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Processed versus fresh frozen bone for impaction bone grafting in revision hip arthroplasty (Review)

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[Intervention Review]

Processed versus fresh frozen bone for impaction bone grafting in revision hip arthroplasty

Timothy N Board[1], Susan Brunskill[2], Carolyn Doree[2], Chris Hyde[2], Peter R Kay[3], RM Dominic Meek[4], Robert Webster[5], George Galea[6]

[1]The Centre for Hip Surgery, Wrightington Hospital, Wigan, UK. [2]Systematic Review Initiative, NHS Blood and Transplant, Oxford, UK. [3]Wrightington Hospital, Wigan, UK. [4]Orthopaedic Department, Southern General Hospital, South Glasgow University Hospitals NHS Trust, Glasgow, UK. [5]National Blood Service, Sheffield, UK. [6]Scottish National Blood Transfusion Service, Edinburgh, UK

Contact address: Timothy N Board, The Centre for Hip Surgery, Wrightington Hospital, Appley Bridge, Wigan, Lancashire, WN6 9EP, UK. tim@timboard.co.uk.

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ABSTRACT

Background

Impaction grafting is a technique to restore bone loss both in the femur and the acetabulum during revision hip arthroplasty surgery. Initially impaction grafting was undertaken using fresh frozen femoral head allografts that were milled to create morselized bone pieces that could be impacted to create a neo-cancellous bone bed prior to cementation of the new implant. Results of medium and long term outcome studies have shown variable results using this technique. Currently both processed and non-processed allograft bone are used and the purpose of this review was to analyse the evidence for both.

Objectives

To determine the clinical effectiveness of processed (freeze dried or irradiated) bone in comparison to fresh frozen (unprocessed) bone.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1985 to 2008), EMBASE (1985 to 2008), CINAHL(1985 to 2008) and the National Research Register. Additional sources were also searched. Handsearching of relevant journals and conference abstracts was also undertaken. Searches were complete to 31 August 2008.

Selection criteria

Randomised controlled trials that compared different types of bone for impaction grafting.

Data collection and analysis

Three hundred and sixty references were identified from the searches. Following detailed eligibility screening, three hundred and fifty nine references did not meet the eligibility criteria. Further details are required about one trial in order to determine it's eligibility.

Main results

No trials were identified that met the criteria for inclusion in the review.

Authors' conclusions

Good quality randomised controlled trials are required in this area so that a surgeon's choice of bone graft can be informed by evidence rather than personal preference.

PLAIN LANGUAGE SUMMARY

Processed versus fresh frozen bone for repairing the bone in revision hip surgery

This summary of a Cochrane review presents what we know from research about the advantages and disadvantages of using fresh frozen bone or processed bone for repairing the hip bone during surgery.

The review shows that no studies were found that compared the clinical utilities of processed versus fresh frozen bone in revision hip surgery.

What is revision hip surgery and what are processed and fresh frozen bone?

The most common problem with hip replacements is that the prosthesis used to replace the original diseased bone begins to loosen over time. This happens because some bone is lost at the hip joint over the years. This usually happens 10 or more years after having the operation. Sometimes another surgery, called a "revision surgery" is needed to remodel the lost bone. During this type of surgery a technique called impaction grafting can be used to replace the lost bone. Impaction grafting involves the pressing of small bone chips into the top of the thigh bone or the cavities either side of the hip bone.
Two types of bone can be used: processed or unprocessed (fresh frozen). The bone comes from donors and is stored and processed in "Tissue Establishments", similar to the way blood is donated and stored. Bone donations are thoroughly screened prior to use. Processing the donated bone prior to use in impaction grafting limits the rare possibility of transmitting infections e.g. HIV or Hepatitis. However there is concern that processed bone is less clinically satisfactory than fresh frozen bone.

