Stakeholder Feedback Form - Vertebroplasty or Kyphoplasty in Symptomatic Osteoporotic Painful Vertebral Compression Fractures Unresponsive to Non-Surgical Treatment

Zusammenfassung der Stakeholderkommentare

Alle unten aufgeführten Stakeholder wurden zum Scoping-Bericht konsultiert. Curafutura, H+, santésuisse, SGNC/SGNR/SO & SGS (konsolidierte Stellungnahme), SMCF, SMVS und Swiss Medtech haben Stellungnahmen zum Bericht eingereicht. Stellungnahmen welche nicht im vorgegebenen Feedbackformular eingingen, wurden sinngemäss ins Feedbackformularformat übergetragen.

Dieser Scoping-Bericht hat zum Ziel die Durchführbarkeit eines Health Technology Assessment (HTA) zu ermitteln, und zwar aufgrund der Menge und der Qualität der vorhandenen Primärliteratur, die während der Scoping-Phase identifiziert wurden. In einem Scoping-Bericht werden keine Studienergebnisse analysiert. Ausserdem, dienen weder ein Scoping-Bericht, noch ein HTA- Bericht dazu, nationale Behandlungsrichtlinien zu erstellen. Es ist die Aufgabe von den jeweiligen Fachgesellschaften, Behandlungsrichtlinien zu erarbeiten.

Verschiedene Stakeholder haben moniert, warum percutaneous vertebroplasty (PVP) und percutaneous balloon kyphoplasty (PBK) nicht mit einander verglichen werden. Im originalen HTA-Antrag zur Re-evaluation wurde die individuelle Überprüfungen von PVP und PBK beantragt und kein Vergleich von beiden. Zudem ist anzumerken, dass in einem HTA die Wirksamkeit einer Leistung generell zu der Standardtherapie beurteilt wird. Des Weiteren bemerkten mehrere Stakeholder, dass «vertebral height loss» und «kyphotic wedge angle» als Ergebnis (outcome) auszuwerten seien. Diese Forderung wird teilweise nachgekommen, indem diese als Surrgoratergebnisse aufgenommen werden, wenn zu wenig patientenrelevante Ergebnisse (z.B. Schmerzen, Mobilität oder Lebensqualität) vorhanden sind.

Die individuellen Kommentare der Stakeholder sind in alphabetischer Reihenfolge der Stakeholder aufgelistet:

Stakeholder 1 – Curafutura

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
General comment	Overall	Neben dem Vergleich von Vertebroplasty und Kyphoplasty mit konservativer Behandlung sollte die Gelegenheit auch genutzt werden, um Vertebroplasty mit Kyphoplasty zu vergleichen, sind doch die Kostenunterschiede signifikant. Auch Risiken und Nutzen wie z.B. Komplikationsrate und Lebensqualität weisen grosse Unterschiede auf. Bei Kyphoplasty bestehen in der KLV verschiedenen Einschränkungen und es müsste geprüft werden, ob diese gelockert oder verschärft, oder aber auch auf Vertebroplasy ausgeweitet werden müssten.		☐Accepted ☐Accepted with modification ☒Turned down This is outside of the scope of the planned assessment.
Specific comment	Lines 710 - 722	Aufgrund der Beschreibung zum Kostenvergleich muss geschlossen werden, dass der Forschergruppe das schweizerische Finanzierungssystem im stationären und ambulanten Bereich nicht im Detail bekannt ist, ebenso wenig wie die Verfügbarkeit von Kostendaten.	Einsetzen einer kleinen Begleitgruppe aus dem Bereich Gesundheitsökonomie und Kostenmanagement (Leistungserbringer) sowie	☐Accepted ☐Accepted with modification ☒Turned down

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
			Leistungsabgeltung und Tarife (Versicherer). Die Begleitgruppe müsste sich auch Gedanken zu den Auswirkungen mit den neuen, sich abzeichnenden Finanzierungsmodelle (EFAS, ambulante Pauschalen usw.) machen.	The authors of the scoping report are supported by the FOPH in obtaining all relevant information pertaining to outpatient (i.e. TARMED) and inpatient (i.e. DRG) care. Direct requests for cost data made to industry or insurers will be conducted through the FOPH.
Specific comment	Line 725	Sinnvoll wäre es Vertebroplasty nicht nur mit konservativer Behandlung zu vergleichen, sondern mit Kyphoplasty	Erstellen einer zusätzlichen PICO-Box mit für Vertebroplasty mit comparator Kyphoplasty oder vice versa. Entsprechende Ausweitung der Literatursuche und Verarbeitung.	☐Accepted ☐Accepted with modification ☒Turned down This is outside of the scope of the planned assessment. The evaluation aims to determine the efficacy of each intervention independently of one another, i.e. compared to placebo/sham or conservative management.
Specific comment	Line 726 ff	Der Katalog der HTA Sub-Questions, welche mituntersucht werden sollen, ist eindrücklich und grundsätzlich nachvollziehbar. Allerdings ist der Katalog derart umfangreich, dass die meisten Fragen mit der vorhandenen Datenbasis kaum geklärt werden können. Es ist zu befürchten, dass viele Unterfragen jeweils nur in einzelnen Studien untersucht wurden und damit die Evidenz für klare Aussagen fehlen wird.	Nach einer weiteren groben Sichtung der Literatur sollen Kapitel 7 überarbeitet und die Anzahl Unterfragen pragmatisch reduziert werden. Man sollte sich auf Fragen konzentrieren, die in mehreren Studien zu finden und miteinander vergleichbar sind.	☐Accepted ☒Accepted with modification ☐Turned down We agree that the list of questions posed by the EUnetHTA Core Model are comprehensive. The list provided already represents a selection of questions that are most relevant to an evaluation of PVP and PBK. Some additional sub-questions have been removed to ensure only the most relevant questions are addressed in the HTA report.

Stakeholder 2 – H+ Hospitals of Switzerland

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
Specific comment	Overall	- Die unklare Evidenz in der Literatur bedeutet nicht, dass das Verfahren per se unwirksam und obsolet ist. - Ein neues HTA wird kaum neuen Erkenntnisse liefern. - Es braucht eine sorgfältige, interdisziplinäre Indikationsstellung, im Rahmen einer interdisziplinären Indikationskonferenz (Wirbelsäulenzentrum / Spine Center) mit klaren Indikationskriterien (erfolglose konservative Therapie, radiologische Kriterien). - Bei sorgfältiger Indikationsstellung können die minimal invasiven Verfahren einem betroffenen Patienten aber helfen. - Die Indikationskriterien sind in Form einer nationalen Guideline durch die Fachgesellschaften festzulegen. - Zur Qualitätskontrolle sollte das Verfahren in das bereits geplante Schweizerische Wirbelsäulenregister aufgenommen werden		Acknowledged

Stakeholder 3 – Santesesuisse

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change*	Action
General comment	Overall	Guter Aufbau und klare Strukturierung des Berichtes.		None required
General comment	Overall	Die im Scoping-Bericht zitierte Literatur ist oft nicht frei zugänglich. Da die Literatur integraler Bestandteil des Scoping-Berichts ist, sollte diese in geeigneter Form verfügbar sein.	Die Literatur sollte in geeigneter Form den Adressaten des Berichts zur Verfügung stehen.	☐Accepted ☐Accepted with modification ☒Turned down The FOPH currently does not have a system for storing or disseminating literature as part of the HTA process. Some citations referenced in the report are freely accessible online. Stakeholders will need to find other means to access the other citations at this stage.
1) Specific comment	Section 1. Policy Question	Weitgehend nachvollziehbare aber dennoch zu kurze Herleitung der Entscheidungsfrage im Kapitel 1 (Policy Question). Die inhaltliche Darstellung und Erläuterung der unterschiedlichen Ergebnisse aus der Literatur sowie der verschiedenen Guidelines mit teilweise unterschiedlichen Empfehlungen fehlt		☐Accepted ☒Accepted with modification

