Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie

KCE reports vol. 39A

Federaal Kenniscentrum voor de gezondheidszorg
Centre fédéral d'expertise des soins de santé
2006

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Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie

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KCE reports vol.39A

Titel :	Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie
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Conflict of interest :	R.W. was consultant for Schering Plough Belgium and BMS International; Y.B. was reviewer for Kyphon, Inc.
Disclaimer:	De experts en validatoren werkten mee aan het wetenschappelijk rapport maar zijn niet verantwoordelijk voor de beleidsaanbevelingen. Deze aanbevelingen vallen onder de volledige verantwoordelijkheid van het KCE.
Layout:	Dimitri Bogaerts, Nadia Bonnouh

Brussel, september 2006

Studie nr 2005-04
Domein : Good Clinical Practive (GCP)

MeSH : Low Back Pain ; Intervertebral Disk ; Fractures, Compression ; Surgical Procedures, Operative
NLM classification : WE 755

Taal : Nederlands, Engels
Format : Adobe® PDF™ (A4)

Wettelijk depot : D/2006/10.273/38

Hoe refereren naar dit document?
Vlayen J, Camberlin C, Paulus D, Ramaekers D. Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie. Good Clinical Practice (GCP). Brussel: Federaal Kenniscentrum voor de gezondheidszorg (KCE); 2006. KCE reports 39A (D/2006/10.273/38)

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Voorwoord

De behandeling van chronische lage rugpijn blijft een enorme uitdaging vormen voor de moderne geneeskunde. Lage rugpijn leidt maatschappelijk tot heel wat langdurig werkverlet en arbeidsongeschiktheid. De meest geschikte aanpak van deze problematiek vormt trouwens het onderwerp van een apart KCE rapport dat eind dit jaar zal afgerond worden.

In dit rapport worden op vraag van het RIZIV twee 'rapid assessment' gepresenteerd van nieuwe chirurgische technieken in het domein van de lage rugpijn: totale discusprothese voor de behandeling van degeneratief lumbaal discuslijden enerzijds, en vertebroplastie / ballon kyfoplastie voor de behandeling van wervelindeukingsfracturen anderzijds.

'Rapid assessments' zijn iets nieuws in de Belgische context en onderscheiden zich van een volledige 'health technology assessments'. Eén belangrijk verschil is dat ze beduidend sneller het daglicht zien. Beleidsmakers willen vaak het antwoord op hun vraag van vandaag gisteren al hebben. De druk van producenten, opinieleiders en soms zelfs patiënten laat niet altijd toe om bvb. een jaar te wachten tot een volledig HTA beëindigd is.

Deze nieuwe technologieën kunnen mogelijks baten voor de patiënt geven, maar dragen ook risico op complicaties en zijn meestal duur. De wetenschappelijke bewijzen van hun werkzaamheid op relevante patiëntenuitkomsten en lange termijn veiligheid zijn vaak nog beperkt of virtueel onbestaande, vermits de klinische studies nog dikwijls lopende zijn. De onderzoekers of de producent zijn vaak bereidwillig om al interim of voorlopige resultaten ter beschikking te stellen. De interpretatie van dergelijke preliminaire informatie die de toets van peer review en publicatie nog niet doorstaan heeft, blijft een riskante onderneming. Anderzijds wil dit ook zeggen dat de finale resultaten van die studies mogelijks de conclusies van een rapid assessment zullen nuanceren of zelfs tegenspreken.

De in dit rapport behandelde nieuwe wervelzuil technologieën vormen een goede illustratie van een majeure uitdaging waarmee de meeste Westerse systemen geconfronteerd worden. Voor nieuwe technologieën zoals diegenen die in dit rapport worden besproken is er heel wat beweging, getuige de informatiestroom die tot op het einde bleef toekomen. Het KCE hoopt dat dit rapport een houvast biedt om een weloverwogen beslissing te nemen.

Dit rapport kwam tot stand dankzij een vruchtbare samenwerking tussen het KCE en haar kennisnetwerk. Onze dank gaat dus naar de externe experten en de producenten van de betrokken technologieën voor hun gewaardeerde input.

Jean-Pierre Closon
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Executive summary

Dit rapport bevat twee 'rapid assessments' die de klinische en kosteneffectiviteit evalueren van enkele opkomende technieken in het domein van lage rugpijn: totale discusprothese voor de behandeling van degeneratief lumbaal discuslijden enerzijds, en vertebroplastie en ballon kyfoplastie voor de behandeling van lumbale wervelindeukingsfracturen anderzijds. Uitgaande van HTA rapporten, systematische reviews en klinische studies wordt een samenvatting gegeven van de evidentie over de efficiëntie, klinische effectiviteit en veiligheid van deze 3 technieken. Het rapport volgt de standaard KCE methodologie van een HTA rapport, zonder echter uitgebreid in te gaan op patiëntenaspecten, ethische aspecten en organisationele aspecten.

Totale discusprothese

Achtergrond

Conservatieve, niet-chirurgische behandeling is dikwijls de eerste keuze bij chronische lage rugpijn veroorzaakt door degeneratief discuslijden. Bij sommige patiënten brengt deze behandeling echter weinig tot geen beterschap, en wordt de stap naar chirurgie gezet. Lumbale arthrodese wordt in deze omstandigheden als 'gouden standaard' aanzien. De laatste jaren wordt ook totale discusprothese als alternatief voor lumbale arthrodese aangeboden. Een discusprothese bestaat uit 2 metalen eindplaatjes en een flexibele synthetische kern. Momenteel zijn er 6 types internationaal beschikbaar, waarvan er 4 in België gebruikt worden.

Doelstellingen

Het doel van deze 'rapid assessment' is de beschikbare klinische en economische evidentie samen te vatten voor totale discusprothese in vergelijking met conservatieve behandeling of lumbale arthrodese, en dit voor de volgende indicaties: degeneratief discuslijden, lumbale discushernia, post-laminectomie syndroom, chronische lage rugpijn refractair aan conservatieve behandeling en gefaalde lumbale arthrodese.

Methodologie

In meerdere electronische databanken werd gezocht naar HTA-rapporten, systematische reviews en gerandomizeerde studies (RCT). Deze zoektocht werd aangevuld met een nazicht van de grijze literatuur en contacten met de industrie. Relevante studies werden o.b.v. titel en abstract geselecteerd door 1 onderzoeker. De geselecteerde studies werden vervolgens o.b.v. de full-text beoordeeld op hun kwaliteit door 1 onderzoeker, en nadien door een 2^{e} onafhankelijke onderzoeker en een groep van externe experten. Studies van lage kwaliteit werden geëxcludeerd. Van de geïncludeerde klinische studies werden de volgende gegevens geëxtraheerd: studie design, aantal en type patiënten, interventie, comparator, uitkomstvariabelen en resultaten.

Resultaten

Klinische effectiviteit en veiligheid

Van de 24 potentieel relevante studies werden uiteindelijk 7 studies geïncludeerd: 2 HTA-rapporten, 2 systematische reviews, en 3 artikels die de resultaten van 1 unieke RCT beschreven. Er werden bovendien een 5-tal lopende RCT's gevonden.

De geïncludeerde HTA-rapporten en systematische reviews hadden vergelijkbare zoekresultaten en de meerderheid verwees naar de in dit rapport geïncludeerde RCT. De meeste auteurs beschouwden totale discusprothese als een experimentele interventie o.b.v. de beschikbare evidentie.

In de geïncludeerde RCT werden 304 patiënten met symptomatisch degeneratief discuslijden, refractair aan conservatieve behandeling gedurende 6 maanden, gerandomiseerd naar totale discusprothese met de Charité discusprothese (n = 205) of anterieure lumbale interlaminaire fusie (ALIF) (n = 99). Klinische uitkomsten waren o.a. pijn, functionele beperking, neurologische status en patiëntentevredenheid. Na een follow-up van 2 jaar bleek alleen de patiëntentevredenheid significant beter in de interventionele groep t.o.v. de controlegroep. Wat betreft de veiligheid verschillen de cijfers gerapporteerd in de studie van de cijfers weergegeven in een FDA-rapport, en het is niet duidelijk welke cijfers correct zijn. Device-gerelateerde verwikkelingen (rugpijn, pijn t.h.v. onderste ledematen, verplaatsing van device, inzakking) kwamen frequenter voor in de interventionele groep (7.8% vs. 4.0%), terwijl device failure (heringreep, revisie, verwijderen van device, bijkomende fixatie) frequenter voorkwam in de controlegroep (8.1% vs. 5.4%). Bij 2 patiënten behandeld met een discusprothese en 1 patiënt behandeld met fusie diende het implantaat verwijderd te worden – een potentieel gevaarlijke ingreep gezien de omliggende anatomische structuren, waar echter geen harde evidentie voor werd teruggevonden.

De geïncludeerde RCT heeft enkele belangrijke minpunten. De beoordelaars waren niet geblindeerd voor de toegewezen behandeling. Bovendien bleek de keuze van ALIF als comparator niet voor de hand liggend. Men is het in de literatuur immers niet eens over de superioriteit van lumbale arthrodese t.o.v. conservatieve behandeling. Een vergelijking tussen totale discusprothese en conservatieve behandeling is wenselijker.

Economische evaluatie

Geen enkele originele economische studie werd teruggevonden.

De prijs voor een discusprothese varieert in België van €2.400 tot €3.100, wat minder is dan bvb. in de Verenigde Staten. Het jaarlijkse budget voor het RIZIV bij terugbetaling van lumbale discusprothesen wordt geschat op €2.375.000, uitgaande van 1.000 ingrepen per jaar.

Conclusies

- De kwaliteit van de beschikbare klinische evidence voor de effectiviteit van totale discusprothese voor de behandeling van chronische lage rugpijn is laag. Bovendien bestaat er bezorgdheid over de veiligheid van deze techniek. Verwikkelingen op lange termijn worden dan ook best systematisch bijgehouden in observationele studie registers. Momenteel, en tot de resultaten van goede primaire studies beschikbaar worden, dient totale discusprothese als een experimentele interventie beschouwd te worden, die idealiter enkel uitgevoerd wordt bij zorgvuldig geselecteerde patiënten in het kader van klinische studies. Het design van deze klinische studies is bij voorkeur dat van een gerandomiseerde studie, waarbij totale discusprothese vergeleken wordt met de correcte comparators (waaronder conservatieve behandeling).
- Deze aanbevelingen zijn in tegenstelling met de huidige praktijk in sommige Belgische ziekenhuizen, waar patiënten behandeld worden met deze experimentele techniek buiten de setting van een klinische studie. Enkel registreren van patiënten behandeld met deze invasieve techniek in een register op vrijwillige basis is maatschappelijk gezien onaanvaardbaar. Het verplicht rapporteren van belangrijke verwikkelingen (sterfte, heringreep, permanente handicap, …) gerelateerd aan deze ingrepen wordt zelden gedaan.
- Hoewel economische gegevens ontbreken, kan men er van uit gaan dat de invloed op het budget van deze ingreep, de hospitalisatie en de behandeling van eventuele verwikkelingen aanzienlijk is, zelfs zonder directe terugbetaling van het implantaat.

Vertebroplastie en kyfoplastie

Achtergrond

Wervelindeukingsfracturen zijn een belangrijke oorzaak van acute rugpijn, chronische rugpijn en wervelzuilvervorming. De meeste patiënten kunnen adequaat behandeld worden met conservatieve behandelingen, zoals pijnmedicatie, bedrust, bracing, bisfosfonaten of calcitonine, maar voor patiënten die niet reageren op conservatieve therapie kan chirurgie overwogen worden. Momenteel is er grote interesse voor de zogenaamde minimaal invasieve ingrepen, zoals vertebroplastie (VP) en ballon kyfoplastie (BK). In beide gevallen wordt cement geïnjecteerd in de aangetaste wervel, in het geval van BK gebeurt dit na het creëren van een holte d.m.v. een ballon.

Doelstellingen

Het doel van deze 'rapid assessment' is de beschikbare klinische en economische evidentie samen te vatten voor VP en BK voor de volgende indicaties: osteoporotische wervelindeukingsfracturen, traumatische wervelindeukingsfracturen, botmetastasen en hemangiomata.

Methodologie

In meerdere electronische databanken werd gezocht naar HTA-rapporten, systematische reviews en RCT's. Deze zoektocht werd aangevuld met een nazicht van de grijze literatuur en contacten met de industrie. Relevante studies werden o.b.v. titel en abstract geselecteerd door 1 onderzoeker. De geselecteerde studies werden vervolgens o.b.v. de full-text beoordeeld op hun kwaliteit door 1 onderzoeker, en nadien door een 2e onafhankelijke onderzoeker en een groep van externe experten. Studies van lage kwaliteit werden geëxcludeerd. Van de geïncludeerde klinische studies werden de volgende gegevens geëxtraheerd: studie design, aantal en type patiënten, interventie, comparator, uitkomstvariabelen en resultaten.

Resultaten

Klinische effectiviteit en veiligheid

Van de 16 potentieel relevante HTA-rapporten werden er 6 geïncludeerd (4 over BK, 2 over VP). Vier van de 6 potentieel relevante systematische reviews werden eveneens geïncludeerd (2 over BK en 2 over VP). Geen enkele gepubliceerde RCT werd teruggevonden, doch er werden 5 lopende RCT's geïdentificeerd. Van 1 van deze 5 RCT's konden preliminaire resultaten opgevraagd worden. Gezien de beperkte gegevens uit RCT's werd de evidentie uitgebreid met de gegevens van 5 niet-gerandomiseerde gecontroleerde studies.

De geïncludeerde HTA-rapporten en systematische reviews verwijzen in het algemeen naar dezelfde evidentie. De houding t.o.v. VP en BK verschilt echter van studie tot studie, waarbij sommigen de beschikbare evidentie onvoldoende vinden en anderen positiever staan t.o.v. de ingrepen, doch met restricties (geselecteerde patiënten, i.k.v. prospectieve studies, …).

De 1-maand resultaten van een lopende RCT, waarbij 300 patiënten met een niet-traumatische wervelindeukingsfractuur gerandomiseerd werden naar BK (n = 149) of conservatieve behandeling (n = 151), suggereren een voordeel van BK wat betreft levenskwaliteit, pijn en functionele beperking. Deze bevindingen bevestigen de resultaten van niet-gerandomiseerde gecontroleerde studies: na 1 jaar verbetert BK de pijnscores meer dan conservatieve behandeling of VP, en na 6 maanden verbetert BK de functionele beperking meer dan conservatieve behandeling. Voor VP daarentegen werd na 2 jaar geen verschil waargenomen in pijnscore of functionele beperking t.o.v.

conservatieve behandeling. Deze niet-gerandomiseerde studies vertoonden echter belangrijke methodologische beperkingen.

Gebaseerd op een meta-analyse van case series blijkt BK een relatief veilige procedure te zijn, hoewel er een vrij hoge incidentie van cementlekkage werd vastgesteld (10 – 23%). In een klein aantal gevallen treedt er een lekkage op naar kritische plaatsen (epidurale ruimte, naburige bloedvaten, …), doch in mindere mate dan na een VP (0.1% vs. 4%).

Economische evaluatie

Het materiaal voor ballon kyfoplastie kost ongeveer € 3.600, wat 5 tot 10 maal duurder is dan het materiaal voor vertebroplastie. Deze cijfers vindt men ook terug in de Europese en Amerikaanse literatuur. Een Deense studie vergeleek de kosten voor een vertebroplastie met die van conservatieve behandeling, doch kon op basis van de gebrekkige bestaande literatuur geen kosteneffectiviteitanalyse doen. In een recent abstract werd de incrementele kosteneffectiviteitratio geschat op €4.065 per QALY ten voordele van ballon kyfoplastie ten opzichte van conservatieve behandeling. De details van deze studie zijn echter onvoldoende gekend.

Het jaarlijkse budget voor het RIZIV bij terugbetaling van het ballon kyfoplastie materiaal wordt geschat op €2.700.000, uitgaande van 600 ingrepen per jaar.

Conclusies

- De klinische effectiviteit van vertebroplastie voor de behandeling van niet-traumatische wervelindeukingsfracturen blijft onzeker. Slechts één niet-gerandomiseerde gecontroleerde studie kon hooguit een equivalentie aantonen tussen VP en conservatieve behandeling. Daarenboven heerst er grote bezorgdheid over de incidentie van cementlekkages na VP. Momenteel, en tot de resultaten van de lopende RCT's beschikbaar worden, dient VP als een experimentele interventie beschouwd te worden, die idealiter enkel uitgevoerd wordt bij zorgvuldig geselecteerde patiënten in het kader van klinische studies. Rekening houdend met de beschikbare gegevens over effectiviteit en veiligheid is het design van deze klinische studies bij voorkeur dat van een RCT met voldoende power om de superioriteit aan te tonen t.o.v. conservatieve behandeling.
- De effectiviteit van BK voor de behandeling van niet-traumatische wervelindeukingsfracturen wordt aangetoond in niet-gerandomiseerde gecontroleerde studies van matige kwaliteit: BK verbetert de pijnscores t.o.v. conservatieve behandeling. De preliminaire resultaten van 1 lopende RCT bevestigen de klinische effectiviteit op korte termijn, maar de voordelen op lange termijn blijven onzeker. Gebaseerd op een meta-analyse van case series blijkt BK een relatief veilige procedure te zijn.
- Wat betreft de eventuele terugbetaling van BK hebben beleidsmakers de keuze tussen de volgende mogelijkheden:

  1.Wait-and-see, o.w.v. de beperkte evidence voor de klinische voordelen op lange termijn, de kleine benefit/risk ratio, het feit dat verschillende RCT's lopend zijn, en het gebrek aan kosteneffectiviteit gegevens;

  2. Terugbetaling onder duidelijke criteria, naar analogie met de klinische studies (volwassen patiënten met een pijnlijke, niet-traumatische, thoracale of lumbale (D5 – L5) wervelindeukingsfractuur van ≤ 3 maanden oud). Het opstarten van een register voor de opvolging van tot nog toe ongekende verwikkelingen is te overwegen, maar zal een moeilijke opgave zijn voor deze populatie, waar een belangrijke loss to follow-up te verwachten is;
- Gezien dit een nieuwe techniek is waar een leercurve te verwachten is, wordt BK best uitgevoerd door een multidisciplinair team. Voor bejaarde patiënten met comorbiditeiten, polymedicatie en valproblemen wordt best overleg gepleegd met geriater en huisarts. Training met de techniek en strikte opvolging van de instructies van de producent zijn een voorwaarde om een aanvaardbaar niveau van expertise te bereiken.

