Supplementary file

Appendix 1: Medline/Embase/Cinahl/AMED search strategy

Any field
No limitations
1: Randomised control trial (exploded)
2: Double blind (exploded)
3: Single blind (exploded)
4: Placebo (exp)
5: Comparative study (exp)
6: 1 OR 2 OR 3 OR 4 OR 5
7: meta-analysis or systematic review
8: metanalysis exp
9: quantitative review
10: quantitative overview
11: statistical pool
12: 7 or 8 or 9 or 10 or 11
13: Cohort studies exp
14: cohort stud
15: exp prospective studies
16: prospective stud
17: relative risk
18: incidence exp
19: 13 or 14 or 15 or 16 or 17 or 18
20: exp case- control studies
21: case control stud
22: exp retrospective studies
23: retrospective stud
24: exp odds ratio
25: odds ratio
26: 20 or 21 or 22 or 23 or 24 or 25
27: exp cross sectional
28: cross sectional
29: exp risk
30: prevalence exp
31: 27 or 28 or 29 or 30
32: Raynaud Disease
33: Raynaud
34: 32 or 33
35: Epidemiology
36: 19 or 26 or 31 or 35
37: 34 and 36 (incidence or risk or prevalence or epidemiology) and raynauds
38: 32 and 35 (raynauds and epidemiology)
39: 30 and 32 ( prevalence and raynaud disease)
40: 18 and 32 (incidence and raynaud disease)
41: 12 and 33 (systematic review and raynauds disease)
42: 6 and 32 (RCT and Raynauds disease)
PubMed search strategy

#1 Search randomised control trials
#2 Search double blind
#3 Search single blind
#4 Search placebo
#5 Search comparative study
#6 Search (((#1) OR #2) OR #3) OR #4) OR #5
#7 Search meta-analysis
#8 Search systematic review
#9 Search quantitative review
#10 Search quantitative overview
#11 Search statistical pool
#12 Search (((#7) OR #8) OR #9) OR #10) OR #11
#13 Search cohort studies
#14 Search "cohort studies"[All Fields]
#15 Search prospective studies
#16 Search "prospective studies"[All Fields]
#17 Search relative risk
#18 Search incidence
#19 Search (((#13) OR #14) OR #15) OR #16) OR #17) OR #18
#20 Search case control
#21 Search "case control"[All Fields]
#22 Search retrospective studies
#23 Search "retrospective studies"[All Fields]
#24 Search odds ratio
#25 Search "odds ratio"[All Fields]
#26 Search (((#20) OR #21) OR #22) OR #23) OR #24) OR #25
#27 Search cross sectional
#28 Search "cross sectional"[All Fields]
#29 Search risk
#30 Search prevalence
#31 Search (((#27) OR #28) OR #29) OR #30
#33 Search Raynauds Disease
#34 Search Raynaud
#35 Search (#33) OR #34
#36 Search Epidemiology
#37 Search (((#19) OR #26) OR #31) OR #36
#38 Search (#35) AND #37 (incidence or risk or prevalence or epidemiology) and raynauds
#39 Search (#33) AND #36 raynauds and epidemiology
#40 Search (#30) AND #33 prevalence and raynaud disease
#41 Search (#18) AND #33 incidence and raynaud disease
#42 Search (#12) AND #33 systematic review and raynauds disease
#43 Search (#6) AND #33 RCT and Raynauds disease
### Summary meta-analysis for risk factors/associations (Female)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.57</td>
<td>0.344736</td>
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<tr>
<td>8</td>
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<td>0.289061</td>
<td>1.52</td>
<td>4.72</td>
</tr>
<tr>
<td>9</td>
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<td>0.560023</td>
<td>1.69</td>
<td>15.18</td>
</tr>
<tr>
<td>10</td>
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<td>0.25</td>
<td>6.01</td>
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<td>11</td>
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<td>1.22</td>
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<td>12</td>
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<td>0.308414</td>
<td>0.8</td>
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<td>13</td>
<td>0.91</td>
<td>0.380383</td>
<td>0.43</td>
<td>1.91</td>
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<td>14</td>
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<td>1.08</td>
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<td>1.026172</td>
<td>1.01</td>
<td>56.4</td>
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<td>16</td>
<td>1.22</td>
<td>0.206463</td>
<td>0.69</td>
<td>1.55</td>
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<tr>
<td>17</td>
<td>1.44</td>
<td>0.190619</td>
<td>0.99</td>
<td>2.09</td>
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<tr>
<td>18</td>
<td>1.32</td>
<td>0.661326</td>
<td>0.36</td>
<td>4.81</td>
</tr>
</tbody>
</table>