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		sowohl in diesem als auch in den nachfolgenden Kapiteln. Die aktuelle Evidenzlage hinsichtlich der beiden Eingriffe sowie der internationalen Guidelines werden nicht erläutert. Die erwähnten Guidelines stammen aus unterschiedlichen Jahren (2010 - 2019). Aus den Erläuterungen geht nicht hervor, ob und welche Auswirkungen die neuesten Reviews auf die Guidelines haben. Es geht aus dem Dokument nicht hervor, weshalb im vorgesehenen HTA nur die PVP im Vergleich zur Scheinbehandlung bzw. zur konservativen Behandlung aber nicht gegenüber der PKB verglichen werden soll. Dabei zu beachten ist, dass die PKP teilweise als Weiterentwicklung der PVP bezeichnet wird. Zudem zeigt sich im Versorgungsatlas in einigen Regionen teilweise höhere Raten für PVP und in anderen Regionen solche für PKP. Es fehlen bezüglich PKB Angaben zu Evidenzbasis und Entscheidungsgrundlagen, welche zu der bestehenden KLV-Regelung geführt hatten. Bezüglich der conflicting results aus der Literatur (Zeile 74) findet sich lediglich ein Verweis auf die Cochrane Review von Buchbinder et al (2018). Dies erstaunt insofern, als in der Review im Vergleich zur Schein-Behandlung nach Korrektur für Verzerrungen (aufgrund der Heterogenität) kein bedeutender klinisch relevanter Vorteil von PVP und kein Unterschied zwischen PVP und PKB festgestellt werden konnte (Buchbinder S.30-37: Discussion). Gemäss den Autoren der Studie wäre zudem aufgrund zusätzlicher Forschung keine anderslautenden Schlussfolgerungen zu erwarten (Buchbinder S.34: Implications for research). Eine entsprechende Anmerkung findet sich im vorliegenden Dokument erst in Kapitel 8 (Zeilen 783-784) wobei angemerkt wird, dass sich die zu erwartenden Ergebnisse bezüglich der Wirksamkeit der PVP gegenüber derjenigen aus der Cochrane Review von Buchbinder kaum stark unterscheiden werden. Gleichzeitig besteht zwischen der Cochrane Review und dem beabsichtigten aktuellen HTA hinsichtlich der jeweils berücksichtigten Studien eine grosse Überlappung (Zeile 410).		☐Turned down Guideline concordance, and an interrogation of the available evidence, is beyond the scope of the scoping report. The policy context merely outlines the question posed by the FOPH. The text and citations on conflicting results in the literature have been adapted. Comparisons with Cochrane Review have been removed.
2) Specific comment	Sections 2 – 4	Grundsätzlich gute zusammenfassende Darstellung des medizinischen Hintergrundes (2. Medical Background), der Interventionen PVP und PKB, der alternativen Behandlungsoptionen (3. Technology) sowie der Literatursuche (4. Systematic Search Strategy). Ungenügende Darstellung der unterschiedlichen Indikationen / Kontraindikationen für PVP oder PKP. Auch die regional unterschiedliche Verteilung der Eingriffe wird nur ansatzweise erläutert, wobei beispielsweise weder auf die Häufigkeiten der ambulanten Durchführung noch auf die aktuelle Verteilung der Häufigkeiten jeweils von PVP und PKB sowie PVP/PKB im Detail eingegangen wird (z.B. im Versorgungsatlas zeigt sich in einigen Regionen eine höherer PVP Rate und eine tiefere PKB Rate etc.). Abgesehen von der Tabelle 1 (Zeile 328) fehlt eine Erläuterung zur Bedeutung und der allfälligen Berücksichtigung der laufenden Studien im geplanten HTA.		☐Accepted ☒Accepted with modification ☐Turned down Regional variability is mentioned in the policy question and context section. Results from ongoing studies will only be included in the effectiveness/safety assessment if their results are available and published. Based on the list of studies identified, this is unlikely to occur. However, in the HTA report

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				there is a subchapter dedicated to ungoing studies to highlight possible future developments.
3) Specific comment	Section 5	Nachvollziehbare Synthese der Evidenzbasis, wobei die inhaltlichen Ergebnisse und Schlussfolgerungen der angeführten Studien nicht erwähnt werden. Die Cochrane Review von Buchbinder et al und die aktuelle Review werden bezüglich PICO und Design tabellarisch gegenübergestellt (Tabelle 4, Zeile 405). Zudem wird auf die in der aktuellen Review nicht zu verwendenden Studien hingewiesen, wobei die diesbezügliche Begründung sehr spärlich ausfällt. Beispielsweise wird nicht erläutert, weshalb der VOPE trial wegen nicht verfügbaren publizierten Daten ausgeschlossen werden soll, obwohl er in der Cochrane Review berücksichtigt wurde (Zeile 414-415). Die für die aktuelle Review wichtigen und relevanten inhaltlichen Ergebnisse und Schlussfolgerungen aus der Arbeit von Buchbinder werden nicht erwähnt. Dies scheint insbesondere auch daher erstaunlich, weil in dieser umfassenden Cochrane Review insgesamt kaum relevante Vorteile der PVP gefunden wurden und von weiteren Studien keine anderen Schlussfolgerungen zu erwarten wären (s.a. diesbezügliche Bemerkungen zu Kapitel 1.). Zudem seien gemäss Buchbinder aufgrund der aktuellen Literatur keine Untergruppen von Patienten zu erwarten, welche von der PVP profitieren würden. Diese Aussagen der Cochrane Review sind zumindest zu erläutern.		☐Accepted ☒Accepted with modification ☐Turned down The scoping report focuses on published literature. Unpublished data from the VOPE trial may be collected for the HTA. Subgroup analyses are pre-defined based on factors that may impact the direction or size of effect of the intervention. They are not influenced by available evidence. Comparisons to the Cohrane Review have been removed in line with other feedback.
4) Specific comment	Section 5.2 / page 27 / line 530f	Eine „de-novo“ ökonomische Beurteilung wird im Grundsatz unterstützt soll aber in Abhängigkeit von Wirksamkeit und Sicherheit der Intervention beurteilt werden. Zeigt sich keine Wirksamkeit oder ist die Sicherheit nicht gegeben ist keine ökonomische Analyse in Betracht zu ziehen.		☒Accepted ☐Accepted with modification ☐Turned down Agree. As stated in report “The decision to conduct a de novo economic evaluation will be guided by the findings of the safety and effectiveness review.”
5) Specific comment	Section 6	Aus den Erläuterungen im Kapitel 6 geht nicht hervor, warum in der aktuellen Review die PVP mit der Scheinbehandlung und der konservativen Therapie aber nicht mit der PKB verglichen werden soll. Aufgrund der fehlenden Regulierung bzw. Erwähnung der PVP in der KLV bzw. in der Richtlinie der Schweizerischen Gesellschaft für Spinale Chirurgie (SGS) sind für die PVP die Kriterien der jeweiligen Indikationsstellung im klinischen Alltag nicht bekannt. Gemäss den Richtlinien der SGS für die PKB wird bei nicht erfüllten Kriterien die konservative Behandlung und nicht eine PVP empfohlen. Auch in Anbetracht der regional unterschiedlichen Raten von PVP und PKB wäre auch der Vergleich von PVP und		☐Accepted ☒Accepted with modification ☐Turned down The aim of the scoping report is to inform a decision on possible changes to the reimbursement status of PVP and PBK in

