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Technical Support Institution with
National Health Mission
Ministry of Health and Family Welfare,
Government of India

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Dear Dr. Sharmila

With reference to your letter on 'study on clinical effectiveness and costs of implants', the following is placed for your perusal:

1. We analyzed Six Hundred Thirty One randomized control trials (Annexure Binder-I & II) on Hip and Knee implants including Cemented and Un-cemented implants categories, and various sub-categories including Stainless Steel, Titanium, Cobalt Chromium, ceramic on ceramic and metal on poly-ethylene. A detailed assessment report is attached (Annex-III)

2. The data on landing cost of implants is captured from leading supplier and tabulated in the report. The valid cost of Hip & Knee implants appears to be the following:

Hip Implants: Un-cemented: 86,000/-; Cemented: Rs.45, 000/-

Knee Implants: Un-cemented: 97,000/-; Cemented: Rs.54, 000/-

3. The cost suggested above includes service tax. Since there remains an ambiguity on the number of units/pack, the patient remains unaware of actual cost/unit of implant. It is also suggested that:

- Packaging of implants should ensure unit wise packing
- MRP to be made mandatory on all implant packs
- Hospital handling charges to be substituted with service tax as applicable

Please let us know if you require any further clarifications.

Thanking You,

Sanjiv Kumar

Dr. Sanjiv Kumar

Smt. Dr. Sharmila Mary Joseph, IAS

Member Secretary, National Pharmaceutical Pricing Authority

Dept. of Pharmaceuticals, Govt. of India

Encl:

1. Annex- I & II (Binders on 631 RCTs)

2. Annex- III : Assessment report

Cc:

PPS to Joint Secretary (Policy)

Office of the M.S (NPPA)
Dy. No. 1568
Date: 23/10/15

Health Technology Assessment On Orthopedic Implants

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Health Technology Assessment on Orthopedic Implants

Introduction:

Musculoskeletal disease (MSDs) conditions are prevalent and their impact is pervasive. They are the most common cause of severe long term pain & morbidity, having a substantial influence on health and quality of life, imposing on enormous burden of cost on the healthcare system. WHO estimates that 40% of people over the age of 70 years suffer from OA knee, about 80% of the people at some time in their life have had low back pain at some point in their life. Osteoporotic hip fracture, injuries and diseases of the musculoskeletal system account for more than 20% of patient visits to primary care physicians. The global prevalence of MSDs ranges from 14% to as high as 42%.

Despite their enormous impact in India, MSDs do not receive the due attention due to perception that MSDs are less serious and unlike Cardio-vascular Diseases, other neurological diseases AIDS, and Cancer, which are largely considered fatal, the MSDs are considered, nonfatal and chronic and are tend to be seen as a consequence of ageing and the only solution for this problem is Joint replacement surgery. Even the awareness about joint replacement surgery is very low in India. Surveys conducted in urban areas reveal that only about 10 per cent of people are aware about detection and prevention of MSD such as Osteoporosis, Osteoarthritis, Rheumatoid arthritis etc. It is therefore, imperative to raise awareness about MSD in all its forms among the medical community, patients and the public. Conferences and meetings where both patients and healthy people are invited to spread awareness/knowledge regarding arthritis, its prevention and management could be an effective method to enhance awareness.

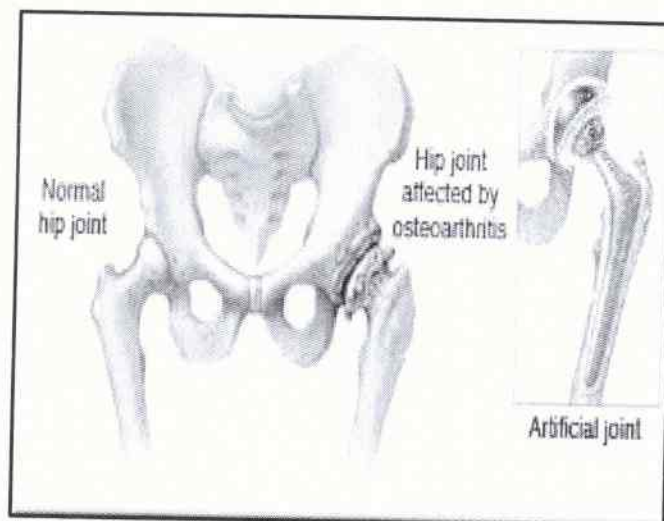
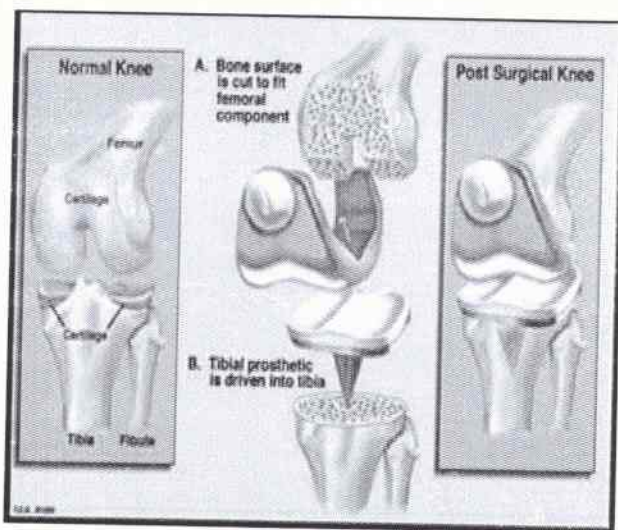
The joint replacement in India is projected to grow at about 25-30 per cent over the next coming years, owing to an increase in the ageing population, sedentary lifestyle, booming economy, better healthcare infrastructure and the opening up of the insurance sector. With over 70,000 hip and knee replacements being performed every year, the growth rate of the orthopaedic implants is estimated to be more than 25 per cent per annum for the next five to six years.

Therefore, on request of National Pharmaceutical Pricing Authority, Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers, GOI (NPPA) to National Health Systems Resource Centre, a technical support institution under Ministry of Health & Family Welfare, the Division of Healthcare Technology undertook an assessment of clinical effectiveness, cost effectiveness and cost variations of Orthopaedic Implants.

Musculoskeletal Diseases (MSD):

Musculoskeletal Disorders are one of the major causes of morbidity, have a substantial influence on health and quality of life and impose an enormous burden of cost on the healthcare system. The existing knowledge on musculoskeletal conditions comprise over 150 diseases and syndromes usually associated with pain. They can broadly be categorized as joint diseases, spinal disorders and conditions resulting from trauma. The burden of musculoskeletal disorders is global hence, WHO declared 2000-2010 as the Bone and Joint decade.

Most common conditions comprising MSD are Osteoarthritis, Rheumatoid arthritis, Avascular necrosis and Trauma. These conditions are chronic and the best available treatment is Knee or Hip Arthroplasty to improve the quality of life. We need to insert orthopedic implants to restore the normal joint structure.

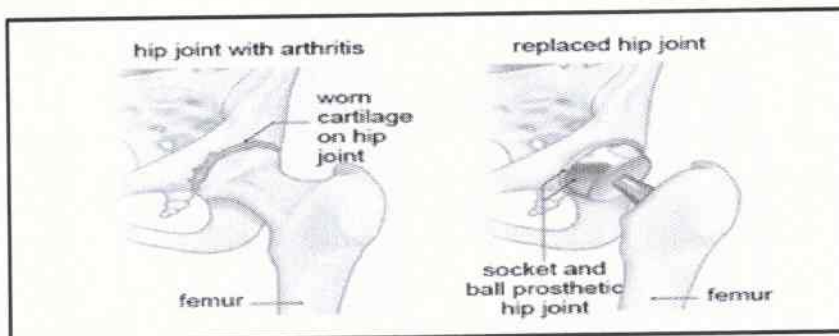


Orthopedic Implant:

An orthopaedic implant is a medical device made up of substance or combination of substances (other than a drug), synthetic or natural in origin, that can be used for any period of time as a whole or part of a system that treats, augments or replaces any tissue, organ or function of the human body. Widely Orthopedic implants are used in HIP & Knee Arthroplasty's.