BACKGROUND

Hip arthroplasty is one of the most successful surgical advances of the last century with some 60,000 hip arthroplasties being performed annually in the UK. However artificial joints have a limited lifespan and it is not uncommon for prostheses to fail after a period of 10 or more years. Consequently there is a rising demand for revision arthroplasty where the old prosthesis is replaced. Commonly, failure of the prosthesis is associated with a large degree of bone loss in the hip region. In order to reconstitute this bone loss a technique called impaction grafting is often employed during the revision procedure. Impaction grafting involves the progressive compaction of morselized (small fragments) bone chips into the femoral canal or acetabular cavity. The prosthesis is then cemented in place, creating a three layer composite - implant, cement and graft. The bone graft undergoes remodeling with time and become incorporated into the skeleton (Ling 1993; Nelisson 1995; Linder 2000; Ullmark 2002b). Long term outcome studies of hip revision with impaction grafting report wide variation in results (Slooff 1984; Gie 1993; Leopold 1999; Ullmark 2002a; Schreurs 2003; Lie 2004; Schreurs 2004a; Schreurs 2004b), one as high as 100% survival at 10.4 years (Schreurs 2005) and other results are less convincing when impaction grafting is performed without the use of cement as demonstrated by a 28% survival at 15.3 years (Jeffery 2003). Other methods of revision hip arthroplasty include uncemented components without impaction grafting and cemented components without impaction grafting.

Impaction grafting is most commonly performed using fresh frozen femoral head allograft (fresh frozen bone). The frozen femoral head is thawed at the time of surgery and milled to the required size. The most commonly used alternative to fresh frozen bone graft is processed bone (freeze dried or irradiated bone). It is these two graft types that will be investigated in this review. Less frequently used graft types include xenograft, autograft and artificial bone. These bone types will not be included as both xenograft and autograft are used so rarely for revision surgery to be considered irrelevant. Artificial bone is a different entity entirely and is beyond the scope of this review.

The surgical technique is the same whether processed or fresh frozen bone is used. The use of fresh frozen bone is currently associated with the best long term results (Schreurs 2005), however, there are two areas of concern. Firstly, due to the remaining bone marrow and cells in the graft there is a risk of disease transmission: there have been four cases worldwide of HIV transmission via non processed bone allograft (Simonds 1992; Simonds 1993) and four cases of hepatitis C virus transmission (Conrad 1995). Transmission of new variant Creutzfeldt Jakob disease (vCJD) is also a possibility but has not been reported. Secondly, the presence of bone marrow cells and fat have been shown to have a deleterious effect on bony ingrowth in-vitro and may hinder bone incorporation and remodeling (van der Donk 2003). Results from cohort studies using processed bone have shown variable results (Tokgozoglu 2000; de Roeck 2001; Buckley 2005; de Roeck 2001; Robinson 2002; Tokgozoglu 2000) but it is not clear if the type of bone graft or minor variations in technique are responsible for the variations in outcome.

Processed bone has less potential for disease transmission but the mechanical properties are generally poorer than fresh frozen bone (Pelker 1984; Tokgozoglu 2000). Although the removal of the bone marrow is a benefit of processed bone in that this reduces the risk of disease transmission, the current open process for the removal of bone marrow followed by sterilisation with gamma irradiation is not well liked by surgeons. (Marczynski 1993). Over the last 10 to 15 years in the USA all bone is issued as processed (undertaken through a variety of methods) and fresh frozen bone is hardly ever used. (Strong 1992; Tomford 1994). Newer methods of processing bone that avoid the use of irradiation are being developed by the National Health Service Blood and Transplant and the Scottish National Blood Transfusion Service.

In summary, when used in impaction grafting for revision arthroplasty of the hip, fresh frozen bone is thought to produce better long term results, but with an associated increased risk of disease transmission. Conversely, the use of processed bone may be associated with poorer results but a reduced risk of disease transmission. A new directive from the European Parliament came into force in April 2006, which includes rigorous standards for tissue banking facilities ensuring a necessary minimisation of disease transmission risk and that quality standards are met whenever any processing or storage takes place. Consequently it has become paramount to perform this review in order to identify any differences in outcome of revision hip arthroplasty using either fresh frozen bone or processed bone.

OBJECTIVES

To determine the clinical effectiveness of processed (freeze dried or irradiated) bone in comparison to fresh frozen (unprocessed) bone.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.
Trials of any duration were considered, although the ideal duration is a minimum of 3 years.

Types of participants

Adults (aged over 18 years) undergoing revision hip arthroplasty with impaction bone grafting.

Types of interventions

Different types of bone used for impaction grafting.