**Fixed effects (inverse variance)**
- Pooled odds ratio = 1.625034 (95% CI = 1.431853 to 1.844279)
- Z (test test odds ratio differs from 1) = 7.519142  P < 0.0001

**Non-combinability of studies**
- Cochran Q = 20.538923 (df = 17)  P = 0.2476
- Moment-based estimate of between studies variance = 0.016185
- I² (inconsistency) = 17.2% (95% CI = 0% to 53%)

**Random effects (DerSimonian-Laird)**
- Pooled odds ratio = 1.647191 (95% CI = 1.424271 to 1.905002)
- Z (test test odds ratio differs from 1) = 6.726861  P < 0.0001

**Bias indicators**
- Begg-Mazumdar: Kendall's tau = 0.215686  P = 0.2291
- Egger: bias = 1.035266 (95% CI = -0.298385 to 2.368917)  P = 0.1193
Summary meta-analysis for risk factors/associations (Female)

Summary meta-analysis plot [fixed effects]

- Sahin 2003: 1.32 (0.36, 4.81)
- Suter 2005: 1.44 (0.99, 2.09)
- Brand 1997: 1.22 (0.69, 1.55)
- Voulgari 2000: 7.55 (1.01, 56.40)
- Smyth 1999: 0.91 (0.43, 1.91)
- Suter 2007: 1.48 (1.08, 2.01)
- Heslop 1983: 2.14 (1.22, 3.75)
- Onbas 2005: 1.46 (0.80, 2.68)
- Purdie 2009: 5.07 (1.69, 15.18)
- Ivona 2001: 1.22 (0.25, 6.01)
- Keil 1991: 2.17 (1.02, 4.62)
- Harada 1991: 2.18 (1.23, 3.86)
- Iwata 1991: 2.67 (1.52, 4.72)
- Smyth 1999: 0.91 (0.43, 1.91)
- Suter 2007: 1.48 (1.08, 2.01)
- Voulgari 2000: 7.55 (1.01, 56.40)
- Brand 1997: 1.22 (0.69, 1.55)
- Suter 2005: 1.44 (0.99, 2.09)
- Sahin 2003: 1.32 (0.36, 4.81)
- combined: 1.63 (1.43, 1.84)
Summary meta-analysis for risk factors/associations (Female)

Summary meta-analysis plot [random effects]

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakir 2008</td>
<td>2.57 (1.31, 5.06)</td>
</tr>
<tr>
<td>De Angelis 2008</td>
<td>1.10 (0.58, 2.09)</td>
</tr>
<tr>
<td>Gallo 1994</td>
<td>1.57 (0.71, 1.88)</td>
</tr>
<tr>
<td>Fraenkel 1999</td>
<td>1.73 (1.17, 2.56)</td>
</tr>
<tr>
<td>Jones 2003</td>
<td>1.54 (1.01, 2.33)</td>
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<tr>
<td>Keil 1991</td>
<td>2.17 (1.02, 4.62)</td>
</tr>
<tr>
<td>Harada 1991</td>
<td>2.18 (1.23, 3.86)</td>
</tr>
<tr>
<td>Iwata 1991</td>
<td>2.67 (1.52, 4.72)</td>
</tr>
<tr>
<td>Purdie 2009</td>
<td>5.07 (1.69, 15.18)</td>
</tr>
<tr>
<td>Ivona 2001</td>
<td>1.22 (0.25, 6.01)</td>
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<td>Heslop 1983</td>
<td>2.14 (1.22, 3.75)</td>
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<tr>
<td>Onbasi 2005</td>
<td>1.46 (0.80, 2.68)</td>
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<tr>
<td>Smyth 1999</td>
<td>0.91 (0.43, 1.91)</td>
</tr>
<tr>
<td>Suter 2007</td>
<td>1.48 (1.08, 2.01)</td>
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<tr>
<td>Voulgari 2000</td>
<td>7.55 (1.01, 56.40)</td>
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<tr>
<td>Brand 1997</td>
<td>1.22 (0.69, 1.55)</td>
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<tr>
<td>Suter 2005</td>
<td>1.44 (0.99, 2.09)</td>
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<tr>
<td>Sahin 2003</td>
<td>1.32 (0.36, 4.81)</td>
</tr>
<tr>
<td>combined</td>
<td>1.65 (1.42, 1.91)</td>
</tr>
</tbody>
</table>
Summary meta-analysis for risk factors/associations (Family history)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>11.8</td>
<td>0.540395</td>
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<td>2</td>
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</tr>
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Fixed effects (inverse variance)
Pooled odds ratio = 16.551505 (95% CI = 7.441944 to 36.81193)
Z (test test odds ratio differs from 1) = 6.881377  P < 0.0001

