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2 Executive Summary: Comments on the Assessment Report (AR)

- The Assessment Report **appropriately classified the invasive control procedures (so-called "sham" arm) of the Buchbinder and Kallmes studies as interventions,** referred to in the Assessment Report as **"Operative Placebo with Local Anaesthesia"** OPLA. (6, 7) Both studies involved the placement of needles and administration of anaesthesia (either directly to the spine or via the hand/forearm) and were as such, invasive procedures with potential therapeutic effects beyond that obtainable with a true placebo.
- Subsequent to the publication of these studies in the New England Journal of Medicine (NEJM), **position statements from the medical community identified severe limitations that pose challenges to interpretation of these studies. Further, Dr. William Clark, an interventional radiologist involved in the Kallmes study (7), who reported that he "regard(s) the study as meaningless"** (8, 9, 12) Areas for concern included high non-participation rates, the inclusion of patients with chronic fractures, measurement of —overall pain rather than back pain, significant crossover from non-invasive management (NIM), potential analgesic effect from facet injection, as well as limited statistical power.
- PVP had an ICER well below the standard threshold of £20,000 per QALY in the Assessment Group's foundation analysis, as well as in the base case submitted by Johnson and Johnson Medical. **PVP with either low or high viscosity cements is cost-effective relative to non-invasive management for patients with osteoporotic vertebral compression fractures.**
- The incremental cost-effectiveness of various cements for either PVP or BKP was not addressed in Johnson and Johnson Medical's submission as such analyses were outside of the scope for this MTA, but was attempted by the Assessment Group (AG) despite limitations in the available evidence base to support this appraisal. It is recognised that the evidence base concerning cement viscosity is emerging and therefore it is recommended that **the decision on which viscosity cement is suitable to different patients, is left to the judgment of the clinician.**
- **There are very few alternative treatment options to PVP or BKP for patients unresponsive to non-invasive management other than months of severe pain, restricted mobility and poor quality of life and depression in up to 40% of cases.** It is reported that patients with VCFs are confined to bed nine times more often than those without VCFs, increasing their risk of further VCFs which can further complicate recovery. The impact of VCFs on quality of life (QoL) has been shown to be comparable with chronic obstructive pulmonary disease (COPD), a point which should not be underestimated.

<u>Limitations of Assessment Report (AR)</u>

1. **The Assessment Group appears to have relied extensively on the opinion of one clinician**, who reported routine, first-line use of facet joint injections for treatment of osteoporotic compression fractures. **This practice is not representative across the wider clinical community in England and Wales.**
2. The original scope published by NICE states that "people with painful osteoporotic vertebral fractures" are the patient population of interest. (1) **The most accurate outcome will be a result of the use of the most granular data available.** Although identical to HES data, The Dr Foster Intelligence[1] data tools offer an additional level of diagnostic-specificity than is available through HES, which allows a more accurate estimation of the relevant patient population and incidence of VCFs.(2)
3. **The AR is inconsistent in its classification of the control arms** from the Buchbinder and Kallmes studies. Despite having identified the "Sham"/ placebo arms within these studies as an "Operative Placebo with Local anaesthesia" (OPLA), the AR at times refers to these as placebo comparators, and suggests that results of these studies raise questions about the clinical benefit of PVP. **This inconsistency in classification makes it difficult to interpret the findings and undermines the quality of the final report presented by the authors.**
4. **The Assessment Report fails to draw necessary conclusions on the analysis presented.**

Comparison of the Assessment Report (AR) and the J and J Medical Submission

Invasive Control Procedure or "Sham" NEJM Studies

- The invasive control procedures performed in the Kallmes and Buchbinder studies clearly cannot be considered as a SHAM or placebo, as both involve an invasive procedure. (6,7)
- Therefore, it is not possible to conclude from these studies that the treatment effect associated with vertebroplasty (PVP) is due to a 'placebo effect'.
- These two publications are significantly flawed and highlight the challenges of conducting adequately powered RCTs of vertebroplasty, including barriers to recruitment and the need for appropriate patient selection. (6, 7)

Clinical Effectiveness:

- For people with painful osteoporotic VCFs refractory to analgesic treatment, vertebroplasty (PVP) performs significantly better in unblinded trials than NIM/OPM (non-invasive management) in terms of improving quality of life, reducing pain and disability.
- For patients that are refractory to conservative treatment, PVP and BKP are the only routinely performed treatments available.
- There is some evidence that PVP and BKP are associated with reductions in mortality; however, this effect has not been fully investigated in clinical trials with a randomisation procedure, so the causal mechanisms remain unclear.