Table of contents

1 INTRODUCTION

These rapid assessments are primarily concerned with the clinical and cost-effectiveness of emerging spine technologies for the treatment of low back pain: intervertebral disk replacement, and vertebroplasty and balloon kyphoplasty. Based on other existing HTA reports, systematic reviews and clinical trials, the objective is to provide a clear synthesis of the evidence on efficacy, clinical effectiveness and safety of the three technologies. This report follows the standard methodology of HTA reports of the KCE. However, in contrast to full HTA reports, patient issues, ethical issues and organisational issues will not be addressed extensively.

The report is divided into two major parts: the first part concerns intervertebral disk replacement, and the second part deals with both balloon kyphoplasty and vertebroplasty. Both parts follow the same logic, first describing the background and the technology under consideration, followed by a description of the clinical and economical literature, and a discussion on the findings. Each part of the report ends with conclusions and recommendations about the use of the addressed technologies.

2 INTERVERTEBRAL DISK REPLACEMENT

2.1 BACKGROUND

A number of disc diseases can lead to chronic low back pain (LBP), with degenerative disc disease (DDD) being one of the most important reasons [1]. At present, non-surgical therapy – including physical therapy, rehabilitation, infiltrations, and psychosocial approaches – is often the first-line treatment for chronic low back pain associated with DDD [2, 3], but many patients do not respond to such treatments [4-7]. The evidence-base of these interventions will be the subject of a separate KCE report on the diagnosis and treatment of LBP.

In 2004, NICE considered spinal fusion as the gold standard surgical treatment for DDD that is not responsive to conservative treatment for more than 6 months [8]. However, as in other fields of orthopaedic surgery, joint arthrodesis cannot be generally considered an optimal solution, since joint motion is not preserved. Therefore, inspired by the results of total hip and knee replacement, the first types of artificial lumbar discs were developed in the fifties [9]. After a partial or total anterior or posterior discectomy, the prosthetic disc aims to restore disc height, hereby maintaining or restoring spinal mobility and avoiding adjacent joint degeneration. The main indication for intervertebral disc replacement is DDD. Other indications are herniated lumbar intervertebral disc, post-laminectomy syndrome, chronic low back pain not responsive to conservative treatment, and failed anterior fusion [8] .

In Belgium, these discs are already being placed in several hospitals. The aim of this report is to summarize the existing clinical and economical evidence on intervertebral disc replacement for patients with the above mentioned indications, compared to conservative treatment or arthrodesis. In case of a lack of economical evidence, the possible costs associated with intervertebral disc replacement in Belgium will be estimated.

2.2 TECHNOLOGY DESCRIPTION

Prosthetic discs are typically made of two metallic endplates (e.g. made of tungsten, cobalt-chromium or cobalt-chromium-molybdenum (CCM) alloy) with teeth or a fin on each endplate that can be inserted into the adjacent vertebrae (figure 1). These metallic endplates may be coated with hydroxyapatite to promote the anchoring to the bone. A flexible synthetic core (e.g. made of high density polyethylene) is provided between the endplates to maintain the range of motion in the operated area.

Currently, six types of disc prostheses are internationally available: SB Charité III, Acroflex, Prodisc II, Flexicore, Maverick, and Kineflex. The devices considerably differ mechanically. While the Acroflex disk is a one-piece device consisting of 2 titanium endplates with a rubber core adhered between them, both the Charité disk and the Prodisc II are three-piece devices comprised of 2 metal endplates (cobalt-chromium alloy) and a ultrahigh-molecular-weight polyethylene core ('metal on poly'). The Flexicore, Maverick, and Kineflex disks are 'metal on metal' disks. The Flexicore disk is inserted as a single unit (the superior and inferior portions are linked by a captured ball-and-socket joint), while the Maverick disk is a two-piece device and the Kineflex disk a three-piece device (2 CCM endplates and a CCM core). Both the Charité and Flexicore disks have 6 teeth on each endplate, while the Prodisc II, Maverick and Kineflex disks have a fin on each endplate to anchor the disk. Most devices have a central centre of rotation, only the Maverick disk has a posterior centre of rotation.

Artificial lumbar discs are implanted using a retroperitoneal anterior approach, avoiding the major nerves and vascular structures. Once the target intervertebral disc is reached, the neurosurgeon or orthopaedic surgeon first performs a discectomy. The disc space is maintained using distraction devices. A trial prosthesis is then inserted in the disc space in order to determine the most appropriate artificial disc device, which includes considerations such as height, angle, and size. Once those parameters are obtained, the trial disc is replaced by the permanent artificial disc. Fluoroscopy and/or

other imaging techniques can be used to ensure correct central positioning of the disc. Gradual release of the distraction devices and a confirmatory radiograph complete the implantation.

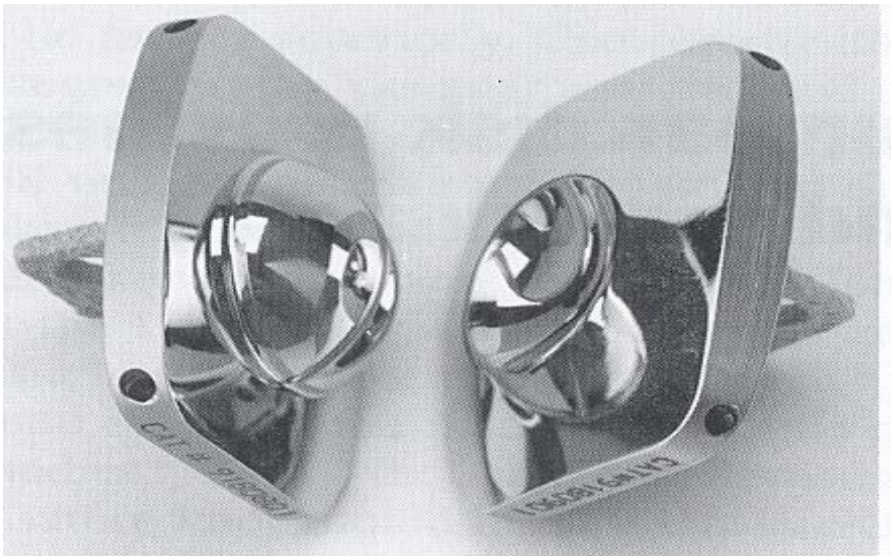

Figure 1 : Maverick disk (source: Medtronic Belgium, with permission).

2.3 CLINICAL EFFECTIVENESS

2.3.1 Methods

2.3.1.1 Search strategy

An iterative search strategy was performed, first searching for existing health technology assessments (HTA) and systematic reviews, and subsequently for randomized controlled trials (RCTs). Finally, as indexing and MeSH terms are often not developed yet for emerging technologies, a complementary search was done of the grey literature via Google and via contacts with suppliers and manufacturers of artificial lumbar disks.

HTA reports and systematic reviews were searched in the HTA database, Medline (Ovid), Pre-Medline (Ovid), and Embase. RCTs were searched in Medline (Ovid), Pre-Medline (Ovid), Embase, and the Cochrane Library.

The search date was February 2006.

2.3.1.2 Search terms

For the HTA database the following search-string was used:

(disk or disc)/Subject Headings Exploded AND (artificial OR prosthe OR replacement)/Title & Abstract

The search algorithm used for Medline is provided in appendix.

For Embase the following search-string was used:

(('intervertebral disk hernia'/exp/dm_su/mj) OR ('intervertebral disk degeneration'/exp/dm_su/mj) OR ('lumbar disk hernia'/exp/dm_su/mj) OR (intervertebral AND (disc OR disk) AND replacement) OR ((disc OR disk) AND 'prosthesis'/exp/mj) OR ('low back pain'/exp/dm_su/mj)) AND ([meta analysis]/lim OR [systematic review]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [embase]/lim AND [2000-2006]/py

For the search in the Cochrane Library and Pre-Medline, we used the following search string: (disk or disc) and (artificial or prosthe$ or replacement).

Finally, for the Google search the following search terms were used in combination: disk, disc, replacement, artificial, prosthesis, technology assessment, systematic review, randomized.

Overall, the search was limited to reports and articles published between 2000 and 2006. No language restriction was used.

The title and abstract of citations were reviewed for relevance by one reviewer (JV). In case the abstract could not provide enough information, the full-text article was retrieved. The following in and exclusion criteria were used to select relevant papers:

Inclusion: HTA, systematic review, meta-analysis, RCT; intervertebral disk replacement for the following conditions: degenerative disk disease, herniated lumbar intervertebral disk, post-laminectomy syndrome, failed conservative treatment for chronic low back pain, failed anterior fusion in the lumbar region; major outcomes of interest: pain reduction, adverse events, mortality, health-related quality of life.

Exclusion: narrative reviews, letters, commentaries, case series, case studies; nucleus replacement device, prosthetic disk nucleus; target conditions other than mentioned above.

2.3.1.3 Quality assessment

The quality of the selected papers was assessed by one reviewer (JV) on the basis of the full-text and quality controlled by a second internal reviewer and a group of external experts. To assess the quality of HTA reports, the INAHTA checklist was used (www.inahta.org) (see appendix). The quality of systematic reviews and RCTs was assessed using the checklists of the Dutch Cochrane Centre (www.cochrane.nl) (see appendix).

Quality assessment was summarized as good, average or poor quality (according to the quality of evidence grading for interventional procedures of ASERNIP, http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPsReviewProcess/Classifications_Syst.htm). HTA reports or systematic reviews received a poor quality appraisal when the search of the literature was insufficient and no quality assessment of included studies was reported. Since the subject of this report was a surgical procedure, quality assessment of the RCTs did not comprise the blinding of the surgeons (and even the patients). However, two major criteria were the randomization process and the blinding of the assessors: an RCT received a poor quality appraisal when at least one of these two criteria was negative.

Poor quality studies were excluded from further review.

2.3.1.4 Data extraction strategy

As for clinical trials, information was captured about the study design, number and type of patients included, intervention, comparator, outcome variables and results.Results

2.3.1.5 HTA reports

Eight possible HTA reports were identified. Only two of these – the CTAF and the NICE report – were considered as fair quality reports and were included [8, 10]. The remaining six were graded as poor quality and therefore excluded from further review [11-16]. The quality appraisal of the eight identified HTA reports and the evidence tables of the two included HTA reports are provided in appendix.

California Technology Assessment Forum HTA report [10]

This report focused on intervertebral disk replacement with the SB Charité III disk. Other devices were not considered because of limited data on clinical outcomes in the literature. The literature search (through December 2004) revealed four uncontrolled case series and one randomized controlled trial. This RCT, which was found to have important methodological flaws [17], found significantly improved pain and ODI scores after disk replacement as compared to spinal fusion. On the basis of this weak evidence, the author of the HTA report concluded that further data were needed in order to determine whether the SB Charité III disk meets the five technology assessment criteria of CTAF.

National Institute for Clinical Excellence HTA report [8]

This report was based on a rapid review of the published literature by ASERNIP-S [18] and also focused on the SB Charité III disk. An extensive literature search revealed 11 published studies (1 RCT, 1 non-randomized comparative study, and 9 case series) and one RCT in progress. All studies identified by CTAF [10] (see above) were also found by NICE. However, the methodological drawbacks of the included RCT [17] were not discussed in the same detail as CTAF did [10]. The authors concluded in their guidance that the evidence was adequate to support the use of intervertebral disk replacement. However, they stressed the need for long-term data and the audit and review of clinical outcomes of all patients having intervertebral disk replacement.

2.3.1.6 Systematic reviews

Three possible systematic reviews were identified. One Chinese systematic review could not be assessed because of the unavailability of the full-text [19], and was not included. The two other systematic reviews were found to be of fair quality and were included [20, 21] (see appendix for quality appraisal and evidence table).

The literature search by de Kleuver et al. was thorough, although EMBASE and the grey literature were not searched [21]. It was performed through January 2002, and could therefore not identify the RCT of Geisler et al. [17]. Nine articles (all observational studies) were identified, of which the majority was also identified in the HTA report of NICE [8]. On the basis of the identified evidence, de Kleuver et al. considered intervertebral disk replacement an experimental procedure [21].

The systematic review of the Evidence Based Practice Group (EBPG) had as primary objective to investigate the safety and effectiveness of intervertebral cervical disk replacement [20]. Their secondary objective was the identification of reviews or systematic reviews on artificial vertebral disks in general (including lumbar) through a 'non-systematic' literature search. However, the search strategy was as thorough as the one used by de Kleuver et al., and included a search of the websites of INAHTA-members, but not EMBASE. Three HTA reports [8, 13, 15], one systematic review [21], and one RCT [17] were identified. Based on the evidence, the EBPG considered intervertebral disk replacement at an experimental stage.

2.3.1.7 Randomized clinical trials

Thirteen reports on RCTs were identified (figure 2). Six reports described the interim and final results of one and the same RCT with the SB Charité III disk. The interim reports were not included for further analysis [22-24]. The three final reports were graded as fair quality and were included (obviously as one study) [17, 25, 26].

Six other reports described the interim results of one RCT with the Prodisc II disk [27-32]. Three articles were excluded, because more recent reports were found that included the same patients [28, 30, 32]. The remaining three articles were found to be of low quality (no information on the blinding of the randomization or on the blinding of the outcome assessors) and were also excluded.

Finally, one abstract – obtained through contacts with manufacturers – described the interim results of an RCT with the Maverick disk [33], but this report was also excluded because of a low quality. The quality appraisal of the identified RCTs and the evidence tables of the included articles are provided in appendix.

In the included (multi-center non-blinded) RCT, 304 patients with single-level symptomatic DDD and non-responding to conservative treatment for 6 months were randomized to either intervertebral disk replacement with the SB Charité III disk (n = 205) or anterior lumbar interbody fusion with BAK cage (n = 99), and followed for 2 years [17, 25, 26]. Main clinical outcomes were pain (assessed on a visual analog scale), functional impairment (assessed by the Oswestry Disability Index), self-perceived health (assessed by the SF-36 Health Survey), neurological status, and patient satisfaction. After 2 years of follow-up, only patient satisfaction was significantly higher in the interventional group compared to the control group [25]. The overall complication rate, the neurological complication rate and the number of device failures were equivalent between both groups [17, 25] (see below).

An important drawback of the study was that no blinded outcome assessors were used (at least it wasn't mentioned in the manuscript). Instead, outcomes as pain and functional ability were assessed by the patients themselves using subjective instruments (VAS and ODI respectively). In these kinds of studies it must be possible to have the patients assessed by objective blinded assessors (e.g. physiotherapists).

Above this, the EBPG found major design problems based on data available on the US FDA website [20]. For example, violation was found on the in- and exclusion criteria (similar proportions among both groups), and no patients who violated the protocol were excluded from the primary effectiveness analysis [20]. Finally, patients were not blinded for their therapy.

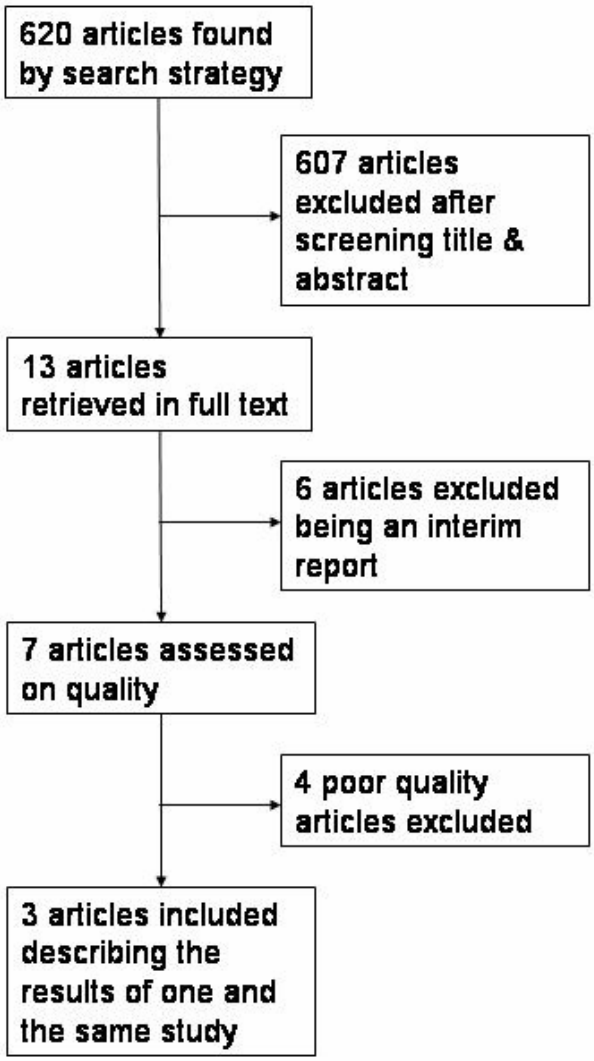

Figure 2 : Search results (flow diagram) of RCTs.

2.3.1.8 Harms and complications

As mentioned above, the only published RCT found equivalent complication rates between disk replacement and spinal fusion [17, 25]. However, the data provided in the published articles slightly differ from those provided by the FDA [34], and it is not very clear which data are right.