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change*	Action
		PKB von Interesse. Bezüglich der Central Research Questions stellt sich für die Untersuchung von PVP und PKB die Frage nach dem Comparator: Wie weit eignet sich eine Vergleichsgruppe von Patienten mit nicht-chirurgischer Behandlung, wenn in der Review insgesamt nur Patienten mit persistierender schmerzhafter OVCF trotz vorgängiger nicht-chirurgischer Therapie einbezogen werden. Aus solchen Vergleichsgruppen würden sich auch ethische Fragen ergeben. Ausgehend von Ergebnissen und Schlussfolgerungen von Buchbinder (s. Bemerkungen Kapitel 1) wird bezüglich der PVP nicht eindeutig ersichtlich, warum trotz weitgehender Überlappung der einzubeziehenden Studien mit der vorgeschlagenen Review welche zusätzlichen und neuen Erkenntnisse hinsichtlich Wirksamkeit und Sicherheit gewonnen werden sollen. Dabei scheint sich die zu untersuchende Population im Wesentlichen lediglich durch das Einschlusskriterium persistierende schmerzhafte OVCF unter nicht-chirurgischer bzw. medikamentöser Therapie zu unterscheiden. Zu beachten ist, dass auch in den von Buchbinder berücksichtigen Studien vorbestehende konservative Behandlungen zumindest teilweise enthalten sind und eine Subgruppenanalyse keine Unterschiede ergab. Der erste und zweite Satz zur Population der PVP (Zeile 605-608) ist unklar, da sich die KLV nur zur PKP aber nicht zur PVP äussert. Im zweiten Satz geht bezüglich dem Nebensatz for whom non-surgical treatments are contraindicated nicht hervor, was damit gemeint ist. Vermutlich fehlt hier ein or. Im Zusammenhang mit den Kriterien der Studienpopulation wird weder für die PVP noch für die PKP eindeutig klar, ob als Bedingung die schmerzhafte OVCF ohne Verbesserung unter medikamentöser Behandlung (z.B. analog PKP in KLV, Tabelle 4, Tabelle 9, Tabelle 10fxe) oder unter multimodalen nicht-chirurgischer Behandlung (inkl. Physiotherapie, Bracing, Bettruhe, Lifestyleanpassung etc.) gilt (z.B. Zeile 278, Zeile 607). Auch bleibt die Dauer und Intensität der allfälligen nicht-chirurgischen Behandlung unberücksichtigt, wobei die europäischen Richtlinien anscheinend mindestens 3 Wochen empfehlen. Betreffend Kommentar zu PICO s. vorgängige Erläuterungen. Die Outcome-Parameter sowie die Kriterien für die MCID werden gut und detailliert beschrieben.		Switzerland. In addressing this aim, the research question aims to identify the efficacy/effectiveness and safety of PVP and PBK. Both may have beneficial effects, which may not be apparent in trials comparing PVP and PBK. Therefore, the most relevant comparisons to address this research question are trials compared with sham or conservative management. The referenced sentence has been corrected.
6) Specific comment	Section 8	In Zeile 783-784 wird angemerkt, dass sich die zu erwartenden Ergebnisse bezüglich der Wirksamkeit der PVP gegenüber derjenigen aus der Cochrane Review von Buchbinder kaum stark unterscheiden werden, wobei die Ergebnisse bezüglich Sicherheit auch auf Studien mit geringerem Evidenzgrad erweitert würden (s. Bemerkungen zu Kapitel 1).		☒Accepted ☐Accepted with modification ☐Turned down All comparisons to the Cohrane Review have been removed.

*Only one comment had a suggestion written in this column by the stakeholder. For the other comments, suggested changes have been inferred from the comment text.

Stakeholder 4 – Related professional societies (SGNC, SGNR, SO & SGS)

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
Specific comment	Overall	Besides pain[…] fractures of the thoracolumbar spine can lead to loss of vertebral height, wedging of several vertebrae, and end up in severe kyphotic deformity. This deformities have profound biomechanical and physiological impact including decreased mobility (and its consequences such as deep venous thrombosis and pulmonary embolism), impaired ventilation, further loss of bone and muscle mass, in the final consequence patients with OCVF's have a high risk for chronic pain, reduced quality of life and significant higher mortality risk.	Consider including vertebral height loss and kyphotic wedge angle as outcomes	☐Accepted ☐Accepted with modification ☒Turned down The inclusion of surrogate measures (e.g. vertebral height, wedge angle) will be re-considered in the HTA report only in the absence of data on direct patient-relevant outcomes (i.e. pain, mobility, quality of life).
Specific comment	Overall	With respect to the RCTs examining the role of VA to date, marked heterogeneity exists in all aspects of trial design including patient inclusion and exclusion criteria, clinical evaluation both pre and post randomization, the active treatment type offered, the intervention delivered in the control arm and the nature of the primary and secondary outcome measures obtained. In particular, the sham procedure used as control in 3 out of 4 blinded RCTs seemed more an active control than a real sham pure placebo control; in fact, in those trials it was not demonstrated that augmentation was ineffective, but rather that patients in the control arm were doing fairly better as well. Unfortunately, the same positive results could not be replicated using the "sham procedure" out of its placebo masking. As for basically all conservative, minimally-invasive and surgical spinal treatments, evidence is elusive. Using subjective primary and secondary outcome measures such as self-reported pain scales raises concerns over data reliability and accuracy.	Include suitable controls.	☐Accepted ☐Accepted with modification ☒Turned down All available RCTs comparing PVP or PBK to a relevant comparator intervention were identified.
Specific comment	Overall	Finally, improved device- and material-technology is offering increased safety (such as for high viscosity cements and improved fluoroscopic technology) and effectiveness in obtaining vertebral height restoration and kyphosis correction (such as with percutaneous internal fixation devices, e.g. vertebral body stents and Spinejack); these advances are not captured by the RCTs so far.	Note potential effects of new technologies in VA.	☐Accepted ☐Accepted with modification ☒Turned down The current evaluation was specifically targeted towards vertebroplasty and kyphoplasty. Alternative vertebral augmentation procedures, e.g. Spinejack and stents etc, are beyond the scope of the assessment.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
Specific comment	Overall	[It is noted that this stakeholder response included a significant amount of references, using large retrospective studies for safety and efficacy data]	Consider using large retrospective studies as evidence	☒Accepted ☐Accepted with modification ☐Turned down The value of large-scale retrospective studies is acknowledged, and these study designs will be considered for inclusion at the HTA stage.

