

**Table S1: Search strategy**

|                                     |                                                                                                      |
|-------------------------------------|------------------------------------------------------------------------------------------------------|
| <b>Responsible searcher: Kunath</b> |                                                                                                      |
| <b>Last searched: 07.04.2012</b>    |                                                                                                      |
| <b>Medline (Ovid)</b>               |                                                                                                      |
| 1                                   | Prostatic Neoplasms/                                                                                 |
| 2                                   | (prostat* adj3 (cancer* or tumor* or neoplas* or carcinom* or malign*)).tw.                          |
| 3                                   | Gynecomastia/                                                                                        |
| 4                                   | (breast* adj3 (pain* or tenderness* or swelling* or enlarg*)).tw.                                    |
| 5                                   | (gynecomast* or gynaecomast* or mastodyn*).mp.                                                       |
| 6                                   | Tamoxifen/                                                                                           |
| 7                                   | (Tamoxifen* or Soltamox* or Tomaxithen* or Nolvadex* or ICI 47699* or ICI 46474* or ICI 46,474*).mp. |
| 8                                   | 1 or 2                                                                                               |
| 9                                   | 3 or 4 or 5                                                                                          |
| 10                                  | 6 or 7                                                                                               |
| 11                                  | 8 and 9 and 10                                                                                       |
| <b>Embase</b>                       |                                                                                                      |
| 1                                   | CT=("PROSTATE TUMOR"; "PROSTATE CANCER"; "PROSTATE ADENOCARCINOMA"; "PROSTATE CARCINOMA")            |
| 2                                   | (prostat* and (cancer* or tumor* or neoplas* or carcinom* or malign*))/same sent                     |
| 3                                   | CT="GYNECOMASTIA"                                                                                    |
| 4                                   | (breast* and (pain* or tenderness* or swelling* or enlarg*))/same sent                               |
| 5                                   | (gynecomast* or gynaecomast* or mastodyn*)/ same sent                                                |
| 6                                   | CT="TAMOXIFEN"                                                                                       |
| 7                                   | (tamoxifen* or soltamox* or tomoxithen* or nolvadex*)/same sent                                      |
| 8                                   | 1 OR 2                                                                                               |
| 9                                   | 3 OR 4 OR 5                                                                                          |
| 10                                  | 6 OR 7                                                                                               |
| 11                                  | 8 AND 9 AND 10                                                                                       |
| <b>Cochrane Library</b>             |                                                                                                      |
| 1                                   | MeSH descriptor Prostatic Neoplasms explode all trees                                                |
| 2                                   | (prostat* NEAR/3 (cancer* or tumor* or neoplas* or carcinom* or malign*))                            |
| 3                                   | MeSH descriptor Gynecomastia explode all trees                                                       |
| 4                                   | (breast* NEAR/3 (pain* OR tenderness* OR swelling* OR enlarg*))                                      |
| 5                                   | MeSH descriptor Tamoxifen explode all trees                                                          |
| 6                                   | (tamoxifen* OR soltamox* OR tomoxithen* OR nolvadex*)                                                |
| 7                                   | (gynecomast* or gynaecomast* or mastodyn*)                                                           |
| 8                                   | (1 OR 2)                                                                                             |
| 9                                   | (3 OR 4 OR 5)                                                                                        |
| 10                                  | (6 OR 7)                                                                                             |
| 11                                  | (8 AND 9 AND 10)                                                                                     |