Looking in more detail at the complication data, device-related adverse events (defined as back and lower extremities pain, implant displacement, and subsidence) were more frequent in the investigational group (7.8% vs. 4.0% in the control group; odds ratio 2.01, 95% CI 0.65 – 6.18) (figure 3). On the other hand, device failure (defined as re-operation, revision, removal, or supplemental fixation) occurred more frequently in the control group (8.1% vs. 5.4% in the interventional group; odds ratio 0.64, 95% CI 0.25 – 1.66) (figure 3).

Two interventional subjects and one control subject required removal of their implant. This is a major concern – particularly at the L5S1-level – because of the neighbouring anatomical structures. However, no hard safety data exist about implant removal.

The interventional group also experienced more superficial wound infection (6.3% vs. 2.0% in the control group) (figure 3). However, in the control group 18.2% reported pain at the donor graft site, and 9.1% had pseudo-arthrosis.

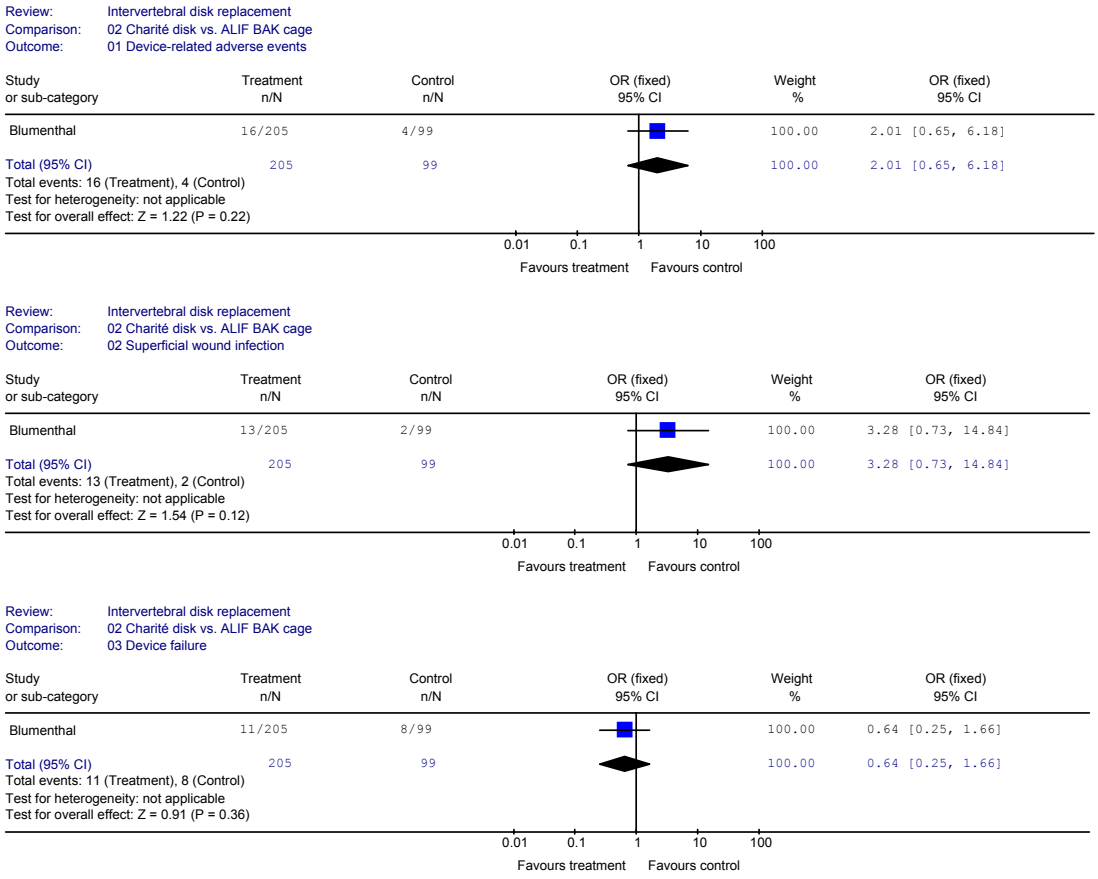

Figure 3 : comparison of adverse events between the Charité disk and ALIF BAK cage [17, 25, 34].

2.3.1.9 Ongoing trials

Several trials comparing intervertebral disc replacement with spinal fusion are currently ongoing. In October 2004, the FDA approved the Charité disc based on the 2-year results of a randomized controlled trial comparing the disc to anterior fusion with the BAK cage [35]. A post-approval trial is now following implanted patients during 5 years [36]. In Europe, the RESORD trial is ongoing [8]. The newer devices (Flexicore, Maverick, and Kineflex) also have ongoing randomized controlled trials [33, 37].

2.4 ECONOMIC EVALUATION

2.4.1 Methodology

The following databases were searched using filters for economic or cost studies: Medline, Premedline, Econlit, Embase, Centre for Reviews and Dissemination databases (HTA database, DARE and NHSEED) (see appendix for search strategy). No publication date or language restrictions were applied.

Based on the abstracts of the 58 unique references obtained, 9 references were selected. Three reports were manually retrieved. No original economic evaluation was found.

Suppliers and manufacturers of artificial lumbar disks were invited to submit any relevant information about their products. Some information was provided on prices, incidence and prevalence figures, and on the number of patients who received an artificial disk.

Currencies were converted using the 27 februari 2006 exchange rates (1 USD=0.84€, 1 AUD= 0.62€, 1 CAD=0.74 €).

2.4.2 Marketing of artificial disks

The first artificial disks were implanted in Europe in the 1980s. Between 1987 and 2004, more than 7000 Charité disks, 2000 ProDisc disks and 2000 Maverick disks have been implanted worldwide [38].

After Europe and Asia, artificial disks were introduced in the US and Canada. Canada licensed the SB Charité III disk in 2003 and the U.S. Food and Drug Administration gave the first approval in 2004. This approval was submitted to certain conditions: for spinal arthroplasty in skeletally mature patients with DDD at one level from L4-S1, confirmed by patient history and radiographic studies, with no more than 3 mm spondylolisthesis, and with a failed conservative treatment longer than 6 months. The approval was also submitted to an annual reporting of a 5-year follow-up of patients included in the FDA-regulated trial that had led to the approval. As a consequence, DePuy Spine requires mandatory, extensive surgeon training (http:/spine-health.com/topics/surg/charite/charite03.html). Artificial disks from other manufacturers (ProDisc, Synthes Inc.; MAVERICK, Medtronic, Sofamor Danek; Flexicore, StrykerSpine; Kineflex, Spinal Motion) are approved for investigational use only and are currently being evaluated. Of these, ProDisc has received an approvable letter (prior to approved order) on January 5th 2006.

The 2005 U.S. market price of a Charité artificial disk is €9,680 (2 x €4,550 for the endplates plus €590 for the core) [39], which is in the €7,500 - €10,000 range reported by other authors [12 38]. The ASERNIP report indicated an Australian price around €4,040 for the same device in 2003 [18]. The Australian and European prices range from €3,800 to €4,200 [40]. In Belgium, prices for a complete disk (endplates and core) range from €2,236 to €2,940 which is cheaper than the prices cited above.

The available disks on the Belgian market are:

- Charité artificial disk (DepuySpine, Johnson&Johnson)
- Mobidisc (LDR medical, distributed by Inspine)
- A-MAV and O-MAV (Medtronic, Sofamor Danek),
- ProDisc (B Braun – Aesculap)

About 140 and 120 patients were treated with the Charité disk in Belgium in 2004 and 2005 respectively; A-MAV or O-MAV artificial disks were implantated in about respectively 500 and 590 patients during the periods May 2003 - April 2004 and May 2004 - April 2005 (personal communications from manufacturers).

2.4.3 Economic consequences

There is currently no reimbursement granted in Belgium, neither for the prosthesis nor for the medical act (no honorarium fee).

In 2005, the National Institute for Illness and Invalidity Insurance made an estimation of the possible impact on the Health Insurance budget of the reimbursement of the implant. They estimated the number of patients at 1,000 per year. If the reimbursement was fixed at €2,375, the material would hence cost €2.375.000 per year. Concerning the honorarium fee, in the absence of a specific code, surgeons could currently use the general billing code (281654-281665) "Arthrodesis or inter-body screw fixation by anterior approach". The fee for this code amounts to €720. No proposition about the reimbursement has been made by the Institute to the Minister of Health yet.

The Harvard Pilgrim Health Care health plan estimated that 50% of the increase in annual spinal fusions in the United States (currently estimated at 300,000-350,000) might be eligible for artificial disk replacement with the Charité artificial disk [40]. As there are less American patients eligible for total disk replacement under FDA restrictions than European patients, this percentage is supposed to be even higher in Europe. Total cost (including prosthesis) for artificial disc replacement surgery in the U.S. ranges from €29,500 to €37,800 ($35,000-$45,000), and many insurance companies only provide partial or no coverage (considering that the technology is still experimental). In comparison, the cost of a lumbar body fusion is about €20,200 (€16,200 for the procedure and €4,000 for the BAK cage).

In Belgium, the price of an artificial disk amounts to €2500, while materials for anterior lumbar interbody fusion (ALIF) cost €2200 and for posterior lumbar interbody fusion (PLIF) from €2400 to €3800 (according to the type of material chosen) (personal communication from manufacturers and experts). The Belgian prices for these different techniques are thus in the same range.

According to a U.S. report, the savings from a shorter length of stay would be absorbed by the cost of the disk (€8,400-10,000 compared to a €3,400-4,200 for the fusion material) [12]. However, the FDA-regulated RCT comparing the Charité disk to fusion [39] estimated that the U.S. costs for fusion cage are probably the same as for a disk replacement (hospital stay, professional and medical devices included). According to the same author, procedure time was 2 hours and the length of hospital stay 4 days for a disk replacement. ICSI reported a length of stay of 3 to 5 days (depending on a single or multilevel replacement) [12]. In a prospective multicenter study cited by the HAS (formerly ANAES), the length of stay for a fusion ranged from 3-4 days (one level) to 5-7 days (two levels) [15]. No information was available on the eventual differences between the posterior, anterior or oblique approaches. In Belgium, no difference in length of stay can be observed between both procedures, being about 3 to 5 days (personal communication from experts).

2.4.4 Market trends

In 2004, according to spine market analysts 50 percent of the U.S. spine arthroplasty market, representing 70% of the world spine arthroplasty market, was occupied by artificial disk replacement (versus 44% for fusion and 6% for disc nucleus replacement) [41]. According to a financial consulting institution, disc replacement (including nucleus replacement, which is not covered in the present report) will represent 70% of the spinal surgery in the United States by 2010, absorbing 47.9% of the actual fusion market [38].

2.5 DISCUSSION

The HTA reports and systematic reviews that were included in the present report found a similar low quality body of evidence (only de Kleuver et al. did not find the RCT with the SB Charité III disk, since it was published after their systematic review). Most authors considered intervertebral disk replacement an experimental procedure; only NICE was more positive about it. Nevertheless, the RCT that was identified by most authors and that was also included in the present report only showed an equivalence between the SB Charité III disk and anterior lumbar interbody fusion (ALIF), and moreover was of questionable quality [17, 25, 26].

The choice of the comparator in the published and ongoing RCTs is a point of discussion. Some identified RCTs used ALIF as comparator, which is also the fact for most ongoing RCTs (except for the RCT with the Kineflex disk [37], that uses the SB Charité III disk as comparator), others used circumferential fusion (i.e. the combination of an anterior and posterior approach) as comparator. No trial was found comparing disk replacement to the 'best conservative treatment'. However, the literature concerning fusion surgery is conflicting [42]. Three trials comparing lumbar fusion to conservative treatment showed conflicting results [42]. Two recent trials of good quality showed marginal or no superiority of fusion surgery [43, 44], and in only one trial, lumbar fusion was found to be clearly superior to non-surgical treatment for chronic low back pain [45]. However, the control group of this trial was treated with physical therapy techniques similar to the treatment the patients received without success before randomization. Therefore, the control group may have been close to the natural history of the disease [45]. Given the findings of these three studies, studies comparing intervertebral disk replacement to conservative treatment are warranted.

Information on the economic evaluation of artificial disks is lacking. Therefore, ongoing and future trials should ideally gather economic and cost information apart from clinical outcomes information. However, of the ongoing trials none was found to include an economical evaluation.

In conclusion, the evidence-base supporting the use of intervertebral disk replacement for DDD relies on one RCT with important limitations. Given this poor quality of evidence; given the fact that information on long-term results and adverse events (i.e. exceeding 2 years) of this invasive procedure is still lacking; given the fact that there is insufficient information on the prevention of adjacent level disease, on the wear and tear of the polyethylene core, and on the clinical outcomes after revision or conversion surgery; and given the fact that numerous RCTs are ongoing, intervertebral disk replacement has to be considered an experimental procedure for the time being. In addition, future RCTs examining the clinical efficacy of intervertebral disk replacement should consider comparison to state-of-the-art conservative treatment.

Key points intervertebral disk replacement

- **The quality of evidence on the efficacy of intervertebral disk replacement for the treatment of chronic low back pain remains poor to date.**
- **Furthermore, there are safety concerns related to this technique and long term adverse events are to be followed conscientiously in trial registers.**
- **At present and until the results of high-quality primary research become available, this technique has to be considered experimental, and should ideally be limited to carefully selected patients treated in clinical trials in research centres. The experimental design of choice is a randomized controlled trial, comparing disk replacement with the correct comparator (preferentially conservative treatment).**
- **This recommendation highly contrasts with the current practice in some Belgian hospitals, where patients are being treated with this experimental technique outside the protocol of a high-quality clinical trial. Just recording patients treated with these invasive techniques in a voluntary registry is unacceptable from a societal point of view. At present, even the mandatory reporting of important adverse events related to these techniques (death, reintervention, permanent handicap, ...) to the Ministry of Public Health is rarely done (personal communication Ministry of Public Health, Medical Devices Dept.).**
- **Economic data are lacking. Budget impact related to the surgery, hospital stays and the treatment of possible complications is expected to be considerable even without direct reimbursement of the implant.**

3 BALLOON KYPHOPLASTY AND VERTEBROPLASTY

3.1 BACKGROUND

Vertebral fractures are an important source of acute back pain, chronic back pain and spinal deformity. Most frequently, such fractures are caused by osteoporosis (post-menopausal, corticoid-induced). Based on extrapolations of data from the Netherlands [46], the incidence of osteoporotic vertebral fractures in Belgium can be estimated at 10.000 cases per year [47]. Non-osteoporotic causes of vertebral fractures are trauma, bone metastases and more rarely haemangiomas.

Conservative management includes analgesics, bed rest and external bracing. Medical treatment with bisphosphonates or calcitonin is another option [48, 49], but large randomized controlled trials are lacking supporting their routine use [50]. Pain related to malignant vertebral fractures can also successfully be relieved with radiotherapy [51].

Most patients become symptom free with conservative management within weeks. However, some patients do not respond to these therapies, and for these patients surgery may be considered. Recently, there has been increased interest in minimally invasive interventions, including vertebroplasty and balloon kyphoplasty. Vertebroplasty was introduced in the mid-1980s for the treatment of painful haemangiomas [52], and was subsequently applied to osteoporotic fractures and bone metastases. Balloon kyphoplasty is a recent variation of vertebroplasty, and was first performed in the late nineties.

The aim of this report is to summarize the existing clinical and economical evidence on vertebroplasty and balloon kyphoplasty for patients with the above mentioned indications. In case of a lack of economical evidence, at least an estimation will be made of the costs associated with these procedures in Belgium.

3.2 TECHNOLOGY DESCRIPTION

Vertebroplasty and balloon kyphoplasty both are minimally invasive procedures designed to provide pain relief and spine stabilization in case of a vertebral fracture. One or more vertebral levels can be treated during one session.

During vertebroplasty, bone cement – usually polymethylmethacrylate (PMMA) – is injected through one or two biopsy needles placed through the skin and through the pedicles into the ventral third of the cancellous bone of the vertebral body (figure 1). The bone cement is injected in a liquid state at a high pressure until a filling of the vertebral body and an even distribution of the PMMA into the cancellous bone, as visualised under fluoroscopy or computer tomography, is achieved. The procedure is usually performed under local anaesthesia.

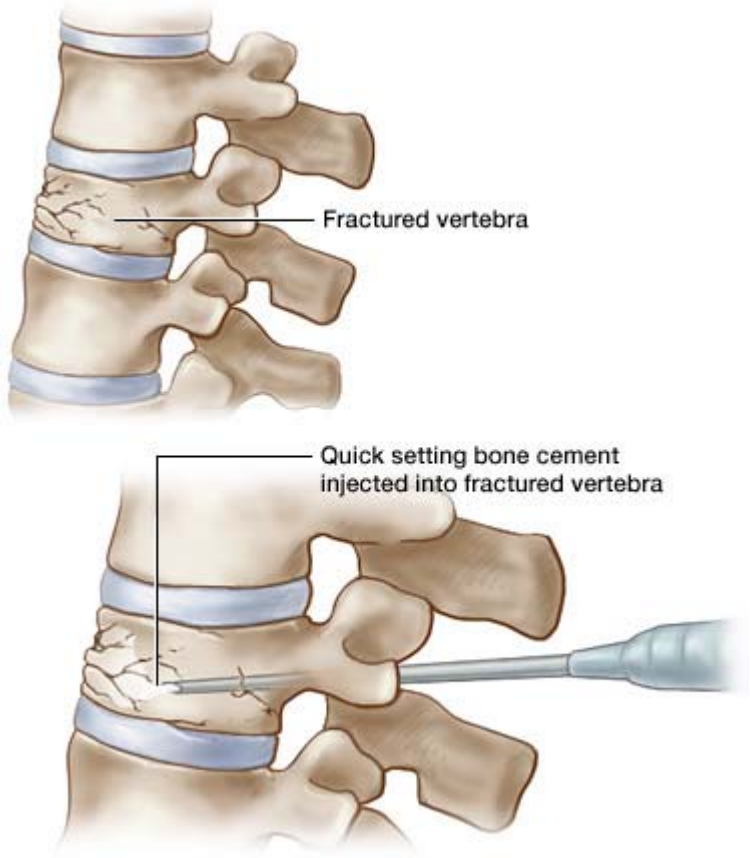

Figure 1 : Vertebroplasty (source : Adventist Midwest Health, with permission) .