Types of outcome measures

The following outcomes were sought:

Primary outcomes

Validated outcomes:
Arthroplasty revision rate
Dislocation rate
Re-operation rate (even without new implants)
Roentgen stereophotogrammetric analysis (RSA) for stability of implanted components
Mortality
General HRQoL tools (e.g. SF36)
Validated functional self-assessment questionnaires (Oxford, WOMAC, AAOS) or scores (Harris)
Patients assessment of pain with validated tools

Patient's satisfaction

Post-operative complications
a. Superficial wound infection.
b. Deep wound infection (infection around the implant)
c. Superficial hematoma
d. Deep hematoma
e.Thromboembolic complications (deep thrombosis, pulmonary embolism) fat embolism
f. Heterotopic ossification
g. Others, e.g. post-operative stiffness requiring manipulation under anaesthesia
h. Any medical complication (as detailed in each individual study), pneumonia, bladder infection

Secondary outcomes

Technical outcomes:
1) Radiological measurements (based on plain radiographs, computed tomograms, Positron Emmision Tomography (PET), Radioisotopic scans). Figures on validity and reliability of the reported method will be carefully checked, in particular assessing:
a. immediate post-operative component malpositioning
b. follow-up evidence of mobilisation
c. lack of remodeling

2) Range of motion
3) Leg length discrepancy

4) Operative details:
a. Length of incision (in millimetres)
b. Operative time (in minutes)
c. Operative blood loss (in millimetres)
d. Intra-operative blood loss (in millimetres)
e. Post-operative blood loss (in millimetres)
f. Post operative blood transfusion (number of units)

5) Perioperative complications:
a. Intra-operative fracture at the time of surgery (acetabulum or femur)
b. Periprosthetic fracture after surgery
c. Nerve damage
d. Damage to other anatomical structures
e. Other surgical complications (as detailed in each study)

6) Post-operative care outcomes:
a. Days to mobilisation
b. Length of hospital stay (days)
c. Length of rehabilitation centre stay (days)

7) Final outcome measures:
a. Days to dislocation
b. Residence at final follow-up (return to living at home, discharge location)
c. Mobility (use of walking aids, return of mobility)
d. Clinical rating scales (filled in by an external assessor) (Charnley, Merle d'Aubigne etc) (less reliable and valid).

Timing of outcome assessment

Outcome measurement for arthroplasty revision rate were sought for 3, 5 and 10 year following arthroplasty as per UK National Institute for Health and Clinical Excellence recommendations. Measurements at time points up to 2 years were sought for all other primary, technical and operative detail outcome measures.

Search methods for identification of studies

Electronic searches

The following sources were searched:
- Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library* Issue 3, 2008)
- MEDLINE (1950 to 2008)
- EMBASE (1974 to 2008)
- CINAHL (1982 to 2008)
- LILACS
- KoreaMed
- PakMediNet
- IndMed
- the National Blood Service Systematic Review Initiative's database of RCTs established from searches of the main haematology and blood transfusion journals (Transfusion, Transfusion Medicine, Vox Sanguinis, British Journal of Haematology) and conference abstracts (American Society of Haematology, British Society of Haematology, British Blood Transfusion Society, International Society of Blood Transfusion, American Association of Blood Banks), 1980 to present;
- the websites of the International Health Technology Assessment Agencies through the International Network of Agencies of Health Technology Assessment (INAHTA) and the International Society of Technology Assessment in Health Care (ISTAHC);
- the databases NHSEED (NHS Economic Evaluation Database), DARE (Database of Abstracts of Reviews of Effects) and HTA, accessed via *The Cochrane Library*
- The British Library's Zetoc database
- reference lists of relevant papers
- the following databases of ongoing trials:

- Current Controlled Trials Register: http://www.controlled-trials.com (includes ISRCTN, National Research Register, UK Clinical Trials Gateway)
- Clinical Trials.gov: http://www.clinicaltrials.gov/
- UK Clinical Trials Network (UKCRN)
- WHO ICTRP (includes Australian New Zealand Clinical Trials Registry)

Search strategies can be found in Appendices for CENTRAL (Appendix 1), MEDLINE and CINAHL (Appendix 2), and EMBASE (Appendix 3). These were combined with search filters adapted from the MEDLINE RCT search filter validated by the Cochrane Collaboration (Higgins 2008). Searches were undertaken to 31 August 2008. No date or language restrictions were applied to the searches.

Searching other resources

In addition the following journals and conference abstracts were handsearched in order to identify reports of RCTs:

Journals

Advances in Tissue Banking
European Journal of Orthopaedics

Conference Abstracts

American Orthopaedic Research Society

American Hip Society (1998 to 2008)
British Hip Society
British Orthopaedic Association (1998 to 2008)
British Orthopaedic Research Society (1999 to 2008)
European Federation of Orthopaedics and Traumatology (EFFORT)
European Hip Society (1998 to 2008)
European Orthopaedic Research Society (EORS) (2005, 2006).