**Table S2: Adverse events: Tamoxifen (10 or 20 mg daily) vs. no additional therapy or placebo**

| Outcome                               | Studies                                      | Participants (N=) | Risk Ratio (M-H, Fixed, 95% CI), I <sup>2</sup> |
|---------------------------------------|----------------------------------------------|-------------------|-------------------------------------------------|
| discontinuation due to adverse events | Fradet 2007, Saltzstein 2005                 | 166               | 0.92 (0.38-2.23), 28%                           |
| total adverse events                  | Boccardo 2005                                | 77                | 0.94 (0.52, 1.70), -                            |
| serious adverse events                | Boccardo 2005, Saltzstein 2005               | 148               | 1.07 (0.33, 3.49), 0%                           |
| rash                                  | Boccardo 2005, Saltzstein 2005, Perdona 2005 | 249               | 0.64 (0.25, 1.61), 0%                           |
| fever                                 | Boccardo 2005, Perdona 2005                  | 178               | 4.21 (0.48, 36.76), 0%                          |
| neurologic events                     | Boccardo 2005, Perdona 2005                  | 178               | 0.79 (0.18, 3.47), 9%                           |
| cardiovascular events                 | Boccardo 2005, Perdona 2005                  | 178               | 1.06 (0.35, 3.15), 0%                           |
| respiratory events                    | Boccardo 2005                                | 77                | 3.24 (0.14, 77.06), -                           |
| intercurrent infections               | Boccardo 2005                                | 77                | 2.16 (0.20, 22.86), -                           |
| myelotoxicity                         | Boccardo 2005, Perdona 2005                  | 178               | 0.35 (0.04, 3.30), 0%                           |
| hot flashes                           | Boccardo 2005, Perdona 2005, Fradet 2007     | 273               | 1.70 (0.75, 3.86), 0%                           |
| breast pain                           | Saltzstein 2005                              | 71                | 0.88 (0.74, 1.04), -                            |
| gynecomastia                          | Saltzstein 2005                              | 71                | 0.77 (0.52, 1.15), -                            |
| pharyngitis                           | Saltzstein 2005, Fradet 2007                 | 166               | 1.00 (0.41, 2.44), 0%                           |
| vasodilation                          | Saltzstein 2005                              | 71                | 2.57 (0.53, 12.39), -                           |
| accidental injury                     | Saltzstein 2005                              | 71                | 3.09 (0.34, 28.26), -                           |
| asthenia                              | Fradet 2007, Saltzstein 2005, Perdona 2005   | 267               | 0.62 (0.27, 1.39), 0%                           |
| back pain                             | Saltzstein 2005                              | 71                | 7.19 (0.39, 134.39), -                          |
| dizziness                             | Saltzstein 2005, Fradet 2007                 | 166               | 2.93 (0.91, 9.43), 0%                           |
| sinusitis                             | Saltzstein 2005                              | 71                | 7.19 (0.39, 134.39), -                          |
| constipation                          | Saltzstein 2005, Perdona 2005, Fradet 2007   | 267               | 0.98 (0.42, 2.29), 21%                          |
| decreased libido                      | Saltzstein 2005                              | 71                | 2.06 (0.20, 21.68), -                           |
| diarrhea                              | Saltzstein 2005, Perdona 2005, Fradet 2007   | 267               | 1.62 (0.63, 4.16), 0%                           |
| dyspnea                               | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| gastritis                             | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| nausea                                | Saltzstein 2005                              | 71                | 0.69 (0.12, 3.86), -                            |
| pain                                  | Saltzstein 2005                              | 71                | 1.03 (0.15, 6.90), -                            |
| pelvic pain                           | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| periodontal abscess                   | Saltzstein 2005                              | 71                | 2.06 (0.20, 21.68), -                           |
| Pruritus                              | Saltzstein 2005, Perdona 2005                | 172               | 3.07 (0.64, 14.81), 0%                          |
| somnolence                            | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| urinary frequency                     | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| urinary retention                     | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| urinary tract disorder                | Saltzstein 2005                              | 71                | 2.06 (0.20, 21.68), -                           |
| urinary urgency                       | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| vomiting                              | Saltzstein 2005                              | 71                | 5.14 (0.26, 103.37), -                          |
| abdominal pain                        | Saltzstein 2005                              | 71                | 3.08 (0.13, 73.23), -                           |
| paresthesia                           | Saltzstein 2005                              | 71                | 0.51 (0.05, 5.42), -                            |
| urinary tract infection               | Saltzstein 2005                              | 71                | 3.08 (0.13, 73.23), -                           |
| dry skin                              | Saltzstein 2005                              | 71                | 0.21 (0.01, 4.13), -                            |
| hypercholesterolemia                  | Saltzstein 2005                              | 71                | 0.15 (0.01, 2.74), -                            |
| hypertension                          | Saltzstein 2005                              | 71                | 0.21 (0.01, 4.13), -                            |
| peripheral edema                      | Saltzstein 2005                              | 71                | 0.21 (0.01, 4.13), -                            |
| urticaria                             | Saltzstein 2005                              | 71                | 0.21 (0.01, 4.13), -                            |
| anemia                                | Perdona 2005                                 | 101               | 3.06 (0.13, 73.35), -                           |
| erectile dysfunction                  | Fradet 2007                                  | 95                | 0.86 (0.08, 9.11), -                            |