Balloon kyphoplasty is a modified vertebroplasty technique. First, two small incisions are made to gain access to the fractured vertebra(e) (figure 2). Two transpedicular or extrapedicular channels are created by a hand drill, through which an inflatable bone tamp is inserted into the collapsed vertebral body. The inflated balloon elevates the endplates, and thereby restores the height and kyphotic angle of the vertebral body. The balloon is then deflated and removed, and the created space is filled with bone cement (usually PMMA). In comparison to vertebroplasty, more viscous cement can be used with less pressure, thereby decreasing the risk of cement extrusion. The procedure is performed under local or general anaesthesia and is also assisted by fluoroscopy.

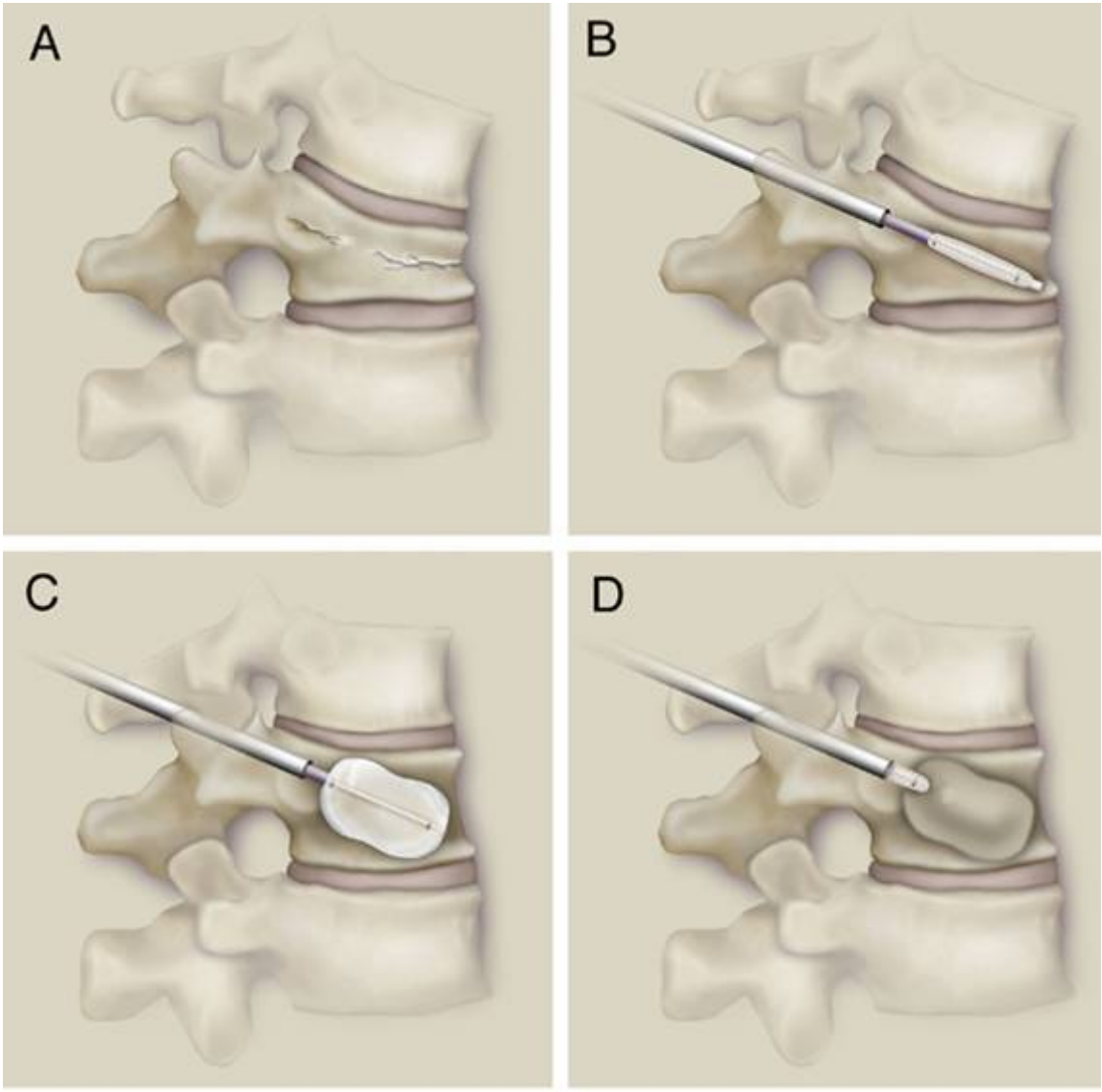

Figure 2 : Kyphoplasty (source: Kyphon Inc, http://www.kyphon.com/, with permission)

3.3 CLINICAL EFFECTIVENESS

3.3.1 Methods

3.3.1.1 Search strategy

An iterative search strategy was performed, first searching for existing health technology assessments (HTA) and systematic reviews, and subsequently for randomized controlled trials (RCTs). Finally, as indexing and MeSH terms are not developed yet in the case of emerging technologies, a complementary search was done of the grey literature via Google and via contacts with suppliers and manufacturers.

HTA reports and systematic reviews were searched in the HTA database, Medline (Ovid), Pre-Medline (Ovid), and Embase. RCTs were searched in Medline (Ovid), Pre-Medline (Ovid), Embase, and the Cochrane Library.

The search date was February 2006.

3.3.1.2 Search terms

For the HTA database the following search-string was used:

((disk OR disc) AND balloon)/Title & Abstract OR (kyphoplast)/Title & Abstract OR (vertebroplast)/Title & Abstract

The search algorithm used for Medline is provided in appendix.

For Embase the following search-string was used:

(('osteoporosis'/exp/dm_su/mj) OR ('spine fracture'/exp/dm_su/mj) OR ('compression fracture'/exp/dm_su/mj) OR ('spinal cord compression'/exp/dm_su/mj) OR ('pathologic fracture'/exp/dm_su/mj) OR ('kyphoplasty'/exp/mj) OR ((disc OR disk) AND ('balloon'/exp OR 'balloon')) OR ('percutaneous vertebroplasty'/exp/mj)) AND ([meta analysis]/lim OR [systematic review]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [embase]/lim AND [2000-2006]/py

For the search in the Cochrane Library and Pre-Medline, we used the following search string: kyphoplast$ or vertebroplast$.

Finally, for the Google search the following search terms were used in combination: kyphoplasty, vertebroplasty, technology assessment, systematic review, randomized.

Overall, the search was limited to reports and articles published between 2000 and 2006. No language restriction was used.

The title and abstract of citations were reviewed for relevance by one reviewer (JV). In case the abstract could not provide enough information, full-text of the article was retrieved. The following in and exclusion criteria were used to select relevant papers:

Inclusion: HTA, systematic review, meta-analysis, RCT; balloon kyphoplasty or vertebroplasty for the following conditions: osteoporotic compression fractures, vertebral fractures caused by malignancy, hemangiomata; major outcomes of interest: pain reduction, adverse events, mortality, health-related quality of life.

Exclusion: narrative reviews, letters, commentaries, case series, case studies; target conditions other than mentioned above.

3.3.1.3 Quality assessment

The quality of the selected papers was assessed by one reviewer (JV) on the basis of the full-text and quality controlled by a second internal reviewer and a group of external experts. To assess the quality of HTA reports, the INAHTA checklist was used (www.inahta.org) (see appendix). The quality of systematic reviews and RCTs was assessed using the checklists of the Dutch Cochrane Centre (www.cochrane.nl) (see appendix).

Quality assessment was summarized as good, average or poor quality (according to the quality of evidence grading for interventional procedures of ASERNIP, http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPsReviewProcess/Classifications_Syst.htm). HTA reports or systematic reviews received a poor quality appraisal when the search of the literature was insufficient and no quality assessment of included studies was reported. Since the subject of this report was a surgical procedure, quality assessment of the RCTs did not comprise the blinding of the surgeons (and even the patients). However, two major criteria were the randomization process and the blinding of the assessors: an RCT received a poor quality appraisal when at least one of these two criteria was negative.

Poor quality studies were excluded from further review.

3.3.1.4 Data extraction strategy

As for clinical trials, information was captured about the study design, number and type of patients included, intervention, comparator, outcome variables (pain, functional ability, safety) and results. Information about surrogate endpoints (kyphotic angle, vertebral height) was not extracted because of the limited importance for patients.

A meta-analysis was performed using the software of Review Manager.

3.3.2 Results

3.3.2.1 HTA reports

Sixteen completed HTA reports were identified: six concerning balloon kyphoplasty, seven concerning vertebroplasty, and three concerning both. Above this, three ongoing projects were found (one concerning balloon kyphoplasty [53], two concerning vertebroplasty [54, 55]). Of the completed HTA reports, one report could not be assessed because of unavailability of the full-text [56] and another report was excluded because it was written in Danish [57]. Two reports were not assessed because more recent reports were found published by the same agency [58, 59]. Two unpublished HTA reports about kyphoplasty were identified through contacts with Kyphon Inc [60, 61].

Of the twelve remaining reports, the two unpublished reports were rated as having a good quality and were included [60, 61]. Four other fair quality reports were also included in our review [62-65]. Six HTA reports (including the two reports of BCBS and the report of AHRQ, who used a very poor search strategy) were graded as poor quality reports and were excluded from further review [66-71]. The quality appraisal of all identified HTA reports and the evidence tables of the included reports are provided in appendix.

Balloon kyphoplasty

Agencia de Evaluación de Tecnologías Sanitarias HTA report [60]

The scope of this unpublished report of good quality was the treatment of osteoporotic and neoplastic vertebral compression fractures with balloon kyphoplasty. A thorough literature search until October 2004 identified one systematic review, two HTA reports, eleven cohort and case-control studies, and 12 case series. The results indicated significant improvements in pain intensity, functional capacity, and quality of life. However, the identified evidence demonstrated substantial methodological limitations and short follow-up periods. The authors concluded that balloon kyphoplasty can be considered clinically adequate for the treatment of recent and painful vertebral fractures. However, the authors indicated that there is a particular need for prospective studies of good methodological quality in order to resolve the uncertainty, and suggested that patients treated with balloon kyphoplasty should be systematically included in a prospective clinical study.

University of Birmingham [61]

This unpublished report of good quality, which was commissioned by Kyphon Inc., focused on the treatment of osteoporotic and neoplastic vertebral compression fractures with balloon kyphoplasty and vertebroplasty. The literature search (through March 2004) identified three systematic reviews and a large body of non-randomized comparative studies and case series. Quality appraisal identified two controlled trials being little prone to bias [72, 73]. Both procedures were found to have significant improvements in pain relief, functional capacity, and quality of life, although balloon kyphoplasty appeared to have a superior adverse event profile. The authors concluded that both therapies are effective in the management of patients with osteoporotic vertebral compression fractures that are refractory to conventional medical therapy. However, they also stressed the need for confirmation of these conclusions by the results from the ongoing randomized controlled trials.

National Institute for Health and Clinical Excellence HTA report [62]

This report focused on balloon kyphoplasty for vertebral compression fractures. A 'rapid review' of the literature (through June 2005) revealed one unpublished systematic review, two HTA reports, three non-randomized controlled trials, five case series, a review of complications reported to the FDA, and an unpublished registry report. The literature review formed the basis for an updated guidance published on April 26, 2006, stating that the current evidence on the safety and efficacy of balloon kyphoplasty for vertebral compression fractures appears adequate to support its use. This positive advice was mainly based on the fact that the three non-randomized studies indicated that balloon kyphoplasty provides improved pain scores both compared to conventional medical care and vertebroplasty. However, it was stressed that the procedure should only be carried out provided that normal arrangements are in place for consent, audit, and clinical governance.

Ontario Ministry of Health and Long-Term Care HTA report [64]

This report also focused on balloon kyphoplasty for the treatment of osteoporotic and neoplastic vertebral compression fractures. The literature search (through September 2004) identified one non-randomized controlled trial and eleven case series. The conclusion of the report, based on evidence from level 3a and level 4 studies, was that balloon kyphoplasty is as effective as vertebroplasty at relieving pain associated with vertebral compression fractures due to osteoporosis. Compared to vertebroplasty, it also results in lower fracture rates in adjacent vertebra and in fewer neurological complications due to cement leakage. However, the procedure should be restricted to facilities with sufficient volumes.

Vertebroplasty

National Institute for Health and Clinical Excellence HTA report [63]

This report focused on percutaneous vertebroplasty for the treatment of osteoporotic and neoplastic vertebral compression fractures. It was based on a rapid review of the published literature by ASERNIP-S. A systematic review of the literature (through October 2002) revealed one systematic review, two non-randomized controlled trials, 32 case series, and 6 case reports. It was concluded that the evidence appeared adequate to support the use of percutaneous vertebroplasty, provided that normal arrangements are in place for consent, audit and clinical governance.

Centre for Clinical Effectiveness HTA report [65]

The focus of this report was the safety and efficacy of percutaneous vertebroplasty for symptomatic osteoporotic vertebral compression fractures. The literature search (through April 2002) identified one systematic review and six case series. The author concluded that the evidence was insufficient to support the use of percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fractures.

3.3.2.2 Systematic reviews

Balloon kyphoplasty

No systematic reviews about balloon kyphoplasty were found through the literature search, but two reviews were supplied by Kyphon Inc (Bouza 2006; Taylor 2006). The systematic review of Bouza et al. formed the basis for the HTA report of the Agencia de Evaluación de Tecnologías Sanitarias [60], and will therefore not be discussed separately. The systematic review of Taylor et al. is an update of the literature review performed for the HTA of Taylor et al. [61], and was presented at the 2006 HTAi meeting in Adelaide, Australia [74]. Based on confidential information provided by Kyphon Inc, this review was assessed as being of good quality. During the 2006 HTAi meeting, also a third systematic review about balloon kyphoplasty was identified [75], which was rated as being of fair quality. The quality appraisal of the identified systematic reviews and the evidence table of the included reviews are provided in appendix.

Taylor et al. performed a broad literature search through March 2004 and updated this search to April 2006 [74]. They included 43 papers in their review: 8 comparative studies (4 prospective controlled trials and 4 retrospective studies) and 35 case series. The authors concluded that – compared to conventional medical management and vertebroplasty – balloon kyphoplasty provided superior pain relief and greater improvements in functional capacity. Based on the results of the case series, the authors also concluded balloon kyphoplasty to provide a rapid and marked improvement in health-related quality of life and to be a safe procedure.

The review of Newton et al. was presented as an abstract at the 2006 HTAi meeting in Adelaide, Australia [75]. A complete quality appraisal of the review was therefore not possible because of the limited methodology description. The main objective of the review was to identify the evidence on the safety and effectiveness of balloon kyphoplasty compared to conventional surgery. However, a description of conventional surgery was not provided. The authors performed a thorough literature search through October 2004. They identified 2 cohort studies and 17 case series that assessed the safety of balloon kyphoplasty compared to conventional surgery, and 2 cohort studies and 14 case series that assessed the effectiveness of balloon kyphoplasty compared to conventional surgery. The authors concluded that the available evidence was insufficient to make conclusions on the safety and effectiveness of balloon kyphoplasty compared with conventional surgery. They advised that higher quality primary research is needed before balloon kyphoplasty may receive funding within Australia.

Vertebroplasty

Two systematic reviews about vertebroplasty were identified through the literature search [76, 77], and a third was identified as an abstract at the 2006 HTAi meeting [78]. The reviews of Hendrikse et al. and Merlin et al. were found to be of fair quality, and were included [76, 78]. The other systematic review was excluded because of a poor quality (only English literature searched and no quality appraisal of the identified studies) [77]. The quality appraisal of the identified systematic reviews and the evidence table of the included reviews are provided in appendix.

Hendrikse et al. focused their systematic review on percutaneous vertebroplasty for osteoporotic vertebral compression fractures. They performed a search in Medline and the Cochrane Library through August 2002 [76]. Twelve observational studies (4 prospective and 8 retrospective) were identified, of which the majority was also identified by the HTA reports of NICE and CCE [63, 65]. The authors concluded that percutaneous vertebroplasty seems to be an effective and safe procedure for the treatment of osteoporotic vertebral compression fractures, but should be preserved for carefully selected patients non-responsive to conservative treatment.

The review of Merlin et al. was also presented as an abstract at the 2006 HTAi meeting, which made a full quality appraisal impossible [78]. They performed a thorough literature search through November 2004, and identified 72 studies reporting on the safety of

vertebroplasty and 30 studies reporting on the effectiveness of vertebroplasty. They concluded that the evidence was insufficient to determine if vertebroplasty is as safe as or safer than medical management. Furthermore, they concluded that vertebroplasty appeared to be more effective than conventional medical management at treating symptomatic vertebral compression fractures in the short term, and as effective in the long term. Based on this evidence, interim public funding for vertebroplasty was recommended in Australia for patients with painful osteoporotic vertebral compression fractures and for patients with pain from metastatic deposits or multiple myeloma in a vertebral body.