Stakeholder 5 - Société de Médecine du Canton de Fribourg (SMCF)

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
		Nous trouvons pour le moins curieux de confier ce rapport à des épidémiologistes australiens, dans un pays qui s'est prononcé contre les vertébroplasties et ceci à la suite de deux études (RCT) les plus controversée de la littérature sur les prise en charge des fractures vertébrales. Ce RCT écrit par le Prof Buchbinder et al. en 2009, ainsi que l'étude de Kallmes et al. en 2009, ont été fortement décriés pour des problèmes méthodologiques graves, en particulier un traitement chirurgical incorrect versus des opérations placebo. Ces deux études sont à l'origine de la prise de position de l'Australie et de l'American Academy of Orthopaedics Surgeon (AAOS) qui se prononcent contre la vertébroplastie, mais il eut été correct de mentionner que l'AAOS se prononce en faveur de la kyphoplastie. Il eut probablement également été correct de citer les prises de positions de sociétés internationales telle que l'ISASS, ou de mentionner d'autres pays que l'United Kingdom ayant fait effectuer des HTA, par exemple l'Irlande en 2013. Et enfin de tenir compte des innombrables éditoriaux de revues des plus variées concernant ces études controversées.		☐Accepted ☒Accepted with modification ☐Turned down A conflict of interest statement has been added to the Scoping Report.
		Dans leurs conclusions de la faisabilité, les auteurs suggèrent que leurs conclusions ne différeront pas de la plus récente revue Cochrane, revue qui est écrite par les auteurs justement décriés des deux études mentionnées plus haut ! Il existe donc un sérieux risque de biais dans cette étude HTA, si l'on ne pondère pas en examinant également les résultats cliniques en enlevant des comparaisons des études qui ne correspondent pas à la pratique actuelle de la majorité des chirurgiens et radiologues de par le monde.		☒Accepted ☐Accepted with modification ☐Turned down The intention of this comparison was to highlight the fact that no new RCT evidence has been

				identified since the Cochrane report was published. We accept that our analysis may find different results to the Cochrane review, depending on how studies are grouped etc. All comparisons to the Cochrane Review have been removed from the Scoping report to avoid any ambiguity on this issue.
		De plus il faudrait pour le moins signaler que les techniques actuelles ne comportent pas que les vertébroplasties et kyphoplasties à ballonnet, mais d'autres techniques chirurgicales, parfois associées à des spondylodèse par système pédiculaires, et dans d'autres lésions que les fractures ostéoporotiques mais également sont utilisées dans des fractures traumatiques et dans certaines tumeurs vertébrales, dans certains cas de métastases ou de myélome multiple.		☐Accepted ☐Accepted with modification ☒Turned down These indications are outside of the scope of the planned evaluation.

Stakeholder 6 – La Société Médicale du Valais (SMVS) / Die Walliser Ärztegesellschaft (VSÄG)

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
Specific comment	Overall	Si une HTA est réalisée, l'analyse devra être stratifiée par âge de fracture aiguë ou non aiguë, conformément aux restrictions actuelles et aux critères de remboursement similaires utilisés internationalement. Il nous semble peu probable qu'une telle HTA arrive à d'autres conclusions que celles déjà connues. Nous adhérons à la combinaison de MRC / Angleterre, AAOS, NASS et à la directive allemande. En cas de non-réponse au traitement conservateur de trois semaines ou de douleurs qui ne peuvent être gérées thérapeutiquement en fonction des critères d'évolution liés au patient (Patient related outcome), une réévaluation clinique est entreprise et, le cas échéant, une kyphoplastie ou vertébroplastie est proposée.		☒Accepted ☐Accepted with modification ☐Turned down This subgroup analysis has already been pre-defined on page 31.

Stakeholder 7 - Swiss Medtech

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
General comment: Scope of HTA	Overall	We would suggest extending the scope of the HTA review to "percutaneous vertebral augmentation" techniques, as when considering the current clinical practice in Switzerland for the treatment of OVCFs, therapies beyond vertebroplasty and kyphoplasty are administered. This is a particularly pertinent question if vertebroplasty and/or kyphoplasty are removed from reimbursement, in order to understand what available treatment options could provide in terms of clinical, patient safety and long-term cost-effectiveness.	Assessment of all procedures under the category of "percutaneous vertebral augmentation" to treat painful OVCFs	☐Accepted ☐Accepted with modification ☒Turned down This is outside of the scope of the planned assessment.
General comment: Possibility of bias	Overall	The credibility of any HTA is strongly dependent on objectivity. However, there is a lack of transparency regarding the selection, qualification and possible conflict of interests of the authors. With regard to the uniformly Australian authorship together with the current withhold of reimbursement of PVP/PBK in Australia, there remains some doubt as to whether the required objectivity is guaranteed. Despite the notable differences in the objectives of the HTA and the 2018 Cochrane review, the authors make a rather prejudiced statement: "…the results of the clinical efficacy/effectiveness in this review is unlikely to differ from the Cochrane review…" (cp 783-4) [1]. Despite their existence, no other (positive) reviews are being discussed in detail. While no possible consequences of the HTA on the future reimbursement of PVP/PBK status have been formulated, there is multiple reference to a potential disinvestment (cp 558; 731; 752). Disconcertingly, the report states that the HTA sub-questions have been specifically selected based on their relevance in the context of a potential disinvestment (cp 731).	Disclosure of the selection process/criteria of the HTA assignment to the authors Proof of qualification of the authors. For the evaluation, we suggest to have a more diverse group of experts from different origins (country-wise) and in terms of clinical expertise. Declaration of conflict of interests of the authors Formulate sub-questions of the HTA irrespective of its outcome Exclude section "comparison to 2018 Cochrane review" p.21 (review articles are not planned to be included in the evaluation)	☐Accepted ☒Accepted with modification ☐Turned down A conflict of interest statement has been added to the Scoping Report. The purpose of the evaluation is to inform a possible change to the reimbursement of these interventions, either by reducing the eligible indications, removing the reimbursement, or leaving the reimbursement unchanged. Disinvestment is the underlying policy context behind why the evaluaton is being conducted, which does impact the relevant sub-questions to be addressed in the HTA. As stated elsewhere, comparisons to the Cochrane review have been removed to avoid ambiguity on these issues.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
1) Evidence (Efficacy)	1. Policy Question Page 8 Line 72-74 4. Database and Search Strategy Page 14ff Line 262ff	The controversy over the efficacy of Percutaneous Vertebroplasty (PVP) and Percutaneous Balloon Kyphoplasty (PBK) mentioned in the HTA scoping report is dating back to the year 2009. Although dozens of single-center, single-arm studies had shown a beneficial effect of these procedures on pain reduction, only few randomized controlled trials (RCT)s had so far been published [2]. As none of these trials had been blinded, the efficacy was questioned based on the results of two sham-controlled randomized trials published simultaneously [3, 4]. Several experts have in the meantime claimed that these studies have been flawed [5, 6]. The main points of criticism being methodological aspects such as inadequately low volume of cement used in the verum group as well as the patients being included too late in the clinical course. The Cochrane review refers to PVP only [7].	Recognition of the full body of clinical studies including the large number of smaller studies with lower levels of evidence Suggest adding "in vertebroplasty" to the end of sentence in Line 74 Critical appraisal of the Buchbinder et al, 2009 and Kallmes et al, 2009 studies based on the well-founded expert criticisms	☐Accepted ☒Accepted with modification ☐Turned down Noted for HTA stage. Changed to "In the literature regarding vertebroplasty.." Such appraisal is not within the scope of this report.
2) Current worldwide expert view & reimbursement status of PVP/PBK	1. Policy Question Page 8 Line 72-74	A systematic review concluded that three out of four identified clinical guidelines published between 2010 and 2013 recommended the use of PVP/PBK for the management of vertebral compression fracture [8]. The supporters were namely: The National Institute for Health and Care Excellence Guidelines, the Canadian Association of Radiologists as well as the American College of Radiology. Only the American Academy of Orthopedic Surgeons recommended against the use of PVP/PBK in response to the 2009 publications. However, it has been claimed that the decision would have been different had the results of the VERTOS II trial been included in their review[9]. The positive results of this study were published in Lancet only on August 9th, 2010 [10]. Recent email correspondence (30/09/2019) with William O Shaffer, MD, FAAOS. FAOA, Chief Medical Officer & Medical Director at American Academy of Orthopaedic Surgeons: "*We have discovered NASS (North AMERICAN Spine Society) has already started on a systematic review on this subject so will defer to them, as such we are not updating this guideline*." [11] The Society of Interventional Radiology (SIR) affirms the value of the clinical care pathway recently published in the Spine Journal [12]. This was a multispecialty panel	In an HTA assessment, an overview of the reimbursement status of European countries should be referenced as planned in this scoping report.	☐Accepted ☐Accepted with modification ☒Turned down An overview of the reimbursement status of PVP and PBK in other European countries may be conducted in the HTA report, but is outside the scope of the scoping report.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
		using the RAND/UCLA appropriate method for the management of vertebral fragility fractures [13]. Importantly, as recent as of July 2019, the joint consensus statement of 2014 by the Society of Interventional Radiology (SIR), American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), American College of Radiology (ACR), American Society of Neuroradiology (ASNR), American Society of Spine Radiology (ASSR), Canadian Interventional Radiology Association (CIRA) and the Society of NeuroInterventional Surgery (SNIS) corroborate the legitimacy of PVP/PBK is still being endorsed by these parties [14, 15]. Several economic studies concluded that PVP/PBK were cost-effective [16-18]. An HTA from Denmark stated that PVP was profitable compared to conservative treatment[19]. Based on an HTA from the UK, the National Institute for Health and Care Excellence (NICE) issued a review decision in January 2016 in which they held onto the conclusion from their technology appraisal of 2013 that both, PVP and PBK were cost-effective [20, 21]. In line with the growing body of evidence on efficacy, safety and cost-effectiveness, reimbursement of PVP/PBK is today insured among almost all European countries. In the US system the Medicare MAC Administrators recently held an all MAC CAC meeting to discuss the evidence and therapy and collectively decided to expand coverage based on the current pathway publications and strong mortality evidence [22]. With regard to the Australian government having suspended the reimbursement of these procedures in 2011, one should be informed that a new application for public funding issued by the Interventional Radiology Society of Australasia is now under evaluation by the authorities [23]. Importantly, the clinical aspects are receiving a special consideration in this review. In fact, the final decision is expected at the end of 2019.		
3) Development of the inpatient costs in Switzerland	1. Policy Question Page 8 Line 67ff 5. Synthesis of Evidence Base 5.2 Evidence Base Pertaining to Costs,	Switzerland has a high disease burden from osteoporosis. As stated in the HTA scoping protocol, demographic projections and the natural trajectory of the disease will result in an increase incident of OVCF. This is reflected by the increasing numbers of PVP and PBK over the years. In 2013 a total of 1151 and 777 patients have been treated in inpatient care in Switzerland for PVP and PBK, respectively, whereas in 2017 (most recent data available), the numbers increased to 1423 and 1071, respectively [24, 25] (TABLE 1). However, at the same time, the cost weight for the procedures have been reduced, especially for PBK. As a result of this intervention, the total expenditure for PVP/PBK did not increase (25.76 Mio in 2017 vs 26.76 Mio in 2013) (TABLE 1).	Inclusion of the actual costs of inpatient PVP/PBK based on data from the Federal Statistical Office (BFS) and other real-world data collected in Swiss hospitals	☒Accepted ☐Accepted with modification ☐Turned down Cost data will be included in the budgetary impact evaluaton conducted in the HTA report.