Non-combinability of studies
Cochran Q = 0.91092  (df = 1)  P = 0.3399
Moment-based estimate of between studies variance = 0
I² (inconsistency) = *%  (95% CI = *% to *%)

Random effects (DerSimonian-Laird)
Pooled odds ratio = 16.551505 (95% CI = 7.441944 to 36.81193)
Z (test test odds ratio differs from 1) = 6.881377  P < 0.0001

Bias indicators
Begg-Mazumdar: Kendall's <too few strata> *
Egger: bias = <too few strata> (95% CI = * to *)  P = *

Summary meta-analysis plot [fixed effects]
Summary meta-analysis for risk factors/associations (Family history)

Summary meta-analysis plot [random effects]

Freedman 1996
11.80 (4.10, 34.10)

Smyth 1999
25.90 (7.66, 87.60)

combined
16.55 (7.44, 36.81)

odds ratio (95% confidence interval)
### Summary meta-analysis for risk factors/associations (marital status)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.79</td>
<td>0.256126</td>
<td>0.48</td>
<td>1.31</td>
</tr>
<tr>
<td>2</td>
<td>0.49</td>
<td>0.217288</td>
<td>0.32</td>
<td>0.75</td>
</tr>
<tr>
<td>3</td>
<td>0.39</td>
<td>0.448991</td>
<td>0.16</td>
<td>0.93</td>
</tr>
<tr>
<td>4</td>
<td>0.87</td>
<td>0.453522</td>
<td>0.36</td>
<td>2.13</td>
</tr>
</tbody>
</table>

**Fixed effects (inverse variance)**
- Pooled odds ratio = 0.594495 (95% CI = 0.445635 to 0.793078)
- Z (test test odds ratio differs from 1) = -3.536538  P = 0.0004

**Non-combinability of studies**
- Cochran Q = 3.61024  (df = 3)  P = 0.3067
- Moment-based estimate of between studies variance = 0.020022
- I² (inconsistency) = 16.9% (95% CI = 0% to 73%)

**Random effects (DerSimonian-Laird)**
- Pooled odds ratio = 0.598367 (95% CI = 0.430621 to 0.831457)
- Z (test test odds ratio differs from 1) = -3.059622  P = 0.0022

**Bias indicators**
- Begg-Mazumdar: Kendall's tau = 0.333333  P = 0.75 (low power)
- Egger: bias = 0.318768 (95% CI = -9.008236 to 9.645771)  P = 0.8966
Summary meta-analysis for risk factors/associations (marital status)

Summary meta-analysis plot [fixed effects]

De Angelis 2008
0.79 (0.48, 1.31)

Fraenkel 1999
0.49 (0.32, 0.75)

Keil 1991
0.39 (0.16, 0.93)

Voulgari 2000
0.87 (0.36, 2.13)

combined
0.59 (0.45, 0.79)

Summary meta-analysis plot [random effects]

De Angelis 2008
0.79 (0.48, 1.31)

Fraenkel 1999
0.49 (0.32, 0.75)

Keil 1991
0.39 (0.16, 0.93)

Voulgari 2000
0.87 (0.36, 2.13)