3.3.2.3 Randomized clinical trials

No completed RCTs were identified. However, five ongoing RCTs were identified: two comparing balloon kyphoplasty to conservative treatment [79, 80], one comparing balloon kyphoplasty to vertebroplasty [81], one comparing vertebroplasty to conservative treatment [82], and one comparing vertebroplasty to placebo [83]. Of the FREE trial, Kyphon Inc. provided the preliminary 1 month results [80]. In this ongoing 2-year study, 300 patients with non-traumatic vertebral fracture (mostly due to primary osteoporosis, in 8 patients due to steroid-dependent osteoporosis, and in 3 from multiple myeloma) were randomized to either balloon kyphoplasty (BKP) (n=149) or non-surgical treatment (NST) (n=151). Because of a lack of a golden standard for non-surgical management of vertebral compression fractures, subjects randomized to the control group received non-surgical treatments (such as pain medication, bed rest, bracing, physiotherapy, rehabilitation programs, walking aids) according to the hospital's protocol. Primary outcome of the study was the change in quality of life as measured by SF-36 at one month. Secondary outcomes at one month included the SF-36 subscales, the global health measure EQ-5D, patient reported back pain measured on a 10-point numeric rating scale, back function using the Roland Morris Disability Questionnaire, and device- and procedure-related safety. Mean improvement in quality of life at 1 month was 7.0± 8.9 for BKP ($p<0.0001$) and 1.8± 7.2 for NST ($p=0.005$) ($p<0.0001$ for difference). Mean improvement in pain score at 1 month was 3.3±2.6 for BKP and 1.4±2.1 for NST ($p<0.0001$ for difference). Mean improvement in disability at 1 month was 5.8±6.2 for BKP and 1.9±4.0 for NST ($p<0.0001$ for difference). BKP was well tolerated with no bone cement-related serious adverse events and no relevant procedure-related serious adverse events. Thirty-one patients (14 in the BKP group, 17 in the NST group) were excluded from analysis, mainly because of unavailability of the 1 month data due to early withdrawal.

3.3.2.4 Non-randomized controlled trials

To increase the evidence-base, it was decided to perform an additional literature search for non-randomized controlled trials. The literature review of NICE [62] was taken as a starting point and completed with a search from June 2005 to April 2006 using the same search strategy as described above. Apart from the 3 controlled trials found by NICE – two comparing balloon kyphoplasty to conservative treatment [72, 73, 84] and one comparing balloon kyphoplasty to vertebroplasty [85] –, one additional trial was identified comparing vertebroplasty to conservative treatment [86]. Above this, one controlled trial comparing balloon kyphoplasty and vertebroplasty was identified through contacts with manufacturers [87].

The quality of the identified trials is low. Only one study used an independent assessor for the clinical follow-up, but in this study it was unclear whether an intention-to-treat analysis was used [85]. Diamond et al. used an independent assessor of the radiographs, but did not state whether the other outcomes were also independently assessed [86]. However, they used an intention-to-treat analysis. Pflugmacher et al. used two examiners for the radiological parameters working independently of each other, but they did not state whether these examiners were blinded for the clinical results [87]. The two other studies did not use independent assessors [73, 84].

The reporting of the outcomes was very heterogeneous across the trials, making it difficult to compare them. For example, pain was evaluated by a visual analogue scale

(VAS) in all trials, but in two studies a score of 10 represented maximum pain [85, 87], in another study a score of 100 was used for maximum pain [73], and in a fourth study a score of 100 was used for minimum pain [84]. For one study it was unclear what score represented maximum pain [88]. New fractures were defined as a height reduction of at least 20% in 2 studies [84, 88], the three other studies did not provide a definition [73, 85, 87]. Cement leakage was reported in only two studies [84, 85].

Pain

Compared to conservative treatment, balloon kyphoplasty improved pain scores significantly at 6 months [73, 84] (figure 3) and at 12 months postoperative [84]. Balloon kyphoplasty also significantly improved pain scores at 12 months postoperative compared to vertebroplasty in the study of Grohs et al. [85], but not in the study of Pflugmacher et al. [87] (figure 4). Diamond et al. did not find a difference in pain scores between vertebroplasty and conservative treatment at 2 years of follow-up [86].

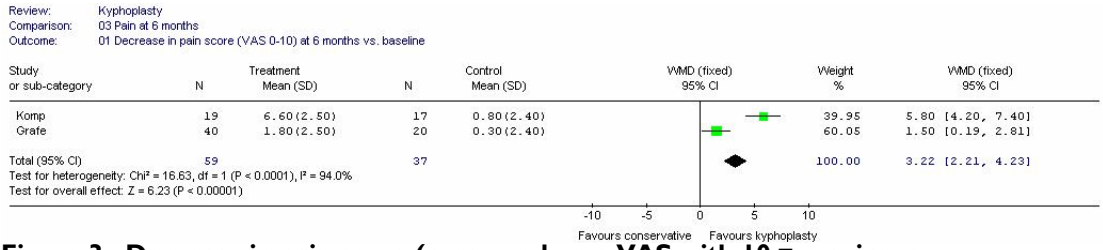

Figure 3 : Decrease in pain score (measured on a VAS with 10 = maximum pain) at 6 months vs. baseline for balloon kyphoplasty vs. conservative treatment.

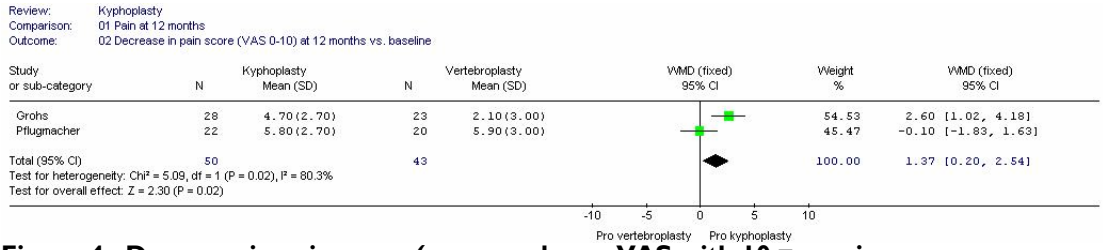

Figure 4 : Decrease in pain score (measured on a VAS with 10 = maximum pain) at 12 months vs. baseline for balloon kyphoplasty vs. vertebroplasty.

Functional ability

Improvement on the Oswestry Disability Index (ODI) score was similar for balloon kyphoplasty and vertebroplasty at 12 months postoperative [85, 87] (figure 5). However, balloon kyphoplasty significantly improved the ODI score at 6 months postoperative compared to conservative treatment [73]. Diamond et al. did not find a difference in functional ability between vertebroplasty and conservative treatment at 2 years of follow-up [86].

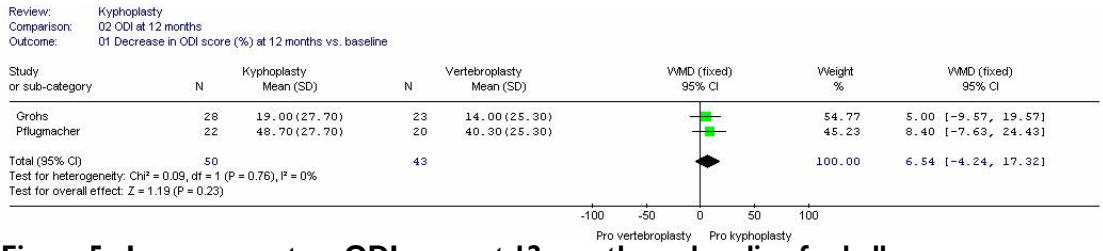

Figure 5 : Improvement on ODI score at 12 months vs. baseline for balloon kyphoplasty vs. vertebroplasty.

Safety

A lower incidence rate of new vertebral fractures was found in patients treated with balloon kyphoplasty compared to those treated with conservative treatment [73, 84]. Grohs et al. reported a higher incidence rate in balloon kyphoplasty vs. vertebroplasty treated patients [85], but this difference was not statistically significant.

Cement leakage to critical areas was higher in vertebroplasty vs. balloon kyphoplasty treated patients [85]. Overall, cement leakage was reported in 10 – 23% of kyphoplasty interventions [84, 85, 87] and in 19 – 28% of vertebroplasty interventions [85, 87]. In the systematic review of Taylor et al., symptomatic cement leakages were reported in 4% of vertebroplasty cases and in 1/1000 kyphoplasty cases [74].

3.4 ECONOMIC EVALUATION

3.4.1 Methodology

The following databases were searched using filters for economic or cost studies: Medline and Premedline, Econlit, Embase, Centre for Reviews and Dissemination (HTA database, DARE and NHSEED) (see appendix for strategy search). No publication date or language restrictions were applied. Based on the abstracts of the 122 unique references obtained, 18 HTA reports and 32 references were selected from which 6 original articles were found relevant. Five additional reports were manually retrieved and downloaded.

No original full economic evaluation was found. References reporting only outcomes were excluded. Two costing studies were found in HTA reports. The first one was judged of good quality and the other one of poor quality, using the Drummond checklist for economic evaluations [89] (see appendix).

Finally, at the third annual meeting of HTAi (July 2006), an abstract was identified comparing the cost-effectiveness of balloon kyphoplasty and conventional medical management.

Suppliers and manufacturers of material for balloon kyphoplasty or percutaneous vertebroplasty were invited to submit any relevant information about their products, per mail or during meetings. Some information was provided on technical issues, on ongoing studies, and on incidence and prevalence of osteoporotic fractures in Belgium.

Given prices include all the material needed for a one level procedure (except auxillary costs such as gloves) unless otherwise specified. This includes needles and cement for the vertebroplasty and balloons, injectors and cement for the balloon kyphoplasty).

Currencies were converted using the 27 februari 2006 exchange rates (1 USD=0.84€, 1 AUD= 0.62€, 1 CAD=0.74 €, 1 DKK=0.13 €).

3.4.2 Marketing of material for balloon kyphoplasty and vertebroplasty

Bone cements and bone void fillers designed for other purposes than treatment of vertebral compression fractures have been modified for the use of vertebroplasty and balloon kyphoplasty. The U.S. FDA has approved the PMMA (polymethylmehtacrylate) bone cement from Kyphon, Inc. (KyphX HVR) for balloon kyphoplasty. Their KyphX® inflatable bone tamp is approved since 1998. Several other orthopaedic companies have an approval for bone cement products for purposes other than vertebroplasty since 1976, but since 1999 PMMA bone cement has been reclassified by the FDA and requires special controls. Death and serious injuries following the use of bone cement have to be reported to the FDA that has issued recommendations for its use (contraindication in case of on-site infection, warnings about blood pressure changes or cardiovascular adverse events) and cautioned about complications due to leakage. The FDA has only begun to clear bone cements in vertebral compression fractures due to osteoporosis since April 2004 and has updated its 2002 warning against side effects. In Europe, the CE mark was granted in 2000.

Beside PMMA bone cement, the CORTOSS™ bis-GMA composite has received a European CE approval in 2003 for use in vertebral augmentation. It is not approved in the U.S yet. Its formal application in Europe since 2002 was for bone screws fixation. It is claimed to overcome some of the PMMA weak points: on demand mixing, inherently opaque, no volatile monomers, lower exotherm and biomechanically stronger.

3.4.3 Economic consequences

3.4.3.1 Material costs: international comparison

All the costs described below concern a one vertebra level procedure, and increase with the number of levels of vertebrae treated.

In Denmark, the DACEHTA compared the direct costs of percutaneous vertebroplasty to conservative treatment for a period of 6 weeks starting from the management decision, including examination costs, hospital stay, personal material (€2,475 versus €2,370 with a certain degree of uncertainty). Without any comparable data on the effectiveness of percutaneous vertebroplasty compared to conservative treatment, they concluded that conducting a cost-effectiveness analysis was impossible [57]. Hence, RCTs are planned to gather information in Denmark.

Table 1 : Cost structure of vertebroplasty material (DACEHTA, 2004).

	Danish costs (€)
Medical material (gloves, …)	67
Anesthetics (incl. syringe)	13
Canules (2/vertebra)	107
Cement (20g / vertebra)	201
Blendingsystem and injector	134
Drugs (narcotics, analgesics and antibiotics)	134
Total	657

In the 2004 Canadian HTA report [64], the costs of balloon kyphoplasty were compared to the costs of vertebroplasty. For balloon kyphoplasty, the extra device costs amounted to €2,600 versus vertebroplasty in Canada and anaesthesia was more frequently required (difference in physician's fee and reimbursement anaesthetics = €35). The total costs (devices, anaesthetics and medical fees) amounted to €3,100 for balloon kyphoplasty against €540 for vertebroplasty. These numbers include more or less a €360 margin for adverse events treatment. The methods of calculation of this margin or the differences in follow-up after treatment were not reported. No device

costs were taken into account for vertebroplasty. Another Canadian source mentioned a cost of €220 - €440 in 2002 for vertebroplasty that includes material but also physician fees [69].

In Australia, the costs of vertebroplasty are between €220 - €440 (including physician's fees and material, but not pre-examinations and hospital fees). The cost of balloon kyphoplasty material alone is around €3,800 (and is not yet approved in Australia) [90].

In 2005, the Ministry of Health of Italy estimated the material costs for vertebroplasty to be between €500 and €725 (mean = €608) or between €695 and €1832 for a complete kit (mean = €1053), based on five hospital practices [91]. For balloon kyphoplasty, material costs amounted to €3,173 - 3,534 (mean = €3,400) [92]. To these costs the Italian DRG-reimbursement should be added, which is the same for both procedures. In a recent article in the European Journal of Trauma, reported material costs were respectively more or less €200 and €3,000 [93].

The table below summarizes the material costs information found in the literature compared to Belgian prices. We did not add the costs of the procedure as they differ from one healthcare system to another and thus cannot be compared. Depending on the cement used (one level: PMMA €80 or phosphocalcic cement €485), the kyphoplasty material in Belgium ranges from €3,470 to €4,000. Additional material for an extra vertebra costs €3,000 (2 extra balloons and 6 extra bone filler devices).

Table 2 : Cost of vertebroplasty (needles + cement) and balloon kyphoplasty (whole kit + cement) material from different countries in Euro.

	USA (2004) [68, 94]	Canada (2002) [69]	Australia (2003) [90]	Denmark (2004) [57]	Italy (2005) [91, 92]	Spain (2005) [95]	Belgium (2006) (from experts and Kyphon)
Vertebroplasty	340 - 460	330	-	440	600 - 1050	1100	450
Balloon Kyphoplasty	2860-2940 (*)	2860 (*)	3840	-	3400	4250	3600

(*) For balloon kyphoplasty : American prices from literature date from 2004 and the Canadian ones from 2002. Now, the 2006 Kyphon catalog gives canadian prices from 3500 to 3600 € and American prices from 2950 € to 3020 €, all of them cement excluded.

3.4.3.2 Procedural costs

Both procedures can be done on an outpatient basis and either with sedation and an analgesic or under general anaesthesia, depending on the general condition of the patient as well as on the number of levels that are treated. According to a Canadian report and an American report, both from 2004, a balloon kyphoplasty lasted around 60 to 90 minutes per level treated and patients were observed for a few hours; some patients might require an overnight stay [68] [64]. Currently the procedure times are reduced. According to the Kyphon website, a vertebroplasty lasts 30 to 45 minutes. Vallejo et al. reported even faster times: 20 minutes for a vertebroplasty and 30-45 minutes for a balloon kyphoplasty [96]. The longer operation time required for balloon kyphoplasty could increase the costs [68].

3.4.3.3 Cost-effectiveness

In an abstract presented at the most recent HTAi meeting, balloon kyphoplasty was estimated to be cost-effective compared to conventional medical management [97]. The incremental cost-effectiveness ratio was estimated at €4,065 per QALY following a Markov Model with a 2 years horizon for a 70 year-old woman suffering from primary osteoporosis and presenting a first vertebral compression fracture. Sensitivity analyses

were performed, but detailed results were not reported. Whether all branches were fully described on the horizon is not clear (e.g. the complication cost).

3.4.3.4 Belgian situation

Currently, no reimbursement is granted for balloon kyphoplasty or vertebroplasty in Belgium, neither for the material nor for the medical act (no honorarium fee). The nomenclature numbers most often used by surgeons are 281514-281525 (reduction of a dislocation, fracture or fracture-dislocation of the spine) – reimbursed at €354.51 for both procedures – and 589116-589120 (percutaneous occlusion under radiographic control of venous and arterial vascularisation of one or more organs), reimbursed at €680.08 for vertebroplasty. A last option used by surgeons for a vertebroplasty are 281971 – 281982 (resection-reconstruction of one or more vertebrae) reimbursed at € 775.49.

In 2005, the National Institute for Illness and Invalidity Insurance estimated the impact of reimbursement of balloon kyphoplasty on the Health budget. They estimated the number of patients at 600 per year. If the reimbursement was fixed at €4,256.28 for the devices (single or double-level) and €84.69 for the bone cement (per level), the material would cost €2,629,989 per year, considering a double-level intervention in 50% of the cases. Concerning the honorarium fee, a proposition was made at €272, giving 600 x 272= €163,200 for honorarium fees. No definitive proposition about the reimbursement has been made by the Institute to the Minister of Health yet.

Balloon kyphoplasty and vertebroplasty could benefit to more than 2,000 patients a year, suffering from a vertebral fracture due to osteoporosis, according to a personal communication from a manufacturer.

3.4.4 Market trends

A newcomer on the kyphoplasty market is the Disc-o-Tech Sky Bone Expander (Disc-o-Tech Medical Technologies, Israel) claimed to reduce operative time and costs thanks to a unilateral approach (http://www.disc-o-tech.com/Articles/Article.asp?CategoryID=4&ArticleID=109) [91] (material prices amounts to €1,000 according to experts). It should be noted that this technique was not considered as a balloon kyphoplasty procedure as encompassed in the reimbursement project or in the present report. To date, no published studies are available on this device. However, a recent abstract raised some serious doubts on the safety of the procedure [98].

Another experimental technique is the cavity creation vertebroplasty, where a manual curettage in the vertebral body is done previous to a bone cement injection. The price of a kit for such a technique would be much higher than the conventional vertebroplasty (almost €1,000) [96].