Cost-effectiveness:

- The results of the Assessment Group's foundation analysis, PVP had an ICER of £7,802 which is cost-effective and well below the standard threshold of £20,000 per QALY.
- In the base case submitted by Johnson and Johnson Medical, the ICER for vertebroplasty vs. NIM was £4,392 in the base case, and ranged from £568–£13,595 in the scenarios considered

Cement Type

- PVP with either low or high viscosity cements is cost-effective relative to non-invasive management for patients with osteoporotic vertebral compression fractures. The incremental cost-effectiveness of various cements for either PVP or BKP was not addressed in Johnson and Johnson Medical's submission as such analyses were outside of the scope for this MTA.
    - The AR attempted subgroup analyses on different types of cement viscosity. Given this was not part of the intentions of the assessment as detailed in the scope, and the Assessment Group excluded the only RCT level evidence on the differential safety profile of High Viscosity cement[1] (18), we feel this subgroup analysis is not robust. Had the scope detailed that cement type was a consideration of the appraisal we would have investigated these differences more completely.
    - It is difficult to assess the different cement types in cost-effectiveness analyses, given the current limited availability of comparative level 1 evidence related to HV vs. LV cements. This is to be expected as HV cement has been developed more recently so the evidence is less developed for this technology.
    - The clinical advisor to the Assessment Group confirmed there is a role for cements of differing viscosity in treating this patient population but this decision should be based on clinical

judgement and based on individual patient characteristics until evidence to investigate this specific point has been generated.

- High viscosity (HV) cement was developed to mitigate safety concerns associated with low viscosity (LV) cement by allowing for greater control of speed and location of cement placement within the vertebra. Although complications associated with PVP are rare, they can be serious if cement leakage occurs within the spinal canal or vasculature. In such instances, hardened cement can cause paralysis or lead to a fatal pulmonary embolism. The selection of cement used during PVP and BKP procedures should be left to clinician discretion and be informed by individual patient characteristics.

[1] *Anselmetti, (18) a study on the use of HV cement (Confidence Spinal Cement System®) in VBA, reported no significant difference in the rate of intradiscal leakage for HV and LV cement, 6.1% vs. 13.0%, respectively However, the rate of venous leakage in the study, which is more likely to lead to clinically significant complications, was significantly lower with HV cement, at 8.2%, compared to 41.3% with LV cement (p<0.0001).*

3 Critique of Assessment Report:

5. **Recognition that the so-called "Sham" treatment arms within the Buchbinder and Kallmes studies are interventions referred to as "Operative Placebo with Local anaesthesia" (OPLA):** We were encouraged to see that the Assessment Report appropriately classified the invasive control procedures (so-called "sham" arm) of the Buchbinder and Kallmes studies as interventions, referred to as OPLA. (6, 7) Both studies involved the placement of needles and administration of anaesthesia (either directly to the spine or via the hand/forearm) and were as such, invasive procedures with potential therapeutic effects beyond that obtainable with a true placebo.
6. **However, the AR is inconsistent in its classification of the control arms from the Buchbinder and Kallmes studies.** Despite having identified the "Sham"/ placebo arms within these studies as an "Operative Placebo with Local anaesthesia" (OPLA), the AR at times refers to these as placebo comparators, and suggests that results of these studies raise questions about the clinical benefit of PVP. This inconsistency in classification makes it difficult to interpret the report.
7. **VCF incidence rates in the AR were neither relevant nor recent**: The AR model uses data on the incidence of vertebral compression fractures (VCFs) drawn from a large scale prospective Scottish study. (3) Although these are UK-specific data and report VCF rates, this data set is not truly reflective of NICE's population of interest for this appraisal, namely England and Wales and could include patients with VCFs due to malignancy and trauma. Although published in 1998, Singer et al analyse a two year period during 1992 and 1993, a time span over which meaningful changes in screening and diagnosis of VCF may have transpired. (3) In contrast, Johnson and Johnson Medical extracted data from the NHS data source (SUS) by Dr Foster Intelligence[1], which relates to a much more recent and thus relevant period between April 2010 and March 2011. (2) Further, this data source allows for the specific identification of patients with symptomatic osteoporotic VCFS presenting for hospital treatment either non-surgical or an intervention such as PVP or BKP. *(See Appendix A).*
8. **Calculation of Length of Stay is not limited to osteoporotic VCFs**: The Assessment Group (AG) relied on the length of stay (LoS) provided by Medtronic and sourced from the standard HES data. These data are likely to overstate LoS by including VCFs of non-osteoporotic etiology (for example, trauma or tumor). In contrast, the Johnson & Johnson submission identified average LoS for the specific population of patients with osteoporotic fractures within the HES / Dr Foster dataset. Both HES and the Dr Foster data use the Secondary Users Service (SUS) data which are routinely collected in the NHS, so the source is the same.
9. **Inadequate clinical input; Reliance on one clinical advisor:**