Data collection and analysis

Selection of studies

One review author (CD) screened, all titles and abstracts of papers identified by the review search strategy for relevancy to the review question. Only studies clearly irrelevant were excluded at this stage. All other studies were assessed on the basis of their full text for inclusion/exclusion using the criteria indicated above (type of studies, participants, interventions and outcome measures).

At this stage, two review authors (TB, SJB) independently assessed eligibility. Disagreements were resolved between the two review authors. Details of why studies were excluded were recorded. No trials were identified that met the criteria for inclusion in the review.

Further aspects of the method defined in the protocol were thus not employed but will be used in future updates if eligible trials are identified for inclusion. In future updates the following methods will be used.

Data extraction and management

Aside from details relating to included study quality the following two groups of data will be extracted.

(1) Study characteristics: place of publication, date of publication, population characteristics, setting, detailed nature of intervention, detailed nature of comparator, detailed nature of outcomes. A key purpose of these data will be to explain clinical heterogeneity in included studies independently from analysis of results.

(2) Results of included studies in respect of each of the main outcomes indicated in the review question. Reasons why an included study did not contribute data on a particular outcome will be carefully recorded and the possibility of selective reporting of results on particular outcomes considered. For dichotomous outcomes the numbers of outcomes in treatment and control groups will be recorded. For continuous outcomes, mean and standard deviation will be recorded.

Data extraction will be undertaken by two review authors (TB, GG) working independently. Data will be extracted onto study specific data extraction forms which will be created and piloted specifically for this review. Following resolution of any disagreements, the consensus data will be recorded onto a third data extraction form and transcribed into the systematic review computer software (Review Manager 2008) by a third review author (SB).

Assessment of risk of bias in included studies

The two review authors (TB, GG) undertaking the data extraction will independently assess risk of bias for each trial using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). Any disagreements will be resolved by discussion or by involving a third (CH) assessor.

The following are the criteria that will be used to assess the risk of bias in the included trials:
(1) Generation of random sequence.
(2) Concealment of treatment allocation schedule.
(3) Blinding of clinician (person delivering the treatment), participant and outcome assessors to treatment allocation.
(4) Completeness of the outcome data, checking for possible attrition bias through withdrawals, loss to follow-up and protocol violations.
(5) Selective reporting bias, checking that all of a study's prespecified outcomes and all expected outcomes of interest to the review have been reported.
(6) Other sources of bias in the included trials. An assessment will be made as to whether each trial was free of problems, not identified through 1 to 5 above, that could put it at risk of bias.
(7) An overall risk of bias assessment would be made based on items 1-6 above. An explicit judgement about whether studies are at high risk of bias will be made according to criteria given in The Cochrane Handbook (Higgins 2008).The likely magnitude and direction of the bias will be assessed with reference to items 1-6, with particular emphasis on the likely impact the bias would have had on the findings.

Criteria 1 to 6 above will be rated according to criteria identified in The Cochrane Handbook (Higgins 2008). This assigns ratings of adequate, inadequate or unclear to items 1 to 5, and a rating of yes, no or unclear to item 6. These ratings will be recorded in each trial's 'Risk of Bias' table. In addition, a narrative summary of the findings of this assessment will be provided alongside the individual ratings. The overall risk of bias assessment will be reported in the results section of this review.

Measures of treatment effect

Dichotomous data for each arm in a particular study will be expressed as proportion or risks and the treatment effect as a risk ratio (RR) with 95% confidence intervals. Continuous data for each arm in a particular study will be expressed as mean and standard deviation and the treatment effect as weighted mean difference (WMD) if outcomes are measured in the same way between trials. Where outcomes are measured using different methods, the treatment effect data will be combined and analysed using the standardised mean difference.

Dealing with missing data

Where possible, missing data will be sought directly from the author(s) of the individual trial(s). For all included trials, levels of attrition will be noted and the impact of including trials with high levels of missing data in the overall assessment of treatment effect will be explored in sensitivity analyses. For all outcomes, analyses will be carried out, as far as possible, on an intention-to-treat basis.