3.5 DISCUSSION

The evidence-base for both balloon kyphoplasty and vertebroplasty is weak. No completed randomized controlled trials were found, and the identified non-randomized controlled trials were of low quality and heterogeneous with regard to the outcomes measured. The identified HTA reports and systematic reviews generally referred to this same body of evidence. Nevertheless, there is some evidence coming from one ongoing RCT (preliminary 1 month results) suggesting that balloon kyphoplasty might be an effective procedure in the short term [80], hereby confirming the results of low-quality non-RCTs.

The fact that no completed RCTs were found is not surprising. First, it is an often used excuse that it is difficult for surgical procedures in general to conduct an RCT because of the difficulties with blinding the patients and/or the assessors. Second, the spectacular marketing and patient testimonies about balloon kyphoplasty and vertebroplasty on the internet obstruct the recruitment of control patients, as they initially refuse to be enrolled in the control arm.

Important methodological flaws were identified in all selected primary studies. For most studies it was unclear whether an intention-to-treat analysis was used, and only a minority used independent assessors. Most studies also paid a lot of attention to surrogate endpoints, e.g. kyphotic angle and vertebral height, which intentionally were not analysed in the present report because of the small importance for the patient. Of the identified reports and primary studies, some were produced by or in collaboration with one and the same author [61, 72, 74]. However, the competing interests of the authors were always clearly declared.

Based on the available evidence, balloon kyphoplasty appears to be a fairly safe procedure. However, some studies reported a rather high rate of cement leakages in 10 to 23% of cases [84, 85, 87]. Cement leakage is mostly asymptomatic but leakage to critical areas (such as epidural space, segmental vessels) – which is reported at a higher rate in vertebroplasty than in balloon kyphoplasty – can lead to pulmonary embolism, neurological deficits or reoperation (removal of cement). However, none of these latter complications were reported in the selected trials, probably because of the small sample size. Nevertheless, a meta-analysis of case series clearly demonstrated a higher incidence rate of symptomatic cement leakages after vertebroplasty than after balloon kyphoplasty [74].

In patients treated with balloon kyphoplasty, a lower incidence rate of new vertebral fractures was found compared to conservative treatment [73, 74, 84]. This is explained by favourable changes in the spinal biomechanics after balloon kyphoplasty [84].

A general conclusion of the economic evaluation is that currently balloon kyphoplasty material is five to ten times more expensive than the vertebroplasty material. If we take into account that balloon kyphoplasty generally requires general anaesthesia, and sometimes a night at the hospital, the difference could be even higher, ranging from ten to twenty times according to some authors [94].

As the information on economic evaluation of vertebroplasty and balloon kyphoplasty is lacking, ongoing and future well-conducted trials should ideally gather economic and costs information apart from patient outcomes information, in particular in the comparison of each of both techniques with conservative medical therapy. A lot can be expected from the VERTOS-II (Percutaneous Vertebroplasty Versus Conventional Therapy) trial that will be conducted in 2 Dutch centres and one Belgian centre (A.Z. Sint Lucas, Gent) [82]. This trial will include a cost-effectiveness analysis from a one-year Dutch and Belgian societal perspective. Results are expected by May 2008. At the University of Alabama, the FREE (Fracture Reduction Evaluation) trial – an RCT supported by Kyphon, Inc. – will study balloon kyphoplasty versus standard medical therapy, including the economic aspects at different time intervals up to 1 year and the cost-effectiveness (costs/QALY) at 1 and 2 years [80]. Finally, the ongoing Investigational Vertebroplasty Efficacy and Safety Trial (INVEST) – conducted at the Mayo clinic (Minnesota) – will include a cost-effectiveness analysis of balloon kyphoplasty versus vertebroplasty [83].

The position of other countries and/or organisations towards this limited evidence-base varies. Some countries or organisations call for more primary research before funding balloon kyphoplasty (e.g. Australia [75], Canada [64], AHRQ [66]) or vertebroplasty. Other countries or organisations recently approved funding or supported the use of balloon kyphoplasty (e.g. NICE [99]) or vertebroplasty (e.g. Australia [78], NICE [63]).

Policy makers are challenged with a difficult decision. One option is to keep the current position and to not approve reimbursement, because of the limited evidence of clinical benefits and the weak benefit/risk ratio, for which this report provides a contemporary and up-to-date review of the current scientific knowledge. Another option is to approve reimbursement under certain conditions in accordance with clinical trials (adult patients with a painful non-traumatic thoracic or lumbar (T5 – L5) vertebral compression fracture of ≤ 3 months old [80]) and to set up a registry for the follow-up of so far unknown adverse events. For public health reasons, these conditions could even be applied upstream in a market authorization procedure by the Ministry of Public Health, prior to any reimbursement submission, as it is currently the case for drugs. Safety and efficacy of each drug have to be established and reported before any

introduction of this drug on the Belgian market. Finally, an option is to approve funding without any restriction or follow-up, since for other reimbursed orthopaedic procedures high-quality primary research proving patient benefits were never asked in the past.

Key points vertebroplasty

- **The efficacy of vertebroplasty for non-traumatic vertebral fractures is uncertain. Only one non-randomized controlled trial at the most showed equivalence between vertebroplasty and conservative treatment.**
- **Above this, there are some safety concerns about the rate of cement leakages after vertebroplasty.**
- **At present and until the results of further ongoing RCTs become available, this technique has to be considered experimental, and should be limited to carefully selected patients treated in research centres. Taken into consideration the available data on efficacy and safety, the experimental design of choice for this interventional procedure should be a randomized controlled trial with sufficient power to show superiority over conservative treatment.**

Key points kyphoplasty

- **There is average quality of evidence on the efficacy of balloon kyphoplasty for the treatment of non-traumatic vertrebral compression fractures coming from non-randomised clinical studies: kyphoplasty appears to reduce pain scores compared to conventional therapy. There is only limited evidence from randomised trials: The preliminary results of one ongoing RCT confirm the short term clinical effectiveness. Long term benefits are still uncertain.**
- **Based on a meta-analysis of case series, balloon kyphoplasty appears to be relatively safe.**
- **Concerning the reimbursement of the procedure, policy makers are faced with a difficult decision and have the choice between following options:**
- **1. Wait-and-see, because of the limited evidence of long term clinical benefits and the weak benefit/risk ratio and the fact that trials are still ongoing and cost-effectiveness data mostly lacking;**
- **2. Reimbursement under certain criteria in accordance with clinical trials (adult patients with a painful non-traumatic thoracic or lumbar (T5 – L5) vertebral compression fracture of ≤ 3 months old). The instigation of a registry for the follow-up of so far unknown adverse events can be considered, but will be difficult to establish in this patient population where a large loss to follow-up is to be expected;**
- **Since this is still an emerging technology and a learning curve can be expected, the technique should be performed by a multidisciplinary team. For part of the elderly patients that present with co-morbidities, multiple drugs and fall problems, a discussion with a geriatric specialist and the general practitioner is to be recommended. Training in this technique and a strict adherence to the manufacturers' instructions is needed to reach an appropriate level of expertise in the procedure.**

4 REFERENCES

1. Borenstein D. Epidemiology, etiology, diagnostic evaluation, and treatment of low back pain. Current Opinion in Rheumatology. 1996;8(2):124-9.
2. Philadelphia P. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions for low back pain. Physical Therapy. 2001;81(10):1641-74.
3. Guzman J, Esmail R, Karjalainen K, Malmivaara A, Irvin E, Bombardier C. Multidisciplinary bio-psycho-social rehabilitation for chronic low-back pain. Cochrane Database of Systematic Reviews. 2006;1:1.
4. Khadilkar A, Milne S, Brosseau L, Robinson V, Saginur M, Shea B, et al. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. Cochrane Database of Systematic Reviews. 2006;1:1.
5. Assendelft WJJ, Morton SC, Yu Emily I, Suttorp MJ, Shekelle PG. Spinal manipulative therapy for low-back pain. Cochrane Database of Systematic Reviews. 2006;1:1.
6. Nelemans PJ, de Bie RA, de Vet HCW, Sturmans F. Injection therapy for subacute and chronic benign low-back pain. Cochrane Database of Systematic Reviews. 2006;1:1.
7. Ostelo R, van Tulder MW, Vlaeyen JWS, Linton SJ, Morley SJ, Assendelft WJJ. Behavioural treatment for chronic low-back pain. Cochrane Database of Systematic Reviews. 2006;1:1.
8. National Institute for Clinical E. Prosthetic intervertebral disc replacement. London: National Institute for Clinical Excellence (NICE). 2004:2.
9. Fernstrom U. Arthroplasty with intercorporal endoprothesis in herniated disc and in painful disc. Acta Chirurgica Scandinavica Supplementum. 1966;357:154-9.
10. Tice JA. Artificial disc replacement for degenerative disc disease of the lumbar spine. San Francisco, California: California Technology Assessment Forum; 2005 February 16, 2005. Available from:
11. Blue Cross Blue Shield A. Artificial vertebral disc replacement. Chicago IL: Blue Cross Blue Shield Association (BCBS). 2005:17.
12. Institute for Clinical Systems I. Lumbar artificial intervertebral discs. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI). 2005:19.
13. Ontario Ministry of H, Long-Term C. Artificial discs: applications to cervical and lumbar spinal surgery for degenerative disc disease. Toronto: Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care (MAS). 2004:17.
14. Wang JC. Lumbar disc arthroplasty. Spine Journal. 2005;5(1):95-103.
15. Haute Autorite de Sante/French National Authority for H. Disc prostheses and arthrodesis in degenerative disease of the lumbar spine. Paris: Haute Autorite de Sante/French National Authority for Health (HAS). 2000.
16. Artificial Disc (Total Disc Replacement) as an Alternative to Spinal Fusion for Degenerative Disc Disease: Harvard Pilgrim Health Care; 2004 December, 2004 (revised May, 2005). Available from:
17. Geisler FH, Blumenthal SL, Guyer RD, McAfee PC, Regan JJ, Johnson JP, et al. Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charite intervertebral disc. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004. 2004;1(2):143-154.
18. ASERNIP-S. Artificial intervertebral (lumbar) disc replacement. Rapid Review. Adelaide: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical; 2003 May

2003. New and Emerging Techniques - Surgical. Available from: http://racsdev.gmp.usyd.edu.au/asernip-s/net-s/procedures/Artificial_Intervertebral_Disc_Replacement_May2003.pdf

19. He Z-S, Bai J-P, Xilin B-L-R, Jin G-L, Wu T-X, Li J. Artificial total disc replacement for lumbar degenerative disc disease: A systematic review. Chinese Journal of Evidence-Based Medicine. 2005;5(2):136-139.

20. Martin CWaWEBPG. Artificial cervical and lumbar disc implants: A review of the literature. Vancouver: WorksafeBC; 2005 2005 April 13. Available from: http://www.worksafebc.com/health_care_providers/Assets/PDF/artificial_cervical_lumbar_disc.pdf

21. de Kleuver M, Oner FC, Jacobs WCH. Total disc replacement for chronic low back pain: background and a systematic review of the literature. European Spine Journal. 2003;12(2):108-16.

22. McAfee PC, Fedder IL, Saiedy S, Shucosky EM, Cunningham BW. Experimental design of total disk replacement-experience with a prospective randomized study of the SB Charite. Spine. 2003;28(20):S153-62.

23. McAfee PC, Fedder IL, Saiedy S, Shucosky EM, Cunningham BW. SB Charite disc replacement: report of 60 prospective randomized cases in a US center. Journal of Spinal Disorders & Techniques. 2003;16(4):424-33.

24. Guyer RD, McAfee PC, Hochschuler SH, Blumenthal SL, Fedder IL, Ohnmeiss DD, et al. Prospective randomized study of the Charite artificial disc: data from two investigational centers. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):252S-259S.

25. Blumenthal S, McAfee PC, Guyer RD, Hochschuler SH, Geisler FH, Holt RT, et al. A prospective, randomized, multicenter Food and Drug Administration Investigational Device Exemptions study of lumbar total disc replacement with the CHARITE(trademark) artificial disc versus lumbar fusion - Part I: Evaluation of clinical outcomes. Spine. 2005;30(14):1565-1575.

26. McAfee PC, Cunningham B, Holsapple G, Adams K, Blumenthal S, Guyer RD, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITEtrade; artificial disc versus lumbar fusion - Part II: Evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. Spine. 2005;30(14):1576-1583.

27. Delamarter RB, Bae HW, Pradhan BB. Clinical results of ProDisc-II lumbar total disc replacement: report from the United States clinical trial. Orthopedic Clinics of North America. 2005;36(3):301-13.

28. Delamarter RB, Fribourg DM, Kanim LEA, Bae H. ProDisc artificial total lumbar disc replacement: introduction and early results from the United States clinical trial. Spine. 2003;28(20):S167-75.

29. Auerbach JD, Wills BPD, McIntosh TC, Balderston RA. Lumbar disc arthroplasty versus fusion for single-level degenerative disc disease: Two-year results from a randomized prospective study. Seminars in Spine Surgery. 2005;17(4):310-318.

30. Zigler JE. Clinical results with ProDisc: European experience and U.S. investigation device exemption study. Spine. 2003;28(20):S163-6.

31. Zigler JE. Lumbar spine arthroplasty using the ProDisc II. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):260S-267S.

32. Zigler JE, Burd TA, Vialle EN, Sachs BL, Rashbaum RF, Ohnmeiss DD. Lumbar spine arthroplasty: early results using the ProDisc II: a prospective randomized trial of arthroplasty versus fusion. Journal of Spinal Disorders & Techniques. 2003;16(4):352-61.

33. Gornet MF, Mathews HH, Burkus JK, Johnson II DR, Rahn KA. MAVERICK total disc replacement: a review of 12-month data from five investigational centers. The Spine Journal. 2005;5(4, Supplement 1):S57.

34. Administration FaD. Approval letter of CHARITÉ Artificial Disc Rockville MD: FDA; 2004 [updated cited May 23, 2006]. Approval letter of CHARITÉ Artificial Disc. Available from: http://www.fda.gov/cdrh/pdf4/p040006a.pdf

35. Tillman DB. Approval letter. Rockville MD: Food and Drug Administration; 2004 [updated October 26, 2004; cited March 28, 2006]. Approval letter. Available from: http://www.fda.gov/cdrh/pdf4/p040006a.pdf

36. ClinicalTrials.gov. CHARITE™ Vs. ALIF 5-Year Follow-Up. Rockville: ClinicalTrials.gov; 2005 [updated December 8, 2005; cited March 28, 2006]. CHARITE™ Vs. ALIF 5-Year Follow-Up. Available from: http://clinicaltrials.gov/show/NCT00215332

37. ClinicalTrials.gov. Kineflex Artificial Disc System to Treat DDD. Rockville: ClinicalTrials.gov; 2006 [updated March 1, 2006; cited March 28, 2006]. Kineflex Artificial Disc System to Treat DDD. Available from: http://clinicaltrials.gov/show/NCT00292292

38. Singh K, Vaccaro AR, Albert TJ. Assessing the potential impact of total disc arthroplasty on surgeon practice patterns in North America. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):195S-201S.

39. Morrow T. Spinal disc technology seeks to replace body's engineering marvel. Managed Care. 2005;14(6):67-8.

40. HealthCare HP. Artificial Disc (Total Disc Replacement) as an Alternative to Spinal Fusion for Degenerative Disc Disease: Harvard Pilgrim HealthCare; 2004 [updated May, 2005; cited May 23, 2006]. Artificial Disc (Total Disc Replacement) as an Alternative to Spinal Fusion for Degenerative Disc Disease. Available from: http://www.harvardpilgrim.org/pls/portal/docs/PAGE/PROVIDERS/MEDMGMT/STATEMENTS/ARTIFICIAL_%20DISC6.05.PDF

41. Viscogliosi A VJ, Viscogliosi M. Beyond Total Disc. The future of Spine Surgery. New York: Viscogliosi Brothers LLC; 2004 May 2004. Spine Industry Analysis series. Available from: http://a788.g.akamaitech.net/7/788/915/ec84ccbf519a9a/images.gomez.com/images/Alerts/SAReport%202004.pdf

42. van Tulder MW, Koes B, Malmivaara A. Outcome of non-invasive treatment modalities on back pain: an evidence-based review. European Spine Journal. 2006;15(1).

43. Fairbank J, Frost H, Wilson-MacDonald J, Yu L-M, Barker K, Collins R, et al. Randomised controlled trial to compare surgical stabilisation of the lumbar spine with an intensive rehabilitation programme for patients with chronic low back pain: the MRC spine stabilisation trial.[see comment][erratum appears in BMJ. 2005 Jun 25;330(7506):1485]. BMJ. 2005;330(7502):1233.

44. Brox JI, Reikeras O, Nygaard O, Sorensen R, Indahl A, Holm I, et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: a prospective randomized controlled study. Pain. 2006;122(1-2):145-55.

45. Fritzell P, Hagg O, Wessberg P, Nordwall A, Swedish Lumbar Spine Study G. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. Spine. 2001;26(23):2521-32; discussion 2532-4.

46. (CBO) KvdG. Osteoporose Tweede Herziene Richtlijn. Alphen aan den Rijn: CBO; 2002 2002. Available from:

47. (RIZIV/INAMI) RvZ-el. De doelmatige behandelingen voor de preventie van breuken ten gevolge van osteoporose. Brussel: RIZIV/INAMI; 2005 May 26, 2005. Available from:

48. Wong R, Wiffen PJ. Bisphosphonates for the relief of pain secondary to bone metastases. Cochrane Database of Systematic Reviews. 2006;1:1.

49. Lyritis GP, Ioannidis GV, Karachalios T, Roidis N, Kataxaki E, Papaioannou N, et al. Analgesic effect of salmon calcitonin suppositories in patients with acute pain due to recent osteoporotic vertebral crush fractures: a prospective double-blind, randomized, placebo-controlled clinical study. Clinical Journal of Pain. 1999;15(4):284-9.

50. Martinez MJ, Roque i Figuls M, Alonso Coello P, Catala E, Garcia JL, Ferrandiz M. Calcitonin for metastatic bone pain. Cochrane Database of Systematic Reviews. 2006;1:1.