- The AG appears to have relied extensively on the opinion of one clinician, who reported routine, first-line use of facet joint injections for treatment of osteoporotic compression fractures. This practice is not representative across the wider clinical community in England and Wales.
- The Clinical Advisor estimated the average selling price (ASP) of lower-viscosity cements, which is quoted in the report. Unless validated, this ASP cannot be taken as a robust data point for inclusion in the modeling as it might apply only to a subset of NHS providers eligible for volume-based discounts, rather than mean ASPs across all NHS Trusts. We therefore recommend the ASPs are validated by NICE using NHS procurement data.
- Given PVP is being considered as a class, it would be more appropriate to use an ASP calculated across all cement types.

- PVP with all cement types (including high and low viscosity cements) is cost-effective relative to non-invasive management for patients with osteoporotic vertebral compression fractures. A comparison of cost effectiveness between various cement types was outside of the scope of this appraisal but was attempted by the AG despite limitations in the available evidence base to support this appraisal.
  - The AR attempted subgroup analyses on different types of cement viscosity. Given this was not part of the intentions of the assessment as detailed in the scope, and the Assessment Group excluded the only RCT level evidence on the differential safety profile of High Viscosity cement1 (18), we feel this subgroup analysis is not robust. Had the scope detailed that cement type was a consideration of the appraisal we would have investigated these differences more completely in our submission.
  - It is difficult to assess the different cement types in cost-effectiveness analyses, given the current limited quantity of comparative level 1 evidence related to HV vs. LV cements. This is to be expected as HV cement has been developed more recently so the evidence is less developed for this technology.
  - The clinical advisor to the Assessment Group confirmed there is a role for cements of differing viscosity in treating this patient population but this decision should be based on clinical judgement and based on individual patient characteristics until evidence to investigate this specific point has been generated.
- High viscosity (HV) cement was developed to mitigate safety concerns associated with low viscosity (LV) cement by allowing for greater control of speed and location of cement placement within the vertebra. Although complications associated with PVP are rare, they can be serious if cement leakage occurs within the spinal canal or vasculature. In such instances, hardened cement can cause paralysis or lead to a fatal pulmonary embolism. The selection of cement used during PVP and BKP procedures should be left to clinician discretion and be informed by individual patient characteristics.

[1] *Anselmetti, (18) a study on the use of HV cement (Confidence Spinal Cement System®) in VBA, reported no significant difference in the rate of intradiscal leakage for HV and LV cement, 6.1% vs. 13.0%, respectively However, the rate of venous leakage in the study, which is more likely to lead to clinically significant complications, was significantly lower with HV cement, at 8.2%, compared to 41.3% with LV cement (p<0.0001)*

4 Variation in Estimates of Incidence and Length of Stay

4.1 Incidence of Osteoporotic Vertebral Fractures (VCFs)

NICE state that “people with malignancy-related vertebral fractures and those with neuropathy in the absence of osteoporotic compression fractures are outside the scope of this appraisal.” (1) The Assessment Report (AR) highlights some considerable variation in estimates of the incidence of painful vertebral fractures as reported within submissions for this MTA.