<table>
<tr><th>Stakeholder, Comment No</th><th>Location in doc. (chapter, line, page)</th><th>Comment</th><th>Suggested change</th><th>Action</th></tr>
<tr><td></td><td>Budget Impact and Cost-Effectiveness Page 27 Lines 496ff</td><td>
<table>
<tr><td colspan="7">PVP</td></tr>
<tr><td>year</td><td colspan="3">2013</td><td colspan="3">2017</td></tr>
<tr><td>CHOP code</td><td>DRG*)</td><td>cost weight</td><td># cases**)</td><td>DRG</td><td>cost weigl</td><td># cases**)</td></tr>
<tr><td>81.65.00</td><td>I53Z</td><td>1.075</td><td>2</td><td>I69B</td><td>0.876</td><td>2</td></tr>
<tr><td>81.65.10</td><td>I53Z</td><td>1.075</td><td>517</td><td>I10C</td><td>1.017</td><td>673</td></tr>
<tr><td>81.65.11</td><td>I53Z</td><td>1.075</td><td>236</td><td>I10C</td><td>1.017</td><td>316</td></tr>
<tr><td>81.65.12</td><td>I53Z</td><td>1.075</td><td>204</td><td>I10C</td><td>1.017</td><td>243</td></tr>
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<tr><td>81.65.99</td><td>I53Z</td><td>1.075</td><td>8</td><td>I10C</td><td>1.017</td><td>2</td></tr>
<tr><td>Total no. of cases</td><td></td><td></td><td>1151</td><td></td><td></td><td>1423</td></tr>
<tr><td>Costs PVP (Mio)***)</td><td></td><td></td><td>12.37</td><td></td><td></td><td>14.47</td></tr>
<tr><td colspan="7">PBK</td></tr>
<tr><td>year</td><td colspan="3">2013</td><td colspan="3">2017</td></tr>
<tr><td>CHOP code</td><td>DRG*)</td><td>cost weight</td><td># cases**)</td><td>DRG</td><td>cost weigl</td><td># cases**)</td></tr>
<tr><td>81.66.00</td><td>I09C</td><td>1.852</td><td>1</td><td>I69B</td><td>0.876</td><td></td></tr>
<tr><td>81.66.10</td><td>I09C</td><td>1.852</td><td>586</td><td>I10C</td><td>1.017</td><td>857</td></tr>
<tr><td>81.66.11</td><td>I09C</td><td>1.852</td><td>128</td><td>I10C</td><td>1.017</td><td>131</td></tr>
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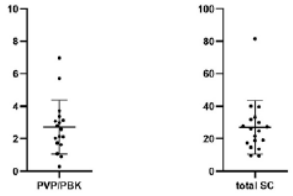
<tr><td>81.66.99</td><td>I09C</td><td>1.852</td><td>1</td><td>I10C</td><td>1.017</td><td>1</td></tr>
<tr><td>Total no. of cases</td><td></td><td></td><td>777</td><td></td><td></td><td>1071</td></tr>
<tr><td>Costs PBK (Mio)***)</td><td></td><td></td><td>14.39</td><td></td><td></td><td>11.29</td></tr>
<tr><td colspan="7"></td></tr>
<tr><td>Total costs PVP+PBK (Mio)</td><td></td><td></td><td>26.76</td><td></td><td></td><td>25.76</td></tr>
<tr><td colspan="7">*) ICD-10 diagnosis code M80.00
**) published case numbers per CHOP code
***) base rate=10'000, assuming normal length of hospital stay ("Normallieger")</td></tr>
</table>
Data sources: [24, 25]
</td><td></td><td></td></tr>
<tr><td>4)</td><td>Chapter 2. Medical Background 2.1 Health condition Page 9-10: Line 98-99</td><td>There is also a mortality risk associated with osteoporotic VCFs, that should be highlighted in addition to other complications.
People with spinal fractures are at increased risk of complications and death compared with people who don't have spinal fractures.</td><td>Include the mortality risk associated with OVCFs</td><td>☒Accepted
☐Accepted with modification
☐Turned down
Added risk of mortality to this health condition paragraph with the given citation.</td></tr>
<tr><td>5)</td><td>Chapter 2. Medical Background</td><td>Reference 2 - US Medicare MAC's in their draft local coverage decisions defined acute fractures as less than 6 weeks and less.</td><td>Nil</td><td>☐Accepted</td></tr>
</table>

