**Appendices**

Appendix 1: Using Stata to obtain relative risks by sex and the female to male ratio of relative risks from Cox proportional hazards regression models.

Comments are in blue, and prefixed by an asterisk on every line, commands are in red, and the rest is output.

**. \* The problem to solve is finding relative risks (RRs) for diabetes by sex,**

**. \* and the female to male ratio of RRs, the RRR, adjusting for continuous age**

**. \* and SBP, and smoking(defined as 0=never, 1=previous, 2=current smoker)**

**. \* Note that sex is coded 0=women; 1=men in the database**

**. \* Set the failure time variable**

**. stset time\_MI,failure(MI)**

 **failure event: MI != 0 & MI < .**

**obs. time interval: (0, time\_MI]**

 **exit on or before: failure**

**------------------------------------------------------------------------------**

 **474,212 total observations**

 **0 exclusions**

**------------------------------------------------------------------------------**

 **474,212 observations remaining, representing**

 **5,183 failures in single-record/single-failure data**

 **1.2375e+09 total analysis time at risk and under observation**

 **at risk from t = 0**

 **earliest observed entry t = 0**

 **last observed exit t = 3,671**

**. \*\* Sex-stratified analyses, to obtain RRs for women and men**

**. \* Women**

**. stcox age sbp i.smoking diabetes if sex==0**

 **failure \_d: MI**

 **analysis time \_t: time\_MI**

**Iteration 0: log likelihood = -18503.658**

**Iteration 1: log likelihood = -18081.017**

**Iteration 2: log likelihood = -17939.854**

**Iteration 3: log likelihood = -17934.419**

**Iteration 4: log likelihood = -17934.383**

**Iteration 5: log likelihood = -17934.383**

**Refining estimates:**

**Iteration 0: log likelihood = -17934.383**

**Cox regression -- Breslow method for ties**

**No. of subjects = 263,939 Number of obs = 263,939**

**No. of failures = 1,493**

**Time at risk = 690522741**

 **LR chi2(5) = 1138.55**

**Log likelihood = -17934.383 Prob > chi2 = 0.0000**

**------------------------------------------------------------------------------**

 **\_t | Haz. Ratio Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **age | 1.069493 .0044099 16.29 0.000 1.060885 1.078172**

 **sbp | 1.017851 .0013098 13.75 0.000 1.015287 1.020421**

 **|**

 **smoking |**

 **1 | 1.305345 .0773789 4.50 0.000 1.162164 1.466166**

 **2 | 3.936892 .2677192 20.15 0.000 3.445637 4.498187**

 **|**

 **diabetes | 2.967393 .2429644 13.28 0.000 2.527437 3.483933**

**------------------------------------------------------------------------------**

**. \* Men**

**. stcox age sbp i.smoking diabetes if sex==1**

 **failure \_d: MI**

 **analysis time \_t: time\_MI**

**Iteration 0: log likelihood = -44948.011**

**Iteration 1: log likelihood = -44299.159**

**Iteration 2: log likelihood = -44277.008**

**Iteration 3: log likelihood = -44276.957**

**Iteration 4: log likelihood = -44276.957**

**Refining estimates:**

**Iteration 0: log likelihood = -44276.957**

**Cox regression -- Breslow method for ties**

**No. of subjects = 210,273 Number of obs = 210,273**

**No. of failures = 3,690**

**Time at risk = 546931571**

 **LR chi2(5) = 1342.11**

**Log likelihood = -44276.957 Prob > chi2 = 0.0000**

**------------------------------------------------------------------------------**

 **\_t | Haz. Ratio Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **age | 1.051295 .0025201 20.87 0.000 1.046367 1.056245**