Hip Arthroplasty

Hip arthroplasty is a surgical procedure in which the hip joint is replaced by a prosthetic implant. Hip replacement surgery can be performed as a total replacement or a hemi replacement. Such joint replacement orthopaedic surgery is generally conducted to relieve arthritis pain or in some hip fractures. A total hip replacement consists of replacing both the acetabulum and the femoral head while hemiarthroplasty generally only replaces the femoral head. As shown in the figure-



Indications for Total Hip Replacement

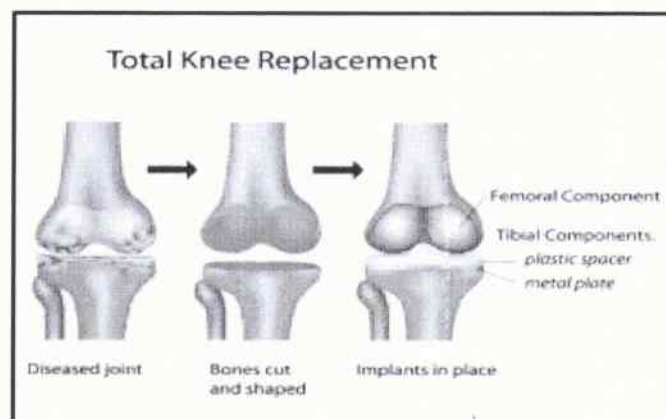
1. Avascular necrosis hip
2. Primary osteoarthritis
3. Post traumatic osteoarthritis
4. Rheumatoid arthritis
5. Fracture neck femur/Non union neck femur
6. Inter-trochanteric fracture
7. Pathological fracture
8. Tuberculosis Hip
9. Post Infectious arthritis
10. Old perthes disease
11. Aseptic loosening/Failed ' HR
12. Infected THR
13. Failed bipolar prosthesis

Knee Arthroplasty-

Knee arthroplasty is a surgical procedure to replace the weight-bearing surfaces of the knee joint to relieve pain and disability. It is most commonly performed for osteoarthritis, and also for other knee diseases such as rheumatoid arthritis and psoriatic arthritis. In patients with severe deformity from advanced rheumatoid arthritis, trauma, or long-standing osteoarthritis, the surgery may be more complicated and carry higher risk. Osteoporosis does not typically cause knee pain, deformity, or inflammation and is not a reason to perform knee replacement. Debilitating pain from osteoarthritis is much more common in the elderly.

Knee replacement surgery can be performed as a partial or a total knee replacement. In general, the surgery consists of replacing the diseased or damaged joint surfaces of the knee with metal and plastic components shaped to allow continued motion of the knee.

The operation typically involves substantial postoperative pain, and includes vigorous physical rehabilitation. The recovery period may be 6 weeks or longer and may involve the use of mobility aids (e.g. walking frames, canes, crutches) to enable the patient's return to preoperative mobility.



Indications for Total knee replacement

1. Primary osteoarthritis
2. Post traumatic arthritis
3. Rheumatoid arthritis
4. Post infectious arthritis
5. Infected TKR
6. Aseptic loosening/failed TKR
7. Periprosthetic fracture
8. Aneurysmal bone cyst distal end femur
9. Osteosarcoma distal femur
10. Giant cell tumors distal femur/proximal tibia
11. Other neoplasms of distal femur/proximal tibia
12. Others

Categories of materials used for orthopedic implants:

A) Category I - Metal Alloys:

1. Titanium alloys 2. Cobalt chrome alloys 3. Stainless steel

B) Category II- Nonmetals:

1. Ceramics & Bioactive glasses 2. Polymers (Bone cement, polyethylene)

A) Category I - Metal Alloys:

1. Titanium & Titanium alloys-

| Composition | |
|-------------|------------|
| Metal | Percentage |
| V | 4% |
| Hb | 7 % |
| Molybdenum | 5-15 % |
| Al | 6 % |

Physical properties:

It is strong, Lightweight, Corrosion Resistant, Cost-efficient, Non toxic, Biocompatible (non-toxic and not rejected by the body), Long-Lasting, Non-ferromagnetic, Osseointegration, Long range availability, Flexibility and elasticity rivals that of human bone.

2. Cobalt chrome alloys

| Composition | |
|--|------------|
| Metal | Percentage |
| Cobalt | 30-60% |
| Chromium | 20-30% |
| Minor amounts of carbon, nickel and molybdenum added | |

Physical properties

Resistance to wear & corrosion, Stamina, Very high Young's modulus

3. Stainless Steel

| Composition | |
|-------------|------------|
| Metal | Percentage |
| Chromium | 18% |
| Nickel | 16% |
| Molybdenum | 3% |
| Carbon | 0.03% |

| 316L | |
|--------------------|-----|
| Molybd | 3% |
| Nickel | 16% |
| Low carbon content | |

Physical Properties-

1. Strong 2. Relatively ductile 3. Biocompatible 4. Relatively cheap 5. Reasonably resistant to corrosion

B, Category II- Nonmetals

1. Ceramics

| |
|---|
| Composition |
| Silica (silicon oxide) |
| Zirconia (Zirconium oxide) |
| Hydroxyapatite (HA) |
| Compounds of metallic elements |
| Aluminium bound ionically or covalently with nonmetallic elements |
| Alumina (aluminium oxide) |

Physical Properties:

Chemically inert & insoluble, Best biocompatibility, Very strong, Osteoconductive.

2. Polymer

Consists of many repeating units of a basic sequence (monomer)

Most commonly used are:

Polymethylmethacrylate (PMMA, Bone cement) & Ultrahigh Molecular Weight Polyethylene (UHMWPE)

a. PMMA(Bone Cement)

Mainly used to fix prosthesis in place – can also be used as void fillers

Available as liquid and powder

The liquid contains:- The monomer N,N-dimethyltoluidine (the accelerator), Hydroquinone (the inhibitor)

The powder contains:- PMMA copolymer, Barium or Zirconium oxide (radio-opacifier), Benzoyl peroxide (catalyst)

b. UHMWPE

A polymer of ethylene with MW of 2-6million it is used for acetabular cups in THR prostheses

Metal on polyethylene is gold standard bearing surface in THR having high success rate.

Osteolysis produced due to polyethylene wear debris causes aseptic loosening

Biodegradable Polymers

Over all uses -

Pins, Bone plates, Screws, Bars, Rods, Wires, Posts, Expandable rib cages, Spinal fusion cages, Finger and toe Knee, Hip replacements and Maxio-facial prosthetics etc.

Objectives of Health Technology Assessment (HTA):

With a growing population of orthopedic patients, rising awareness about the impact of joint problems, and the importance of surgical treatments, there is a marked increase in orthopaedic cases. As orthopedic implants are very costly we cannot provide service to all the patients who belong to weaker sections of the society. But if the price of orthopaedic implants is reduced we can have Universal coverage for all orthopedic patients.

With over 2000 articles on the subject, there exist substantial evidence on Cemented versus Uncemented orthopedic Implants and on efficacy of different metals and non metals as orthopedic implants.

Objectives of this review-

- i. To assess the clinical effectiveness of Cemented Versus Uncemented Knee Orthopedic Implants
- ii. To assess the clinical effectiveness of Cemented Versus Uncemented Hip Orthopedic Implants
- iii. To assess the clinical effectiveness of different types of metals and non metals used as Orthopedic implants.
- iv. To evaluate the price variations among different types of Orthopedic Implants.

Methodology:

Systematic review is a practical research method in the field of medicine for searching targeted document. It applies predesigned methodologies to identify and access relevant literature, then summarizes conclusions from individual studies to answer specific research question. The major advantage of systematic literature review is to study the research phenomena across a wide range of settings and empirical methods. The secondary advantage is the usage of Meta - analytic technique. This technique will increase the likelihood of detecting real effects than individual studies.

Systematic literature review comprises following steps - Literature search from evidence-based databases, literature filter by criteria, data extraction according to our outcome and data analysis in legible diagrams.

The Literature search was conducted in three parts to complete this HTA report.

- A) Literature Search for Knee Arthroplasty
- B) Literature Search for Hip Arthroplasty
- C) Literature Search for different metals and non metals used for Orthopedic Implants.

