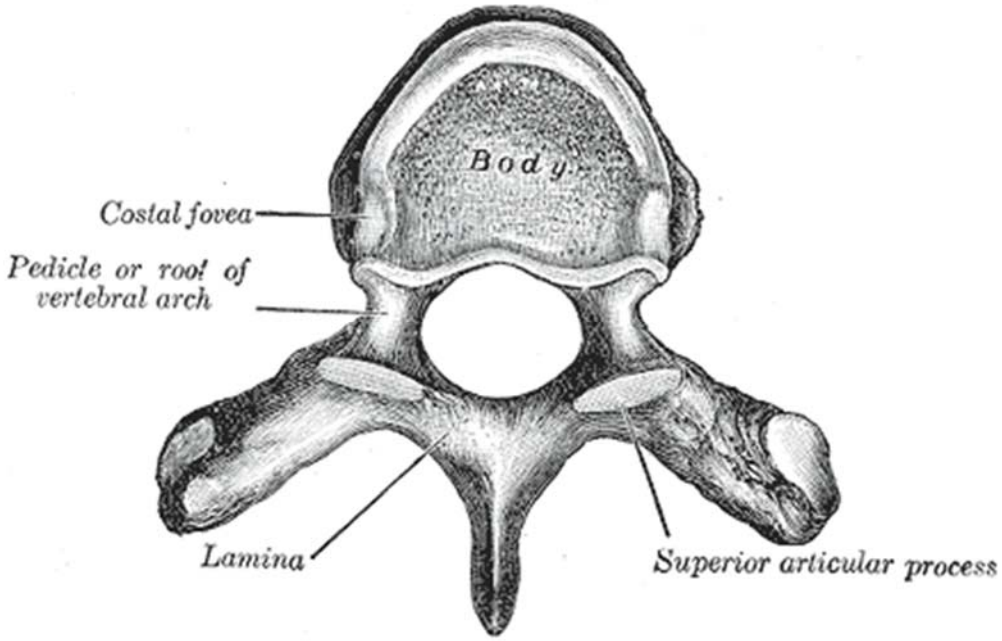
KCE REPORT 255S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

PERCUTANEOUS VERTEBROPLASTY AND BALLOON KYPHOPLASTY

SUPPLEMENT





KCE REPORT 255S
HEALTH TECHNOLOGY ASSESSMENT

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

PERCUTANEOUS VERTEBROPLASTY AND BALLOON KYPHOPLASTY

SUPPLEMENT

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COLOPHON

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1. BELGIAN SITUATION

1.1. Reimbursement schedule

1.1.1. INAMI – RIZIV billing codes for vertebroplasty and balloon kyphoplasty

Code	Label (Fr / Nl)	Key letter	Tariff (*)
Procedure for ballon kyphoplasty			
(589676) - 589680	Cyphoplastie percutanée par ballonnet pour le traitement de fractures par enfoncement d'un corps vertébral (par corps vertébral) / Percutane ballonkyphoplastie voor de behandeling van indeukingsfracturen van een wervellichaam (per wervellichaam)	I 400	€ 305.35
Balloon kyphoplasty material before July the 1st, 2014			
(683012) - 683023	Matériel de consommation pour cyphoplastie avec ballon, utilisé à l'occasion de la prestation 589676-589680/ Gebruiksmateriaal voor kyphoplastie met ballon gebruikt naar aan leiding van de verstrekking 589676-589680	U 4121	
(683034) - 683045	Ciment pour cyphoplastie avec ballon utilisé conjointement à la prestation 683012-683023, par niveau, maximum 2 niveaux / Cement voor kyphoplastie met ballon gebruikt samen met de verstrekking 683012-683023, per niveau, maximum 2 niveaus	U 82	
Balloon kyphoplasty material between July the 1st, 2014 and April the 1st, 2015.			
(162971) - 162982	Matériel de consommation pour cyphoplastie avec ballon, utilisé à l'occasion de la prestation 589676-589680 de la nomenclature / Gebruiksmateriaal voor kyphoplastie met ballon gebruikt naar aanleiding van de verstrekking 589676-589680 van de nomenclatuur		€ 4257.64
(162993) - 163004	Ciment pour cyphoplastie avec ballon utilisé conjointement à la prestation 162971-162982, par niveau, maximum deux niveaux / Cement voor kyphoplastie met ballon gebruikt samen met de verstrekking 162971-162982, per niveau, maximum twee niveaus		€ 82.08
Balloon kyphoplasty and vertebroplasty material from April the 1st, 2015.			
(162993) - 163004	Ciment pour cyphoplastie avec ballon utilisé conjointement à la prestation 162971-162982, par niveau, maximum deux niveaux / Cement voor kyphoplastie met ballon gebruikt samen met de verstrekking 162971-162982, per niveau, maximum twee niveaus		€ 82.08
(171975) - 171986	Ciment pour vertébroplastie, par niveau, maximum 2 niveaux / Cement voor vertebroplastie, per niveau, maximum 2 niveaus		€ 82.08

(Ambulatory) - (*) situation at 01/08/2015

1.1.2. Reimbursement conditions for balloon kyphoplasty:

Reimbursement is limited to

Vertebral compression fractures caused by osteoporosis, single- or multi-level, inferior to T5, without neurological compression and without neurological defect sign, if the following criteria are met:

- Persistent pain of more than 8 weeks linked to the fracture and for which the pain medication therapy administered during at least 8 weeks has failed or caused very troublesome side effects; the situation must have been written in a report by the physician in charge of the pain treatment; the intervention must take place in the 4 months after the first objective findings of the VCF unless a progression of the fracture has been demonstrated.
- Loss of height between 20% and 60%.
- Dorsal wall is maintained.
- Presence of a bony oedema.
- Fractures classified A1.1, A1.2 , A1.3 or A2.3 according to the AO classification (Arbeitsgemeinschaft für Osteosynthesefragen classification).
- In a man with a T-score, calculated in comparison with a male reference population, during a dual energy xray absorptiometry examination:
  - <-2.5 at the lumbar level (L1-L4 or L2-L4) OR
  - <-1 at the hip level (total or femoral neck zone).
- In a woman with a glucocorticoid-induced osteoporosis, treated since more than 3 months with a daily oral dosis of 7.5 mg prednisone or equivalent, administered in a recognized scientific indication:
  - The patient must be post-menopausal without hormonal substitution OR
  - she must present a T-score <-1.5 at the level of the lumbar spine (L1-L4 or L2-L4) or at the hip level (total or femoral neck zone), calculated in comparison with a female reference population, during a dual energy xray absorptiometry examination.
- In a post-menopausal woman presenting a a T-score <-2.5 at the level of the lumbar spine (L1-L4 or L2-L4) or at the hip level (total or femoral neck zone), calculated in comparison with a female reference population, during a dual energy xray absorptiometry examination.

B. Vertebral compression fractures caused by Kahler's myeloma without neurological compression and without neurological defect sign, if the following criteria are met:

- Persistent pain of more than 6 weeks linked to the fracture and for which the pain medication therapy administered during at least 6 weeks has failed or caused very troublesome side effects; the situation must have been written in a report by the physician in charge of the pain treatment.
- Dorsal wall is maintained.
- Presence of a bony oedema.
- Fractures classified A1.1, A1.2., A1.3 or A2.3 according to the AO classification (Arbeitsgemeinschaft für Osteosynthesefragen classification).

In both cases (A and B), this diagnosis is made based on the three following examinations:

- An antero-posterior plain film radiography; and
- a MRI or CT-scan when there is contraindication for MRI; and
- a bone scintigraphy without SPECT; and
- a DEXA-scan in case of osteoporotic VCF.

The documents proving that the conditions are satisfied must be kept in a file and provided to the advisory physician if requested.

A maximum of 2 BKPs can be billed per two calendar years (exceptions can be made requiring the authorization of the College of Medical Directors).

1.2. Diagnoses found in the RHM-MZG data

1.2.1. Most frequent 3-digit ICD-9-CM codes of principal diagnosis in the case of vertebroplasty

Ranking	3 digit ICD-9-CM code		Number of stays	Percentage
1	733	OTHER DISORDERS OF BONE AND CARTILAGE	1107	51.90%
2	805	FRACTURE OF VERTEBRAL COLUMN WITHOUT MENTION OF SPINAL CORD INJURY	566	26.53%
3	722	INTERVERTEBRAL DISC DISORDERS	111	5.20%
4	198	SECONDARY MALIGNANT NEOPLASM - METASTASE - OF OTHER SPECIFIED SITES	72	3.38%
5	724	OTHER AND UNSPECIFIED DISORDERS OF BACK	28	1.31%
6	203	MULTIPLE MYELOMA AND IMMUNOPROLIFERATIVE NEOPLASMS	24	1.13%
7	721	SPONDYLOSIS AND ALLIED DISORDERS	24	1.13%
8	996	COMPLICATIONS PECULIAR TO CERTAIN SPECIFIED PROCEDURES	22	1.03%
9	228	HEMANGIOMA AND LYMPHANGIOMA, ANY SITE	20	0.94%
10	491	CHRONIC BRONCHITIS	14	0.66%
11	Other		145	6.8%
TOTAL			**2133**	**100%**

Source: RHM-MZG 2008-2011

1.2.2. Five-digit ICD-9-CM codes of principal diagnosis in the case of Other disorders of bone and cartilage (733.xx) in the case of vertebroplasty

Ranking	5 digit ICD-9-CM code		Number of stays	Percentage
1	733.00	OSTEOPOROSIS, UNSPECIFIED	10	0.47%
2	733.01	SENILE OSTEOPOROSIS	2	0.09%
3	733.13	PATHOLOGIC FRACTURE OF VERTEBRAE	1048	49.13%
4	733.19	PATHOLOGIC FRACTURE OF OTHER SPECIFIED SITE	2	0.09%
5	733.22	ANEURYSMAL BONE CYST	3	0.14%
6	733.49	ASEPTIC NECROSIS OF BONE, OTHER	1	0.05%
7	733.81	MALUNION OF FRACTURE	2	0.09%
8	733.82	NONUNION OF FRACTURE	27	1.27%
TOTAL			**1107**	**51.90%**