The Johnson and Johnson Medical submission includes estimated incidence of patients requiring hospitalization for severe pain due to osteoporotic VCFs, as derived from Dr Foster Intelligence [1] (2). The data used in Dr Foster Intelligence[1] originates from the same Commissioning Data Sets (known as the SUS dataset) reported quarterly by every NHS secondary care provider in England. The Dr Foster Unit at Imperial College receives NHS data and anonymises all patient identifiers. Dr Foster Intelligence[1] (2) files are at the individual patient-level and detail the care provided through admitted, outpatient and accident and emergency. Although identical to HES data, The Dr Foster Intelligence[1] data tools permit cross-tabulation of procedures by diagnoses and other patient-level characteristics, allowing for greater precision in identification of target patient populations. (2)

Consistent with NICE's final scope for this MTA, Johnson and Johnson Medical's incidence estimate considers vertebroplasty (PVP), kyphoplasty, (BKP) and non-invasive management (NIM) for patients requiring treatment of osteoporotic VCFs. Based on this analysis, it is estimated that there were 473 VBA, 225 BKP and 6,375 NIM patients treated in the inpatient or day case setting between April 2010 and March 2011. These estimates are lower than those reported by Hospital Episode Statistics (HES) as quoted by Medtronic and Synthes in their submissions. However, given the additional level of diagnostic-specificity offered by Dr Foster Intelligence[1] tools, Johnson and Johnson Medical were able to estimate incidence specific to VCFs of osteoporotic origin (rather than those of malignancy or trauma) thus adhering to the decision problem for this MTA. *Please see Appendix B for details of the data collection protocol and Appendix C for a schematic showing the derivation of the patient groups described.*

The AG's model uses data on the incidence of vertebral compression fractures (VCFs) drawn from a large scale prospective Scottish study. (3) Although this data set is UK specific, it may not be representative of NICE's population of interest for this appraisal, namely England and Wales. Further, it could include patients with VCFs of non-osteoporotic origin (e.g., malignancy and trauma). Although published in 1998, Singer et al analyse data from 1992 and 1993. Since this time, evolving diagnostics and treatments are likely to have affected change in the incidence of VCFs (3). The data Johnson and Johnson Medical extracted from Dr Foster Intelligence[1] relates to a much more recent and thus relevant period between April 2010 and March 2011. (2) These data are also suitable for identification of symptomatic fractures that present clinically for treatment.

4.2 Length of Stay (LoS) for Comparators of Interest

The Assessment Report (AR) highlights considerable uncertainty regarding the lengths of stay associated with each comparator arm. In the Johnson & Johnson Medical submission, to determine accurate length of hospital stay, an analysis was run using The Dr Foster Intelligence[1] (2) on all hospital discharges between 1st April 2008 and 31st March 2011 (*For details of Dr Foster data collection methodology* see Appendices *B and C as well as Section 1.1).* An analysis of M80 ICD-10 codes was performed, which is data reported for patients specifically with a diagnosis of osteoporosis with pathological fracture. A subsequent analysis of procedural codes specific to vertebroplasty and kyphoplasty (OPCS code V444 and V445, respectively) was undertaken and the number of patients treated with these two interventions could then be accurately determined. Patients with hospitalisation for osteoporosis with pathological fracture were classified as having received non-invasive management (NIM) only when they had "null procedures", i.e. no procedural code was assigned during hospitalisation.

The Assessment Group (AG) concluded that length of stay (LoS) data from Medtronic's submission, sourced from the standard HES data were most appropriate for use in its cost effectiveness model. These estimates are likely to overstate significantly average LoS for patients with VCFs of osteoporotic origin, as the data source includes patients who received PVP or BKP for malignancy or trauma.

[1] *This information is published with kind permission of Dr Foster Intelligence. All rights are reserved. No further copying or reproduction of this information is permitted without consent from Dr Foster Intelligence. Dr Foster extracted the data, but did not conduct any analysis on the data and therefore does not necessarily endorse any conclusions drawn from the data.*

It is noteworthy that the AG's clinical advisor commented that the average LoS in the more than two thousand vertebral augmentation procedures he has undertaken at his facility was less than 6 hours and that the majority of these interventions (VBA or BKP) in Oxford are day case procedures, not normally requiring admission. LoS results from published clinical trials of PVP and BKP also suggest that the AG's LoS estimates for these procedures are overstated. Finally, lower LoS estimates than those used by the AG are consistent with expert opinion provided by clinical advisors to Johnson & Johnson Medical in an Advisory Board held on the 18th November 2011 in London. This clinical advisory board comprised interventional radiologist, general practitioners, spinal surgeons and geriatricians with experience in treating vertebral compression fractures.