 **sbp | 1.013238 .0009097 14.65 0.000 1.011456 1.015022**

 **|**

 **smoking |**

 **1 | 1.173581 .0441693 4.25 0.000 1.090127 1.263424**

 **2 | 2.345507 .1045069 19.13 0.000 2.149366 2.559546**

 **|**

 **diabetes | 1.654616 .0874023 9.53 0.000 1.49188 1.835103**

**------------------------------------------------------------------------------**

**. \* (or could use the "bysort sex:" prefix to do both in one command)**

**. \* Note that the "i." prefix designates an indicator (categorical) variable**

**. \* and the "c." index designates a continuous variable**

**. \*\* Interaction model**

**. \* Since I would like to estimate the female to male RRR, I need to make**

**. \* men the reference group, but the current coding has women as the reference**

**. \* (because of the pre-defined coding of sex). One way of doing this is to**

**. \* simply recode sex as 0=men; 1 =women, which would be the case if sex was**

**. \* redefined as 1-sex (in fact, I would recommend defining a new variable,**

**. \* say sex2, rather than overwriting the original). This will work in any**

**. \* statistical software.**

**. \* In Stata a neater way of achieving the women/men RRR is to use the "ib"**

**. \* prefix; precisely, "ib1." tells Stata to take the group coded 1 for sex**

**. \* as the reference**

**. stcox ib1.sex##c.age ib1.sex##c.sbp ib1.sex##smoking ib1.sex##diabetes**

 **failure \_d: MI**

 **analysis time \_t: time\_MI**

**Iteration 0: log likelihood = -67335.846**

**Iteration 1: log likelihood = -65903.409**

**Iteration 2: log likelihood = -65344.382**

**Iteration 3: log likelihood = -65322.823**

**Iteration 4: log likelihood = -65322.793**

**Refining estimates:**

**Iteration 0: log likelihood = -65322.793**

**Cox regression -- Breslow method for ties**

**No. of subjects = 474,212 Number of obs = 474,212**

**No. of failures = 5,183**

**Time at risk = 1237454312**

 **LR chi2(11) = 4026.11**

**Log likelihood = -65322.793 Prob > chi2 = 0.0000**

**------------------------------------------------------------------------------**

 **\_t | Haz. Ratio Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex |**

 **0 Female | .0572753 .0180353 -9.08 0.000 .0308983 .1061697**

 **age | 1.051347 .0025202 20.89 0.000 1.046419 1.056298**

 **|**

 **sex#c.age |**

 **0 Female | 1.017191 .0048513 3.57 0.000 1.007726 1.026744**

 **|**

 **sbp | 1.013236 .0009097 14.65 0.000 1.011455 1.01502**

 **|**

 **sex#c.sbp |**

 **0 Female | 1.004549 .0015762 2.89 0.004 1.001464 1.007643**

 **|**

 **smoking |**

 **1 | 1.17345 .0441645 4.25 0.000 1.090004 1.263283**

 **2 | 2.34461 .1044663 19.12 0.000 2.148546 2.558567**

 **|**

 **sex#smoking |**

 **0 Female#1 | 1.112452 .0781136 1.52 0.129 .9694202 1.276587**

 **0 Female#2 | 1.681066 .1366622 6.39 0.000 1.433463 1.971438**

 **|**

 **1.diabetes | 1.65516 .0874309 9.54 0.000 1.492371 1.835707**

 **|**

**sex#diabetes |**

 **0 Female#1 | 1.7916 .1745684 5.98 0.000 1.480138 2.168601**

**------------------------------------------------------------------------------**

**. \* Note that this also produces the male RR.**

**. \* To use the interaction model to get the female RR, without having to deal with**

**. \* covariances, use the same code without the ib prefix to change the reference.**

**. stcox i.sex##c.age i.sex##c.sbp i.sex##smoking i.sex##diabetes**

 **failure \_d: MI**

 **analysis time \_t: time\_MI**

**Iteration 0: log likelihood = -67335.846**

**Iteration 1: log likelihood = -65903.409**

**Iteration 2: log likelihood = -65344.382**

**Iteration 3: log likelihood = -65322.823**

**Iteration 4: log likelihood = -65322.793**

**Refining estimates:**

**Iteration 0: log likelihood = -65322.793**

**Cox regression -- Breslow method for ties**

**No. of subjects = 474,212 Number of obs = 474,212**

**No. of failures = 5,183**

**Time at risk = 1237454312**

 **LR chi2(11) = 4026.11**

**Log likelihood = -65322.793 Prob > chi2 = 0.0000**

**------------------------------------------------------------------------------**

 **\_t | Haz. Ratio Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex |**

 **1 Male | 17.45953 5.4978 9.08 0.000 9.418879 32.36427**

 **age | 1.06942 .0044095 16.28 0.000 1.060812 1.078098**

 **|**

 **sex#c.age |**

 **1 Male | .9830999 .0046887 -3.57 0.000 .973953 .9923328**

 **|**

 **sbp | 1.017845 .0013098 13.75 0.000 1.015281 1.020416**

 **|**

 **sex#c.sbp |**

 **1 Male | .9954716 .001562 -2.89 0.004 .9924149 .9985377**

 **|**

 **smoking |**

 **1 | 1.305406 .0773831 4.50 0.000 1.162217 1.466237**

 **2 | 3.941445 .2680142 20.17 0.000 3.449647 4.503357**

 **|**

 **sex#smoking |**

 **1 Male#1 | .8989152 .0631196 -1.52 0.129 .7833385 1.031544**

 **1 Male#2 | .5948605 .0483591 -6.39 0.000 .5072438 .6976113**

 **|**

 **1.diabetes | 2.965385 .2427957 13.28 0.000 2.525734 3.481566**

 **|**

**sex#diabetes |**

 **1 Male#1 | .5581604 .0543856 -5.98 0.000 .4611268 .6756125**

**------------------------------------------------------------------------------**

**. \* Again, a general method, useable in any statistical software, is to swap**

**. \* the codes for sex, and then run the regression again, just as suggested above**

**. \* A neater option in Stata is to use the lincom command which deals with the**

**. \* covariances directly, and does not require fitting the interaction model**

**. \* twice; for example code such as:**

**. \* lincom 1.diabetes + 1.sex#1.diabetes,hr**

**. \* placed after running an initial regression model with sex coded as 0=men;**

**. \* 1=women, will - together with the results from the regression model itself -**

**. \* give all the 3 statistics required**

Appendix 2: Using Stata to obtain rates by sex and the female to male difference in rate differences from Poisson regression models.