Source: RHM-MZG data 2008-2011

1.2.3. Most frequent 3-digit ICD-9-CM codes of principal diagnosis in the case of kyphoplasty

Ranking	3 digit ICD-9-CM code		Number of stays	Percentage
1	733	OTHER DISORDERS OF BONE AND CARTILAGE	1507	64.08%
2	805	FRACTURE OF VERTEBRAL COLUMN WITHOUT MENTION OF SPINAL CORD INJURY	610	25.94%
3	203	MULTIPLE MYELOMA AND IMMUNOPROLIFERATIVE NEOPLASMS	24	1.02%
4	724	OTHER AND UNSPECIFIED DISORDERS OF BACK	24	1.02%
5	198	SECONDARY MALIGNANT NEOPLASM - METASTASE - OF OTHER SPECIFIED SITES	21	0.89%
6	722	INTERVERTEBRAL DISC DISORDERS	15	0.64%
7	491	CHRONIC BRONCHITIS	11	0.47%
8	338	PAIN, NOT ELSEWHERE CLASSIFIED	10	0.43%
9	737	CURVATURE OF SPINE	10	0.43%
10	806	FRACTURE OF VERTEBRAL COLUMN WITH SPINAL CORD INJURY	9	0.38%
11	Other		111	4.72%
TOTAL			**2352**	**100%**

Source: RHM-MZG 2008-2011

1.2.4. Five-digit ICD-9-CM codes of principal diagnosis in the case of Other disorders of bone and cartilage (733.xx) in the case of kyphoplasty

Ranking	5 digit ICD-9-CM code		Number of stays	Percentage
1	733.00	OSTEOPOROSIS, UNSPECIFIED	21	0.89%
2	733.01	SENILE OSTEOPOROSIS	4	0.17%
3	733.09	OTHER OSTEOPOROSIS	5	0.21%
4	733.10	PATHOLOGIC FRACTURE, UNSPECIFIED SITE	3	0.13%
5	733.13	PATHOLOGIC FRACTURE OF VERTEBRAE	1455	61.86%
6	733.19	PATHOLOGIC FRACTURE OF OTHER SPECIFIED SITE	3	0.13%
7	733.20	CYST OF BONE (LOCALIZED), UNSPECIFIED	1	0.04%
8	733.81	MALUNION OF FRACTURE	2	0.09%
9	733.82	NONUNION OF FRACTURE	12	0.51%
10	733.95	STRESS FRACTURE OF OTHER BONE	1	0.04%
TOTAL			**1507**	**64.01%**

Source: RHM-MZG data 2008-2011

2. CLINICAL EFFECTIVENESS AND SAFETY

2.1. PICO

2.1.1. PICO for Vertebroplasty and selection criteria

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Adult patients (18 years of age or older) with vertebral compression fracture due to osteoporosis, malignancy (metastases, myeloma), haemangioma, osteonecrosis or trauma.	
Intervention	Vertebroplasty	
Comparator	• Conservative (non-surgical) treatment only for osteoporotic VCF or combined with specific radiation therapy, chemotherapy or surgical tumour removal for VCF due to other causes • Kyphoplasty	
Outcomes	• Mortality • Pain and analgesics use • Mobility • Functional capacity • Health Related Quality of Life • Spine anatomy • Safety	
Study design	HTAs, systematic reviews, randomised controlled trials	Narrative reviews, observational studies, letters, editorials, notes, abstracts

2.1.2. PICO for Kyphoplasty and selection criteria

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Adult patients (18 years of age or older) with vertebral compression fracture due to osteoporosis, malignancy (metastases, myeloma), haemangioma, osteonecrosis or trauma.	
Intervention	Kyphoplasty	
Comparator	• Conservative (non-surgical) treatment only for osteoporotic VCF or combined with specific radiation therapy, chemotherapy or surgical tumour removal for VCF due to other causes • Vertebroplasty	
Outcomes	• Mortality • Pain and analgesics use • Mobility • Functional capacity • Health Related Quality of Life • Spine anatomy • Safety	
Study design	HTAs, systematic reviews, randomised controlled trials	Narrative reviews, observational studies, letters, editorials, notes, conference abstracts

2.2. Search strategy

2.2.1. General search strategy

The search is primarily based on the MeSH term Vertebroplasty introduced in 2008. Additionally, a new MeSH term Kyphoplasty was introduced in 2011 but this term is included within the Vertebroplasty term and was therefore not added as a separate MeSH term in the search. However, additional search terms, both as MeSH and free text were added to allow for indexing errors or missing indexing.

Additionally, we consulted the EUnetHTA POP[a] and INAHTA databases and the ClinicalTrials.gov database (search words 'vertebroplasty' OR 'kyphoplasty').