In Summary, we would urge the Committee to refer back to the original scope published by NICE which states that "people with painful osteoporotic vertebral fractures" are the patient population of interest.(1) The most accurate outcome will be a result of the use of the most granular data available. Although identical to HES data, The Dr Foster Intelligence[1] data tools offer an additional level of granularity than is available through HES, which allows a more accurate estimation of the relevant patient population.(2)

5 Comparators

5.1 Invasive Control Procedure ("sham")

It is appropriate that the Assessments Report (AR) recognises the "Sham" procedures included in the Buchbinder and Kallmes studies as interventional arms as they involved injection of anaesthetic into the vertebra or the area adjacent to it. (6, 7) Both studies involved placement of needles and administration of anaesthesia (either directly to the spine or via the hand/forearm) and were therefore categorized as invasive procedures or 'operative placebo with local anaesthesia' (OPLA) within the AR.

These two studies are significantly flawed and highlight the challenges of conducting adequately powered RCTs of PVP, including barriers to recruitment and the need for careful patient selection. (6, 7) Subsequent to the publication of these studies in the New England Journal of Medicine (NEJM), position statements from the medical community identified severe limitations that pose challenges to interpretation of these studies. Further, Dr. William Clark, an interventional radiologist involved in the Kallmes study (7), who reported that he "regard(s) the study as meaningless" (8, 9, 12) Areas for concern included high non-participation rates, the inclusion of patients with chronic fractures, measurement of —*overall* pain rather than back pain, significant crossover from NIM, potential analgesic effect from facet injection, as well as limited statistical power. Further, the studies' investigators did not require clinical correlation of fracture level/imaging with physical examination (percussion, palpation, motion testing), which is particularly important for verification of symptomatic VCFs in elderly patients. Taken together, these issues limit the generalisability and validity of the studies for real-world clinical management of VCFs. In order to address these limitations and generate new evidence for a relevant sub-population of patients with VCFs, investigators currently are recruiting patients to participate in VERTOS IV, which will compare vertebroplasty to sham procedure among patients with radiographically confirmed acute VCFs (≤ 6 weeks of pain).(11)

Johnson and Johnson submitted a de novo cost-effectiveness model to determine the cost-effectiveness of PVP, BKP, and NIM, (termed OPM in the AR). The results of this cost-effectiveness analysis are in line with the results of the Klazen et al trial (10), which found that the ICER for PVP vs. NIM was well below the £20,000 per QALY threshold. The Klazen study used stringent inclusion criteria, including only patients with confirmed acute fractures causing high levels of pain; these patients may represent the group most likely to benefit from PVP.

While the base case and target population analyses demonstrate the cost-effectiveness of PVP vs. BKP and NIM, for completeness, these invasive control procedures (termed "OPLA"" in the AR) were modeled in scenario analyses; in these analyses NIM (termed "OPLA"" in the AR) were dominated by PVP, reflecting the identical cost but the overall better effectiveness of VBA over the invasive control procedure (termed "OPLA"" in the AR).

5.2 Facet Joint Injections

The Assessment Group (AG) includes a hypothetical scenario controlling for the potential influence of facet joint injections for treatment of osteoporotic VCF. This treatment is outside of the scope of the MTA and its inclusion in the AR may have been informed by guidance from the AG's clinical advisor David Wilson, Consultant Musculoskeletal Interventional Radiologist, Oxford University Hospitals and two publications, one of which was co-authored David Wilson. Its aim was to assess facet joint injections as a first line treatment prior to PVP or BKP. Based on NICE's methodology guides these uncontrolled audits would not be deemed of a high enough level of evidence for inclusion in a NICE Technology Assessment.(4,5) The AG, seem to have applied an undue weight on the opinion of one Clinician, whose practice doesn't seem reflective of that of the wider clinical community across England and Wales. In an attempt to validate our initial findings, Johnson and Johnson Medical readdressed the interventional clinical advisors from the advisory board held in 2011 and were able to confirm that they wouldn't endorse the routine, first-line use of facet joint injections.

Indeed no additional evidence comparing Facet Joint Injection to either intervention (PVP or BKP) or against non-invasive management (NIM) was presented in the Assessment Report which would support this approach.

In summary, we refer the committee to refer to the original MTA scope which outlines the decision problem and states that relevant comparators should be the interventions compared with each other and non-invasive management (NIM) (without the use of either intervention).