Comments are in blue, and prefixed by an asterisk on every line, commands are in red, and the rest is output.

**. \* set follow-up time (time\_MI) to be per 10000 per year**

**. stset time\_MI,failure(MI) scale(3652500)**

 **failure event: MI != 0 & MI < .**

**obs. time interval: (0, time\_MI]**

 **exit on or before: failure**

 **t for analysis: time/3652500**

**------------------------------------------------------------------------------**

 **474,212 total observations**

 **0 exclusions**

**------------------------------------------------------------------------------**

 **474,212 observations remaining, representing**

 **5,183 failures in single-record/single-failure data**

 **338.797 total analysis time at risk and under observation**

 **at risk from t = 0**

 **earliest observed entry t = 0**

 **last observed exit t = .0010051**

**. \* note that this is not really necessary for using Poisson regression;**

**. \* its only use here is to get follow-up time (recorded in days) into**

**. \* follow-up time per 10,000 person-years; a simpler alternative would**

**. \* be to use: generate py = time\_MI/(365.25\*10000). Then use py instead**

**. \* of \_t (automatically produced from STSET by STATA) in the following**

**. \*\* Find unadjusted rates by sex**

**. \* Simple calculations - get numerators and denominators and divide 'by hand'**

**. tab sex MI**

 **| MI**

 **Sex | 0 1 | Total**

**-----------+----------------------+----------**

 **0 Female | 262,446 1,493 | 263,939**

 **1 Male | 206,583 3,690 | 210,273**

**-----------+----------------------+----------**

 **Total | 469,029 5,183 | 474,212**

**. total \_t,over (sex)**

**Total estimation Number of obs = 474,212**

 **\_subpop\_1: sex = 0 Female**

 **\_subpop\_2: sex = 1 Male**

**--------------------------------------------------------------**

 **Over | Total Std. Err. [95% Conf. Interval]**

**-------------+------------------------------------------------**

**\_t |**

 **\_subpop\_1 | 189.0548 .04626 188.9642 189.1455**

 **\_subpop\_2 | 149.7417 .0459876 149.6516 149.8318**

**--------------------------------------------------------------**

**. \* This gives the #events and PYs by sex. Dividing the results gives sex-specific**

**. \* rates of 1493/189.0548 = 7.897181 and 3690/149.7417 = 24.64243**

**. \* Poisson model to get the raw components which will produce the same results**

**. \* as above after summation and exponentiation (note exp(\_t) is an offset)**

**. poisson MI sex,exp(\_t)**

**Iteration 0: log likelihood = -32428.542**

**Iteration 1: log likelihood = -32428.542**

**Poisson regression Number of obs = 474,212**

 **LR chi2(1) = 1543.83**

 **Prob > chi2 = 0.0000**

**Log likelihood = -32428.542 Pseudo R2 = 0.0233**

**------------------------------------------------------------------------------**

 **MI | Coef. Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex | 1.137964 .0306724 37.10 0.000 1.077847 1.198081**

 **\_cons | 2.066506 .0258803 79.85 0.000 2.015781 2.11723**

 **ln(\_t) | 1 (exposure)**

**------------------------------------------------------------------------------**

**. gen rate\_female=exp(\_b[\_cons])**

**. dis rate\_female**

**7.8971806**

**. gen rate\_male=exp(\_b[\_cons] + \_b[sex])**

**. dis rate\_male**

**24.642433**

**. \* Unadjusted rates by sex and diabetes status (note use of irr, which produces**

**. \* estimates of relative rates for display purposes)**

**. poisson MI i.sex##i.diabetes,irr exp(\_t)**

**Iteration 0: log likelihood = -32278.822**

**Iteration 1: log likelihood = -32272.65**

**Iteration 2: log likelihood = -32272.641**

**Iteration 3: log likelihood = -32272.641**

**Poisson regression Number of obs = 474,212**

 **LR chi2(3) = 1855.63**

 **Prob > chi2 = 0.0000**

**Log likelihood = -32272.641 Pseudo R2 = 0.0279**

**------------------------------------------------------------------------------**

 **MI | IRR Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex |**

 **1 Male | 3.213225 .104614 35.85 0.000 3.01459 3.424948**

 **1.diabetes | 3.547908 .289811 15.50 0.000 3.023026 4.163924**

 **|**

**sex#diabetes |**

 **1 Male#1 | .5505562 .0534582 -6.15 0.000 .4551466 .665966**

 **|**

 **\_cons | 7.255217 .1993914 72.11 0.000 6.874755 7.656733**

 **ln(\_t) | 1 (exposure)**

**------------------------------------------------------------------------------**

**Note: \_cons estimates baseline incidence rate.**

**. \* Get two-way estimates**

**. margins i.sex#i.diabetes, exp(predict(n)/\_t)**

**Adjusted predictions Number of obs = 474,212**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------------------------------------**

 **| Delta-method**

 **| Margin Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

**sex#diabetes |**

 **0 Female#0 | 7.255217 .1993914 36.39 0.000 6.864417 7.646017**

 **0 Female#1 | 25.74084 1.980065 13.00 0.000 21.85998 29.6217**

 **1 Male#0 | 23.31264 .4069324 57.29 0.000 22.51507 24.11022**

 **1 Male#1 | 45.53712 2.254423 20.20 0.000 41.11853 49.9557**

**------------------------------------------------------------------------------**

**. \* Get the difference of rate differences**

**. margins i.sex#i.diabetes, exp(predict(n)/\_t) contrast (cieffects)**

**Contrasts of adjusted predictions**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------**

 **| df chi2 P>chi2**

**-------------+----------------------------------**

**sex#diabetes | 1 1.52 0.2179**

**------------------------------------------------**

**-------------------------------------------------------------------------------**

 **| Delta-method**

 **| Contrast Std. Err. [95% Conf. Interval]**

**------------------------------+------------------------------------------------**

 **sex#diabetes |**

**(1 Male vs base) (1 vs base) | 3.738849 3.03454 -2.208739 9.686438**

**-------------------------------------------------------------------------------**

**. \* Multiple-adjusted rates by sex and diabetes status**

**. poisson MI i.sex##c.age i.sex##c.sbp i.sex##i.smoking i.sex##i.diabetes,irr exp(\_t**

**> )**

**Iteration 0: log likelihood = -31236.028**

**Iteration 1: log likelihood = -31187.484**

**Iteration 2: log likelihood = -31187.443**

**Iteration 3: log likelihood = -31187.443**

**Poisson regression Number of obs = 474,212**

 **LR chi2(11) = 4026.02**

 **Prob > chi2 = 0.0000**

**Log likelihood = -31187.443 Pseudo R2 = 0.0606**

**------------------------------------------------------------------------------**

 **MI | IRR Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex |**

 **1 Male | 17.49334 5.508837 9.09 0.000 9.436707 32.42837**

 **age | 1.069566 .0044098 16.31 0.000 1.060958 1.078244**

 **|**

 **sex#c.age |**

 **1 Male | .9831599 .0046889 -3.56 0.000 .9740125 .9923931**

 **|**

 **sbp | 1.017829 .0013098 13.73 0.000 1.015265 1.020399**

 **|**

 **sex#c.sbp |**

 **1 Male | .995433 .001562 -2.92 0.004 .9923764 .9984991**

 **|**

 **smoking |**

 **1 | 1.305345 .077378 4.50 0.000 1.162166 1.466165**

 **2 | 3.927642 .2670649 20.12 0.000 3.437584 4.487561**

 **|**

 **sex#smoking |**

 **1 Male#1 | .8982616 .0630735 -1.53 0.127 .7827692 1.030794**

 **1 Male#2 | .5948229 .048355 -6.39 0.000 .5072136 .6975647**

 **|**

 **1.diabetes | 2.96852 .2430543 13.29 0.000 2.528401 3.48525**

 **|**

**sex#diabetes |**

 **1 Male#1 | .558077 .0543781 -5.99 0.000 .4610568 .6755131**

 **|**

 **\_cons | .0089949 .0023886 -17.74 0.000 .0053451 .0151369**

 **ln(\_t) | 1 (exposure)**

**------------------------------------------------------------------------------**

**Note: \_cons estimates baseline incidence rate.**

**. margins i.sex#i.diabetes, exp(predict(n)/\_t)**

**Predictive margins Number of obs = 474,212**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------------------------------------**