As, literature search is an essential component to complete a Systematic Review. This includes literature search for evidences, in particular on clinical effectiveness of orthopedic Implants, as per a pre-defined selection criteria and inclusion criteria. Advanced electronic Literature search was done for searching eligible studies. Databases used for the literature search were- Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, ELSEVIER, Pubmed and Science Direct were searched. Secondary referencing was conducted by reviewing reference lists of key articles and searching citations. These above mentioned databases were searched for Knee, Hip Arthroplasty and for different metals and non metals used for orthopedic implants.

A) Literature Search strategy for Knee Arthroplasty Systematic Review:-

Study selection & Data synthesis:

Using the search strategy described above, all titles and abstracts were retrieved. Duplicate, articles not relevant, and articles that did not meet the inclusion criteria were filtered. Studies selected were a mix of Prospective, Retrospective, Cohort and randomised control trial comparing Cemented Versus Uncemented Orthopedic Implants for Knee Arthroplasties. Two reviewers assessed the studies in order to ensure that they met the inclusion criteria set out for this review.

136 studies were available, among them 100 studies were selected. Among these 55 studies were selected after reading the complete text.

28 studies were rejected with reasons. Finally 9 studies were selected and were included for quantitative synthesis (Meta Analysis). Dichotomous data was extracted from the studies and analyzed using Review Manager (RevMan 5.3). For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Key Words used while searching articles were Cemented and Uncemented Orthopedic Knee Implants, Cemented Knee Orthopaedic Implants, Uncemented Knee Orthopaedic Implants.

Inclusion Criteria:

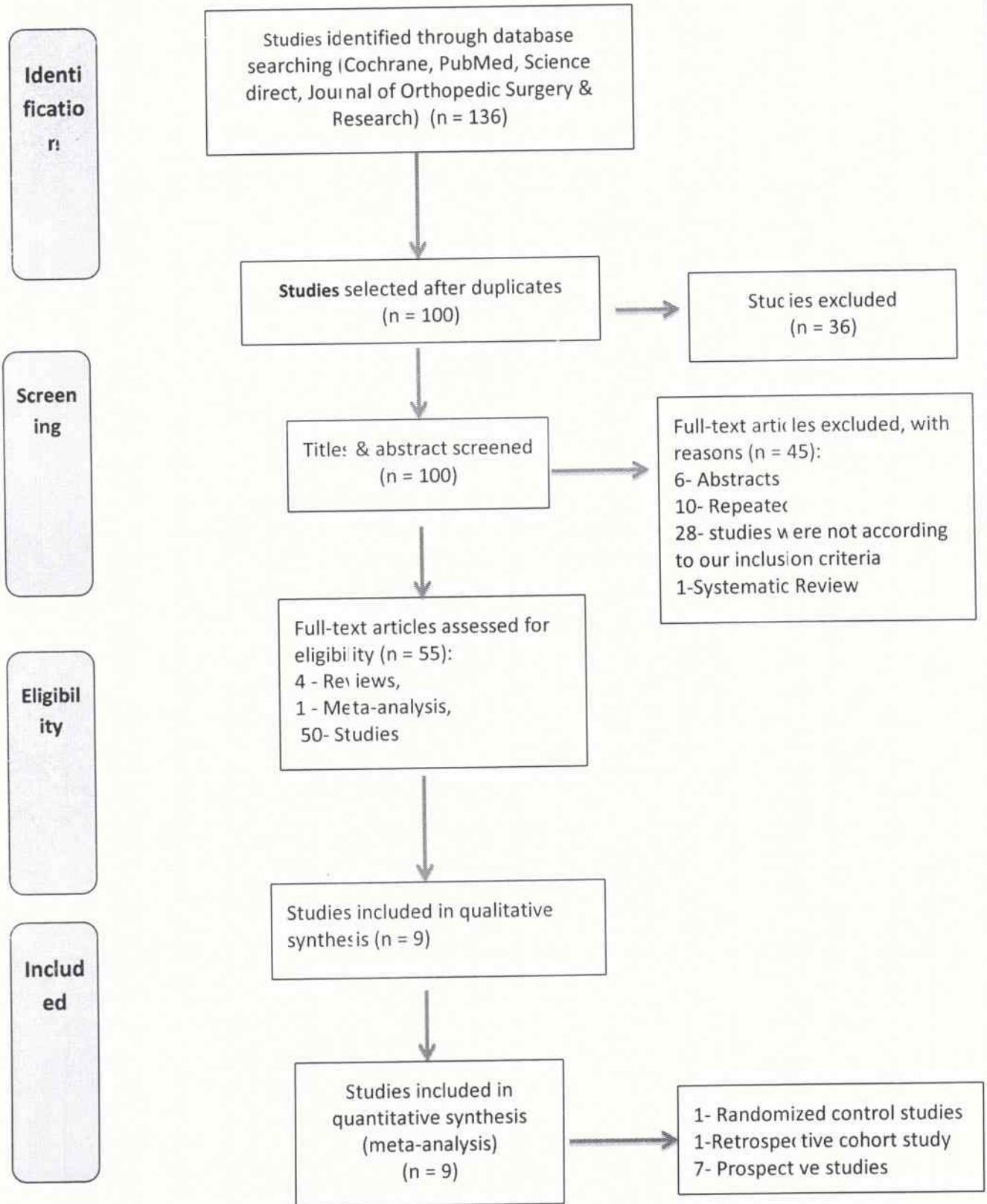
The literature selection criteria are intended to identify primary studies that provide specific evidence about the research topic.

Below mentioned selection criteria was used:-

The PICO parameters used for the selection criteria for the studies on literature search as follows:

| | | |
|----------|--|--|
| P | • Population- Patients in need of Knee Orthopedic Implants | |
| I | • Intervention- Cemented orthopedic Implants | |
| C | • Comparator- Uncemented orthopedic Implants | |
| O | • Outcome- Revision | |

Study Search Diagram for Knee Arthroplasty

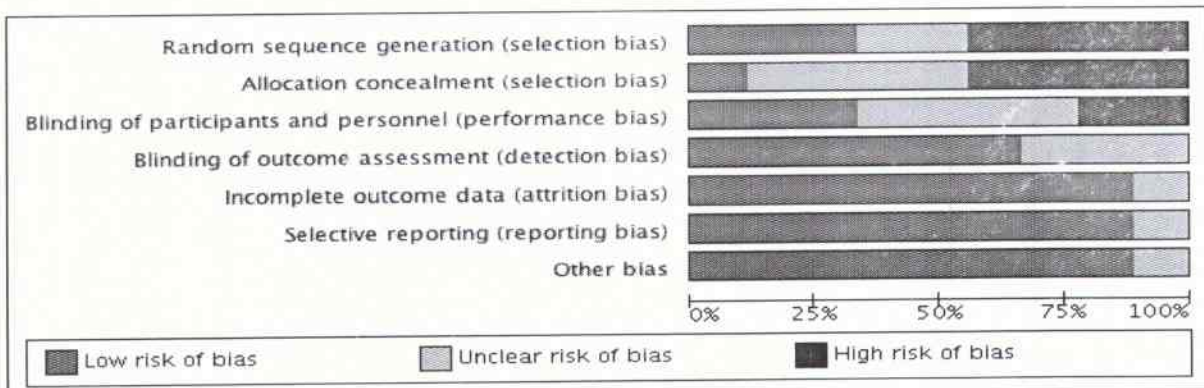


Risk of Bias Assessment for included studies

For methodological quality assessment of included studies, Cochrane Review Manager's Risk of Bias Table was used. Findings of bias assessment of included studies are given below:

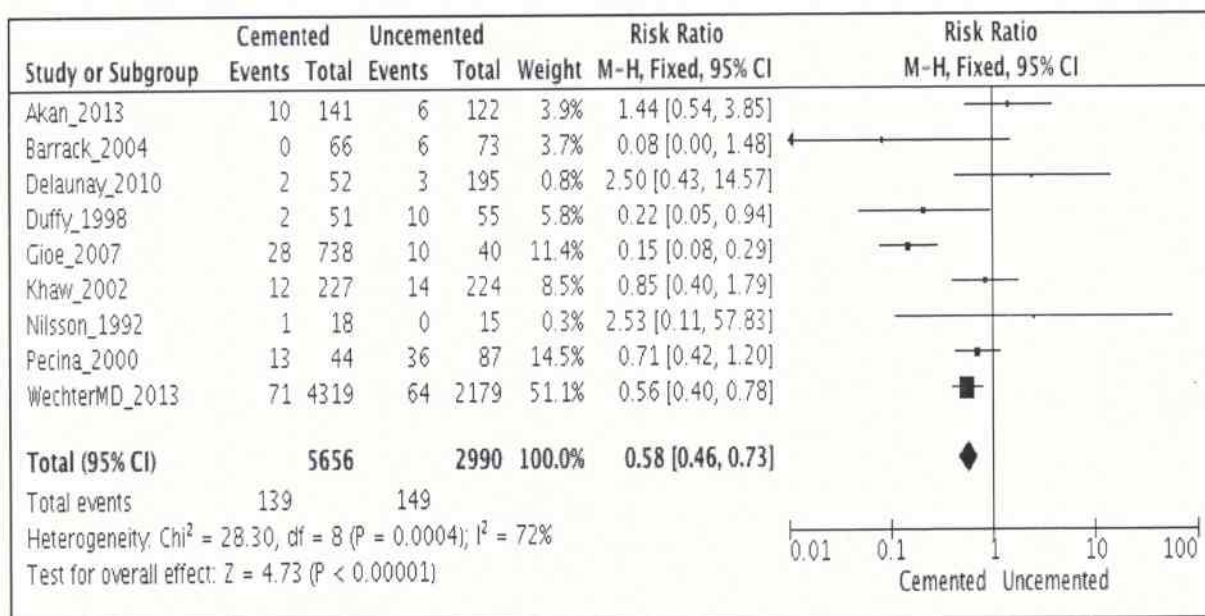
| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|---------------|---|---|---|---|--|--------------------------------------|------------|
| Akan_2013 | ? | ? | ? | + | + | + | + |
| Barrack_2004 | - | - | ? | + | + | + | + |
| Delaunay_2010 | - | - | - | + | + | + | + |
| Duffy_1998 | + | ? | ? | ? | ? | ? | ? |
| Gloe_2007 | - | - | + | + | + | + | + |
| Khaw_2002 | + | + | + | ? | + | + | + |
| Nilsson_1992 | + | ? | + | + | + | + | + |
| Pecina_2000 | - | - | - | ? | + | + | + |
| Wechter_2013 | ? | ? | ? | + | + | + | + |

Risk of Bias Summary -



Forest plot showing comparative data of revision between Cemented Versus Uncemented Orthopedic Knee Implants

A total of 9 studies were finally included for analysis which had revision as outcome. Among all studies, there were 5656 patients in intervention group (Cemented) and 2990 in control group (Uncemented). The findings are summarized in the plot below:



As per the forest plot findings, Risk Ratio = 0.58 which is < 1 and indicates a 42% reduction in incidence of revision in Cemented Knee Orthopedic group compared to Uncemented Orthopedic implant group. It means that cemented orthopedic implant is $1/0.58 = 1.724$ times more effective in reducing revisions. In all cases, $RR = 1$ would mean experimental group is as effective as control group; $RR < 1$ would mean experimental group is more effective than control group for a negative outcome such as revision; an $RR > 1$, experimental group is less effective than control group for a negative outcome.

B) Literature Search strategy for Hip Arthroplasty Systematic Review:-**Study selection & Data synthesis:**

Using the search strategy described above, all titles and abstracts were retrieved. Duplicate, articles not relevant, and articles that did not meet the inclusion criteria were filtered. Studies selected were a mix of Prospective, Retrospective, Cohort and randomised control trial comparing Cemented Versus Uncemented Orthopedic Implants for Hip Arthroplasties. Two reviewers assessed the studies in order to ensure that they met the inclusion criteria set out for this review.

Total studies were identified through database search were 495 studies were excluded during screening. 75 full articles was assessed for systemic analysis. Finally 18 studies were included for quantitative analysis. The study flow diagrams are given below:

The dichotomous data was collected from the studies and analyzed using Review Manager (RevMan 5.3). For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Key Words used while searching articles were Cemented and Uncemented Orthopedic Knee Implants, Cemented Knee Orthopaedic Implants, Uncemented Knee Orthopaedic Implants.

Inclusion Criteria:

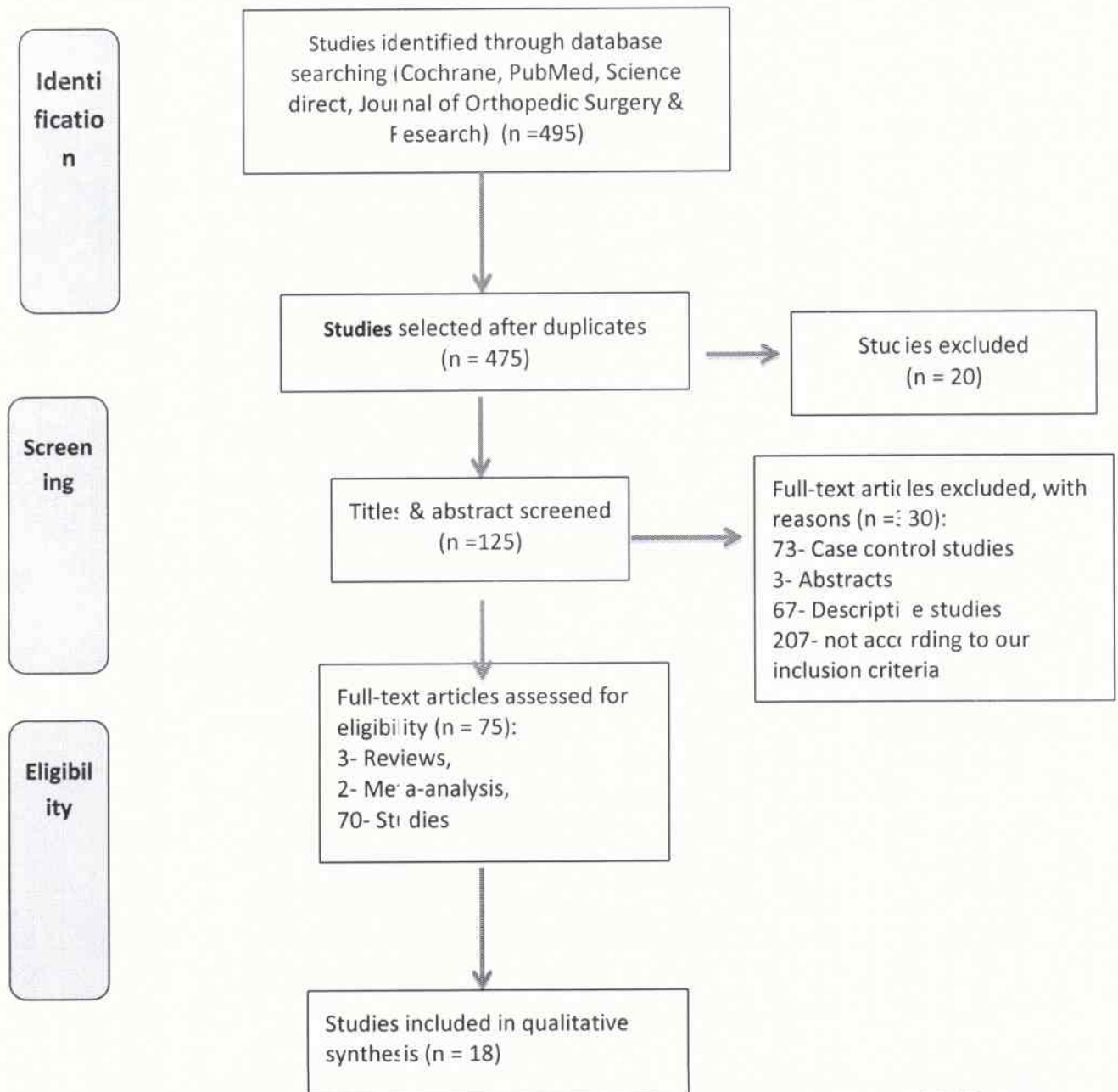
The literature selection criteria are intended to identify primary studies that provide specific evidence about the research topic.