6 Cement Type

PVP with all cement types (including high and low viscosity cements) is cost-effective relative to non-invasive management for patients with osteoporotic vertebral compression fractures. A comparison of cost effectiveness between various cement types was outside of the scope of this appraisal:

- The AR attempted subgroup analyses on different types of cement viscosity. Given this was not part of the intentions of the assessment as detailed in the scope, and the Assessment Group ignored the only RCT level evidence on the differential safety profile of High Viscosity cement[1] (18), we feel this subgroup analysis is not robust. Had the scope detailed that cement type was a consideration of the appraisal we would have investigated these differences more completely.
- It is difficult to assess the different cement types in cost-effectiveness analyses, given the current paucity of comparative level 1 evidence related to HV vs. LV cements. This is to be expected as HV cement has been developed more recently so the evidence is less developed for this technology.
- The clinical advisor to the Assessment Group confirmed there is a role for cements of differing viscosity in treating this patient population, and noted that this decision should be based on clinical judgement and informed by individual patient characteristics until evidence to investigate this specific point has been generated.

High viscosity (HV) cement was developed to mitigate safety concerns associated with low viscosity (LV) cement by allowing for greater control of speed and location of cement placement within the vertebra. Although complications associated with PVP are rare, they can be serious if cement leakage occurs within the spinal canal or vasculature. In such instances, hardened cement can cause paralysis or lead to a fatal pulmonary embolism. The selection of cement used during PVP and BKP procedures should be left to clinician discretion and be informed by individual patient characteristics.

10. *[1]Anselmetti, (18) a study on the use of HV cement (Confidence Spinal Cement System®) in VBA, reported no significant difference in the rate of intradiscal leakage for HV and LV cement, 6.1% vs. 13.0%, respectively However, the rate of venous leakage in the study, which is more likely to lead to clinically significant complications, was significantly lower with HV cement, at 8.2%, compared to 41.3% with LV cement (p<0.0001)*

The evidence from the Anselmetti RCT is also reinforced by other authors' statistical comparison of their findings against the leakage rates reported for low-viscosity cement in non-RCTs. This showed that the rate of venous leakage was significantly lower with high-viscosity cement. Although these aren't RCTs, it is clearly documented that the cement viscosity is an important determinant of cement leakage and filling patterns in vertebral body augmentation and therefore the use of high viscosity cement can reduce the risk of cement leakage (19- 24).

In a study to evaluate the clinical effect of the Confidence Spinal Cement System®, Wang et al found that the system had the following advantages: instantaneous high viscosity, prolonged injectable time duration and controllable directional injection, concluding therefore that it can reduce the risks of bone cement leakage. (25). Similarly, In a retrospective review of his clinical experience with HV cement, Georgy reported that his finding confirmed prior observations that highly viscous cements may increase the safety of vertebral augmentation techniques compared with less viscous cements. (27), additionally, Baroud et al found that cement leakage can be significantly reduced when injecting a cement of an appropriate viscosity. (15)

The Assessment Group (AG) took guidance from their clinical advisor on another important aspect relating to cement types, namely the Average Selling Price (ASP) of lower-viscosity cements. The cost should be for all cements (low and high viscosity) as the scope is to consider PVP not differentiate between cements. Unless validated this cannot be taken as a robust data point for inclusion in the modeling as these prices may reflect large volume-based discounts which may not be available to each NHS provider. We recommend any use of Average Selling Prices should be robust and validated by NICE using NHS procurement data.

It is pertinent to note that in the base cases presented by Johnson and Johnson Medical that VBA using HV cement vs. NIM is already below £20,000 per QALY. **We would refer the committee back to the original scope which does not detail the intention to perform a subgroup analyses on various cement types.** While the evidence base concerning cement selection for PVP is emerging, selection of **cement performance characteristics** required for PVP and BKP **should be left to individual clinician discression.**

7 Other Points for Consideration

7.1 Typographical error

The Assessment Group (AG) comments that there appeared to be a typographical error in the model submitted by Johnson and Johnson Medical; "only 10% of patients receiving BKP were assumed to consume operating room resources; it was assumed that this value was intended to be 100%. As such the overall cost-effectiveness results are likely to be favourable to BKP". This appears to be correct (i.e. there was a typographical error) and this means

that the operating phase of the costs for BKP were too low (by £247) but ONLY when the Strom et al costs were considered, this error favours BKP (i.e. creates bias against PVP).