 **| Delta-method**

 **| Margin Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

**sex#diabetes |**

 **0 Female#0 | 7.987648 .2224028 35.92 0.000 7.551746 8.423549**

 **0 Female#1 | 23.71149 1.83014 12.96 0.000 20.12448 27.2985**

 **1 Male#0 | 22.1283 .3920672 56.44 0.000 21.35986 22.89673**

 **1 Male#1 | 36.65912 1.831037 20.02 0.000 33.07035 40.24789**

**------------------------------------------------------------------------------**

**. margins i.sex#i.diabetes, exp(predict(n)/\_t) contrast (cieffects)**

**Contrasts of predictive margins**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------**

 **| df chi2 P>chi2**

**-------------+----------------------------------**

**sex#diabetes | 1 0.21 0.6493**

**------------------------------------------------**

**-------------------------------------------------------------------------------**

 **| Delta-method**

 **| Contrast Std. Err. [95% Conf. Interval]**

**------------------------------+------------------------------------------------**

 **sex#diabetes |**

**(1 Male vs base) (1 vs base) | -1.193019 2.623924 -6.335815 3.949777**

**-------------------------------------------------------------------------------**

**. \* As another example (not referred to in the text) a similar analysis**

**. \* is done for a variable with 3 levels (smoking status: never/ex/current)**

**. \* which provides two contrasts against the base group (never smoked)**

**. margins i.sex#i.smoking , exp(predict(n)/\_t)**

**Predictive margins Number of obs = 474,212**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------------------------------------**

