

The Cochrane Breast Cancer Group (CBCG)

Newsletter

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What's New

Continued funding from the Australian Department of Health and Ageing

The CBCG is pleased to announce that a further 12 months of infrastructure funding support has been received from the Australian Department of Health and Ageing.

The CBCG moves to RevMan5

In accordance with Cochrane Collaboration policy, the Breast Cancer Group has moved over to the Collaboration's new system for developing and publishing systematic reviews. This incorporates RevMan5 software for review production and Archie, the Cochrane Collaboration central server, for storing and publishing protocols and reviews. A major feature of Archie is that authors now check their reviews in and out using RevMan5 while they are working on them, and also use this server to submit reviews for editorial approval.

In the months between the release of Revman5 in March 2008 and completion of rollout in November 2008, all 35 reviews and 16 protocols registered with the Breast Cancer

Group were converted to Revman5, checked and re-published on The Cochrane Library. Thanks to all authors who provided assistance with this process.

Additional information and tips for authors regarding the new process can be found on pages 5 & 6.

Seeking volunteers to search conference proceedings in breast cancer

The CBCG is currently looking for volunteers who would be interested in searching on-line conference proceedings in breast cancer. The purpose of this activity is to identify relevant trials presented at major conferences and add these to the Specialised Register in Breast Cancer.

Suitable volunteers will need access to a computer, the internet and email. They will also need to have access to a bibliographic software program such as Reference Manager or EndNote, and be proficient with its use.

Volunteers will work at their own pace and in their own time. Some initial instruction and self-guided training resources will be provided. If you are interested, please contact Fergus Tai on ftai@ctc.usyd.edu.au.

Since our last newsletter, three new reviews in breast cancer have been published in The Cochrane Library

Fraction size in radiation treatment for breast conservation in early breast cancer (Issue 3, 2008)

LHRH agonists for adjuvant therapy of early breast cancer in premenopausal women (Issue 4, 2008)

Post operative radiotherapy for ductal carcinoma in situ of the breast Issue 1, 2009)

Full details can be found on pages 2-4



On The Cochrane Library

New Review

James ML, Lehman M, Hider PN, Jeffery M, Francis DP, Hickey BE. Fraction size in radiation treatment for breast conservation in early breast cancer. *Cochrane Database of Systematic Reviews* 2008, Issue 3. Art. No.: CD003860. DOI: 10.1002/14651858.CD003860.pub2.

Background:

Shortening the duration of radiation therapy would benefit women with early breast cancer treated with breast conservation. It may also improve access to radiation therapy by improving efficiency in radiation oncology departments globally. This can only happen if the shorter treatment is as effective and safe as conventional radiation therapy

Objectives:

To assess the effects of altered fraction size on women with early breast cancer who have undergone breast conserving surgery.

Search strategy:

We searched the Cochrane Breast Cancer Group Specialised Register (June 2006), MEDLINE (November 2006), EMBASE (November 2006), reference lists for articles, and relevant conference proceedings. No language constraints were applied.

Selection criteria:

Randomised controlled trials of unconventional versus conventional fractionation in women with early breast cancer who had undergone breast conserving surgery.

Data collection and analysis:

Data extraction was performed independently by the authors with disagreements resolved by discussion. Missing data was sought by contacting the authors concerned

Main results:

Two trials were included and reported on 2644 women. The women were highly selected with node negative tumours smaller than 5 cm and negative pathological margins; 46% of the women had a cup separation size of less than 25 cm. The studies were of high quality. Data for local recurrence and breast appearance were not available in a form which could be combined. Unconventional fractionation (delivering radiation therapy in larger amounts each day but over fewer days than with conventional fractionation) did not appear to affect: (1) local-recurrence free survival (absolute difference 0.4%, 95% CI -1.5% to 2.4%), (2) breast appearance (risk ratio (RR) 1.01, 95% CI 0.88 to 1.17; P = 0.86), (3) survival at five years (RR 0.97, 95% CI 0.78 to 1.19; P = 0.75), (4) late skin toxicity at five years (RR 0.99, 95% CI 0.44 to 2.22; P = 0.98, or (5) late radiation toxicity in sub-cutaneous tissue (RR 1.0, 95% CI 0.78 to 1.28; P = 0.99).

Authors conclusions:

We have evidence from two high quality randomised trials that the use of unconventional fractionation regimes (greater than 2 Gy per fraction) does not affect breast appearance or toxicity and does not seem to affect local recurrence for selected women treated with breast conserving therapy. These are women with node negative tumours smaller than 5 cm and negative pathological margins. Two new trials have been published in March 2008. Their results are consistent with our findings. The results of these trials will be incorporated in the next update of this review.