7.2 Acquisition costs of medical devices decrease significantly over time

Price points are not static with medical devices and are often reflective of a cost to serve or commitment to volume-based agreements. In accordance with the NICE Methods Guide for Technology Appraisals, list prices are the appropriate benchmark for modelling cost-effectiveness. However there must be a recognition that significant discounts are available to the NHS from the quoted list prices based on volume purchased. Unlike with pharmaceuticals, medical devices pricing is not fixed for the life of the patent. Thus, as observed in other competitive markets, such as consumer electronics, prices decrease substantially over time. As a result, acquisition prices and cost per QALY relative to procedures without medical devices will decrease during the appraisal process and thereafter due to market forces. Should NICE rely on using "Average Selling Prices" sourced from Company submissions; it would be prudent to cross-reference these with NHS procurement data to confirm their applicability across the NHS.

8 Conclusion

There are very few alternative treatment options to PVP or BKP for patients unresponsive to non-invasive management other than months of severe pain, restricted mobility and poor quality of life and depression in up to 40% of cases. It is reported that patients with VCFs are confined to bed nine times more often than those without VCFs, increasing their risk of further VCFs which can further complicate recovery. The impact of VCFs on quality of life (QoL) has been shown to be comparable with chronic obstructive pulmonary disease (COPD), a point which should not be underestimated.

Vertebroplasty (PVP) has been shown to be a clinically effective intervention for people with painful osteoporotic VCFs refractory to analgesic treatment. VBA performs significantly better in un-blinded trials than NIM (non-invasive management) in terms of improving quality of life and reducing pain and disability and may be one way to mitigate some of the problems associated with the NIM

Vertebroplasty (PVP) has been shown to be a cost-effective intervention across the range of list prices for cements with high- and low-viscosity, having an ICER well below £20,000 per QALY in the Assessment Group's foundation analysis and in the base case in the model submitted by Johnson and Johnson Medical.

High viscosity (HV) cement was developed to mitigate safety concerns associated with low viscosity (LV) cement. There is RCT evidence which substantiates the difference in venous leakage rates (which although rare, can be clinically significant) between High and Low viscosity cement. However it is recognised that the evidence base concerning cement viscosity is emerging and therefore it is recommended **that the decision on which viscosity cement is suitable to different patients, is left to the judgment of the clinician.**

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10 Appendices

10.1 Appendix A: Dr Foster Intelligence Data Collection Protocol

The Dr Foster Intelligence database was analysed using the following search parameters to obtain the patient population of interest.

For all iterations of data analysis, the following search strategies were used for individual comparator arms:

- **For V444 procedures**: ICD 10 code equal to M80* and OPCS 4.5 code equal to V444.
- **For V445 procedures**: ICD 10 code equal to M80* and OPCS 4.5 code equal to V445
- **For NIM treated patients**: ICD 10 code equal to M80* and OPCS 4.5 field blank (these patients equated to "null" procedures, i.e. no invasive procedures conducted).
- The diagnosis (M80 ICD 10) codes could be listed in any position, i.e. listed as either a primary or secondary diagnosis in order to capture all relevant patients.

The following search strategies were used for all comparator arms:

- The data were queried for hospital discharges for 3 financial years: April 2008–March 2011
- Admissions where the relevant diagnosis code is a primary or secondary diagnosis in the same episode as the dominant diagnosis (usually the first episode, or reason for admission).
- Admissions where the relevant procedure codes are part of the treatment for the same episode as the diagnosis – i.e. they also come from the same episode as the dominant diagnosis. Data come from all acute hospital trusts in England.

These data were then analysed to obtain the various parameters which would inform the model:

Total length of stay

All data identified using the above search parameters was further analysed for total length of patient stay (i.e. date of discharge less date of admission) for each comparator arm (V444, V445 and conservative treatment). The Dr Foster Intelligence tool returned the final Length of stay figure in the reported data. These data were interrogated both for day case procedures and all patients, to assess the overall impact of length of stay for all comparator arms which were reported in the total length of stay section.

Post-operative length of stay

The data identified using the above search parameters was further analysed for post-operative length stay (i.e. date of discharge less date of procedure) for the V444 & V445 comparator arms (as the conservatively treated patients had no coded procedures, this analysis was not possible for this comparator arm).