2.2.2. Detailed search strategy

Medline RCT (OVID)

ID	Search	Hits
1	vertebra.ab,ti.	9132
2	vertebrae.ab,ti.	14 594
3	cervical vertebrae/	28 150
4	Lumbar vertebrae/	40 134
5	Spine/	23 500
6	Low Back Pain/	14 942
7	1 or 2 or 3 or 4 or 5 or 6	110 983
8	Fractures, Compression/	1274
9	(fracture? adj3 compression).ab,ti.	3697
10	8 or 9	4115
11	(fracture? adj3 (spin* or vertebr*)).ab,ti.	12 787
12	Spinal fracture/	10 640
13	11 or 12	17 931
14	7 and 10	1675
15	13 or 14	18 199
16	cement*.ab,ti.	38 628
17	balloon?.ab,ti.	50 781
18	leakage.ab,ti.	43 648
19	polymethylmethacrylate.ab,ti.	3270
20	pmma.ab,ti.	6547
21	Polymethyl Methacrylate/	5440
22	16 or 17 or 18 or 19 or 20 or 21	139 683
23	15 and 22	1598
24	exp vertebroplasty/	1545
25	vertebroplast*.ab,ti.	2263
26	kyphoplast*.ab,ti.	1135
27	24 or 25 or 26	3073
28	23 or 27	3280
29	limit 28 to yr="2006 -Current"	2544
30	limit 29 to systematic reviews	119
31	randomized controlled trial.pt.	400 323
32	controlled clinical trial.pt.	90 694
33	randomized.ti,ab.	341 710
34	placebo.ti,ab.	168 242
35	clinical trials as topic/	176 382
36	randomly.ti,ab.	229 371
37	trials.ti.	50 693
38	31 or 32 or 33 or 34 or 35 or 36 or 37	949 689
39	exp animal/ not humans/	4 094 649
40	38 not 39	876 116
41	29 and 40	257
42	41 not 30	205

[a] POP: Planned and Ongoing Projects Database of projects by EUnetHTA members

Medline SR (OVID)

ID	Search	Hits
1	vertebra.ab,ti.	9122
2	vertebrae.ab,ti.	14 572
3	cervical vertebrae/	28 135
4	Lumbar vertebrae/	40 105
5	Spine/	23 487
6	Low Back Pain/	14 927
7	1 or 2 or 3 or 4 or 5 or 6	110 899
8	Fractures, Compression/	1272
9	(fracture? adj3 compression).ab,ti.	3693
10	8 or 9	4111
11	(fracture? adj3 (spin* or vertebr*)).ab,ti.	12 782
12	Spinal fracture/	10 632
13	11 or 12	17 922
14	7 and 10	1671
15	13 or 14	18 190
16	cement*.ab,ti.	38 621
17	balloon?.ab,ti.	50 773
18	leakage.ab,ti.	43 611
19	polymethylmethacrylate.ab,ti.	3269
20	pmma.ab,ti.	6543
21	Polymethyl Methacrylate/	5435
22	16 or 17 or 18 or 19 or 20 or 21	139 629
23	15 and 22	1595
24	exp vertebroplasty/	1539
25	vertebroplast*.ab,ti.	2260
26	kyphoplast*.ab,ti.	1134
27	24 or 25 or 26	3070
28	23 or 27	3277
29	(malign* or neoplasm* or tumo?r* or metasta* or myelom* or haemangiom* or cancer*).ab,ti.	2 272 687
30	exp neoplasms/	2 703 544
31	osteoporo*.ab,ti.	54 449
32	exp Osteoporosis/	46 502
33	osteonecro*.ab,ti.	6933
34	exp Osteonecrosis/	12 406
35	trauma*.ab,ti.	258 855
36	exp "Wounds and Injuries"/	737 109
37	29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	4 092 763
38	28 and 37	2878
39	28 not 38	399
40	limit 28 to yr="2006 -Current"	2541
41	limit 40 to systematic reviews	119

EMBASE RCT

ID	Search	Hits
#1	vertebra:ab,ti	11 742
#2	vertebrae:ab,ti	17 843
#3	'spine'/exp	133 859
#4	'low back pain'/exp	37 180
#5	#1 OR #2 OR #3 OR #4	172 653
#6	'compression fracture'/exp	3133
#7	(fracture* NEAR/3 compression):ab,ti	4928
#8	#6 OR #7	6008
#9	(fracture* NEAR/3 (spin* OR vertebr*)):ab,ti	17 402
#10	'spine fracture'/exp	23 447
#11	#9 OR #10	28 831
#12	#5 AND #8	2726
#13	#11 OR #12	29 008
#14	cement*:ab,ti	41 854
#15	balloon*:ab,ti	73 592

#16	leakage*:ab,ti	53 874
#17	polymethylmethacrylate:ab,ti	3529
#18	pmma:ab,ti	7097
#19	'poly(methyl methacrylate)'/exp	11 070
#20	#14 OR #15 OR #16 OR #17 OR #18 OR #19	178 258
#21	#13 AND #20	2359
#22	'percutaneous vertebroplasty'/exp	4413
#23	vertebroplast*:ab,ti	3161
#24	kyphoplast*:ab,ti	1714
#25	#22 OR #23 OR #24	4893
#26	#21 OR #25	5208
#27	malign*:ab,ti OR neoplasm*:ab,ti OR tumor*:ab,ti OR tumour*:ab,ti OR metasta*:ab,ti OR myelom*:ab,ti OR haemangiom*:ab,ti OR cancer*:ab,ti	2 773 585
#28	'neoplasm'/exp	3 461 911
#29	osteoporo*:ab,ti	76 879
#30	'osteoporosis'/exp	94 330
#31	osteonecro*:ab,ti	8467
#32	'bone necrosis'/exp	21 995
#33	trauma*:ab,ti	323 443
#34	'injury'/exp	1 585 751
#35	#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	5 503 461
#36	#26 AND #35	4659
#37	#36 AND (2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)	3774
#38	#26 AND (2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)	4215
#39	[medline]/lim	21 490 853
#40	#38 NOT #39	1862
#41	[cochrane review]/lim OR 'systematic review' OR 'meta analyse' OR [meta analysis]/lim OR [systematic review]/lim OR 'meta analyses' OR 'meta analysis' OR 'guideline' OR 'guidelines'	600 691
#42	#40 AND #41	106
#43	#37 NOT #39	1696
#44	#43 AND #41	100
#45	#42 NOT #44	6
#46	random*:ab,ti OR placebo*:de,ab,ti OR (double NEXT/1 blind*):ab,ti	1 141 517
#47	#40 AND #46	234