51. McQuay HJ, Collins SL, Carroll D, Moore RA. Radiotherapy for the palliation of painful bone metastases. Cochrane Database of Systematic Reviews. 2006;1:1.

52. Galibert P, Deramond H, Rosat P, Le Gars D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. Neuro-Chirurgie. 1987;33(2):166-8.

53. Kyphoplasty (project). Comite d'Evaluation et de Diffusion des Innovations Technologiques (CEDIT).

54. Percutaneous vertebroplasty in the treatment of osteoporotic vertebral fractures (project). The Netherlands Organisation for Health Research and Development (ZonMw).

55. Percutaneous vertebroplasty for back pain (project). The Swedish Council on Technology Assessment in Health Care (SBU).

56. Hayes, Inc. Percutaneous vertebroplasty and kyphoplasty. Lansdale, PA: HAYES, Inc. 2004:22.

57. Danish Centre for E, Health Technology A. Percutaneous vertebroplasty. Pain management of osteoporotic vertebral fractures. Copenhagen: Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) (formerly DIHTA). 2004:33.

58. Blue Cross Blue Shield A. Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy. Chicago IL: Blue Cross Blue Shield Association (BCBS). 2004:21.

59. Blue Cross Blue Shield A. Percutaneous vertebroplasty for vertebral fractures caused by osteoporosis and malignancy, or hemangioma. Chicago IL: Blue Cross Blue Shield Association (BCBS). 2004:25.

60. Bouza C, Magro A, Amate JM. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures. Madrid, Spain: Agencia de Evaluación de Tecnologías Sanitarias; 2005. Available from:

61. Taylor RS, Taylor RJ, Fritzell P. Ballon Kyphoplasty for Vertebral Compression Fractures: Health Technology Assessment. Birmingham: University of Birmingham; 2005 March 2005. Available from:

62. National Institute for Health and Clinical E. Interventional procedures overview of balloon kyphoplasty for vertebral compression fractures. London: National Institute for Clinical Excellence (NICE). 2005:27.

63. National Institute for Clinical E. Percutaneous vertebroplasty. London: National Institute for Clinical Excellence (NICE). 2003:2.

64. Ontario Ministry of H, Long-Term C. Balloon kyphoplasty. Toronto: Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care (MAS). 2004:42.

65. Muggli E. Safety and efficacy of percutaneous vertebroplasty in symptomatic osteoporotic vertebral compression fractures. Clayton, Victoria: Centre for Clinical Effectiveness (CCE). 2002:18.

66. Agency for Healthcare R, Quality. Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy and percutaneous vertebroplasty for vertebral fractures caused by osteoporosis and malignancy. Rockville: Agency for Healthcare Research and Quality (AHRQ). 2005.

67. Blue Cross Blue Shield A. Percutaneous vertebroplasty for vertebral fractures caused by osteoporosis or malignancy. Chicago IL: Blue Cross Blue Shield Association (BCBS). 2005:25.

68. Institute for Clinical Systems I. Vertebroplasty and balloon-assisted vertebroplasty for the treatment of osteoporotic compression fractures. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI). 2004.

69. Fisher A. Percutaneous vertebroplasty: a bone cement procedure for spinal pain relief. Ottawa: Canadian Coordinating Office for Health Technology Assessment/Office Canadien de Coordination de l'Evaluation des Technologies de la Sante (CCOHTA). 2002:4.

70. Pichon Riviere A, Augustovski F, Ferrante D, Regueiro A, Garcia Marti S, Glujovsky D, et al. Percutaneous vertebroplasty usefulness for vertebral fracture treatment. Ciudad de Buenos Aires: Institute for Clinical Effectiveness and Health Policy (IECS). 2004.

71. Blue Cross Blue Shield A. Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis or malignancy. Chicago IL: Blue Cross Blue Shield Association (BCBS). 2005:23.

72. Kasperk C, Hillmeier J, Noldge G, Grafe IA, Dafonseca K, Raupp D, et al. Treatment of painful vertebral fractures by kyphoplasty in patients with primary osteoporosis: A prospective nonrandomized controlled study. Journal of Bone and Mineral Research. 2005;20(4):604-612.

73. Komp M, Godolias G, Ruetten S. Minimally invasive therapy for functionally unstable osteoporotic vertebral fracture by means of kyphoplasty: prospective comparative study of 19 surgically and 17 conservatively treated patients. J Miner Stoffwechs. 2004;11(suppl 1):13-15.

74. Taylor R, Fritzell P, Taylor R, Casteels B. Balloon kyphoplasty and vertebroplasty for vertebral compression fractures: a updated comparative systematic review of efficacy and safety. In: Proceedings of the HTAi; 2006; Adelaide, Australia: University of Birmingham; 2006.

75. Newton S, Merlin TL, Hedayati H, Thomson K, Hiller J. Kyphoplasty for treating vertebral compression fractures with kyphosis. In: Proceedings of the HTAi; 2006; Adelaide, Australia: Adelaide Health Technology Assessment; 2006.

76. Hendrikse CA, Kalmijn S, Voormolen MH, Verhaar HJ, Mali WP. Percutaneous vertebroplasty in the treatment of osteoporotic vertebral compression fractures: review of the literature].[see comment. Nederlands Tijdschrift voor Geneeskunde. 2003;147(32):1553-9.

77. Levine SA, Perin LA, Hayes D, Hayes WS. An evidence-based evaluation of percutaneous vertebroplasty. Managed Care. 2000;9(3):56-60.

78. Merlin TL, Newton S, Thomson K, Hiller JE. Brittle bones and painful backs: a systematic review of the safety and effectiveness of vertebroplasty. In: Proceedings of the HTAi; 2006; Adelaide, Australia: Adelaide Health Technology Assessment; 2006.

79. ClinicalTrials.gov. CAFE Study - Cancer Patient Fracture Evaluation Rockville: ClinicalTrials.gov; 2005 [updated December 8, 2005; cited April 10]. CAFE Study - Cancer Patient Fracture Evaluation. Available from: http://clinicaltrials.gov/show/NCT00211237

80. ClinicalTrials.gov. FREE Study - Fracture Reduction Evaluation Rockville: ClinicalTrials.gov; 2005 [updated March 23, 2006; cited April 10]. FREE Study - Fracture Reduction Evaluation. Available from: http://clinicaltrials.gov/show/NCT00211211

81. ClinicalTrials.gov. Cost Effectiveness and Efficacy of Kypho and Vertebro Plasty Trial Rockville: ClinicalTrials.gov; 2006 [updated January 19, 2006; cited April 10]. Cost Effectiveness and Efficacy of Kypho and Vertebro Plasty Trial. Available from: http://clinicaltrials.gov/show/NCT00279877

82. ClinicalTrials.gov. VERTOS-II. Percutaneous Vertebroplasty Versus Conventional Therapy Rockville: ClinicalTrials.gov; 2005 [updated March 17, 2006; cited July 25]. VERTOS-II. Percutaneous Vertebroplasty Versus Conventional Therapy. Available from: http://www.clinicaltrials.gov/ct/show/NCT00232466

83. ClinicalTrials.gov. Vertebroplasty for the Treatment of Fractures Due to Osteoporosis Rockville: ClinicalTrials.gov; 2003 [updated March 15, 2006; cited July 25]. Vertebroplasty for the Treatment of Fractures Due to Osteoporosis. Available from: http://clinicaltrials.gov/ct/show/NCT00068822

84. Grafe IA, Da Fonseca K, Hillmeier J, Meeder P-J, Libicher M, Noldge G, et al. Reduction of pain and fracture incidence after kyphoplasty: 1-Year outcomes of a prospective controlled trial of patients with primary osteoporosis. Osteoporosis International. 2005;16(12):2005-2012.

85. Grohs JG, Matzner M, Trieb K, Krepler P. Minimal invasive stabilization of osteoporotic vertebral fractures: a prospective nonrandomized comparison of vertebroplasty and balloon kyphoplasty. Journal of Spinal Disorders & Techniques. 2005;18(3):238-42.

86. Diamond TH, Bryant C, Browne L, Clark WA. Clinical outcomes after acute osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous vertebroplasty with conservative therapy. Medical Journal of Australia. 2006;184(3):113-7.

87. Pflugmacher R, Kandziora F, Schröder R, Schleicher P, Scholz M, Schnake K, et al. Vertebroplasty and Kyphoplasty in Osteoporotic Fractures of Vertebral Bodies - a Prospective 1-Year Follow-up Analysis. Fortschr Röntgenstr. 2005(177):1670-1676.

88. Diamond TH, Champion B, Clark WA. Management of acute osteoporotic vertebral fractures: A nonrandomized trial comparing percutaneous vertebroplasty with conservative therapy. American Journal of Medicine. 2003;114(4):257-265.

89. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. Bmj. 1996;313(7052):275-83.

90. ASERNIP-S. Kyphoplasty. Procedure Brief. Adelaide: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical; 2003 May 2003. New and Emerging Techniques - Surgical. Available from: http://racsdev.gmp.usyd.edu.au/asernip-s/net-s/procedures/Kyphoplasty.pdf

91. Vertebroplastica percutanea. Roma: Commissione Unica dei Dispositivi Medici, Schede di valutazione tecnologica sui dispositivi medici, Ministero della Salute; 2005. Available from: http://www.ministerosalute.it/imgs/C_17_pagineAree_88_listaFile_itemName_3_file.pdf

92. Cifoplastica percutanea. Roma; 2005. Commissione Unica dei Dispositivi Medici, Schede di valutazione tecnologica sui dispositivi medici, Ministero della Salute. Available from: http://www.ministerosalute.it/imgs/C_17_pagineAree_88_listaFile_itemName_4_file.pdf

93. Armsen N, Boszczyk B. Vertebro-/kyphoplasty history, development, results. European Journal of Trauma. 2005;31(5):433-441.

94. Mathis JM, Ortiz AO, Zoarski GH. Vertebroplasty versus kyphoplasty: A comparison and contrast. American Journal of Neuroradiology. 2004;25(5):840-845.

95. Martinez-Quinones JV, Aso-Escario J, Arregui-Calvo YR. [Percutaneous vertebral augmentation: vertebroplasty and kyphoplasty: operative technique.]. [Spanish]. Neurocirugia (Asturias, Spain). 2005;16(5):427-40.

96. Vallejo R, Benyamin R, Floyd B, Casto JM, Joseph NJ, Mekhail N. Percutaneous cement injection into a created cavity for the treatment of vertebral body fracture: preliminary results of a new vertebroplasty technique. Clinical Journal of Pain. 2006;22(2):182-9.

97. Marchetti M, Caruggi.M, Taylor R. Cost-effectiveness of balloon kyphoplasty for symptomatic vertebral compression fractures in osteoporotic patients. In: Proceedings of the 3rd Annual Meeting of Health Technology Assessment International (HTAi); 2006 July 3rd, 2006; Adelaide, Asutralia; 2006.

98. Foo LSS, Yeo W, Fook-Chong MC, Guo CM, Yue YM, Chen J, et al. P436SA. Sky Bone Expander Kyphoplasty versus Vertebroplasty for Osteoporotic Vertebral Compression Fractures: Early Experience and Results. Osteoporosis International. 2006;17(Suppl 2).

99. National Institute for Clinical E. Balloon kyphoplasty for vertebral compression fractures. London: National Institute for Clinical Excellence (NICE). 2006.

APPENDICES INTERVERTEBRAL DISK REPLACEMENT

CLINICAL STUDIES STRATEGY FOR MEDLINE

1 exp Intervertebral Disk Displacement/su [Surgery]

2 exp Intervertebral Disk/su [Surgery]

3 exp Low Back Pain/su [Surgery]

4 exp Sciatica/su [Surgery]

5 exp Radiculopathy/su [Surgery]

6 exp Lumbar Vertebrae/su [Surgery]

7 exp Arthroplasty/

8 exp Arthroplasty, Replacement/

9 disk.mp. [mp=title, original title, abstract, name of substance word, subject heading word]

10 disc.mp. [mp=title, original title, abstract, name of substance word, subject heading word]

11 7 or 8

12 9 or 10

13 11 and 12

14 1 or 2 or 3 or 4 or 5 or 6 or 13

15 limit 14 to yr="2000 - 2006"

16 limit 15 to meta analysis

17 limit 15 to "reviews (optimized)"

18 limit 15 to "therapy (specificity)"

19 limit 15 to (clinical trial or controlled clinical trial or randomized controlled trial)

20 16 or 17 or 18 or 19

ECONOMIC AND COSTS STUDIES STRATEGY

- Centre for Reviews and Dissemination (HTA)

(disk OR disc)/Subject Headings Exploded AND (artificial OR prosthe OR implant OR replacement)/Title & Abstract

HTA database: 7 Hits

NHS Economic Evaluation Database (NHS EED): 8 Hits

- Econlit (same strategy – Any Field): 4 Hits
- Medline and PreMedline : 29 Hits

For the Medline search on OVID interface, the MesH terms 'Intervertebral Disk' (exploded) was combined with the MeSH term 'Prostheses and Implants' (exploded), the following keywords: 'artificial', (prosthe$ or implant?) or replacement?

Results were combined to the following economics or costs filters:

- the Mc Master University Hedges based on Haynes (medium sensitivity and medium specificity for economics and costs) (http://hiru.mcmaster.ca/hedges/),
- the INTERTASC Quality of life filter available from the University of York website (http://www.york.ac.uk/inst/crd/intertasc/econ.htm),
- Embase: 12 Hits

For the search on Embase database, the same strategy was applied on Embase references only (Medline terms were mapped to Emtree words when possible) and the following filters adapted to Embase were used:

- the economics filter from Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk/methodology/filters.html#econ),
- Emtree term: quality of life/

Grey literature was searched on February 15 through www.google.com (artificial AND (lumbar or vertebral) AND (disk$ OR disc$) AND ("degenerative disk disease") AND (cost$ OR economic$) -CD -DVD –intelligence) in order to retrieve 2 reports (The same research was done in French and Dutch) as well as institution and professional organization sites such as FDA Centre for devices and radiological health register www.fda.gov , www.UNAMEC.be, www.worldspine.org and related sites …. Financial analyses available on charges were not bought.

QUALITY APPRAISAL

Table 1 : HTA reports

INAHTA checklist	ANAES 2000	MAS 2004	NICE 2004	Wang 2004	CTAF 2005	BCBS 2005	HPHC 2005	ICSI 2005
Are contact details available for further information?	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Authors identified?	Yes	No	No	Yes	Yes	Yes	No	Yes
Statement regarding conflict of interest?	No	No	No	No	No	No	No	No
Statement on whether report externally reviewed?	No	No	Partly	No	No	Yes	No	Yes
Short summary in non-technical language?	No	Yes	Yes	No	No	Yes	No	Yes
Reference to the question that is addressed and context of assessment?	No	No	Yes	No	Partly	Partly	No	No
Scope of the assessment specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Description of the health technology?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Details on sources of information?	Yes	Yes	Yes	Yes	Yes	Yes	Partly	Yes
Information on selection of material for assessment?	No	No	Yes	Partly	No	No	No	No
Information on basis for interpretation of selected data?	No	No	Yes	No	Yes	Yes	Partly	Partly
Results of assessment clearly presented?	Yes	Yes	Yes	Yes	Partly	Yes	No	Partly
Interpretation of assessment results included?	Yes	Partly	Yes	No	Yes	Yes	Partly	Yes
Findings of the assessment discussed?	Partly	Partly	Partly	Partly	Yes	Yes	Partly	Yes
Medico-legal implications considered?	No	No	No	No	No	No	No	No
Conclusions from assessment clearly stated?	Partly	Yes	Partly	Yes	Yes	Yes	No	Yes
Suggestions for further action?	Partly	Partly	Yes	No	Partly	No	No	No
Overall appraisal	**Poor**	**Poor**	**Fair**	**Poor**	**Fair**	**Poor**	**Poor**	**Poor**

Table 2 : Systematic reviews

Cochrane checklist	de Kleuver 2003	EBPG 2005
Adequate research question?	Yes	Yes
Adequately performed search?	Partly	Yes
Adequate selection of articles?	Yes	Not stated
Adequate quality appraisal of articles?	Yes	Yes
Adequate description of the data extraction procedure?	No	No
Description of the most important characteristics of the included articles?	Yes	Yes
Adequate handling of clinical and statistical heterogeneity?	No	No
Adequate statistical pooling?	No	No
Overall appraisal	**Fair**	**Fair**

Table 3 : Randomized controlled trials

Cochrane checklist	Geisler 2004, Blumenthal 2005, McAfee 2005	Zigler 2004	Auerbach 2005	Delamarter 2005	Gornet 2005
Randomization?	Yes	Yes	Yes	Yes	Yes
Blinding of randomization?	Yes	Not stated	Not stated	Not stated	Yes
Blinding of patients?	No	No	No	No	No
Blinding of care provider?	No	No	No	No	No
Blinding of outcome assessor?	Not stated	Yes	Yes	Not stated	No
Similar groups at baseline?	Yes	Yes	Yes	Yes	Yes
Follow-up long enough?	Yes	Yes	Yes	Yes	Yes
Intention-to-treat-analysis?	Yes	Not stated	Not stated	Not stated	Not stated
Comparable treatment of groups?	Yes	Yes	Yes	Yes	Yes
Overall appraisal	**Fair**	**Poor**	**Poor**	**Poor**	**Poor**

EVIDENCE TABLES

Table 4 : HTA reports

Study ID	**Intervention**	**Quality Assessment** Good / Fair	**Remarks**	**Conclusions/Recommendations**
NICE 2004	Intervertebral disk replacement	Fair	Included 1 RCT, 1 non-randomized comparative study, and 9 case series	Current evidence on the safety and efficacy of intervertebral disc replacement appears adequate to support the use of this procedure. There is little evidence on outcomes beyond 2–3 years and collection of long-term data is therefore particularly important. Patients should understand the uncertainty about the procedure's long-term efficacy. Audit and review of clinical outcomes of all patients having intervertebral disc replacement should be done.
CTAF 2005	Intervertebral disk replacement	Fair	Focus on Charité Artificial Disc Included 1 RCT and 4 case series	The use of the Charité Artificial Disc does not meet the Technology Assessment criteria 3, 4, or 5 for treatment of DDD of the lumbar spine.