Day case procedures

The proportion of V444 & V445 patients who had day case procedures was assessed. It is worth noting that there is a difference between a LoS of 0 days and day cases. Day cases are planned to last one day, while 0 days LoS

typically means non-day cases where discharge occurs on the same day as admission. Traditional day case patients were reviewed in this subgroup analysis.

Discharge destination

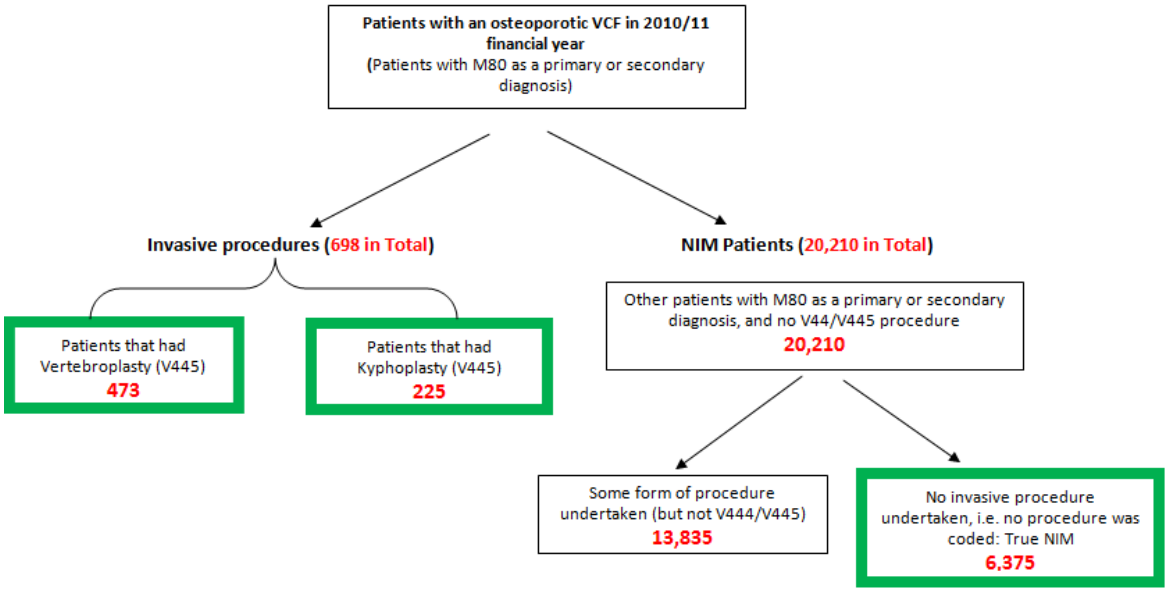
Only destinations with data against them were returned by the Dr Foster Intelligence data query. Table 1 contains the full list of possible destinations.

Table 1: Discharge destination list

ID	Description
19	Usual place of residence, including no fixed abode
29	Temporary place of residence
30	Repatriation from high security psychiatric hospital
37	Penal establishment - court
38	Penal establishment - police station
39	Penal establishment - court and police station excluded
48	High security psychiatric hospital, Scotland
49	NHS - high security psychiatric accommodation
50	NHS - medium secure unit
51	NHS - ward for general patients or the younger physically disabled
52	NHS - ward for maternity patients or neonates
53	NHS - ward for patients who are mentally ill or have learning disabilities
54	NHS run nursing home, residential care home or group home
65	LA Part 3 residential accommodation
66	LA foster care, but not in Part 3 residential accommodation
69	LA home or care
79	Not applicable - patient died or still birth
84	Non-NHS run hospital - medium secure unit
85	Non-NHS (other than local authority) run residential care home
87	Non-NHS run hospital
88	Non-NHS (other than Local Authority) run Hospice
98	Not applicable
99	Not known

10.2 Appendix B: A schematic showing the derivation of the patient groups described.

(*Green boxes represent the three patient groups defined as comparators in the NICE scope)*



10.3 Appendix C: The estimated length of stay in days assumed in the manufacturers' submissions.

	LoS in Days		
Comparator Arm	J&J	Medtronic	Synthes
PVP	3.24	6.2	7.5
BKP	4.48	5.1	5.9
OPM	12.6	9.5	12.4