Assessment of heterogeneity

Statistical heterogeneity will be tested using visual inspection of graphs and the I^2 statistic (with a cut-off of 50%). Potential reasons for observed heterogeneity will be explored in comparisons where there were more than two included trials. Particular emphasis will be placed on study population, treatment, outcome measurement and study quality differences between the included studies. Clinical heterogeneity will be assessed by examining differences in study quality, type of graft used, surgical technique (e.g. choice of bone cements, choice of prosthesis, experience of

surgeon, postoperative rehabilitation regime) and degree of bone loss. Possible explanations for the observed heterogeneity will be discussed within the review.

Assessment of reporting biases

Although it is believed that every effort will have been made to identify unpublished studies, publication bias will be assessed using funnel plots. It is acknowledged that asymmetry, of which publication bias is one cause, is difficult to detect with the small numbers of studies (i.e. less than 10) often encountered in systematic reviews.

Data synthesis

Meta-analysis will be undertaken if there is sufficient data of suitable type. Meta-analysis will be undertaken using the Review Manager software (Review Manager 2008). A fixed-effect model will be used for combining data in the first instance. Where trials were not examining the same intervention or the populations or methods are not similar between the trials suggesting that treatment effects may differ between trials, a random-effects model will be used. If substantial heterogeneity is identified in a fixed-effect model of meta-analysis this will be noted and the analysis repeated using a random-effects model.

Subgroup analysis and investigation of heterogeneity

Subgroup effects that will be examined are: degree of bone loss, cemented or uncemented technique and choice of implant.

Sensitivity analysis

Sensitivity analyses that will be undertaken are the influence of the methodological quality of the trials, for dichotomous data, the influence of participant drop-out and the duration of the trial.

RESULTS

Description of studies

Results of the search

Three hundred and sixty references were identified from the searches: 170 from Embase, 123 from Medline, 25 from the National Research Register, 16 from Cinahl and 13 from CENTRAL. The remaining 13 references were identified from Current Controlled Trials (3), NHSEED (3), HTA (2), Zetoc (2), DARE (1), KoreaMed (1) and Clinical Trials.gov (1). Initial screening of the citations for relevance excluded 353 papers. There was disagreement as to the eligibility of six studies. Following more detailed screening and discussion, these six papers were excluded on the basis of the eligibility of the intervention.

Included studies

No trial was identified that met the inclusion criteria for this review.

Excluded studies

Seven trials were excluded from the review. See the 'Characteristics of excluded studies' for further details. In all cases the reason for exclusion was the ineligibility of the intervention examined in the trial.

Ongoing Studies

No ongoing study was identified.

Studies Awaiting Assessment

There are no studies awaiting assessment for inclusion in this review.

Risk of bias in included studies

Not applicable.

Effects of interventions

No randomised controlled trial met the inclusion criteria for this review. Any newly published, eligible randomised controlled trials will be included in future updates of this review.

DISCUSSION

The objective of this review was to determine the clinical effectiveness of processed (freeze dried or irradiated) bone in comparison to fresh frozen (unprocessed) bone. A comprehensive search strategy was used for this review. Every effort was made to identify relevant studies, including the handsearching of specialised journals and conference abstracts. However no published randomised controlled trials were identified that met our eligibility criteria. Therefore we are unable to draw any conclusions to determine the clinical effectiveness of processed bone in comparison to fresh frozen bone.

A number of RCTs were identified that compared bone graft with bone graft plus additional bone graft substitutes (Johnstone 2006; Kesteris 2006; Munro 2007; Timperley 2006b; Timperley 2007). These studies are not relevant to this review as the bone graft substitutes are used as “bone graft extenders”, that is, they are not designed to replace the use of bone graft. Furthermore they are entirely artificial materials. This review is only interested in the pure use of processed allograft bone in impaction grating and the results from the use of artificial bone cannot be translated for this review question. However, lessons may be learnt from these studies about the conduct of new RCTs in the area of bone grafting generally.

Following a new directive from the European Parliament which came into force in April 2006, which includes rigorous standards for tissue banking facilities ensuring a necessary minimisation of disease transmission risk and that quality standards are met whenever any processing or storage takes place, it is likely that Tissue Banks will feel the need to introduce processing techniques for bone allograft to minimise the disease transmission risk. It is disappointing that there are no RCTs comparing such allograft with the so called “gold standard” of fresh frozen femoral head allograft.