combined
0.60 (0.43, 0.83)
## Summary meta-analysis for risk factors/associations (smoking)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
<th>Study</th>
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<tbody>
<tr>
<td>1</td>
<td>2.03</td>
<td>0.28827</td>
<td>1.15</td>
<td>3.56</td>
<td>Cakir 2008</td>
</tr>
<tr>
<td>2</td>
<td>1.01</td>
<td>0.198398</td>
<td>0.68</td>
<td>1.48</td>
<td>Fraenkel 1999</td>
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<td>3</td>
<td>1.86</td>
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<td>3.88</td>
<td>Keil 1991</td>
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<td>4</td>
<td>2.21</td>
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<td>0.69</td>
<td>7.15</td>
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<td>5</td>
<td>1.31</td>
<td>0.196141</td>
<td>0.89</td>
<td>1.92</td>
<td>Suter 2005</td>
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<td>6</td>
<td>0.81</td>
<td>0.311168</td>
<td>0.44</td>
<td>1.49</td>
<td>Smyth 1999</td>
</tr>
<tr>
<td>7</td>
<td>1.3</td>
<td>0.167147</td>
<td>0.94</td>
<td>1.81</td>
<td>Suter 2007</td>
</tr>
<tr>
<td>8</td>
<td>1.28</td>
<td>0.709785</td>
<td>0.32</td>
<td>5.17</td>
<td>O'Keefe 1993</td>
</tr>
<tr>
<td>9</td>
<td>0.86</td>
<td>0.539871</td>
<td>0.3</td>
<td>2.49</td>
<td>O'Keefe 1992</td>
</tr>
</tbody>
</table>

**Fixed effects (inverse variance)**

- Pooled odds ratio = 1.267571 (95% CI = 1.063649 to 1.510589)
- Z (test test odds ratio differs from 1) = 2.649493  P = 0.0081

**Non-combinability of studies**

- Cochran Q = 8.529249  (df = 8)  P = 0.3835
- Moment-based estimate of between studies variance = 0.005218
- I² (inconsistency) = 6.2% (95% CI = 0% to 57.1%)

**Random effects (DerSimonian-Laird)**

- Pooled odds ratio = 1.27026 (95% CI = 1.055109 to 1.529283)
- Z (test test odds ratio differs from 1) = 2.526517  P = 0.0115

**Bias indicators**

- Begg-Mazumdar: Kendall's tau = 0  P = 0.9195 (low power)
- Egger: bias = 0.386133 (95% CI = -1.650354 to 2.422619)  P = 0.6674

![Bias assessment plot](image)
Summary meta-analysis for risk factors/associations (smoking)

Summary meta-analysis plot [fixed effects]

Summary meta-analysis plot [random effects]
Summary meta-analysis for risk factors/associations (alcohol)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.08</td>
<td>0.154629</td>
<td>0.06 - 0.11</td>
<td>75.389314 - 50.30415</td>
</tr>
<tr>
<td>2</td>
<td>1.38</td>
<td>0.270636</td>
<td>0.81 - 2.34</td>
<td>24.610686 - 49.69585</td>
</tr>
</tbody>
</table>

Fixed effects (inverse variance)
Pooled odds ratio = 0.16124 (95% CI = 0.123934 to 0.209775)
Z (test test odds ratio differs from 1) = -13.592001  P < 0.0001

Non-combinability of studies
Cochran Q = 83.476205  (df = 1)  P < 0.0001
Moment-based estimate of between studies variance = 4.00644
I² (inconsistency) = *%  (95% CI = *% to *%)

Random effects (DerSimonian-Laird)
Pooled odds ratio = 0.329399 (95% CI = 0.020217 to 5.366998)
Z (test test odds ratio differs from 1) = -0.7799  P = 0.4354

Bias indicators
Begg-Mazumdar: Kendall's <too few strata> *
Egger: bias = <too few strata> (95% CI = * to *)  P = *

Summary meta-analysis plot [fixed effects]
Summary meta-analysis for risk factors/associations (alcohol)

Summary meta-analysis plot [random effects]

Suter 2007
0.08 (0.06, 0.11)

Fraenkel 1999
1.38 (0.81, 2.34)

combined
0.33 (0.02, 5.37)

odds ratio (95% confidence interval)
Summary meta-analysis for risk factors/associations (migraine)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.29</td>
<td>0.482176</td>
<td>0.5</td>
<td>3.31</td>
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<td>2</td>
<td>5.25</td>
<td>0.446385</td>
<td>2.19</td>
<td>12.6</td>
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<tr>
<td>3</td>
<td>5.4</td>
<td>0.332283</td>
<td>2.8</td>
<td>10.3</td>
</tr>
<tr>
<td>4</td>
<td>4.38</td>
<td>0.482538</td>
<td>1.7</td>
<td>11.27</td>
</tr>
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<td>5</td>
<td>3.46</td>
<td>0.409258</td>
<td>1.55</td>
<td>7.71</td>
</tr>
<tr>
<td>6</td>
<td>6.23</td>
<td>0.449394</td>
<td>2.58</td>
<td>15.02</td>
</tr>
</tbody>
</table>