Table 5 : Systematic reviews

Study ID	**Intervention**	**Quality Assessment** Good / Fair	**Remarks**	**Conclusions/Recommendations**
de Kleuver 2003	Intervertebral disk replacement	Fair	Search strategy limited to peer-reviewed literature (CDRCT, Current Contents, Medline, Cinahl); no Embase search. Possibility of double-counting of results (inclusion of the study of Griffith et al, see remark on page 111).	The authors concluded that total disk replacement should be considered an experimental procedure and should only be used in strict clinical trials.
Martin 2005	Intervertebral disk replacement	Fair	Primary objective of the SR was to investigate the safety and effectiveness of intervertebral cervical disk implants, and to investigate its relative advantage compared to cervical fusion in treating DDD. The secondary objective of the SR was to summarize available SRs on artificial disk replacement in general (including lumbar disk replacement).	The author expressed his concern on the quality of the study that formed the basis for the approval of the SB Charité III disk by the US FDA. The author concluded that artificial intervertebral disks should be considered still at an experimental stage.

Table 6 : Randomized controlled trials

Study ID	**Patients**	**Intervention/comparator**	**Quality Assessment** Good / Fair	**Outcomes**
Geisler 2004 Blumenthal 2005 McAfee 2005	Patients with single-level symptomatic DDD at L4-L5 or L5-S1 confirmed by provocative discography; failure to respond to nonfusion treatment for a period of at least 6 months.	Intervention: Lumbar total disk replacement with the Charité disk (n = 205) Comparator: ALIF with BAK fusion cage packed with iliac crest autograft (n = 99)	Fair	VAS score at 2y: IDR 31.2 vs. control 37.5, p=0.11 ODI score at 2y: IDR 26.3 vs. control 30.5, p=0.27 Clinical success at 2y: IDR 63.6% vs. control 56.8%, p=0.0004 Equivalent overall complication rate (p=0.68) and device failure (p=0.45)

APPENDICES KYPHOPLASTY AND VERTEBROPLASTY

CLINICAL STUDIES STRATEGY FOR MEDLINE

1 disc.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
2 disk.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
3 1 or 2
4 balloon.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
5 3 and 4
6 kyphoplast$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
7 vertebroplast$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
8 exp Osteoporosis/su [Surgery]
9 exp Osteoporosis, Postmenopausal/su [Surgery]
10 exp Spinal Fractures/su [Surgery]
11 exp Spinal Cord Compression/su [Surgery]
12 exp Fractures, Spontaneous/su [Surgery]
13 exp Fractures, Compression/su [Surgery]
14 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15 limit 14 to yr="2000 - 2006"
16 limit 15 to meta analysis
17 limit 15 to "reviews (optimized)"
18 limit 15 to "therapy (specificity)"
19 limit 15 to (clinical trial or controlled clinical trial or randomized controlled trial)
20 16 or 17 or 18 or 19

ECONOMIC AND COSTS STUDIES STRATEGY

- Centre for Reviews and Dissemination (HTA)

vertebroplast/Title & Abstract OR kyphoplast/Title & Abstract

HTA database: 18 Hits

NHS Economic Evaluation Database (NHS EED): 1 Hit

- Econlit (same strategy – Any Field): 0 Hit
- Medline and PreMedline : 24 Hits

For the Medline search on OVID interface, the words vertebroplast$ or kyphoplast$ were searched in title, original title, abstract, name of substance word or subject heading word.

Results were combined to the following economics or costs filters:

- the Mc Master University Hedges based on Haynes (medium sensitivity and medium specificity for economics and costs) (http://hiru.mcmaster.ca/hedges/),
- the INTERTASC Quality of life filter available from the University of York website (http://www.york.ac.uk/inst/crd/intertasc/econ.htm),
- Embase: 94 Hits

For the search on Embase database, the same strategy was applied on Embase references only. Unlike MeSH thesaurus, Emtree terms 'kyphoplasty' and 'percutaneous vertebroplasty' could be used (as exploded Emtree terms and as text words) . The following filters adapted to Embase were used:

- the economics filter from Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk/methodology/filters.html#econ),
- Emtree term: quality of life/

Grey literature was searched on February 24 through www.google.com (vertebroplast$ OR kyphoplast$ OR cyphoplastie$) in order to retrieve 4 reports as well as institution and professional organization sites such as FDA Centre for devices and radiological health register www.fda.gov , www.UNAMEC.be, www.worldspine.org and related sites …. Financial analyses available on charges were not bought.

QUALITY CHECKLIST FOR ECONOMIC EVALUATIONS APPRAISAL [89]

Study design

The research question is stated
The economic importance of the research question is stated
The viewpoints of the analysis are clearly stated and justified
The rationale for choosing the alternative programmes or interventions compared is stated
The alternatives being compared are clearly described
The form of economic evaluation used is stated
The choice of form of economic evaluation is justified in relation to the questions addressed

Data collection

The sources of effectiveness estimates used are stated
Details of the design and results of effectiveness study are given (if based on a single study)
Details of the method of synthesis or meta-analysis of estimated are given (if based on an overview of a number of effectiveness studies)
The primary outcome measure(s) for the economic evaluation are clearly stated
Methods to value health states and other benefits are stated
Details of the subjects from whom valuations were obtained are given
Productivity changes (if included) are reported separately
The relevance of productivity changes to the study question is discussed
Quantities of resources are reported separately from their unit costs
Methods for the estimation of quantities and unit costs are described
Currency and price data are recorded
Details of currency of price adjustments for inflation or currency conversion are given
Details of any model used are given
The choice of model used and the key parameters on which it is based are justified

Analysis and interpretation of results

Time horizon of costs and benefits is stated
The discount rate(s) is stated
The choice of rate(s) is justified
An explanation is given if costs or benefits are not discounted
Details of statistical tests and confidence intervals are given for stochastic data

The approach to sensitivity analysis is given
The choice of variables for sensitivity analysis is justified
The ranges over which the variables are varied are stated
Relevant alternatives are compared
Incremental analysis is reported
Major outcomes are presented in a disaggregated as well as aggregated form
The answer to the study question is given
Conclusions follow from the data reported
Conclusions are accompanied by the appropriate caveats

QUALITY APPRAISAL OF CLINICAL EVALUATIONS

Table 1 : HTA reports of kyphoplasty alone and of kyphoplasty & vertebroplasty

INAHTA checklist	AETS 2006	Taylor 2005	BCBS 2005	AHRQ 2005	ICSI 2004	NICE 2005	MAS 2004
Are contact details available for further information?	Yes	Yes	Yes	No	Yes	No	Yes
Authors identified?	Yes	Yes	Yes	No	Yes	No	No
Statement regarding conflict of interest?	Yes	Yes	No	No	Yes	No	No
Statement on whether report externally reviewed?	Yes	Yes	Yes	Yes	Yes	No	No
Short summary in non-technical language?	No	No	Yes	No	Yes	Yes	Yes
Reference to the question that is addressed and context of assessment?	Yes	Yes	Partly	Yes	No	Yes	Yes
Scope of the assessment specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Description of the health technology?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Details on sources of information?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Information on selection of material for assessment?	Yes	Yes	Yes	Yes	No	Yes	Yes
Information on basis for interpretation of selected data?	Yes	Yes	Yes	Yes	No	Yes	Partly
Results of assessment clearly presented?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Interpretation of assessment results included?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Findings of the assessment discussed?	Yes	Yes	Yes	Yes	Yes	Partly	Yes
Medico-legal implications considered?	No	No	No	No	No	No	No
Conclusions from assessment clearly stated?	Yes	Yes	Yes	Yes	Yes	Partly	Yes
Suggestions for further action?	Yes	Yes	No	No	Partly	No	Yes
Overall appraisal	**Good**	**Good**	**Poor**	**Poor**	**Poor**	**Fair**	**Fair**

Table 2 : HTA reports of vertebroplasty

INAHTA checklist	BCBS 2005	IECS 2004	CCOHTA 2004	NICE 2003	CCE 2002
Are contact details available for further information?	Yes	Yes	Yes	No	Yes
Authors identified?	Yes	Yes	Yes	No	Yes
Statement regarding conflict of interest?	No	Yes	Yes	No	No
Statement on whether report externally reviewed?	Yes	No	No	No	No
Short summary in non-technical language?	Yes	Yes	Yes	Yes	Yes
Reference to the question that is addressed and context of assessment?	Partly	No	No	Yes	Yes
Scope of the assessment specified?	Yes	Yes	Yes	Yes	Yes
Description of the health technology?	Yes	Yes	Yes	Yes	No
Details on sources of information?	Yes	Yes	No	Yes	Yes
Information on selection of material for assessment?	Yes	Partly	No	Yes	Yes
Information on basis for interpretation of selected data?	Yes	No	No	Yes	Partly
Results of assessment clearly presented?	Yes	Partly	Partly	Yes	Yes
Interpretation of assessment results included?	Yes	Yes	No	Yes	No
Findings of the assessment discussed?	Yes	Partly	No	Yes	No
Medico-legal implications considered?	No	No	No	No	No
Conclusions from assessment clearly stated?	Yes	Yes	Partly	No	Yes
Suggestions for further action?	No	Partly	No	No	No
Overall appraisal	**Poor**	**Poor**	**Poor**	**Fair**	**Fair**

Table 3 : Systematic reviews

Cochrane checklist	Taylor 2006	Newton 2006	Merlin 2006	Hendrikse 2003	Levine 2000
Adequate research question?	Yes	Yes	Yes	Yes	Yes
Adequately performed search?	Yes	Yes	Yes	Yes	Yes
Adequate selection of articles?	Yes	Yes	Yes	Yes	No
Adequate quality appraisal of articles?	Yes	?	?	Yes	No
Adequate description of the data extraction procedure?	Yes	No	No	No	No
Description of the most important characteristics of the included articles?	Yes	No	No	Yes	Yes
Adequate handling of clinical and statistical heterogeneity?	Yes	?	?	No	No
Adequate statistical pooling?	Yes	?	?	No	No
Overall appraisal	**Good**	**Fair**	**Fair**	**Fair**	**Poor**

Table 4 : Non-randomized controlled trials

Cochrane checklist	Komp 2004	Grafe 2005	Grohs 2005	Pflugmacher 2005	Diamond 2006
Randomization?	NA	NA	NA	NA	NA
Blinding of randomization?	NA	NA	NA	NA	NA
Blinding of patients?	No	No	No	No	No
Blinding of care provider?	No	No	No	No	No
Blinding of outcome assessor?	?	No	Yes	?	Partly
Similar groups at baseline?	?	Yes	Yes	?	Yes
Follow-up long enough?	No	?	Yes	Yes	Yes
Intention-to-treat-analysis?	?	Yes	?	?	Yes
Comparable treatment of groups?	Yes	Yes	?	Yes	Yes
Overall appraisal	**Poor**	**Poor**	**Poor**	**Poor**	**Poor**

EVIDENCE TABLES

Table 4 : HTA reports

Study ID	Intervention	Quality Assessment Good / Fair	Remarks	Conclusions/Recommendations
CCE 2002	Percutaneous vertebroplasty	Fair	One systematic review and six case series identified.	Evidence was insufficient to support the use of percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fractures.
NICE 2003	Percutaneous vertebroplasty	Fair	Based on rapid survey of the literature, review of the procedure by one or more specialist advisors and review of the content of the review by ASERNIP-S. One systematic review, 2 non-RCTs, 32 case series, and 6 case reports identified.	Evidence appeared adequate to support the use of percutaneous vertebroplasty, provided that normal arrangements are in place for consent, audit, and clinical governance.
MAS 2004	Balloon kyphoplasty	Fair	Identification of one non-RCT and eleven case series.	Kyphoplasty is a reasonable alternative to vertebroplasty, but should be restricted to high-volume facilities.
NICE 2005	Balloon kyphoplasty	Fair	Identification of one systematic review, 2 HTA reports, 3 non-RCTs, 5 case series, an FDA report, and an unpublished registry report.	Adequate to support the use when special arrangements for consent, audit or research are made.
Taylor 2005	Balloon kyphoplasty and vertebroplasty	Good	Unpublished report. Commissioned by Kyphon Inc. Identification of three systematic reviews and a large body of non-randomized comparative studies and case series.	Both therapies are effective in the management of patients with osteoporotic vertebral compression fractures that are refractory to conventional medical therapy. To be confirmed by the results from the ongoing randomized controlled trials.
AETS 2006	Balloon kyphoplasty	Good	Unpublished report. Identification one systematic review, two HTA reports, eleven cohort and case-control studies, and 12 case series.	Kyphoplasty can be considered clinically adequate for the treatment of recent and painful vertebral fractures, but only as a part of a prospective clinical study.

Table 5 : Systematic reviews

Study ID	**Intervention**	**Quality Assessment** Good / Fair	**Remarks**	**Conclusions/Recommendations**
Taylor 2006	Balloon kyphoplasty	Good		
Newton 2006	Balloon kyphoplasty	Fair		
Merlin 2006	Percutaneous vertebroplasty	Fair		
Hendrikse 2003	Percutaneous vertebroplasty	Fair	Identification of 4 prospective and 8 retrospective observational studies.	Effective and safe procedure for the treatment of osteoporotic vertebral compression fractures, but preserved for carefully selected patients unresponsive to conservative treatment.

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Wettelijk depot : D/2006/10.273/38

KCE reports

1. Effectiviteit en kosten-effectiviteit van behandelingen voor rookstop. D/2004/10.273/1.
2. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase 1). D/2004/10.273/2.
3. Antibioticagebruik in ziekenhuizen bij acute pyelonefritis. D/2004/10.273/5.
4. Leukoreductie. Een mogelijke maatregel in het kader van een nationaal beleid voor bloedtransfusieveiligheid. D/2004/10.273/7.
5. Het preoperatief onderzoek. D/2004/10.273/9.
6. Validatie van het rapport van de Onderzoekscommissie over de onderfinanciering van de ziekenhuizen. D/2004/10.273/11.
7. Nationale richtlijn prenatale zorg. Een basis voor een klinisch pad voor de opvolging van zwangerschappen. D/2004/10.273/13.
8. Financieringssystemen van ziekenhuisgeneesmiddelen: een beschrijvende studie van een aantal Europese landen en Canada. D/2004/10.273/15.
9. Feedback: onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport: deel 1. D/2005/10.273/01.
10. De kost van tandprothesen. D/2005/10.273/03.
11. Borstkankerscreening. D/2005/10.273/05.
12. Studie naar een alternatieve financiering van bloed en labiele bloedderivaten in de ziekenhuizen. D/2005/10.273/07.
13. Endovasculaire behandeling van Carotisstenose. D/2005/10.273/09.
14. Variaties in de ziekenhuispraktijk bij acuut myocardinfarct in België. D/2005/10.273/11.
15. Evolutie van de uitgaven voor gezondheidszorg. D/2005/10.273/13.
16. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid. Fase II : ontwikkeling van een actuarieel model en eerste schattingen. D/2005/10.273/15.
17. Evaluatie van de referentiebedragen. D/2005/10.273/17.
18. Prospectief bepalen van de honoraria van ziekenhuisartsen op basis van klinische paden en guidelines: makkelijker gezegd dan gedaan.. D/2005/10.273/19.
19. Evaluatie van forfaitaire persoonlijk bijdrage op het gebruik van spoedgevallendienst. D/2005/10.273/21.
20. HTA Moleculaire Diagnostiek in België. D/2005/10.273/23, D/2005/10.273/25.
21. HTA Stomamateriaal in België. D/2005/10.273/27.
22. HTA Positronen Emissie Tomografie in België. D/2005/10.273/29.
23. HTA De electieve endovasculaire behandeling van het abdominale aorta aneurysma (AAA). D/2005/10.273/32.
24. Het gebruik van natriuretische peptides in de diagnostische aanpak van patiënten met vermoeden van hartfalen. D/2005/10.273/34.
25. Capsule endoscopie. D/2006/10.273/01.
26. Medico–legale aspecten van klinische praktijkrichtlijnen. D2006/10.273/05.
27. De kwaliteit en de organisatie van type 2 diabeteszorg. D2006/10.273/07.
28. Voorlopige richtlijnen voor farmaco-economisch onderzoek in België. D2006/10.273/10.
29. Nationale Richtlijnen College voor Oncologie: A. algemeen kader oncologisch kwaliteitshandboek B. wetenschappelijke basis voor klinische paden voor diagnose en behandeling colorectale kanker en testiskanker. D2006/10.273/12.
30. Inventaris van databanken gezondheidszorg. D2006/10.273/14.
31. Health Technology Assessment prostate-specific-antigen (PSA) voor prostaatkankerscreening. D2006/10.273/17.
32. Feedback : onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport : deel II. D/2006/10.273/19.
33. Effecten en kosten van de vaccinatie van Belgische kinderen met geconjugeerd pneumokokkenvaccin. D/2006/10.273/21.
34. Trastuzumab bij vroegtijdige stadia van borstkanker. D/2006/10.273/23.
35. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase III)- precisering van de kostenraming. D/2006/10.273/26.
36. Farmacologische en chirurgische behandeling van obesitas. Residentiële zorg voor ernstig obese kinderen in België. D/2006/10.273/28.
37. HTA Magnetische Resonantie Beeldvorming. D/2006/10.273/32.
38. Baarmoederhalskankerscreening en testen op Human Papillomavirus (HPV). D/2006/10.273/35
39. Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie. D/2006/10.273/38