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	2.1 Health condition Page 9-10: Line 106			☒Accepted with modification ☐Turned down There is no standard definition for acute fractures, however this statement has been adapted, citation 2 removed, and the included RCTs added as citations.
6)	Line 136-137	Kyphosis is excluded of the focus of the review – Kyphosis correction with PVP is known to be limited however with PBK is proven to be of clinical value, with a better reduction in loss of mobility (demonstrated in the FREE trial) and a smaller reduction in QoL – also demonstrated in all RCTs with PBK.	Emphasize the clinical impact of kyphosis: it has a demonstrated detrimental impact e.g on lung capacity, loss of appetite, decreased daily activity, etc. Kyphosis correction is a crucial point in the evaluation of successful application of PVP or PBK – we question the decision to exclude it from the HTA.	☐Accepted ☐Accepted with modification ☒Turned down As stated previously, surrogate outcome measures will be considered only in the absence of direct patient-related outcomes.
7)	Chapter 3: Technology 3.2 Percutaneous Balloon Kyphoplasty (PBK) Page 11: Line 166-169	The Swiss Spine registry is no longer mandatory.	Please provide an update on the status of this Registry	☐Accepted ☒Accepted with modification ☐Turned down Thank you for sharing this insight. We will investigate this issue further in the HTA phase of this project.
8)	3.3 Conduct of the Procedures Page 11	Reference to two articles 42 and 43 (from 2010 and 2013) - while in 2013 there was a consensus publication on patient selection and guidance for use based on the RAND/UCLA panel methodology [27]. This was more recently validated by by another publication in 2016 [28].	Refer to appropriateness criteria for treatment of OVCF (decision making	☒Accepted ☐Accepted with modification

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	Line 179		between NSM, PVP and PBK)	☐Turned down The Schupfner citation has been added.
9)	Line 186-187	Our understanding is that PMMA cement hardens in a time of max. 20 minutes (not 1-2 hours)	Clarify with a Swiss physician expert to provide an accurate time for this process	☒Accepted ☐Accepted with modification ☐Turned down This type of data will collected during the HTA phase, either from clinical studies or local experts, and will be used to inform the economic modelling.
10)	Page 12 Line 191	Validate current pricing estimates for PBK	Instead of “additional”, we suggest “up to”	☒Accepted ☐Accepted with modification ☐Turned down Accurate pricing data will be sourced for the HTA report.
11)	Line 192-194	In the VAPOUR trial, the mean median hospital length of stay was reduced by 5.5 days [26]. A 2013 study from the US also showed a reduced length of hospital stay for VP and PBK vs non-operative management [29].	Include impact on length of stay the clinical benefit as well as economic evaluation for all comparative procedures	☒Accepted ☐Accepted with modification ☐Turned down Certainly we will include hospital stay as an outcome in the economic analysis.
12)	Line 198	Cement always has to enter the vertebral body, that’s the goal of the therapy, what is meant is the spinal canal, via which it can have impact on the nerves	Replace “vertebral body” with “spinal canal”	☒Accepted

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
				☐Accepted with modification ☐Turned down Change has been made.
13)	3. Technology 3.1 Percutaneous Balloon Kyphoplasty Page 11 Line 161	The balloon is not inflated with air but with fluid, as this is safer in case of balloon rupture	The balloon is inflated with fluid, then deflated and removed	☒Accepted ☐Accepted with modification ☐Turned down Change has been made.
14) Variation in PVP/PBK procedures between Swiss cantons	3. Technology 3.4 Incidence of the Procedures in Switzerland Page 12 Lines 204-218	The data of the Swiss federal office for statistics allows to compare the different usage of PVP/PBK among hospitals of the different Swiss cantons[30, 31]. It has been claimed that there are regions in Switzerland where patients might be "overtreated" with PVP/PBK.[32]. In contrast to this report stating a 10-fold difference in the procedure rates among Swiss hospital regions in the years 2012/2013, the most recent data collection of the year 2016 reveals a rather modest variation in inpatient procedure rates among the different cantons (TABLE 2). A similar extent of variation can in fact be found for spinal column (SC) surgeries in general. The significance of the difference is unclear but may reflect different disease awareness, diagnosis, referral behavior of general practitioners, specialization of hospitals ("centers of excellence"), besides others.	Provide the newest numbers on procedure rates and compare them to other indicators (eg. Total spinal column procedures)	☐Accepted ☒Accepted with modification ☐Turned down Thank you for suggesting additional data sources. These will be reviewed in the HTA report, considering any adjustment or standardisation applied to each data source.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
		Year 2016 Canton*) PVP/PBK**) No. per 1.0*10^4 total SC***) No. per 1.0*10^4 ratio PVP/PBK : total SC ZH 447 3.09 4805 33.22 9.30 BE 703 6.96 2193 21.73 32.06 VD 239 3.14 2081 27.33 11.48 AG 138 2.14 1599 24.78 8.63 SG 128 2.58 726 14.64 17.63 GE 83 1.74 1431 29.98 5.80 LU 110 2.79 1563 39.61 7.04 TI 130 3.71 1117 31.88 11.64 VS 70 2.11 875 26.37 8.00 FR 62 2.04 529 17.44 11.72 BL 8 0.28 273 9.70 2.93 TG 28 1.06 496 18.81 5.65 SO 151 5.73 503 19.07 30.02 GR 66 3.37 543 27.72 12.15 BS 57 2.99 1554 81.54 3.67 NE 16 0.90 244 13.76 6.56 SZ 25 1.64 144 9.43 17.36 ZG 27 2.25 482 40.14 5.60  *) included are all cantons with >1.0*10^5 inhabitants **) indicator code I.2.13.M ***) indicator code I.2.3.F Data sources: [30, 31]		
15) Pain management and lack of alternative treatments	3. Technology 3.5 Alternative Technologies Considered for this Population Page 13	Osteoporotic vertebral compression fracture (OVCF) patients often present with severe pain. Providing immediate effective pain relief for severely suffering patients represents an ethical responsibility of any doctor as postulated by his and her code of conduct (Hippocratic Oath). Over the last years, several RCTs have convincingly demonstrated the superiority of PVP/PBK over non-surgical treatments in respect to promptness and efficiency of pain relief [10, 33-38]. On the other side, it should be stressed that there is a lack of alternative treatments for OVCF patients. The pharmacological options listed in the HTA Scoping Protocol warrant more critical appraisal. For example, there is serious concern about the safety of opioid use in elderly patients that may increase their risk of falls, confusion, nausea, drug dependency, among others. Second, compared to PVP/PBK, the	Address the ethical responsibility of immediate and effective pain relief of suffering patients Address the social responsibility the state has for the fragile elderly	☐Accepted ☒Accepted with modification ☐Turned down Social and ethical aspects associated with the use of PVP and PBK will be investigated in the HTA report. The choice of comparator is not based on the availability of evidence, but the