Fixed effects (inverse variance)
Pooled odds ratio = 4.112672 (95% CI = 2.932674 to 5.767458)
Z (test test odds ratio differs from 1) = 8.195956  P < 0.0001

Non-combinability of studies
Cochran Q = 7.802203  (df = 5)  P = 0.1675
Moment-based estimate of between studies variance = 0.101857
I² (inconsistency) = 35.9% (95% CI = 0% to 73.6%)

Random effects (DerSimonian-Laird)
Pooled odds ratio = 4.023554 (95% CI = 2.623783 to 6.170096)
Z (test test odds ratio differs from 1) = 6.381951  P < 0.0001

Bias indicators
Begg-Mazumdar: Kendall's tau = -0.2  P = 0.4694 (low power)
Egger: bias = -3.637628 (95% CI = -14.093988 to 6.818732)  P = 0.3888
Summary meta-analysis for risk factors/associations (migraine)

Summary meta-analysis plot [fixed effects]

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakir 2008</td>
<td>1.29 (0.50, 3.31)</td>
</tr>
<tr>
<td>Zahavi 1984</td>
<td>5.25 (2.19, 12.60)</td>
</tr>
<tr>
<td>O'Keefe 1992</td>
<td>5.40 (2.80, 10.30)</td>
</tr>
<tr>
<td>O'Keefe 1993</td>
<td>4.38 (1.70, 11.27)</td>
</tr>
<tr>
<td>Voulgari 2000</td>
<td>3.46 (1.55, 7.71)</td>
</tr>
<tr>
<td>Smyth 1999</td>
<td>6.23 (2.58, 15.02)</td>
</tr>
<tr>
<td>combined</td>
<td>4.11 (2.93, 5.77)</td>
</tr>
</tbody>
</table>

Summary meta-analysis plot [random effects]

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakir 2008</td>
<td>1.29 (0.50, 3.31)</td>
</tr>
<tr>
<td>Zahavi 1984</td>
<td>5.25 (2.19, 12.60)</td>
</tr>
<tr>
<td>O'Keefe 1992</td>
<td>5.40 (2.80, 10.30)</td>
</tr>
<tr>
<td>O'Keefe 1993</td>
<td>4.38 (1.70, 11.27)</td>
</tr>
<tr>
<td>Voulgari 2000</td>
<td>3.46 (1.55, 7.71)</td>
</tr>
<tr>
<td>Smyth 1999</td>
<td>6.23 (2.58, 15.02)</td>
</tr>
<tr>
<td>combined</td>
<td>4.02 (2.62, 6.17)</td>
</tr>
</tbody>
</table>
Summary meta-analysis for risk factors/associations (hypertension)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.96</td>
<td>0.208639</td>
<td>0.64 1.45</td>
<td>92.742301 92.742301</td>
</tr>
<tr>
<td>2</td>
<td>1.70</td>
<td>0.745822</td>
<td>0.395 7.35</td>
<td>7.257699 7.257699</td>
</tr>
</tbody>
</table>

Fraenkel 1999
O Keeffe 1992

Fixed effects (inverse variance)
Pooled odds ratio = 1.000652 (95% CI = 0.674925 to 1.483581)
Z (test test odds ratio differs from 1) = 0.003246 P = 0.9974

Non-combinability of studies
Cochran Q = 0.544457 (df = 1) P = 0.4606
Moment-based estimate of between studies variance = 0
I² (inconsistency) = "% (95% CI = "% to ")

Random effects (DerSimonian-Laird)
Pooled odds ratio = 1.000652 (95% CI = 0.674925 to 1.483581)
Z (test test odds ratio differs from 1) = 0.003246 P = 0.9974

Bias indicators
Begg-Mazumdar: Kendall's <too few strata> *
Egger: bias = <too few strata> (95% CI = * to * ) P = *

Summary meta-analysis plot [fixed effects]
Summary meta-analysis for risk factors/associations (hypertension)

Summary meta-analysis plot [random effects]

- Fraenkel 1999: 0.96 (0.64, 1.45)
- O'Keefe 1992: 1.70 (0.40, 7.35)
- Combined: 1.00 (0.67, 1.48)

Odds ratio (95% confidence interval)
Summary meta-analysis for risk factors/associations (Helicobacter Pylori)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.13</td>
<td>0.764231</td>
<td>0.03</td>
<td>0.6</td>
</tr>
<tr>
<td>2</td>
<td>0.71</td>
<td>0.561705</td>
<td>0.24</td>
<td>2.17</td>
</tr>
</tbody>
</table>