EMBASE SR

ID	Search	Hits
#1	vertebra:ab,ti	11 742
#2	vertebrae:ab,ti	17 843
#3	'spine'/exp	133 859
#4	'low back pain'/exp	37 180
#5	#1 OR #2 OR #3 OR #4	172 653
#6	'compression fracture'/exp	3133
#7	(fracture* NEAR/3 compression):ab,ti	4928
#8	#6 OR #7	6008
#9	(fracture* NEAR/3 (spin* OR vertebr*)):ab,ti	17 402
#10	'spine fracture'/exp	23 447
#11	#9 OR #10	28 831
#12	#5 AND #8	2726
#13	#11 OR #12	29 008
#14	cement*:ab,ti	41 854
#15	balloon*:ab,ti	73 592
#16	leakage*:ab,ti	53 874
#17	polymethylmethacrylate:ab,ti	3529
#18	pmma:ab,ti	7097

#19	'poly(methyl methacrylate)'/exp	11 070
#20	#14 OR #15 OR #16 OR #17 OR #18 OR #19	178 258
#21	#13 AND #20	2359
#22	'percutaneous vertebroplasty'/exp	4413
#23	vertebroplast*:ab,ti	3161
#24	kyphoplast*:ab,ti	1714
#25	#22 OR #23 OR #24	4893
#26	#21 OR #25	5208
#27	malign*:ab,ti OR neoplasm*:ab,ti OR tumor*:ab,ti OR tumour*:ab,ti OR metasta*:ab,ti OR myelom*:ab,ti OR haemangiom*:ab,ti OR cancer*:ab,ti	2 773 585
#28	'neoplasm'/exp	3 461 911
#29	osteoporo*:ab,ti	76 879
#30	'osteoporosis'/exp	94 330
#31	osteonecro*:ab,ti	8467
#32	'bone necrosis'/exp	21 995
#33	trauma*:ab,ti	323 443
#34	'injury'/exp	1 585 751
#35	#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	5 503 461
#36	#26 AND #35	4659
#37	#36 AND (2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)	3774
#38	#26 AND (2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)	4215
#39	[medline]/lim	21 490 853
#40	#38 NOT #39	1862
#41	[cochrane review]/lim OR 'systematic review' OR 'meta analyse' OR [meta analysis]/lim OR [systematic review]/lim OR 'meta analyses' OR 'meta analysis' OR 'guideline' OR 'guidelines'	600 691
#42	#40 AND #41	106
#43	#37 NOT #39	1696
#44	#43 AND #41	100
#45	#42 NOT #44	6

Cochrane

ID	Search	Hits
#1	vertebra:ab,ti	526
#2	vertebrae:ab,ti	526
#3	MeSH descriptor: [Cervical Vertebrae] explode all trees	766
#4	MeSH descriptor: [Lumbar Vertebrae] explode all trees	2130
#5	MeSH descriptor: [Spine] this term only	606
#6	MeSH descriptor: [Low Back Pain] this term only	2100
#7	#1 or #2 or #3 or #4 or #5 or #6	5526
#8	MeSH descriptor: [Fractures, Compression] this term only	95
#9	(fracture* near/3 compression):ab,ti	263
#10	#8 or #9	280
#11	(fracture* near/3 (spin* or vertebr*)):ab,ti	1215
#12	MeSH descriptor: [Spinal Fractures] this term only	630
#13	#11 or #12	1341
#14	#7 and #10	70
#15	#13 or #14	1349
#16	cement*:ab,ti	2246
#17	balloon*:ab,ti	3041
#18	leakage:ab,ti	1899