 **| Delta-method**

 **| Margin Std. Err. z P>|z| [95% Conf. Interval]**

**-------------+----------------------------------------------------------------**

 **sex#smoking |**

 **0 Female#0 | 6.444534 .2492569 25.85 0.000 5.956 6.933069**

 **0 Female#1 | 8.412344 .3797648 22.15 0.000 7.668018 9.156669**

 **0 Female#2 | 25.31182 1.425494 17.76 0.000 22.5179 28.10574**

 **1 Male#0 | 19.29815 .5168352 37.34 0.000 18.28517 20.31113**

 **1 Male#1 | 22.62788 .595442 38.00 0.000 21.46084 23.79493**

 **1 Male#2 | 45.08532 1.619274 27.84 0.000 41.9116 48.25904**

**------------------------------------------------------------------------------**

**. margins i.sex#i.smoking , exp(predict(n)/\_t) contrast (cieffects)**

**Contrasts of predictive margins**

**Model VCE : OIM**

**Expression : predict(n)/\_t**

**------------------------------------------------**

 **| df chi2 P>chi2**

**-------------+----------------------------------**

 **sex#smoking | 2 10.72 0.0047**

**------------------------------------------------**

**-------------------------------------------------------------------------------**

 **| Delta-method**

 **| Contrast Std. Err. [95% Conf. Interval]**

**------------------------------+------------------------------------------------**

 **sex#smoking |**

**(1 Male vs base) (1 vs base) | 1.361927 .9110163 -.4236324 3.147486**

**(1 Male vs base) (2 vs base) | 6.919886 2.226408 2.556206 11.28357**

**-------------------------------------------------------------------------------**

**. \* This illustrates the point that, provided adjusting for all other covariates**

**. \* each time makes sense, we can get a complete set of adjusted sex differences**

**. \* for several risk factors from a single interaction model**

Appendix 3: Copy of the Excel file used to produce the ratio of relative risks, their standard errors and 95% confidence limits, for all the studies in Table 3. Besides the study identifiers, which are reproduced on each page for convenience, items in red and blue were input to Excel and the rest were computed within Excel.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Women** |  |  |  |  |  |  |  |  |
| Study | RRw | RR95LOw | RR95HIw | LnRRw | LnRR95LOw | LnRR95HIw | LnSE1w | LnSE2w | LnSEw |
| Adventist | 2.15 | 1.33 | 3.47 | 0.765468 | 0.285178942 | 1.24415459 | 0.244228 | 0.245045 | 0.244637 |
| APCSC (ANZ) | 2.01 | 1.55 | 2.60 | 0.698135 | 0.438254931 | 0.95551145 | 0.131315 | 0.132592 | 0.131953 |
| APCSC (Asia) | 1.82 | 1.02 | 3.25 | 0.598837 | 0.019802627 | 1.178655 | 0.295826 | 0.295425 | 0.295626 |
| ARIC | 3.16 | 2.64 | 3.78 | 1.150572 | 0.970778917 | 1.32972401 | 0.091404 | 0.091731 | 0.091568 |
| Collins (Indians) | 20.70 | 2.51 | 171.00 | 3.030134 | 0.920282753 | 5.14166356 | 1.077311 | 1.076455 | 1.076883 |
| Collins (Melanesians) | 5.36 | 1.18 | 24.30 | 1.678964 | 0.165514438 | 3.19047635 | 0.77118 | 0.772168 | 0.771674 |
| DECODE | 2.48 | 1.69 | 3.65 | 0.908259 | 0.524728529 | 1.29472717 | 0.197178 | 0.195679 | 0.196428 |
| Dubbo | 1.67 | 1.12 | 2.48 | 0.512824 | 0.113328685 | 0.90825856 | 0.201753 | 0.203824 | 0.202788 |
| EPESE | 3.20 | 1.46 | 7.01 | 1.163151 | 0.378436436 | 1.9473377 | 0.400095 | 0.400364 | 0.40023 |
| Framingham | 5.40 | 2.40 | 12.30 | 1.686399 | 0.875468737 | 2.50959926 | 0.42 | 0.41374 | 0.41687 |
| Hawaii/LA/Hisoshima | 3.29 | 1.79 | 6.55 | 1.190888 | 0.58221562 | 1.87946505 | 0.351315 | 0.310547 | 0.330931 |
| Hisayama | 3.46 | 1.59 | 7.54 | 1.241269 | 0.463734016 | 2.02022218 | 0.397425 | 0.396701 | 0.397063 |
| HUNT I | 2.50 | 2.10 | 2.80 | 0.916291 | 0.741937345 | 1.02961942 | 0.057821 | 0.088956 | 0.073388 |
| Kuopio & N Karelia | 4.89 | 3.84 | 6.24 | 1.587192 | 1.345472367 | 1.83098018 | 0.124382 | 0.123326 | 0.123854 |
| NHANES I | 2.59 | 1.59 | 4.22 | 0.951658 | 0.463734016 | 1.43983513 | 0.24907 | 0.248941 | 0.249005 |
| NHANES III | 2.53 | 1.62 | 3.97 | 0.928219 | 0.482426149 | 1.37876609 | 0.229871 | 0.227445 | 0.228658 |
| Renfrew & Paisley | 1.97 | 1.27 | 3.08 | 0.678034 | 0.2390169 | 1.1249296 | 0.228008 | 0.223988 | 0.225998 |
| Reykjavik | 2.23 | 1.50 | 3.32 | 0.802002 | 0.405465108 | 1.19996478 | 0.203042 | 0.202315 | 0.202678 |
| SHHEC | 3.06 | 2.18 | 4.27 | 1.118415 | 0.779324877 | 1.45161383 | 0.169999 | 0.173005 | 0.171502 |
