Ischaemic stroke
h  Hemorrhagic stroke
i  RR and CI for 19+ cigarettes/day estimated

## References

1      Millett ERC, Peters SAE and Woodward M. Sex differences in risk factors for myocardial infarction: cohort study of UK Biobank participants. *BMJ* 2018; **363**: k4247. [PMID: 30404896 DOI: 10.1136/bmj.k4247]

2      Ng R, Sutradhar R, Yao Z, Wodchis WP and Rosella LC. Smoking, drinking, diet and physical activity-modifiable lifestyle risk factors and their associations with age to first chronic disease. *Int J Epidemiol* 2020; **49**: 113-130. [PMID: 31329872 DOI: 10.1093/ije/dyz078]

3      Wirth J, di Giuseppe R, Wientzek A, Katzke VA, Kloss M, Kaaks R, Boeing H and Weikert C. Presence of gallstones and the risk of cardiovascular diseases: The EPIC-Germany cohort study. *Eur J Prev Cardiol* 2015; **22**: 326-34. [PMID: 24177267 DOI: 10.1177/2047487313512218]

4      Mujahid MS, James SA, Kaplan GA and Salonen JT. Socioeconomic position, John Henryism, and incidence of acute myocardial infarction in Finnish men. *Soc Sci Med* 2017; **173**: 54-62. [PMID: 27923154 DOI: 10.1016/j.socscimed.2016.11.034]

5      Ding N, Sang Y, Chen J, Ballew SH, Kalbaugh CA, Salameh MJ, Blaha MJ, Allison M, Heiss G, Selvin E, Coresh J and Matsushita K. Cigarette smoking, smoking cessation, and long-term risk of 3 major atherosclerotic diseases. *J Am Coll Cardiol* 2019; **74**: 498-507. [PMID: 31345423 DOI: 10.1016/j.jacc.2019.05.049]

6      Schnohr P, Marott JL, Kristensen TS, Gyntelberg F, Grønbæk M, Lange P, Jensen MT, Jensen GB and Prescott E. Ranking of psychosocial and traditional risk factors by importance for coronary heart disease: the Copenhagen City Heart Study. *Eur Heart J* 2015; **36**: 1385-93. [PMID: 25681607 DOI: 10.1093/eurheartj/ehv027]

7      Key TJ, Appleby PN, Bradbury KE, Sweeting M, Wood A, Johansson I, Kühn T, Steur M, Weiderpass E, Wennberg M, Lund Würtz AM, Agudo A, Andersson J, Arriola L, Boeing H, Boer JMA, Bonnet F, Boutron-Ruault MC, Cross AJ, Ericson U, Fagherazzi G, Ferrari P, Gunter M, Huerta JM, Katzke V, Khaw KT, Krogh V, La Vecchia C, Matullo G, Moreno-Iribas C, Naska A, Nilsson LM, Olsen A, Overvad K, Palli D, Panico S, Molina-Portillo E, Quirós JR, Skeie G, Sluijs I, Sonestedt E, Stepien M, Tjønneland A, Trichopoulou A, Tumino R, Tzoulaki I, van der Schouw YT, Verschuren WMM, di Angelantonio E, Langenberg C, Forouhi N, Wareham N, Butterworth A, Riboli E and Danesh J. Consumption of meat, fish, dairy products, and eggs and risk of ischemic heart disease. *Circulation* 2019; **139**: 2835-2845. [PMID: 31006335 DOI: 10.1161/circulationaha.118.038813]

8       Nance R, Delaney J, McEvoy JW, Blaha MJ, Burke GL, Navas-Acien A, Kaufman JD, Oelsner EC and McClelland RL. Smoking intensity (pack/day) is a better measure than pack-years or smoking status for modeling cardiovascular disease outcomes. *J Clin Epidemiol* 2017; **81**: 111-119. [PMID: 27769836 DOI: 10.1016/j.jclinepi.2016.09.010]

9       Chomistek AK, Chiuve SE, Eliassen AH, Mukamal KJ, Willett WC and Rimm EB. Healthy lifestyle in the primordial prevention of cardiovascular disease among young women. *J Am Coll Cardiol* 2015; **65**: 43-51. [PMID: 25572509 DOI: 10.1016/j.jacc.2014.10.024]

10      Kunutsor SK, Spee JM, Kieneker LM, Gansevoort RT, Dullaart RPF, Voerman AJ, Touw DJ and Bakker SJL. Self-reported smoking, urine cotinine, and risk of cardiovascular disease: Findings from the PREVEND (Prevention of Renal and Vascular End-Stage Disease) Prospective Cohort Study. *J Am Heart Assoc* 2018; **7**: [PMID: 29720504 DOI: 10.1161/jaha.118.008726]

11      Peters SAE, Carcel C, Millett ERC and Woodward M. Sex differences in the association between major risk factors and the risk of stroke in the UK Biobank cohort study. *Neurology* 2020; **95**: e2715-e2726. [PMID: 33067404 DOI: 10.1212/wnl.0000000000010982]

12      Manuel DG, Tuna M, Perez R, Tanuseputro P, Hennessy D, Bennett C, Rosella L, Sanmartin C, van Walraven C and Tu JV. Predicting stroke risk based on health behaviours: Development of the Stroke Population Risk Tool (SPoRT). *PLoS One* 2015; **10**: e0143342. [PMID: 26637172 DOI: 10.1371/journal.pone.0143342]

13      Trajkova S, d'Errico A, Ricceri F, Fasanelli F, Pala V, Agnoli C, Tumino R, Frasca G, Masala G, Saieva C, Chiodini P, Mattiello A, Sacerdote C and Panico S. Impact of preventable risk factors on stroke in the EPICOR study: does gender matter? *Int J Public Health* 2017; **62**: 775-786. [PMID: 28643029 DOI: 10.1007/s00038-017-0993-2]

14      Oshunbade AA, Yimer WK, Valle KA, Clark D, 3rd, Kamimura D, White WB, DeFilippis AP, Blaha MJ, Benjamin EJ, O'Brien EC, Mentz RJ, Fox ER, O'Mara CS, Butler J, Correa A and Hall ME. Cigarette smoking and incident stroke in Blacks of the Jackson Heart Study. *J Am Heart Assoc* 2020; **9**: e014990. [PMID: 32517526 DOI: 10.1161/jaha.119.014990]

15      Qin W, Magnussen CG, Li S, Steffen LM, Xi B and Zhao M. Light cigarette smoking increases risk of all-cause and cause-specific mortality: Findings from the NHIS cohort study. *Int J Environ Res Public Health* 2020; **17**: [PMID: 32679883 DOI: 10.3390/ijerph17145122] Erratum appears in Int J Environ Res Public Health. 2020 Aug 25;17(17):6176

16      Nash SH, Liao LM, Harris TB and Freedman ND. Cigarette smoking and mortality in adults aged 70 years and older: Results from the NIH-AARP Cohort. *Am J Prev Med* 2017; **52**: 276-283. [PMID: 27914770 DOI: 10.1016/j.amepre.2016.09.036]


17      Munro HM, Tarone RE, Wang TJ and Blot WJ. Menthol and nonmenthol cigarette smoking: all-cause deaths, cardiovascular disease deaths, and other causes of death among blacks and whites. *Circulation* 2016; **133**: 1861-6. [PMID: 27022064 DOI: 10.1161/circulationaha.115.020536]