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	Lines 220-243 Line 225-226 5. Synthesis of Evidence Base 5.3.3 Ethical Issues Page 30 Line 575ff	benefits of bracing have not convincingly been demonstrated[39]. The same applies to the reference mentioned regarding physiotherapy [40]. Thirdly, whilst it was raised in the HTA scoping report as a possible alternative therapy, neuromodulation is a more invasive therapy compared to PVP/PBK and, to the best of our knowledge, has no evidence base in the OVCF patient population. Neuromodulation, as a more invasive approach is noted as an alternative to PVP/PBK for the management of spinal pain in patients unsuitable for traditional surgical intervention. None of the references provided for neuromodulation in the HTA scoping document describe the use of this therapy in an OVCF specific population – rather describe an overview of the use of neuromoduation in its indicated treatment of chronic neuropathic pain, and its use in children and young people. Whilst it is cited that approximately 10-20% of OVCF patients may develop chronic back pain [41], it should be noted that neuromodulation via spinal cord stimulation is primarily performed for the chronic neuropathic pain stemming from the indications of failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) [42]. In the literature there is one publication dating back to 1999 where neuromodulation via intrathecal drug infusion was used to treat 3 patients with painful OVCFs [43].	Address the social and economic importance of maintaining self-care Involve the patients themselves in the definition of meaningful outcome measures Address the current concerns of opiate consumption Explicitly state the alternative treatments that are currently reimbursed according to the Krankenpflege-Leistungsverordnung (KLV) Demonstrate the clinical evidence with regard to the safety and efficacy as well as cost-effectiveness of alternative therapies such as pharmacological treatment (eg, risks of co-medication of often multimorbid patients; risks associated with opiate use in the elderly etc) Re-assess the inclusion of neuromodulation as an alternative treatment for painful OVCFs	available alternateves in clinical practice. Listing an intervention as a comparator in the scoping report is not an endorsement of its safety or effectiveness. Evaluating the evidence for comparator interventions, as well as PVP and PBK, are outside the scope of the scoping report. These will be investigated through a review of the available evidence in the HTA report. Direct patient input it not typically feasible within the time and resource limitations of an HTA. Neuromodulation has been removed from the report.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
			unresponsive to surgical treatment – either by removing it, or by providing clinical evidence of its use and effectiveness in this patient population. The inclusion of neuromodulation as appropriate alternative treatment for the OVCF population should be discussed and validated with a physician expert.	
16) Swiss data registries and databases	4. Systematic Search Strategy 4.1 Database and Search Strategy Page 14 Line 286	Because of the limited evidence in the early years, the SwissSpine Registry was implemented in 2005 for the actual purpose of gathering relevant information on the safety and efficacy of PBK Switzerland [44]. The SWISSspine registry group concluded that" …[PBK] is a safe and effective treatment concerning pain reduction, QoL improvement, and pain killer consumption and has an acceptable rate of cement extrusions. Postoperative outcome results show clear and significant clinical improvement at early follow-up that remain stable during the first postoperative year."[45]. These findings subsequently led to the coverage of PBK by the basic health insurance. However, despite the specific questions addressed and its direct context to the Swiss patient population, the positive data of the SWISSspine registry does not seem to have been incorporated into the HTA scoping protocol.	Disclosure of the results of the SwissSpine Registry	☐Accepted ☐Accepted with modification ☒Turned down The aim of the scoping report is to establish the PICO criteria for the HTA report. The results of included studies are not discussed at the scoping phase.
17) Information about the VERTOS V study	4.2 PRISMA Flow diagram Table 1 Ongoing clinical trials fitting the inclusion criteria Page 17	The last patient is enrolled on July 2019 – expected final results end Dec 2020 Vertos V intended to enrol 100 patients, not 180	Correct the details listed for the Vertos V study (intended 100 patients; expected results end of December 2020)	☐Accepted ☐Accepted with modification ☒Turned down The data identified on clinicaltrials.gov indicates the estimated enrolement was 180 (NCT01963039). We could not find any information suggesting otherwise.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	Line 328			
18)	5. Synthesis of Evidence Base 5.1 Evidence Base Pertaining to Efficacy, Effectiveness and Safety Page 19 Line 361	Referring to "most studies" – unclear is if this is most studies for both PVP and PBK or that the message is for only the PBK studies	It would be helpful to mention that the message is covering all or a specific treatment option	☒Accepted ☐Accepted with modification ☐Turned down This is all studies for PVP/PBK. This has been clarified.
19)	Line 378	Cochrane Risk of Bias tool – is in press, so not yet publicly available.	We question the use of a tool which is not yet published - how do we know it is validated?	There is no consensus in the HTA community around specific critical appraisal tools. The Cochrane tool has been chosen because it includes a robust analysis of the elements of bias in RCT study design.
20) Mortality benefit	5. Synthesis of Evidence Base 5.2 Evidence Base Pertaining to Costs, Budget Impact and Cost-Effectiveness Page 23 Lines 416ff	In contrast to primary outcome measures, interpretation of secondary endpoints in general requires special caution because of the inadequate power to assess their significance. Unfortunately, functional outcomes have so far merely been studied as secondary outcome measures in the randomized controlled studies. However, here one should refer to the experience of the surgeons regarding the immediate improvement of physical function for patients undergoing PVP/PBK (personal communications). It is widely recognized that early mobilization plays a key factor in reducing morbidity and mortality in the elderly. For example, several studies investigating the management of hip fractures in elderly patients have shown that immediate surgical intervention was associated with a significantly decreased mortality risk and reduced length of hospital stay [46, 47].	Now that there is real-world data suggesting a similar correlation for PVP/PBK and mortality it is important that this evidence is included in the cost-benefit of PVP/PBK in a future HTA	☒Accepted ☐Accepted with modification ☐Turned down Lower levels of evidence will be considered for inclusion in the HTA report in order to address any gaps in the RCT data, either through lack of reporting or lack of power for specific outcomes.
21)	5.2 Evidence Base Pertaining to Costs,	Describes in the FREE trial age of patients with PVP, which should be PBK	Confirm the trial age is correct for both treatment groups	☒Accepted ☐Accepted with modification

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	Budget Impact and Cost-Effectiveness Page 24 Table 6 Overview of within-trial economic evaluations Line 452	Data from Europe has also reported overall higher survival rates and lower cumulative 4-year costs associated with PVP/PBK patients compared that of non-surgical management for OVCF [50].		☐Turned down Typo has been corrected.
22) UK economic models	5. Synthesis of Evidence Base 5.2 Evidence Base Pertaining to Costs, Budget Impact and Cost-Effectiveness Applicability of the economic analyses to the Swiss context Page 27 Lines 497-501	In the UK HTA, three economic models, two provided by the industry and one by the assessment group were presented in detail [6]. These models were cross-validated, and all confirmed to be adequate.	The UK models by Stevenson et al, 2014 may be adapted to the Swiss context	☒Accepted ☐Accepted with modification ☐Turned down Thank you for the suggestion, this has been noted.
23) Reimbursement status in Switzerland	6. Central research questions	Vertebroplasty is not listed in Anhang 1 of the KLV. The restriction to certain patient groups has not been defined by law.	Please clarify	☒Accepted