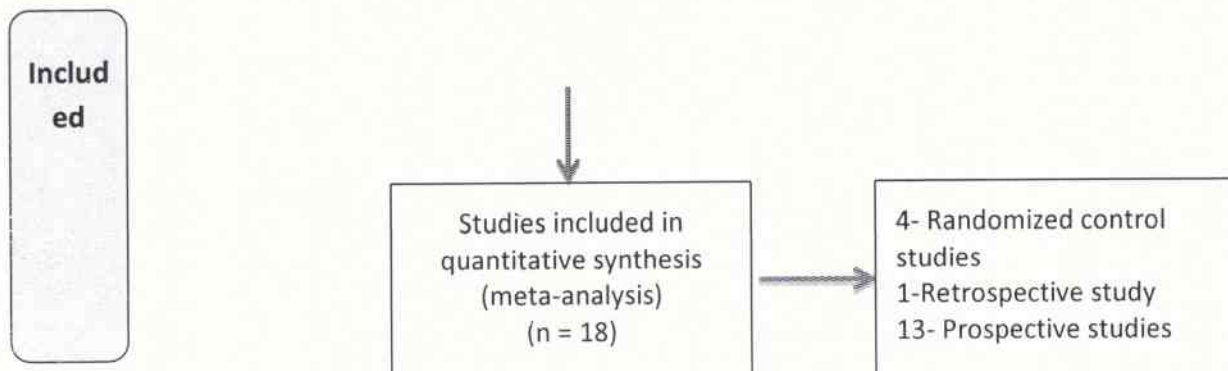
Below mentioned selection criteria was used:-

The PICO parameters used for the selection criteria for the studies on literature search as follows:

| | | |
|---|--|--|
| P | •Population- Patients in need of Hip Orthopedic Implants | |
| I | •Cemented Hip Orthopedic Implants | |
| C | •Uncemented Hip Orthopedic Implants | |
| O | •1. Revision •2. Osteolysis and Infection | |

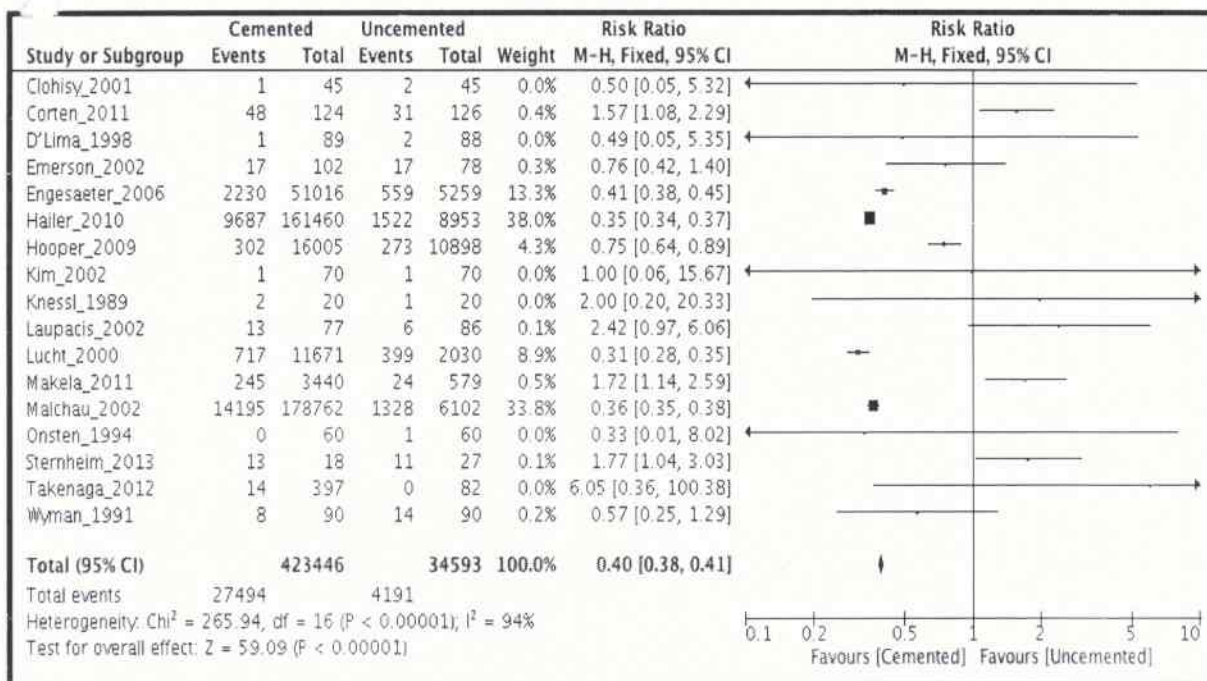
Study Search Diagram





Forest plot showing comparative data of revision between Cemented Versus Uncemented Orthopedic Hip Implants

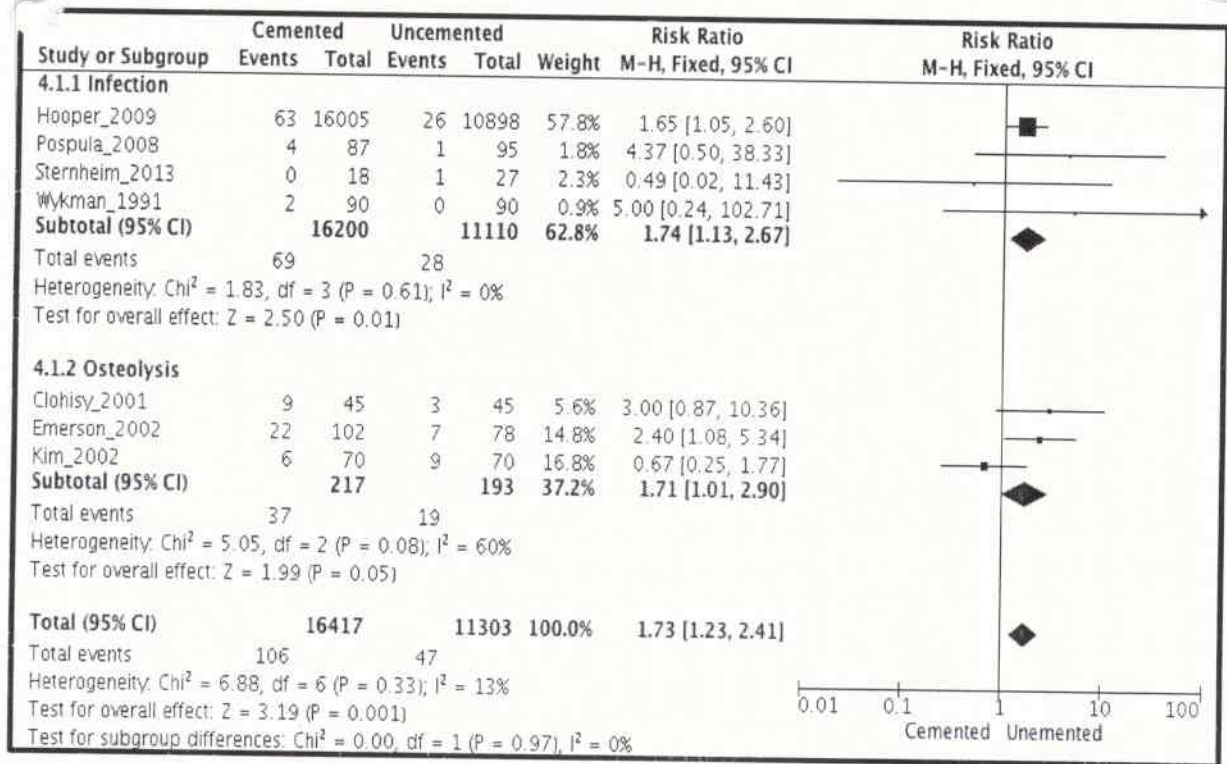
There were a total of 18 studies that measures estimates of revision between Cemented Versus Uncemented Orthopedic Implants. The sample size across studies varied from 178762 in intervention group (Cemented) to 10898 in control group (Uncemented) as maximum to 20 in intervention group (Cemented) and 20 in control group (Uncemented) as minimum. Overall the analysis included 423446 patients in intervention and 34593 patients in control group. Although there was inter-study variations, heterogeneity of 94% was present showing high inter - study variation showing skewed results.