Fixed effects (inverse variance)
- Pooled odds ratio = 0.391428 (95% CI = 0.161211 to 0.950406)
- Z (test test odds ratio differs from 1) = -2.072351  P = 0.0382

Non-combinability of studies
- Cochran Q = 3.204101  (df = 1)  P = 0.0735
- Moment-based estimate of between studies variance = 0.991363
  I² (inconsistency) = % (95% CI = % to %)

Random effects (DerSimonian-Laird)
- Pooled odds ratio = 0.328812 (95% CI = 0.062739 to 1.723299)
- Z (test test odds ratio differs from 1) = -1.316025  P = 0.1882

Bias indicators
- Begg-Mazumdar: Kendall's <too few strata>*
- Egger: bias = <too few strata> (95% CI = * to *)  P = *

Summary meta-analysis plot [fixed effects]
Summary meta-analysis for risk factors/associations (Helicobacter Pylori)

Summary meta-analysis plot [random effects]

- Savasino 2000: 0.13 (0.03, 0.60)
- Herve 2006: 0.71 (0.24, 2.17)
- Combined: 0.33 (0.06, 1.72)

odds ratio (95% confidence interval)
Summary meta-analysis for risk factors/associations (oral contraceptive pill)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.63</td>
<td>0.694011</td>
<td>0.16</td>
<td>2.43</td>
</tr>
<tr>
<td>2</td>
<td>0.71</td>
<td>0.410578</td>
<td>0.32</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Odds Ratio 0.688333 (95% CI = 0.344357 to 1.375903)
Z (test test odds ratio differs from 1) = -1.056916  P = 0.2905

Non-combinability of studies
Cochran Q = 0.021979  (df = 1)  P = 0.8821
Moment-based estimate of between studies variance = 0
I² (inconsistency) = *%  (95% CI = *% to *%)

Random effects (DerSimonian-Laird)
Odds Ratio 0.688333 (95% CI = 0.344357 to 1.375903)
Z (test test odds ratio differs from 1) = -1.056916  P = 0.2905

Bias indicators
Begg-Mazumdar: Kendall's <too few strata>  *
Egger: bias = <too few strata> (95% CI = * to *)  P = *

Summary meta-analysis plot [fixed effects]
Summary meta-analysis for risk factors/associations (oral contraceptive pill)

Summary meta-analysis plot [random effects]

O'Keefe 1993
0.63 (0.16, 2.43)

O'Keefe 1992
0.71 (0.32, 1.60)

combined
0.69 (0.34, 1.38)

odds ratio (95% confidence interval)
Summary meta-analysis for risk factors/associations (Oestrogren replacement therapy)

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Odds Ratio</th>
<th>SE</th>
<th>Approximate 95% CI</th>
<th>% Weight (fixed, random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.21</td>
<td>0.342108</td>
<td>1.13</td>
<td>4.32</td>
</tr>
<tr>
<td>2</td>
<td>2.50</td>
<td>0.378932</td>
<td>1.2</td>
<td>5.3</td>
</tr>
</tbody>
</table>

**Fixed effects (inverse variance)**

Pooled odds ratio = 2.335815 (95% CI = 1.420015 to 3.842238)

Z (test test odds ratio differs from 1) = 3.340923 P = 0.0008

**Non-combinability of studies**

Cochran Q = 0.05833 (df = 1) P = 0.8092

Moment-based estimate of between studies variance = 0

I² (inconsistency) = *% (95% CI = *% to *%)

**Random effects (DerSimonian-Laird)**

Pooled odds ratio = 2.335815 (95% CI = 1.420015 to 3.842238)

Z (test test odds ratio differs from 1) = 3.340923 P = 0.0008

**Bias indicators**

Begg-Mazumdar: Kendall's <too few strata> *

Egger: bias = <too few strata> (95% CI = * to *) P = *

Summary meta-analysis plot (fixed effects)

odds ratio (95% confidence interval)
Summary meta-analysis for risk factors/associations (Oestrogren replacement therapy)

Summary meta-analysis plot [random effects]

1 2 5 10
combined 2.34 (1.42, 3.84)
442 2.50 (1.20, 5.30)
800 2.21 (1.13, 4.32)

odds ratio (95% confidence interval)