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	6.2 Patients Page 31 Line 605-610			☐Accepted with modification ☐Turned down The KLV restrictions are only related to kyphoplasty. This has been clarified in Section 5 (PICO).
24)	6. Central research questions 6.2 Patients Page 31 Line 612-613	PVP/PBK for non-osteoporotic fractures is not the focus of the report – does this mean that for those indications' reimbursement is not in discussion?	Clarify the scope of PVP and impact on non-OVCF indications following this HTA and subsequent funding decision	Correct.
25)	6. Central research questions 6.2 Patients Page 32 Line 617-618	The indication for PBK is based on the Schweizerische Gesellschaft für Spinale Chirurgie guideline on balloon kyphoplasty.	Indications and patient referral methods have changed in Switzerland significantly in recent years in terms of surgical approaches. A standardized patient pathway algorithm across all Swiss centers would be helpful. We recommend updating to guidelines as they are dated from 2004 and in the meantime, practice may have changed.	☐Accepted ☐Accepted with modification ☒Turned down Updating this guidelines is outside the scope of the current project.
26) Limitations of sham studies in vertebral augmentation	Chapter 6. Central Research Question(s)	We challenge the entire statement that sham controls provide the best evidence for relative safety and effectiveness of PVP and PBK. There are a number of limitations of the VA vs sham studies, including selection bias, small enrollment percentage, non-standardized enrollment criteria, the possibility of including non-surgical management into the sham arm, and under powering. The emphasis of VA vs sham	Suggest a more balanced approach in describing the evidence base of sham controls and RCTs against	☐Accepted ☐Accepted with modification

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	6.4 Comparator Pages 32 Line 642-643	studies overlooks the value of other evidence such as large meta analyses that have be subsequently published [51].	standard of care in this treatment population, as well as consultation with physician specialist on the applicability of sham studies in this area.	☒Turned down In theory the best control to determine efficacy is sham procedure. Study selection is, however, not limited to sham controls; active comparators are also considered.
27)	Chapter 6. Central Research Question(s) 6.5 Outcomes Efficacy/effectiveness Pages 33 Line 659	Time points intermediate up to 12 months and long term longer than 12 months – this difference is too small Either intermediate is max 6 months and long term 12 months and longer Or intermediate is up to 12 months and long term is minimally 18 months but preferably 24 months	Please clarify this point with a physician expert	☒Accepted ☐Accepted with modification ☐Turned down We will check with a clinician prior to commencing the HTA report.
28)	Line 672 and 681	Valuable suggestions to take into account to use activity trackers and to evaluate opioid use, however in the time most of the published studies were executed, these devices were not available and opioid use was not an issue, so limited information will have been collected	Just an observation	None
29) Safety analysis	6. Central research questions 6.5 Outcomes Page 34 Lines 685ff	PVP/PBK are low risk procedures, with the mortality in Swiss hospitals remaining constantly well below 1% over the years [30]. When including single arm studies for the safety analysis the adverse events associated with the alternative treatments (e.g. opioid use, see above) should carefully be weighed in. In addition, adverse events associated with progressive fracture compression and retropulsion should be considered.	Include real world data on the safety from Switzerland (SwissSpine Registry etc.)	☐Accepted ☒Accepted with modification ☐Turned down Will use registry data of acceptable design in safety analysis of HTA report.
30)	Chapter 6. Central Research Question(s)	Serious adverse events are defined according ICH-GCP regulations – death, requiring hospitalisation, life threatening, (permanently) disabling. Only when cement leakage and infection lead to a life-threatening event the have to be considered as serious otherwise, they are normal adverse events	Include classification of adverse events and serious adverse events,	☒Accepted

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
	6.5 Outcomes Safety Pages 34 Line 690		according to standardised definitions	☐Accepted with modification ☐Turned down A standardised definition to be added based on the ICH-GCP Regulations. We note this definitions are also supported by the US FDA
31)	6.5 Outcomes Safety Page 34 Line 692-695	Single-level vertebral kyphoplasty is not associated with an increased risk of symptomatic secondary adjacent osteoporotic vertebral compression fractures: a matched case-control analysis [52].	Please clarify this the literature to support this discussion point.	☒Accepted ☐Accepted with modification ☐Turned down We have added a citation noting the hypothesised relationship between vertebral augmentation and subsequent adjacent fracture. Again, the aim of the scoping report is not to answer these research questions, but to identify relevant outcomes for assessment.
32)	Page 34 Line 695	Clinically evident adjacent fracture – question is what is clinically relevant for the reviewers	Define clinically relevant adjacent fractures	☒Accepted ☐Accepted with modification ☐Turned down This sentence has been clarified to mean “symptomatic”.
33)	Page 34 Line 697	Other adverse events – the way how the sentence is written you can read that exposure to radiation is an adverse event	Delete ‘other’ so the sentence becomes: Exposure to radiation and adverse events are important outcomes.	☒Accepted ☐Accepted with modification ☐Turned down

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
				Change has been made as suggested.
34)	8. Feasibility HTA Page 43 Line 806	The recent Australian HTA recommendation from the government was to have additional conversations with physicians and patients directly	We would suggest allowing Swiss patients testify to the effectiveness of their treatments	☐Accepted ☐Accepted with modification ☒Turned down Individual patient testimony is not within the scope of the Swiss HTA program. However, quality of life outcomes, which reflect patient testimonies, are included in the PICO. The results will be analysed in the HTA.
35)	9. References Page 52 Line 1236	The EVOLVE study is not referred to, while a valuable study executed with the goal to show evidence is still similar as previous and leads to continuation of reimbursement (Non-RCT).	Consider inclusion of non-RCT level data	☒Accepted ☐Accepted with modification ☐Turned down 19 non-RCTs were identified in the systematic literature searches. The scoping report only summarised RCTs, but additional levels of evidence will be considered in the HTA report, depending on the outcomes being assessed.
36)	Table 18 Sources of literature (websites) to be searched in the HTA phase Specialty websites	The Geneva Medical Association is mentioned, whereas the Swiss Society of Neurosurgery could be a relevant source.	Re-consider the sources mentioned here and verify if the Swiss Society of Neurosurgery could be a relevant source: https://www.swissneurosurgery.ch/Home	☒Accepted ☐Accepted with modification ☐Turned down This additional resource has been added to the list of grey-literature sources in Appendix A.

Stakeholder, Comment No	Location in doc. (chapter, line, page)	Comment	Suggested change	Action
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curafutura - Die innovativen Krankenversicherer
DVSP - Dachverband Schweizerischer Patientenstellen
FMCH - Dachverband der chirurgisch und invasiv tätigen Fachgesellschaften
FMH - Verbindung der Schweizer Ärztinnen und Ärzte
GDK - Schweizerische Konferenz der kantonalen Gesundheitsdirektorinnen und –direktoren
H+ - Die Spitäler der Schweiz
MTK - Medizinaltarif-Kommission
SAMW - Schweizerische Akademie der Medizinischen Wissenschaften
santésuisse - Die Schweizer Krankenversicherer
Schweizerische Neurologische Gesellschaft
SGR - Schweizerische Gesellschaft für Radiologie
SGV - Schweizerische Gesellschaft der Vertrauens- und Versicherungsärzte
SHG-SCS-SSS - Schweizerische Hirnschlaggesellschaft
SPO – Patientenschutz
Stiftung Osteoporose Schweiz
SVBG/FSAS - Schweizerischer Verband der Berufsorganisationen im Gesundheitswesen
Swiss Medtech
swiss orthopaedics - Schweizerische Gesellschaft für Orthopädie und Traumatologie