As per the analysis above, RR(Risk Ratio)of 0.40means 60% reduction in incidence of revision in cemented Hip orthopedic Implant compared to Uncemented Hip orthopedic Implant.It mens that cemented orthopedic implant is $1/0.40 = 2.5$ times more effective in reducing revisions than uncemented orthopedic implants. In all cases, RR = 1 would mean experimental group is as effective as control group; RR < 1would mean experimental group is more effective than control group for a negative outcome such as revision; an RR > 1, experimental group is less effective than control group for a negative outcome.

B)Forest plot showing comperative data of Infection & Osteolysis between Cemented Versus Uncemented Orthopedic Hip Implants

There were a total of 6 studies that measures estimates of Infection & Osteolysis between Cemented Versus Uncemented Orthopedic Implants. Overall the analysis included 16417 patients in intervention and 11303 patients in control group.

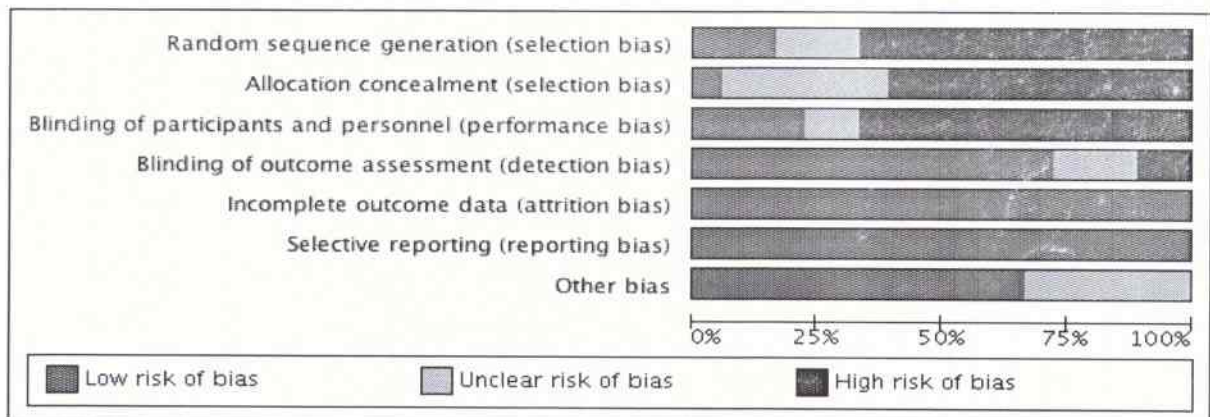


Risk Ratio = 1.73, means 73% less risk of Infection & Osteolysis in cemented Hip Implant compared to Uncemented Hip Implant. It means that cemented orthopedic implant is 1.73 times more effective in reducing Infection & Osteolysis compared to uncemented orthopedic implants. In all cases, $RR = 1$ would mean experimental group is as effective as control group; $RR < 1$ would mean experimental group is more effective than control group for a negative outcome such as revision; an $RR > 1$, experimental group is less effective than control group for a negative outcome.

Risk of Bias Assessment for included studies-

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|-----------------|---|---|---|---|--|--------------------------------------|------------|
| Clohisy_2001 | ? | ? | ? | ? | + | + | + |
| Corten_2011 | + | + | + | + | + | + | ? |
| D'Lima_1998 | + | + | + | + | + | + | ? |
| Emerson_2002 | ? | + | + | + | + | + | ? |
| Engesaeter_2006 | + | + | + | + | + | + | + |
| Haller_2010 | + | ? | + | + | + | + | + |
| Hooper_2009 | ? | + | + | + | + | + | + |
| Kim_2002 | + | ? | + | + | + | + | ? |
| Knessl_1989 | + | + | + | ? | + | + | + |
| Laupacis_2002 | + | + | + | + | + | + | + |
| Lucht_2000 | + | + | + | ? | + | + | + |
| Makela_2011 | + | ? | ? | + | + | + | ? |
| Malchau_2002 | + | + | + | + | + | + | + |
| Onsten_1994 | + | ? | + | + | + | + | + |
| Pospula_2008 | + | + | + | + | + | + | + |
| Sternhelm_2013 | + | + | + | + | + | + | + |
| Takenaga_2012 | + | + | + | + | + | + | ? |
| Wykman_1991 | + | ? | + | + | + | + | + |

Risk of Bias Summary -



CJ Literature Search strategy for comparison of different metals and non-metals used for Orthopedic Implants

Using the search strategy described above, all titles and abstracts were retrieved. Duplicate, articles not relevant, and articles that did not meet the inclusion criteria were filtered. Studies selected were a mix of Randomised clinical trials; Case control studies, Retrospective studies, Prospective studies, double blind prospective randomised control trials which were available on this subject are included in this review. Two reviewers assessed the studies in order to ensure that they met the inclusion criteria set out for this review. 999 studies were available, among these 100 studies were selected after reading the complete text. Further 50 studies & 2-reviews were selected after removing duplicates. Finally 6 studies were selected and were included for quantitative synthesis (Meta Analysis). The dichotomous data was collected from the studies and analyzed using Review Manager (RevMan 5.3). For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

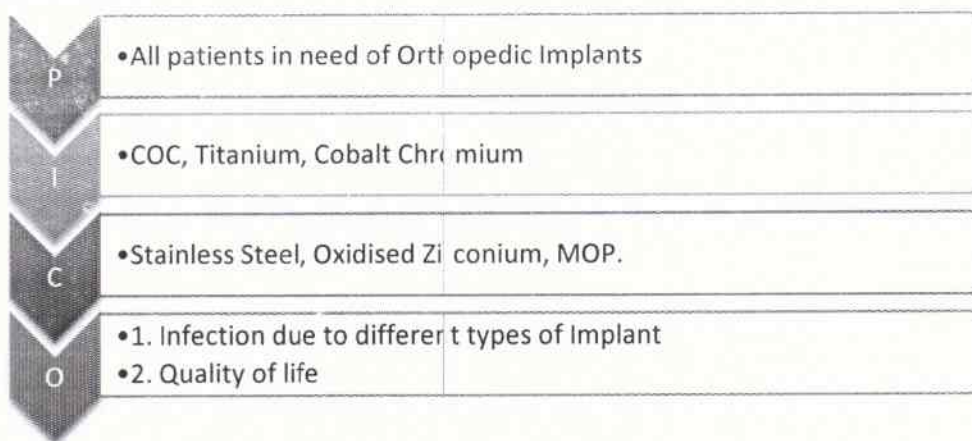
Key Words used while searching articles were used while searching articles were Titanium, Cobalt Chromium and Stainless Steel Orthopaedic Implants, Orthopaedic Implants.

Inclusion Criteria:

The literature selection criteria are intended to identify primary studies that provide specific evidence about the research topic.