| Strong | 2.26 | 1.73 | 2.96 | 0.815365 | 0.548121409 | 1.08518927 | 0.137666 | 0.136349 | 0.137007 |
| Takayama | 0.49 | 0.07 | 3.57 | -0.71335 | -2.659260037 | 1.2725656 | 1.013222 | 0.992811 | 1.003017 |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Men** |  |  |  |  |  |  |  |  |
| Study |  | RRm | RR95LOm | RR95HIm | LnRRm | LnRR95LOm | LnRR95HIm | LnSE1m | LnSE2m | LnSEm |
| Adventist |  | 2.11 | 1.12 | 4.00 | 0.746688 | 0.11332869 | 1.3862944 | 0.32633 | 0.323142 | 0.324736 |
| APCSC (ANZ) |  | 1.58 | 1.32 | 1.90 | 0.457425 | 0.27763174 | 0.6418539 | 0.094096 | 0.091731 | 0.092914 |
| APCSC (Asia) |  | 1.47 | 1.15 | 1.88 | 0.385262 | 0.13976194 | 0.6312718 | 0.125515 | 0.125255 | 0.125385 |
| ARIC |  | 2.38 | 2.02 | 2.80 | 0.8671 | 0.70309751 | 1.0296194 | 0.082918 | 0.083675 | 0.083296 |
| Collins (Indians) |  | 3.15 | 1.29 | 7.69 | 1.147402 | 0.25464222 | 2.0399208 | 0.455366 | 0.45549 | 0.455428 |
| Collins (Melanesians) |  | 1.60 | 0.43 | 5.97 | 0.470004 | -0.8439701 | 1.7867469 | 0.671808 | 0.670395 | 0.671101 |
| DECODE |  | 2.09 | 1.55 | 2.82 | 0.737164 | 0.43825493 | 1.0367369 | 0.152843 | 0.152505 | 0.152674 |
| Dubbo |  | 1.53 | 0.99 | 2.37 | 0.425268 | -0.0100503 | 0.86289 | 0.223277 | 0.222101 | 0.222689 |
| EPESE |  | 1.75 | 0.97 | 3.16 | 0.559616 | -0.0304592 | 1.150572 | 0.301508 | 0.301059 | 0.301283 |
| Framingham |  | 6.10 | 3.40 | 10.90 | 1.808289 | 1.22377543 | 2.3887628 | 0.29616 | 0.298221 | 0.297191 |
| Hawaii/LA/Hisoshima |  | 1.54 | 1.03 | 2.25 | 0.431782 | 0.0295588 | 0.8109302 | 0.193443 | 0.205216 | 0.199329 |
| Hisayama |  | 1.26 | 0.67 | 2.35 | 0.231112 | -0.4004776 | 0.8544153 | 0.318012 | 0.322239 | 0.320126 |
| HUNT I |  | 1.80 | 1.60 | 2.10 | 0.587787 | 0.47000363 | 0.7419373 | 0.078648 | 0.060093 | 0.069371 |
| Kuopio & N Karelia |  | 2.11 | 1.70 | 2.63 | 0.746688 | 0.53062825 | 0.9669838 | 0.112396 | 0.110235 | 0.111315 |
| NHANES I |  | 2.37 | 1.55 | 3.62 | 0.86289 | 0.43825493 | 1.286474 | 0.216114 | 0.216651 | 0.216382 |
| NHANES III |  | 1.29 | 0.91 | 1.85 | 0.254642 | -0.0943107 | 0.6151856 | 0.183951 | 0.178037 | 0.180994 |
| Renfrew & Paisley |  | 1.17 | 0.78 | 1.74 | 0.157004 | -0.2484614 | 0.5538851 | 0.20249 | 0.20687 | 0.20468 |
| Reykjavik |  | 1.34 | 0.97 | 1.87 | 0.29267 | -0.0304592 | 0.6259384 | 0.170035 | 0.164862 | 0.167448 |
| SHHEC |  | 2.49 | 1.84 | 3.37 | 0.912283 | 0.60976557 | 1.2149127 | 0.154403 | 0.154345 | 0.154374 |
| Strong |  | 1.66 | 1.30 | 2.12 | 0.506818 | 0.26236426 | 0.7514161 | 0.124795 | 0.124721 | 0.124758 |
| Takayama |  | 2.96 | 1.59 | 5.50 | 1.085189 | 0.46373402 | 1.7047481 | 0.316101 | 0.317069 | 0.316585 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Women compared to men** |  |  |  |
| Study |  | lnRRR | var1+var2 | SElnRRR | RRR | RRR95LO | RRR95HI |
| Adventist |  | 0.01878 | 0.165301 | 0.406572 | 1.02 | 0.46 | 2.26 |
| APCSC (ANZ) |  | 0.24071 | 0.026045 | 0.161383 | 1.27 | 0.93 | 1.75 |
| APCSC (Asia) |  | 0.213574 | 0.103116 | 0.321117 | 1.24 | 0.66 | 2.32 |
| ARIC |  | 0.283472 | 0.015323 | 0.123786 | 1.33 | 1.04 | 1.69 |
| Collins (Indians) |  | 1.882731 | 1.367092 | 1.169227 | 6.57 | 0.66 | 65.00 |
| Collins (Melanesians) |  | 1.20896 | 1.045858 | 1.022672 | 3.35 | 0.45 | 24.86 |
| DECODE |  | 0.171094 | 0.061893 | 0.248784 | 1.19 | 0.73 | 1.93 |
| Dubbo |  | 0.087556 | 0.090713 | 0.301187 | 1.09 | 0.60 | 1.97 |
| EPESE |  | 0.603535 | 0.250956 | 0.500955 | 1.83 | 0.69 | 4.88 |
| Framingham |  | -0.12189 | 0.262103 | 0.51196 | 0.89 | 0.32 | 2.41 |
| Hawaii/LA/Hisoshima |  | 0.759105 | 0.149248 | 0.386326 | 2.14 | 1.00 | 4.56 |
| Hisayama |  | 1.010157 | 0.26014 | 0.510039 | 2.75 | 1.01 | 7.46 |
| HUNT I |  | 0.328504 | 0.010198 | 0.100986 | 1.39 | 1.14 | 1.69 |
| Kuopio & N Karelia |  | 0.840504 | 0.027731 | 0.166526 | 2.32 | 1.67 | 3.21 |
| NHANES I |  | 0.088768 | 0.108825 | 0.329886 | 1.09 | 0.57 | 2.09 |
| NHANES III |  | 0.673577 | 0.085043 | 0.291622 | 1.96 | 1.11 | 3.47 |
| Renfrew & Paisley |  | 0.52103 | 0.092969 | 0.304908 | 1.68 | 0.93 | 3.06 |
| Reykjavik |  | 0.509332 | 0.069118 | 0.262902 | 1.66 | 0.99 | 2.79 |
| SHHEC |  | 0.206132 | 0.053244 | 0.230748 | 1.23 | 0.78 | 1.93 |
| Strong |  | 0.308547 | 0.034336 | 0.185299 | 1.36 | 0.95 | 1.96 |
| Takayama |  | -1.79854 | 1.106269 | 1.051793 | 0.17 | 0.02 | 1.30 |