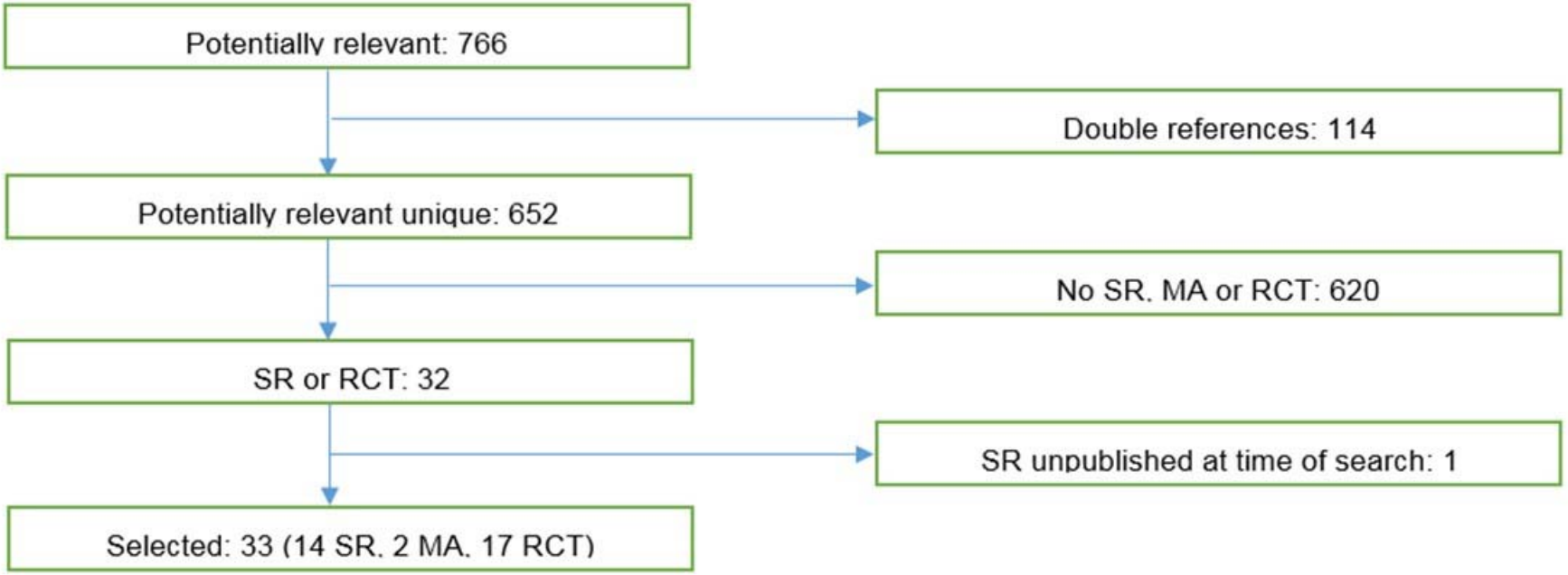
#19	polymethylmethacrylate:ab,ti	155
#20	pmma:ab,ti	307
#21	MeSH descriptor: [Polymethyl Methacrylate] explode all trees	176
#22	#16 or #17 or #18 or #19 or #20 or #21	7426
#23	#15 and #22	123
#24	MeSH descriptor: [Vertebroplasty] explode all trees	119
#25	vertebroplast*:ab,ti	160
#26	kyphoplast*:ab,ti	126
#27	#24 or #25 or #26	249
#28	#23 or #27	255
#29	#28 Publication Year from 2006 to 2014	219

2.3. Search results

From the systematic search in bibliographical databases we originally retrieved 766 references (including many duplicates). From these we selected and reviewed in detail thirteen recent (since 2010) HTAs and systematic reviews. Thirteen RCTs (seventeen publications) were retrieved in full text. We also selected two meta-analyses. Most reviews included only evidence on osteoporotic VCF but there were two on VCF due to malignancies.

The search through the EUnetHTA POP database and the INAHTA database showed no current new projects, but showed two finished projects with HTA reports published in 2014 (one unpublished at the moment of the search). The additional retrieval of clinical trials through the clinicaltrials.gov database yielded 51 clinical trials, the majority within the scope of our PICO. Those are not listed in the flow chart. While writing this report additional full-text articles were retrieved when needed.

2.3.1. Flow chart of selection for systematic search



SR: systematic review, RCT: randomised controlled trial, MA: meta-analysis.

2.4. Methodological quality

Selected studies were evaluated on their methodological quality using the Cochrane´s risk of bias tool for RCTs,[1] and the AMSTAR checklist for systematic reviews.[2]

2.4.1. Systematic review

AMSTAR checklist of systematic reviews for selected SR

	ScHARR[3]
Was an 'a priori' design provided?	Yes
Was there duplicate study selection and data extraction?	Partly*
Was a comprehensive literature search performed?	Yes
Was the status of publication an exclusion criterion?	Yes
Was a list of studies (included and excluded) provided?	Partly
Were the characteristics of the included studies provided?	Yes
Was the scientific quality of the included studies assessed and documented?	Yes
Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes
Were the methods used to combine the findings of studies appropriate?	Yes
Was the likelihood of publication bias assessed?	No
Was the conflict of interest stated? No Yes	Yes
Total	8/11

**Partly: 10% sample checked by second reviewer, data extraction by two reviewers*

2.4.3. RCTs

Cochrane risk of bias table (+= low risk, -= high risk, ?=unclear risk)

RCT	Buchbinder	INVEST	VERTOS	Rousing	VERTOS II	Farrokhi	Blasco	FREE	Liu	KAVIAR	CAFE*
Random sequence generation (selection bias)	+	+	+	+	+	+	?	+	+	+	+
Allocation concealment (selection bias)	+	+	+	+	+	+	?	+	?	?	?
Blinding of participants and personnel (performance bias)	+	+	-	-	-	-	-	-	?	?	-
Blinding of outcome assessment (detection bias)	+	+	-	-	-	-	-	-	+	?*	-
Incomplete outcome data (attrition bias)	+	+	?	?	?	+	?	?	?	?	?
Selective reporting (reporting bias)	?	-	?	?	+	?	+	-	?	?	?
Other bias	+	+	?	?	-	+	?	+	?	?	?