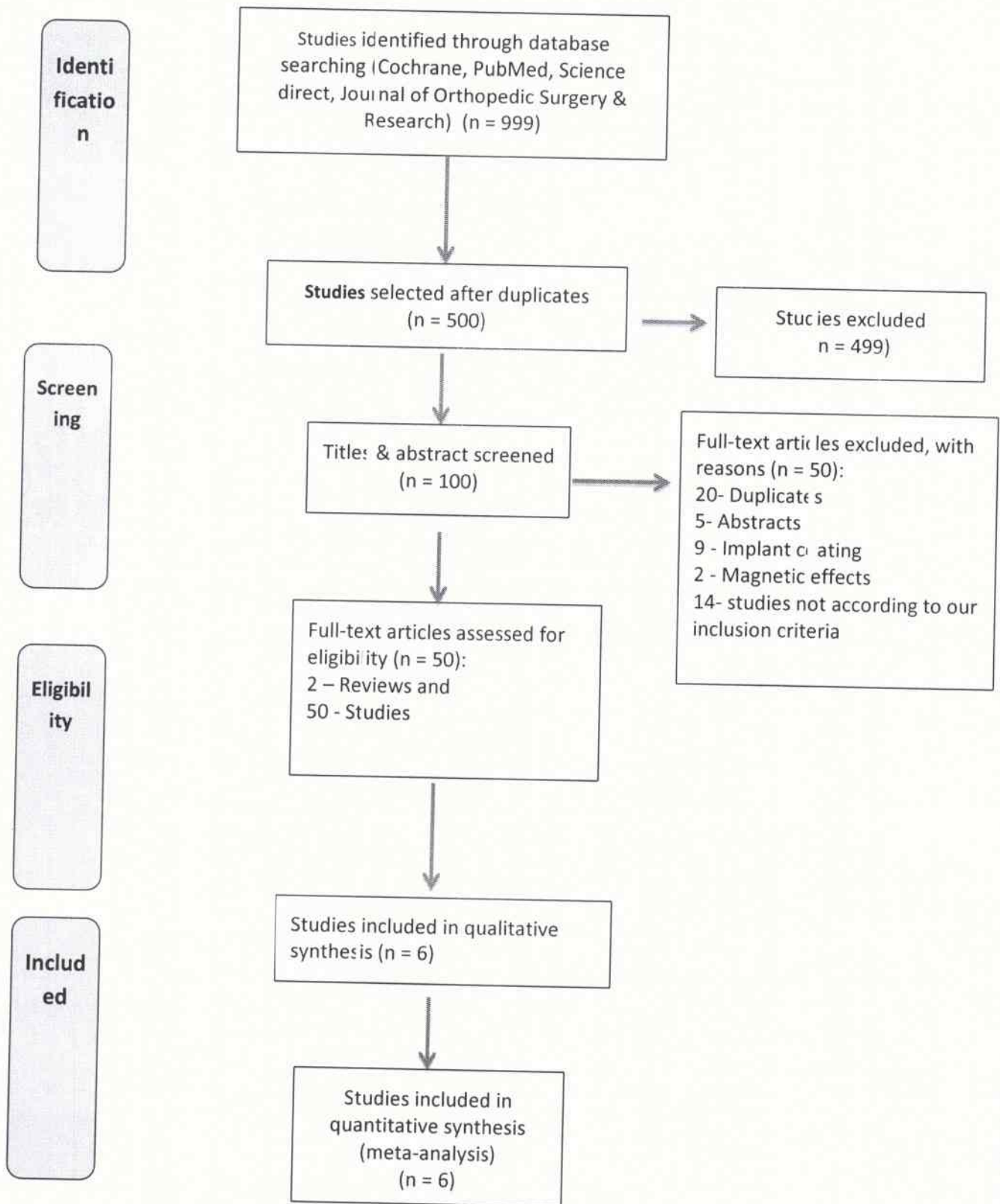
Below mentioned selection criteria was used:-

The PICO parameters used for the selection criteria for the studies on literature search as follows:



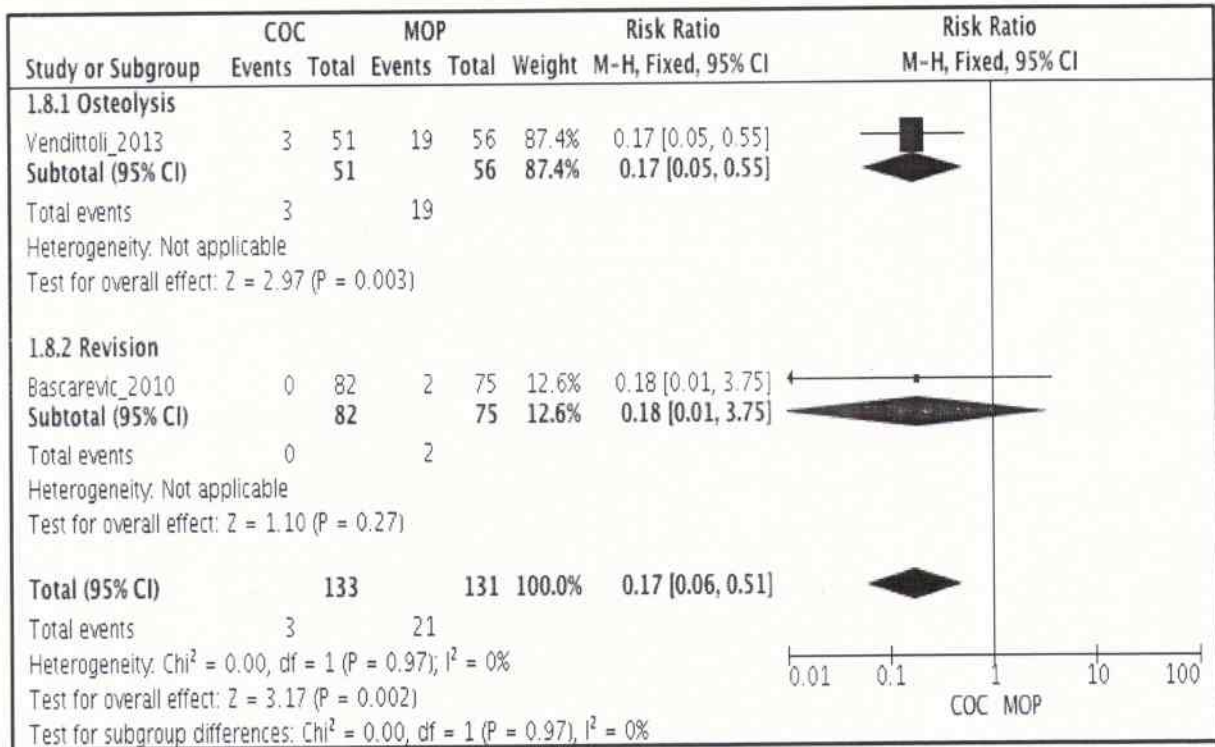
As shown in the figure below:-

Study Search Diagram



Forest plots showing comparison between Ceramic on Ceramic (COC) & Metal on Polymer (MOP) for Osteolysis & Revision:

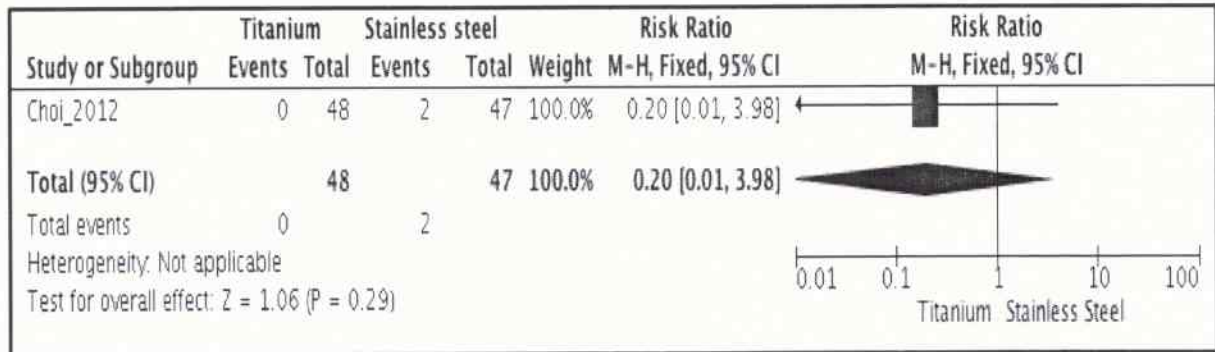
Two studies had estimated outcomes on osteolysis & revision between Ceramic on Ceramic (COC) & Metal on Polymer (MOP). Overall in the analysis there were 133 patients in intervention group and 131 patients in control group.



As per the findings above, a Risk Ratio (RR) of 0.17 denotes a 83% reduction in osteolysis & revision in Ceramic on Ceramic (COC) than Metal on Polymer (MOP) group. It means that COC is $1/0.17 = 5.8$ times more effective in reducing Infection & Osteolysis compared to MOP. In all cases, $RR = 1$ would mean experimental group is as effective as control group; $RR < 1$ would mean experimental group is more effective than control group for a negative outcome such as revision; an $RR > 1$, experimental group is less effective than control group for a negative outcome.