Appendix 4: Excel file containing three columns from Appendix 3 plus three new columns with ancillary data from the constituent studies, created for submission to Stata (see Appendix 5).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study | lnRRR | SElnRRR | Events | %women | Adjusts |
| Adventist | 0.01878 | 0.406572 | 302 | 55 | PSB+ |
| APCSC (ANZ) | 0.24071 | 0.161383 | 3953 | 31 | PSBL |
| APCSC (Asia) | 0.213574 | 0.321117 | 1195 | 27 | PSBL |
| ARIC | 0.283472 | 0.123786 | 1616 | 42 | PSBL |
| Collins (Indians) | 1.882731 | 1.169227 | NA | NA | PSBL |
| Collins (Melanesians) | 1.20896 | 1.022672 | NA | NA | PSBL |
| DECODE | 0.171094 | 0.248784 | 530 | 34 | PSBL |
| Dubbo | 0.087556 | 0.301187 | 463 | 48 | PBL+ |
| EPESE | 0.603535 | 0.500955 | 230 | 55 | PSB+ |
| Framingham | -0.12189 | 0.51196 | 395 | 29 | PSBL |
| Hawaii/LA/Hisoshima | 0.759105 | 0.386326 | 43 | 33 | PSBL+ |
| Hisayama | 1.010157 | 0.510039 | 171 | 34 | PSBL+ |
| HUNT I | 0.328504 | 0.100986 | 4723 | 39 | PSB+ |
| Kuopio & N Karelia | 0.840504 | 0.166526 | 3039 | 31 | PSBL |
| NHANES I | 0.088768 | 0.329886 | 350 | 36 | PSBL |
| NHANES III | 0.673577 | 0.291622 | 973 | 51 | PSBL |
| Renfrew & Paisley | 0.52103 | 0.304908 | 2357 | 59 | PSBL+ |
| Reykjavik | 0.509332 | 0.262902 | 2406 | 29 | PSBL+ |
| SHHEC | 0.206132 | 0.230748 | 2595 | 39 | PSBL |
| Strong | 0.308547 | 0.185299 | 724 | 52 | PSL+ |
| Takayama | -1.79854 | 1.051793 | 106 | 45 | PSB+ |