New Review

Sharma R, Hamilton A, Beith J. LHRH agonists for adjuvant therapy of early breast cancer in premenopausal women. *Cochrane Database of Systematic Reviews* 2008, Issue 4. Art. No.: CD004562. DOI: 10.1002/14651858.CD004562.pub3.

Background:

Approximately 60% of breast cancer tumours in premenopausal women are hormone sensitive (ER+). These patients may be suitable for hormonal treatment. The goal of hormonal therapy is to reduce the

Continued from Page 2....

availability of oestrogen to the cancer cell. This can be achieved by blocking oestrogen receptors with drugs such as tamoxifen, suppression of oestrogen synthesis by LHRH agonists, or ovarian ablation either surgically or by radiotherapy. Chemotherapy can also have a hormonal action by inducing amenorrhoea in premenopausal women.

Objectives:

To assess LHRH agonists as adjuvant therapy for women with early breast cancer.

Search strategy:

The specialised register of the Cochrane Breast Cancer Group was searched on 19 December 2006. The reference lists of related reviews were checked. A final check of the list of trials maintained by the Early Breast Cancer Trialists' Collaborative Group was made in January 2008.

Selection criteria:

Randomised trials of LHRH agonist versus LHRH agonist and tamoxifen, LHRH agonist versus chemotherapy, LHRH agonist versus ovarian ablation, or LHRH agonist versus LHRH agonist and chemotherapy, that recruited premenopausal women with early breast cancer.

Data collection and analysis:

Data were collected from trial reports. We report estimates for the differences between treatments on recurrence free survival, overall survival, toxicity and quality of life using data available in the reports of each trial. Meta-analyses were not performed because of variability in the reporting of the trials and the need for more mature data.

Main results:

We identified 14 randomised trials, involving nearly 12,000 premenopausal women with operable breast cancer, most of whom were ER+. The LHRH agonist in most of these trials was goserelin. For most of the treatment comparisons there are too few trials, too few randomised patients or too little follow-up to draw reliable estimates of the relative effects of different treatments. Four trials (nearly 5000 women) addressed the integration of LHRH agonists into adjuvant hormonal therapy, showing that a combination of an LHRH agonist and tamoxifen might be better than either alone. Insufficient data are available to inform a choice between tamoxifen and goserelin as sole adjuvant therapy. We included twelve trials (more than 10,000 women) of the integration of LHRH agonists into adjuvant chemo-hormonal therapy. Four trials assessed the effects of an LHRH agonist compared to chemotherapy and three other trials investigated a combination of an LHRH agonist and tamoxifen versus chemotherapy. One trial assessed the effects of adding chemotherapy to an LHRH agonist, five trials compared a combination of an LHRH agonist and chemotherapy versus chemotherapy alone, and three trials compared the combination of LHRH agonist, tamoxifen and chemotherapy versus chemotherapy alone. No trials compared an LHRH agonist containing regimen against chemotherapy and tamoxifen. No significant differences in recurrence free survival or overall survival were found between LHRH agonists, with or without adjuvant tamoxifen, and chemotherapy for premenopausal women with ER+ tumours, but hormonal therapy had fewer distressing side effects. The trials point to reductions in recurrence and death for premenopausal women with ER+ tumours who take LHRH agonists, with or without tamoxifen, along with chemotherapy.

Authors conclusions:

For premenopausal women with early breast cancer who are not known to be ER negative, the use of an LHRH agonist, with or without tamoxifen as adjuvant therapy is likely to lead to a reduction in the risk of recurrence and a delay in death. The evidence is insufficient to support the LHRH agonists over chemotherapy, or vice versa, in regard to recurrence free survival and overall survival, but LHRH agonists have fewer or less severe adverse effects. Further follow-up of women in these trials is needed to provide reliable evidence on long term outcomes. Direct randomised comparisons of different durations of LHRH agonists (for example, two years versus longer) and, in the presence of uncertainty, of different LHRH agonists among ER+ or ER unknown premenopausal women are also needed. It is also uncertain how the findings from the CMF-based trials in this review would relate to the use of LHRH agonists with more modern chemotherapy regimens or the comparison of LHRH agonist containing regimens with combinations such as chemotherapy and tamoxifen.

Continued from Page 3....