Forest plots showing comparative data of infection between Titanium & Stainless Steel :

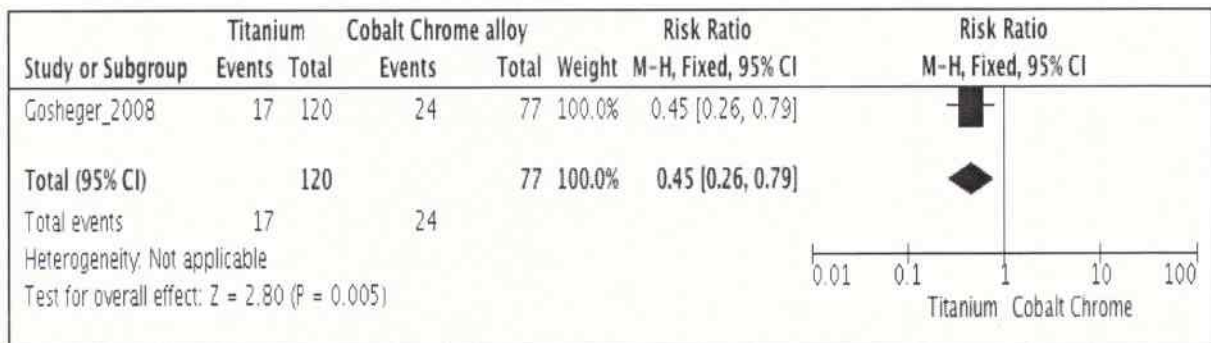
One study had estimated Infection between Titanium & Stainless Steel Orthopedic Implant. Overall in the analysis there were 48 patients in intervention group and 47 patients in control group.



As per the findings above, a Risk Ratio (RR) of 0.20 denotes 80% reduction in infection in Titanium than Stainless Steel. It means that Titanium is $1/0.20 = 5$ times more effective in reducing Infection than Stainless Steel. In all cases, $RR = 1$ would mean experimental group is as effective as control group; $RR < 1$ would mean experimental group is more effective than control group for a negative outcome such as revision; an $RR > 1$, experimental group is less effective than control group for a negative outcome.

Forest plots showing comparative data of infection between Titanium & Cobalt Chrome alloy

One study had estimated Infection between Titanium & Cobalt Chrome alloy Orthopedic Implant. Overall in the analysis there were 120 patients in intervention group and 77 patients in control group.



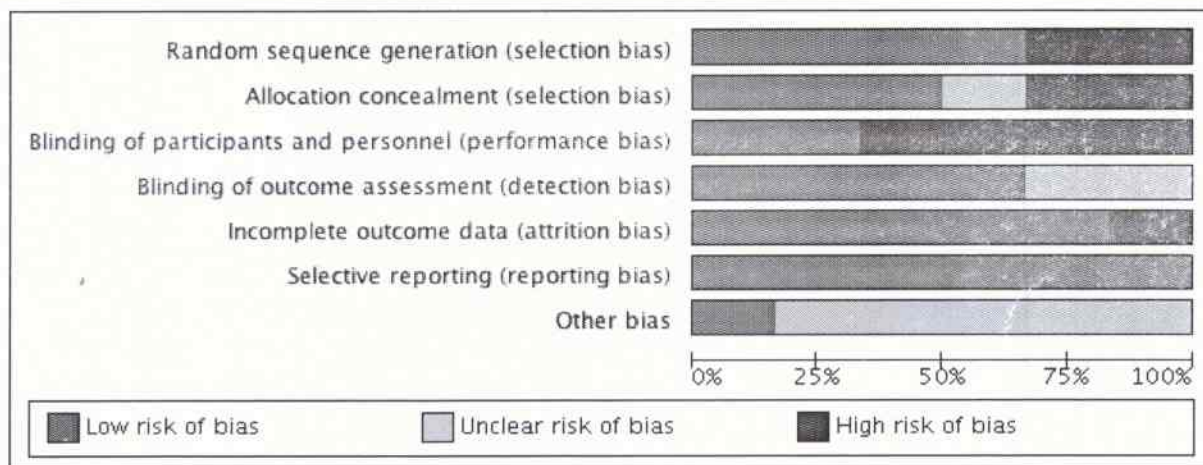
As per the findings above, a Risk Ratio (RR) of 0.45 denotes 55% reduction in infection in Titanium than Cobalt Chrome alloy.

As per the findings above, a Risk Ratio (RR) of 0.45 denotes 80% reduction in infection in Titanium than Stainless Steel. It means that Titanium is $1/0.45 = 2.2$ times more effective in reducing Infection than Stainless Steel. In all cases, RR = 1 would mean experimental group is as effective as control group; RR < 1 would mean experimental group is more effective than control group for a negative outcome such as revision; an RR > 1, experimental group is less effective than control group for a negative outcome.

Risk of Bias Assessment for included studies

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|-----------------|---|---|---|---|--|--------------------------------------|------------|
| Bascarevic_2010 | + | + | - | ? | + | + | ? |
| Choi_2012 | - | - | - | + | + | + | ? |
| D'Antonio_2012 | + | ? | - | + | + | + | ? |
| Gosheger_2008 | - | - | - | ? | - | + | ? |
| Nikolaou_2012 | + | + | + | + | + | + | + |
| Vendittoli_2013 | + | + | + | + | + | + | ? |

Risk of Bias Summery -



Costs and Effects:

Cost-effectiveness analysis is a method of comparing the cost and effectiveness of two or more alternatives. Such comparisons are useful when one of the alternatives being considered is standard care, as this allows the decision maker to consider whether an alternative is better or not. Where mortality is not the only outcome and there are harder to measure events such as revascularization or adverse events, Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs) remain a unit of choice for comparing interventions.

Quality-adjusted life-year (QALY) takes into account both the quantity and quality of life generated by healthcare interventions. It is the arithmetic product of life expectancy and a measure of the quality of the remaining life years. In other words, the QALY is a measure of the value of health outcomes since health is a function of length of life and quality of life. QALY assumes that a year of life lived in perfect health is worth 1 QALY (1 Year of Life \times 1 Utility value = 1 QALY) and that a year of life lived in a state of less than this perfect health is worth less than 1.

Disability-adjusted life year (DALY) is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death. DALYs are calculated by taking the sum of two components- Years of life lost (YLL) and Years of life lived with disability (YLD). Thus $DALY = YLL + YLD$

DALY's lost due to Rheumatoid and Osteoarthritis has been tabulated below:

| Age | Rheumatoid Arthritis(DALY) ('000) | Osteoarthritis(DALY)('000) | Population |
|--------------|-----------------------------------|----------------------------|---------------|
| 30-59 | 353.60 | 1167.20 | 434455 |
| 60-69 | 150.80 | 438.90 | 61272 |
| 70+ | 183.30 | 319.90 | 38962 |
| TOTAL | 687.70 | 1926 | 534689 |

Landeling cost of implants in Hospitals-

| | TKR (Cemented) | TKR (Uncemented) | THR (Cemented) | THR (Uncemented) |
|--------------------------|-------------------|---------------------|-------------------|---------------------|
| Indus C | 38,000.00 | | 26,000.00 | |
| Indus UC | | | | 75,000.00 |
| Smith C | 65,000.00 | | 46,000.00 | |
| Smith UC | | 95,000.00 | | 100,000.00 |
| Depuy C | 68,000.00 | | 50,000.00 | |
| Depuy UC | | | | 70,000.00 |
| Evolutis C | 45,000.00 | | 55,000.00 | |
| Evolutis UC | | 75,000.00 | | 75,000.00 |
| Biored C | 35,000.00 | | | |
| Biored UC | | | | 75,000.00 |
| Sharma C | 35,000.00 | | 21,000.00 | |
| Sharma UC | | | | 59,000.00 |
| Average | 47,666.67 | 85,000.00 | 39600.00 | 75,666.67 |
| Service Tax (14.00 %) | 6,673.33 | 11,900.00 | 5,544.00 | 10,593.33 |
| Total | 54,340.00 | 96,900.00 | 45,144.00 | 86,260.00 |

* UC = Uncemented

* C = Cemented

The proposed price of Hip and Knee implants is suggested as below:

Hip Implants:

Uncemented: 86,000/-

Cemented: Rs.45,000/-

Knee Implants:

Uncemented: 97,000/-

Cemented: Rs.54,000/-

The cost includes service tax. It is also suggested that:

- i. Packaging of implants should ensure unit wise packing
- ii. MRP to be made mandatory on all implant packs
- iii. Hospital handling charges to be substituted with service tax as applicable.