The British National Health Service Blood and Transplant (NHSBT) Tissue Bank at Speke, Liverpool, UK, with the Scottish National Blood Transfusion Service (SNBTS) is currently developing a processed bone allograft using new methodology which avoids the need for irradiation. Whilst an RCT comparing this processed bone with fresh frozen bone prior to general introduction would be the ideal, it would take many years to reliably establish long-term efficacy and safety differences between the two products. Clinical pressure to use such processed bone in the context of a safety measure may not withstand waiting for the outcome of a RCT. Use of short-term surrogate markers of success such as Dual Energy X-ray Absorptiometry (DEXA) to measure bone density of the graft and Roentgen Stereophotogrammteric Analysis (RSA) to measure stability and subsidence of components may provide answers as

to the efficacy of processed bone within two years. Such findings could direct the use of processed bone in clinical practice as long-term findings are awaited.

AUTHORS' CONCLUSIONS

Implications for practice

There are no direct implications for clinical practice identified as a result of this review. However, there is clearly a lack of quality data in this area and well designed clinical trials are required to help inform and guide practice.

Implications for research

As mentioned there is a lack of quality randomised controlled trials in this area. We would therefore propose that a randomised controlled trial be instigated comparing the current gold standard of fresh frozen femoral head allograft with processed femoral head allograft. As overall failure of the surgery with further revision is a long-term outcome that can take 10 years to show results we would propose using short-term surrogate markers of success such as Dual Energy X-ray Absorptiometry (DEXA) to measure bone density of the graft and Roentgen Stereophotogrammteric Analysis (RSA) to measure stability and subsidence of components. Both of these techniques are well used in outcome analysis of hip arthroplasty and can produce results over 12 to 24 months that have been shown to be predictive of long-term success at 10 years.

ACKNOWLEDGEMENTS

None

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Johnstone 2006	This is a randomised controlled trial but does not compare the intervention of interest. This trial compares bone graft A with bone graft B and artifical bone.
Kesteris 2006	This is a randomised controlled trial but does not compare the intervention of interest. This trial compares bone graft A with bone graft B with additional drug.
Munro 2007	This is a randomised controlled trial but does not compare the intervention of interest. This trial compares bone graft A with bone graft B and artifical bone.

Study	Reason for exclusion
Timperley 2006a	This was a randomised controlled trial. Personal communication with the first author (Autumn 2008) discovered that the trial was stopped as it became mandatory for the trialists to wash the bone graft. Therefore the randomisation in this trial between washed and unwashed allograft was no longer a viable option. No published report about this trial has been identified.
Timperley 2006b	This is a randomised controlled trial but does not compare the intervention of interest. This trial compares bone graft A with bone graft B and artifical bone.
Timperley 2007	This is a randomised controlled trial but does not compare the intervention of interest. This trial compares bone graft A with bone graft B and artifical bone.

APPENDICES

Appendix 1. CENTRAL search strategy

#1 BONE TRANSPLANTATION single term (MeSH)
#2 graft* near/5 (impact* OR compact* OR bone* OR fresh OR frozen OR freez* OR irradiat* OR morcel* OR morsel* OR femoral OR femur)
#3 allograft near/5 (impact* OR compact* OR bone* OR fresh OR frozen OR freez* OR irradiat* OR morcel* OR morsel* OR femoral OR femur)
#4 bone* near/5 (processed OR freez* OR frozen OR irradiat* OR impact* OR fresh OR transplant* OR unprocessed OR morcel* OR morsel* OR loss* OR nonprocessed OR reconstitut* OR heat OR autoclave* OR lyophilise* OR lyophilize* OR ethylene OR peracetic OR sterili* OR pasteuri* OR Washed OR lipid)
#5 marburg NEXT bone
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 HIP PROSTHESIS single term (MeSH)
#8 ARTHROPLASTY REPLACEMENT HIP single term (MeSH)
#9 ACETABULUM [su] single term (MeSH)
#10 hip* near/5 (replac* OR revis* OR reconstruct* OR implant* OR reimplant* OR prosthe* OR artificial* OR arthroplast* OR repair*)
#11 femoral near/5 (revis* OR prosthe* OR implant* OR reimplant* OR prosthe* OR artificial* OR repair*)
#12 acetabul* near/5 (revis* OR reconstruct* OR implant* OR reimplant* OR prosthe* OR artificial* OR repair*)
#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 #6 AND #13