New Review

Goodwin A, Parker S, Ghersi D, Wilcken N. Post-operative radiotherapy for ductal carcinoma in situ of the breast (Protocol). *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD000563. DOI: 10.1002/14651858.CD000563.pub3.

Please note: a podcast of this review is now available from http://www.cochrane.org/podcasts/review_summaries/2009issue1/index.html

Background:

The addition of radiotherapy (RT) following breast conserving surgery (BCS) was first shown to reduce the risk of ipsilateral recurrence in the treatment of invasive breast cancer. Ductal carcinoma in situ (DCIS) is a pre-invasive lesion. Recurrence of ipsilateral disease following BCS can be either DCIS or invasive breast cancer. Randomised controlled trials (RCTs) have shown that RT can reduce the risk of recurrence, but assessment of potential long-term complications from addition of RT following BCS for DCIS has not been reported for women participating in RCTs.

Objectives:

To summarise the data from RCTs testing the addition of RT to BCS for treatment of DCIS to determine the balance between the benefits and harms.

Search strategy:

We searched the Cochrane Breast Cancer Group Specialised Register (January 2008), Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2008, Issue 1), MEDLINE (February 2008), and EMBASE (February 2008). Reference lists of articles and handsearching of ASCO (2007), ESMO (2002 to 2007), and St Gallen (2005 to 2007) conferences were performed.

Selection criteria:

RCTs of breast conserving surgery with and without radiotherapy in women at first diagnosis of pure ductal carcinoma in situ (no invasive disease present).

Data collection and analysis:

Two authors independently assessed each potentially eligible trial for inclusion and its quality. Two authors also independently extracted data from published Kaplan-Meier analysis (survival curves) and reported summary statistics. Data were extracted and pooled for four trials. Data for planned subgroups were extracted and pooled for analysis. There were insufficient data to pool for long-term toxicity from radiotherapy.

Main results:

Four RCTs involving 3925 women were identified and included in this review. All were high quality with minimal risk of bias. Three trials compared the addition of RT to BCS. One trial was a two by two factorial design comparing the use of RT and tamoxifen, each separately or together, in which participants were randomised in at least one arm. Analysis confirmed a statistically significant benefit from the addition of radiotherapy on all ipsilateral breast events (hazards ratio (HR) 0.49; 95% CI 0.41 to 0.59, $P < 0.00001$) and ipsilateral DCIS recurrence (HR 0.64; 95% CI 0.41 to 1.01, $P = 0.05$). Pooled analysis for invasive recurrence did not reach statistical significance. All the subgroups analysed benefited from addition of radiotherapy. No significant long-term toxicity from radiotherapy was found. No information about short-term toxicity from radiotherapy or quality of life data were reported.

Authors conclusions:

This review confirms the benefit of adding radiotherapy to breast conserving surgery for the treatment of all women diagnosed with DCIS. No long-term toxicity from use of radiotherapy was identified.

Please note!

Important Information for Breast Cancer Review Authors

Full release of the revised Cochrane Handbook for Systematic Reviews of Interventions (version 5)

The Handbook provides guidance on how to prepare and maintain Cochrane Intervention reviews and Cochrane Overviews of reviews. This is a major revision of the Handbook with virtually all sections being updated. Authors are therefore advised to become familiar with the new requirements on preparing reviews. A summary of the key new material is available from

http://www.cochrane.org/resources/handbook/Handbook_5_WhatsNew.pdf

The Handbook is also available in the following formats:

1. Browseable version

This version is available Online: at <http://www.cochrane-handbook.org>. An offline version is available within the help menu of RevMan5 (version 5.0.17 or later). Please refer to <http://www.cc-ims.net/RevMan> for information relating to RevMan5 and its download.

2. Commercial book

A book version was published by Wiley-Blackwell in September 2008. Please refer to <http://www.wiley.com/WileyCDA/WileyTitle/productCd-470699515.html> for details.

Training for authors in the new methods included in the Handbook is also available. If you are interested in training, please check the list of workshops available in your geographical area at <http://www.cochrane.org/news/workshops.htm>

In addition.....

The CBCG regularly revises their own policies in relation to the development of systematic reviews in breast cancer.

Authors should therefore, in addition to reviewing the revised handbook, also review these regularly. These are published in the group's module on The Cochrane Library and updated every quarter <http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html>

Licence for Publication and Declarations of Interest forms

Authors of Cochrane reviews are advised that *Licence for Publication forms* are now available in RevMan5 (File menu—Reports—Licence for publication form).