**Blinded central radiologist for radiologic outcomes*

The Cochrane risk of bias table (except for the KAVIAR and CAFE trials) is based on the ScHARR report that assesses the internal and external validity of the included trials. The report concludes: *"The quality of the included studies is generally not very high. Much of this is owing to the widespread lack of blinding: the studies at least risk of bias are the double-blinded Buchbinder et al.[4] and INVEST[5] studies, which compare vertebroplasty with an OPLA. The studies which compare vertebroplasty with non-invasive management (Blasco et al.,[6], Farrokhi et al.,[7] Rousing et al.,[8, 9] VERTOS[10] and VERTOS II[11]) vary in quality, that by Farrokhi et al. being at least risk of bias.*

Only three studies (Blasco et al.,[6] FREE[12, 13] and INVEST[5]) appeared to be adequately powered for at least their primary outcomes (pain score in Blasco et al. and INVEST, change in SF–36 PCS score from baseline to 1 month in FREE). Because most studies were underpowered for most outcomes, the absence of a statistically significant treatment effect should not necessarily be taken as evidence that no such difference exists."[3]

The quality of the studies on the effectiveness and safety of vertebroplasty and kyphoplasty for the treatment of non-osteoporotic VCF is very low. Most studies are not-randomised while the only RCT identified (CAFÉ) is small, allowed for cross-over and is industry sponsored. Obviously, setting up trials for those patients is more time- and money intensive because there are fewer patients than for osteoporotic VCF.

3. LITERATURE SEARCH FOR ECONOMIC EVALUATIONS

3.1. Search strategy

Database		Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present	
Date			20/04/2015
Date covered			1946 to present
Search strategy	**#**	**Searches**	**Results**
	1	Economics/	26 593
	2	"Costs and Cost Analysis"/	42 278
	3	"Value of Life"/ec [Economics]	227
	4	exp Economics, Pharmaceutical/ or Economics, Medical/ or Economics, Hospital/ or Economics, Dental/ or Economics, Nursing/	26 722
	5	budget$.ti,ab.	20 160
	6	cost-benefit.mp.	66 258
	7	cost-effectiveness.mp.	37 970
	8	cost-utility.mp.	2753
	9	(cost-minimisation or cost-minimization).mp.	907
	10	or/1-9	187 214
	11	limit 10 to letter	6075
	12	limit 10 to editorial	5092
	13	limit 10 to historical article	2480
	14	or/11-13	13 604
	15	10 not 14	173 610
	16	Animals/	5 442 465
	17	15 not 16	167 274
	18	Cervical Vertebrae/	27 933
	19	Lumbar Vertebrae/	40 004
	20	Spine/	23 300
	21	Low Back Pain/	14 831
	22	18 or 19 or 20 or 21	98 974
	23	Fractures, Compression/	1288
	24	(fracture* adj1 compression).ab,ti.	2911
	25	23 or 24	3356
	26	22 and 25	1158
	27	exp Vertebroplasty/	1581
	28	vertebroplast*.ab,ti.	2294
	29	kyphoplast*.ab,ti.	1159
	30	27 or 28 or 29	3129
	31	26 or 30	3798
	32	limit 31 to (editorial or historical article or letter)	205
	33	31 not 32	3593
	34	17 and 33	41
	35	limit 34 to yr="2006 -Current"	**35**
Note		mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier.	