Appendix 2. MEDLINE and CINAHL (Ovid) search strategy

1. BONE TRANSPLANTATION/
2. (graft$ adj5 (impact$ OR compact$OR bone$ OR fresh OR frozen OR freez$ OR irradiat$ OR morsel$ OR morcel$ OR femoral OR femur)).ti,ab.
3. (allograft$ adj5 (impact$ OR compact$ OR bone$ OR fresh OR frozen OR freez$ OR irradiat$ OR morsel$ OR morcel$ OR femoral OR femur)).ti,ab.
4. (bone$ adj5 (processed OR freez$ OR frozen OR irradiat$ OR impact$ OR compact$ OR fresh OR transplant$ OR unprocessed OR nonprocessed OR morcel$ OR morsel$ OR reconstit$ OR loss$ OR donat$)).ti,ab.
5. (bone$ adj5 (heat OR autoclave$ OR lyophilise$ OR lyophilize$ OR ethylene OR peracetic OR sterilis$ OR steriliz$ OR marburg OR pasteuri $ OR washed OR lipid)).ti,ab.
6. femoral head adj5 frozen.ti,ab.
7. or/1-6
8. HIP PROSTHESIS/
9. ARTHROPLASTY REPLACEMENT, HIP/
10. ACETABULUM su/
11. (hip$ adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR arthroplast$ OR repair$).ti,ab.
12. ((femoral head OR femoral stem) adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR repair$).ti,ab.
13. (acetabul$ adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR repair$).ti,ab.
14. or/8-13
15. 7 AND 14

Appendix 3. EMBASE (Ovid) search strategy

1. BONE TRANSPLANTATION/

2. BONE GRAFT/
3. BONE ALLOGRAFT/
4. (graft$ adj5 (impact$ OR compact$ OR bone$ OR fresh OR frozen OR freez$ OR irradiat$ OR morsel$ OR morcel$ OR femoral OR femur)).ti,ab.
5. (allograft$ adj5 (impact$ OR compact$ OR bone$ OR fresh OR frozen OR freez$ OR irradiat$ OR morsel$ OR morcel$ OR femoral OR femur)).ti,ab.
6. (bone$ adj5 (processed OR freez$ OR frozen OR irradiat$ OR impact$ OR compact$ OR fresh OR transplant$ OR unprocessed OR nonprocessed OR morcel$ OR morsel$ OR reconstit$ OR loss$ OR donat$)).ti,ab.
7. (bone$ adj5 (heat OR autoclave$ OR lyophilise$ OR lyophilize$ OR ethylene OR peracetic OR sterilis$ OR steriliz$ OR marburg OR pasteuri$ OR washed OR lipid)).ti,ab.
8. femoral head adj5 frozen.ti,ab.
9. or/1-8
10.HIP PROSTHESIS/
11.HIP ARTHROPLASTY/
12.TOTAL HIP PROSTHESIS/
13.ACETABULOPLASTY/
14.ARTHROPLASTY/
15.(hip$ adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR arthroplast$ OR repair$).ti,ab.
16.((femoral ADJ head OR femoral ADJ stem) adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR repair$).ti,ab.
17.(acetabul$ adj5 (revis$ OR reconstruct$ OR implant$ OR reimplant$ OR prosthe$ OR artificial$ OR repair$).ti,ab.
18. or/10-17
19. 9 AND 18

WHAT'S NEW

Date	Event	Description
19 September 2008	Amended	CMSG ID: C147-R

HISTORY

Protocol first published: Issue 1, 2007
Review first published: Issue 4, 2009

Date	Event	Description
19 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Tim Board: content expert: preparation of protocol and final review and undertook initial screening of studies.

Susan Brunskill: methodological expert: preparation of protocol and final review.

Carolyn Doree: methodological expert: designed and ran comprehensive search strategies and undertook initial screening of studies.

George Galea: content expert: contributed to preparation of protocol and final review.

Chris Hyde: methodological expert: contributed to preparation of protocol and final review.

Peter Kay: content expert: contributed to preparation of protocol and final review.

Dominic Meek: content expert: contributed to preparation of protocol and final review.

Rob Webster: content expert: contributed to preparation of protocol and final review.

DECLARATIONS OF INTEREST

None known.

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External sources

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INDEX TERMS

Medical Subject Headings (MeSH)

Arthroplasty, Replacement, Hip [*methods]; Bone Transplantation [*methods]; Reoperation; Specimen Handling [methods]; Transplantation, Homologous

MeSH check words

Humans