Appendix 5: Using Stata to perform meta-analysis and produce a forest plot.

Comments are in blue, and prefixed by an asterisk on every line, commands are in red, and the rest is output.

**. \* First cut and paste the meta data from Excel (see Appendix 4)**

**. \*(6 variables, 21 observations pasted into data editor)**

**. \* define a new variable setting the order for the display (optional)**

**gen order=1/selnrrr**

**. \* Meta-analyse and make the forest plot**

**. metan lnrrr selnrrr,eform randomi lcols(study events women adjusts) effect(RRR) xl**

**> ab(0.3, 0.5,2,5) force texts(140) favours(RR higher for men#RR higher for women) s**

**> ortby(order) nobox scheme(s1color)**

 **Study | ES [95% Conf. Interval] % Weight**

**---------------------+---------------------------------------------------**

**Collins (Indians) | 6.571 0.664 64.999 0.29**

**Takayama | 0.166 0.021 1.301 0.35**

**Collins (Melanesians | 3.350 0.451 24.862 0.37**

**Framingham | 0.885 0.325 2.415 1.43**

**Hisayama | 2.746 1.011 7.462 1.44**

**EPESE | 1.829 0.685 4.881 1.49**

**Adventist | 1.019 0.459 2.261 2.19**

**Hawaii/LA/Hisoshima | 2.136 1.002 4.555 2.41**

**NHANES I | 1.093 0.572 2.086 3.20**

**APCSC (Asia) | 1.238 0.660 2.323 3.35**

**Renfrew & Paisley | 1.684 0.926 3.061 3.67**

**Dubbo | 1.092 0.605 1.970 3.75**

**NHANES III | 1.961 1.107 3.473 3.96**

**Reykjavik | 1.664 0.994 2.786 4.72**

**DECODE | 1.187 0.729 1.932 5.16**

**SHHEC | 1.229 0.782 1.932 5.82**

**Strong | 1.361 0.947 1.958 8.08**

**Kuopio & N Karelia | 2.318 1.672 3.212 9.35**

**APCSC (ANZ) | 1.272 0.927 1.745 9.74**

**ARIC | 1.328 1.042 1.692 13.24**

**HUNT I | 1.389 1.139 1.693 15.99**

**---------------------+---------------------------------------------------**

**D+L pooled ES | 1.440 1.274 1.629 100.00**

**---------------------+---------------------------------------------------**

 **Heterogeneity chi-squared = 25.03 (d.f. = 20) p = 0.200**

 **I-squared (variation in ES attributable to heterogeneity) = 20.1%**

 **Estimate of between-study variance Tau-squared = 0.0145**

 **Test of ES=1 : z= 5.81 p = 0.000**

**.**

**. \* Note that, if required, the p value for the test of the null hypothesis of**

**. \* no sex difference (effect size (ES), RRR = 1) is given as 0.000, i.e. p < 0.001**