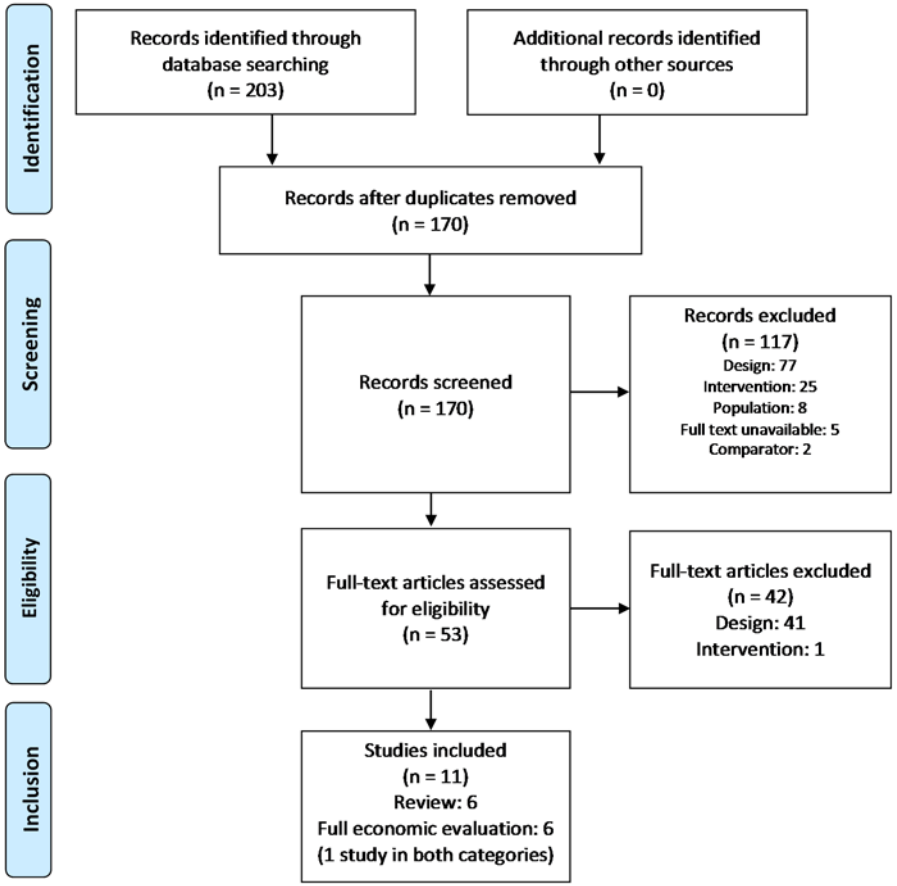
Database		Embase	
Date			20/04/2015
Date covered			No restriction
Search strategy	**#**	**Searches**	**Results**
	#1	vertebra:ab,ti	12 246
	#2	vertebrae:ab,ti	18 481
	#3	'spine'/exp	140 413
	#4	'low back pain'/exp	38 397
	#5	#1 OR #2 OR #3 OR #4	180 382
	#6	'compression fracture'/exp	3354
	#7	(fracture* NEAR/1 compression):ab,ti	4037
	#8	#6 OR #7	5222
	#9	(fracture* NEAR/1 (spin* OR vertebr*)):ab,ti	12 671
	#10	'spine fracture'/exp	24 356
	#11	#9 OR #10	27 196
	#12	#5 AND #8	2727
	#13	#11 OR #12	27 519
	#14	cement*:ab,ti	42 938
	#15	balloon*:ab,ti	76 048
	#16	leakage*:ab,ti	55 884
	#17	polymethylmethacrylate:ab,ti	3615
	#18	pmma:ab,ti	7333
	#19	'poly(methyl methacrylate)'/exp	11 409
	#20	#14 OR #15 OR #16 OR #17 OR #18 OR #19	183 985
	#21	#13 AND #20	2345
	#22	'percutaneous vertebroplasty'/exp	4618
	#23	vertebroplast*:ab,ti	3295
	#24	kyphoplast*:ab,ti	1806
	#25	#22 OR #23 OR #24	5112
	#26	#21 OR #25	5402
	#27	'cost benefit analysis'/exp	66 597
	#28	'cost effectiveness analysis'/exp	104 949
	#29	'cost utility analysis'/exp	6001
	#30	'cost minimization analysis'/exp	2630
	#31	'pharmacoeconomics'/exp	170 072
	#32	#27 OR #28 OR #29 OR #30 OR #31	316 674
	#33	#26 AND #32	172
	#34	#33 AND ([editorial]/lim OR [letter]/lim OR [note]/lim)	24
	#35	#33 NOT #34	148
	#36	#35 AND [2006-2015]/py	**126**

Database		CRD HTA and CRD NHS EED	
Date			20/04/2015
Date covered			No restriction
Search strategy	**#**	**Searches**	**Results**
	1	(vertebra:ab,ti)	0
	2	(vertebrae:ab,ti)	0
	3	(MeSH descriptor: [Cervical Vertebrae] explode all trees)	59
	4	(MeSH descriptor: [Lumbar Vertebrae] explode all trees)	172
	5	(MeSH descriptor: [Spine] this term only)	29
	6	(MeSH descriptor: [Low Back Pain] this term only)	208
	7	(#1 or #2 or #3 or #4 or #5 or #6)	424
	8	(MeSH descriptor: [Fractures, Compression] this term only)	22
	9	((fracture* near/3 compression):ab,ti)	0
	10	(#8 or #9)	22
	11	((fracture* near/3 vertebr*):ab,ti)	0
	12	(MeSH descriptor: [Spinal Fractures] this term only)	89
	13	#11 OR #12	89
	14	#7 AND #10	3
	15	#13 OR #14	91
	16	(cement*:ab,ti)	17
	17	(balloon*:ab,ti)	115
	18	(leakage:ab,ti)	0
	19	(polymethylmethacrylate:ab,ti)	0
	20	(pmma:ab,ti)	1
	21	(MeSH descriptor: [Polymethyl Methacrylate] explode all trees)	8
	22	(#16 or #17 or #18 or #19 or #20 or #21)	138
	23	(#15 and #22)	16
	24	(MeSH descriptor: [Vertebroplasty] explode all trees)	34
	25	(vertebroplast*:ab,ti)	40
	26	(kyphoplast*:ab,ti)	33
	27	(#24 or #25 or #26)	60
	28	(#23 or #27)	60
	29	(#28) FROM 2006 TO 2015	**42**
Note		Searches limited to the HTA and NHS EED databases	

3.2. Selection procedure

The electronic searches returned 203 citations in total (35 in Medline(OVID), 126 in Embase and 42 in CRD HTA & CRD NHS EED). No other publication was identified via manual search. After exclusion of 33 duplicates, 170 unique citations were left. The flow chart of the selection process is presented below.

Flowchart of the economic literature review process



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