**Table S3: Adverse events: Tamoxifen (20 mg daily) vs. anastrozole (1 mg daily)**

| Outcome                               | Studies                        | Participants (N=) | Risk Ratio (M-H, Fixed, 95% CI), I <sup>2</sup> |
|---------------------------------------|--------------------------------|-------------------|-------------------------------------------------|
| discontinuation due to adverse events | Saltzstein 2005                | 71                | 0.86 (0.29-2.55), -                             |
| total adverse events                  | Boccardo 2005                  | 73                | 0.51 (0.31, 0.82), -                            |
| serious adverse events                | Saltzstein 2005, Boccardo 2005 | 144               | 0.82 (0.27, 2.52), 0%                           |
| rash                                  | Saltzstein 2005, Boccardo 2005 | 144               | 1.01 (0.29, 3.56), 47%                          |
| fever                                 | Boccardo 2005                  | 73                | 1.95 (0.18, 20.53), -                           |
| neurologic events                     | Boccardo 2005                  | 73                | 0.16 (0.02, 1.28), -                            |
| cardiovascular events                 | Boccardo 2005                  | 73                | 0.49 (0.13, 1.80), -                            |
| respiratory events                    | Boccardo 2005                  | 73                | 0.97 (0.06, 14.97), -                           |
| intercurrent infections               | Boccardo 2005                  | 73                | 0.49 (0.09, 2.49), -                            |
| myelotoxicity                         | Boccardo 2005                  | 73                | 0.14 (0.01, 2.60), -                            |
| hot flashes                           | Boccardo 2005                  | 73                | 0.97 (0.06, 14.97), -                           |
| breast pain                           | Saltzstein 2005                | 71                | 0.88 (0.74, 1.04), -                            |
| gynecomastia                          | Saltzstein 2005                | 71                | 0.80 (0.54, 1.21), -                            |
| pharyngitis                           | Saltzstein 2005                | 71                | 2.06 (0.56, 7.59), -                            |
| vasodilation                          | Saltzstein 2005                | 71                | 1.71 (0.44, 6.64), -                            |
| accidental injury                     | Saltzstein 2005                | 71                | 7.19 (0.39, 134.39), -                          |
| asthenia                              | Saltzstein 2005                | 71                | 0.77 (0.19, 3.20), -                            |
| back pain                             | Saltzstein 2005                | 71                | 1.03 (0.22, 4.76), -                            |
| dizziness                             | Saltzstein 2005                | 71                | 3.09 (0.34, 28.26), -                           |
| sinusitis                             | Saltzstein 2005                | 71                | 3.09 (0.34, 28.26), -                           |
| constipation                          | Saltzstein 2005                | 71                | 0.69 (0.12, 3.86), -                            |
| decreased libido                      | Saltzstein 2005                | 71                | 2.06 (0.20, 21.68), -                           |
| diarrhea                              | Saltzstein 2005                | 71                | 2.06 (0.20, 21.68), -                           |
| dyspnea                               | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| gastritis                             | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| nausea                                | Saltzstein 2005                | 71                | 2.06 (0.20, 21.68), -                           |
| pain                                  | Saltzstein 2005                | 71                | 1.03 (0.15, 6.90), -                            |
| periodontal abscess                   | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| pruritus                              | Saltzstein 2005                | 71                | 2.06 (0.20, 21.68), -                           |
| somnolence                            | Saltzstein 2005                | 71                | 1.03 (0.15, 6.90), -                            |
| urinary frequency                     | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| urinary retention                     | Saltzstein 2005                | 71                | 2.06 (0.20, 21.68), -                           |
| urinary tract disorder                | Saltzstein 2005                | 71                | 1.03 (0.15, 6.90), -                            |
| urinary urgency                       | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| vomiting                              | Saltzstein 2005                | 71                | 5.14 (0.26, 103.37), -                          |
| abdominal pain                        | Saltzstein 2005                | 71                | 0.51 (0.05, 5.42), -                            |
| paresthesia                           | Saltzstein 2005                | 71                | 1.03 (0.07, 15.81), -                           |
| urinary tract infection               | Saltzstein 2005                | 71                | 0.34 (0.04, 3.14), -                            |
| increased cough                       | Saltzstein 2005                | 71                | 0.15 (0.01, 2.74), -                            |
| peripheral edema                      | Saltzstein 2005                | 71                | 0.34 (0.01, 8.14), -                            |

**Table S4: Adverse events: Tamoxifen (10 mg daily) vs. radiotherapy (single fraction of 12 Gy)**

| Outcome               | Studies      | Participants (N=) | Risk Ratio (M-H, Fixed, 95% CI), I <sup>2</sup> |
|-----------------------|--------------|-------------------|-------------------------------------------------|
| nipple erythema       | Perdona 2005 | 100               | 0.11 (0.03, 0.43), -                            |
| skin irritation       | Perdona 2005 | 100               | 0.03 (0.00, 0.41), -                            |
| pruritus              | Perdona 2005 | 100               | 2.00 (0.38, 10.43), -                           |
| anemia                | Perdona 2005 | 100               | 3.00 (0.13, 71.92), -                           |
| fever                 | Perdona 2005 | 100               | 1.00 (0.06, 15.55), -                           |
| myelotoxicity         | Perdona 2005 | 100               | 0.20 (0.01, 4.06), -                            |
| asthenia              | Perdona 2005 | 100               | 0.40 (0.08, 1.97), -                            |
| cardiovascular events | Perdona 2005 | 100               | 1.50 (0.26, 8.60), -                            |
| neurological events   | Perdona 2005 | 100               | 2.00 (0.19, 21.36), -                           |
| constipation          | Perdona 2005 | 100               | 1.25 (0.36, 4.38), -                            |
| diarrhea              | Perdona 2005 | 100               | 2.00 (0.38, 10.43), -                           |
| hot flashes           | Perdona 2005 | 100               | 1.50 (0.26, 8.60), -                            |