Separate forms **must** be signed by all review authors for all new citation versions of intervention/methodology protocols and reviews. Forms should be sent to the Editorial Base before the protocol or review is published on The Cochrane Library

These are kept by the Editorial Base and a copy sent to the Cochrane Collaboration Secretariat.

In addition all authors are required to complete a *Declaration of Interest questionnaire* for breast cancer reviews at title registration, protocol publication and again when the review is published. These forms will be supplied to authors by the Editorial Base as these are **not** available in RevMan5.

These forms will be kept on file at the Editorial Base and used to determine whether the information on potential conflicts of interest at each stage of the review process is adequate.

Important Information for Breast Cancer Review Authors contd.....

Publication dates for 2009

A full list of relevant dates relating to the next 4 issues of The Cochrane Library is now available from our website <http://www.ctc.usyd.edu.au/cochrane/index.html>

Authors are advised that on average reviews take 6 months to move from draft review, through peer review, copyediting, sign off and publication.

Practical issues when working in RevMan 5

Using the validation report option

The RevMan 5 Validation Report (File > Reports > Validation Report) identifies warnings and errors which authors need to rectify before submitting a protocol or review for publication.

This option will provide a warning that study data is missing in the review however it will not provide details of the study or the outcome with the missing data. A quick way to identify the missing study data is to use the 'Validate as You Type' option. This option is turned on in RevMan5 by going to Tools > Validate as You Type).

Author Reminder:

It is not possible to check in a RevMan5 file to ARCHIE unless that file originates from Archie.

Archie is the system for storing and backing up your revMan5 file. The editorial base will set up the review file for you when the title is registered. Authors are required to open RevMan5 and check out their RevMan file from Archie before starting to prepare a new protocol, new review or updated review. This file should always be checked back into Archie when it is not being used.

An author will not be able to check in a draft to Archie (to share with their review team or editorial base) if they have not first of all checked it out of Archie.

It is also important that authors do not create copies of the RevMan file. Instead, they should either check their edited version back into Archie daily (the ideal situation) or save one version only of their RevMan file locally.

Tips for authors relating to the use of RevMan5 and Archie are currently being prepared. The 'Quick start guide for authors using Archie' available from <http://www.cc-ims.net/authors> is a useful author resource in the meantime.

Coming up in 2009

17th Cochrane Colloquium Singapore

October 11-14 2009

Notable Dates:

Abstract submission: 15th April 2009

Consumer and developing country stipends: 01 June 2009

Early registration: 13th July 2009

Further information is available from the Colloquium website
<http://www.colloquium.info/2009/>

Cochrane Library information

Complimentary copies of The Cochrane Library for authors

In the past complimentary copies of The Cochrane Library were sent to all authors who had updated their review within 10 (Cochrane Library) issues of the previous publication.

RevMan5 provides a new way to identify 'updated' reviews and as such, this also effects the distribution of complimentary CDs.

Effective immediately, complimentary copies will now be sent to those authors who have reviews in the following categories: 'New citation version' and 'New search, conclusions not changed'.

Please refer to the definitions for both of these categories which are available from http://www.cochrane.org/resources/handbook/Handbook_5_WhatsNew.pdf

Short print versions of Cochrane Reviews now available on The Cochrane Library

From Issue 4, 2008 of The Cochrane Library, reviews produced with Revman5 are now also available in a 'short print version'. The short print version contains the Abstract and the Plain Language Summary and is intended to make reviews more accessible, particularly for consumers.

When a review is accessed on The Cochrane Library, three version types are visible from the left hand menu, all in PDF format.

1. Abstract or short print version (Abstract plus Plain Language Summary)
2. Standard (the review without the analysis graphs and the appendices)
3. The full review version.

Authors should note that they now have the option of selecting two or three metaviews for inclusion in the text of the review. For the standard version these will be the only metaview graphs visible using this version.

Podcasts from The Cochrane Library and other multi-media resources

For each issue of The Cochrane Library, audio summaries of selected reviews are now available. These can be found at <http://www.cochrane.org/podcasts/index.html>

The Cochrane Collaboration's website also provides access to the Cochrane Multi-media Portal. Podcasts, and other multi-media from Cochrane Colloquia and meetings can be accessed from this portal <http://www.cochrane.org/multimedia/index.html>

Editor-in-Chief of The Cochrane Library

Dr David Tovey has been appointed as the first Editor-in-Chief of The Cochrane Library. He will commence his post in January 2009 and be based in the UK.

Visit our website:

<http://www.ctc.usyd.edu.au/cochrane/index.html>



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