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SUMMARY WITH CRITICAL APPRAISAL

Laser Spine Surgery for Herniated Discs and/or Nerve Root Entrapment: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Context and Policy Issues

Back pain is a very common condition affecting an estimated 60% to 80% of adults at some point throughout the lifespan.[1,2] In Canada, back pain is the most commonly reported type of chronic pain, accounting for almost one-third of chronic pain among Canadians.[3] For an estimated 80% to 90% of sufferers, back pain is acute and either resolves spontaneously or following medical and/or non-surgical treatment.[4,5] A minority of those whose back pain symptoms persist for longer than 12 weeks are considered to suffer from chronic back pain.[6]

Herniated disc and/or nerve root entrapment are common causes of chronic back pain.[7,8] In patients with herniated disc, the inner nucleus of the disc protrudes through the outer annulus into the intervertebral space — sometimes compressing nerve tissue and causing pain.[9] Nerve root entrapment is sometimes caused by herniated disc, but can also be caused by other conditions — including spinal stenosis[10] — and can result in radicular pain that extends into a limb, causing discomfort and/or disability.[11] Symptoms experienced by patients suffering from these conditions can be extremely variable — from no or minimal discomfort to severe pain, disability and disruption of daily life and activities.[4,7,12] Notably, chronic back pain, such as that produced by herniated disc and/or nerve root entrapment, is described as a significant contributor to disability leave[13] and/or hospital admission.[1]

For patients with chronic back pain caused by herniated disc and/or nerve root entrapment, surgical intervention may be indicated; though, long-term outcomes may be comparable to those in patients who undergo less-invasive, medical or non-surgical therapy.[6,8] Conventional surgery for patients with herniated disc and/or nerve root entrapment involves an open technique that carries an important risk of infection and/or prolonged patient recovery.[5,8] Consequently, minimally invasive surgical approaches have been developed in the past several decades and rely on a variety of particular tools and techniques, including lasers. Often, laser spine surgery for herniated disc is referred to as percutaneous laser disc decompression (PLDD).[7,11,14]

As with other minimally invasive surgical techniques, PLDD uses a catheter or cannula to allow for insertion of a laser surgical tool into the intervertebral space. The laser delivers focused light energy and heat to the disc's nucleus, vaporizing water content and thereby altering the protein structure of the disc, relieving intradiscal pressure.[4] The procedure, like other open and minimally invasive techniques, is intended to reduce disc herniation and/or relieve pressure on any affected nerve root(s).[11] Theoretical and purported benefits of the use of lasers in minimally invasive spine surgical procedures include a lower risk of injury to surrounding tissues; decreased risk of infection, and; shorter recovery time following surgery.[12,15]

Despite more than 25 years since the U.S. Federal Drug Administration (FDA) approved the use of lasers in percutaneous disc decompression[7,8], there is a general consensus in the literature that high-quality evidence informing their use is lacking.[6,11,15] Complicating this gap in the evidence is the rapid proliferation of outpatient laser spine surgical treatment centres that promise favourable outcomes to patients suffering from herniated disc and chronic back pain — sometimes at a considerable cost to the patient.[16,17]

The purpose of this report is to search, synthesize and summarize evidence describing the clinical effectiveness, cost-effectiveness, and evidence-based guidelines addressing laser spine surgery in patients with herniated disc and/or nerve root entrapment.

Research Questions

1. What is the clinical effectiveness of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?
2. What is the cost-effectiveness of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?
3. What are the evidence-based guidelines associated with the use of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?

Key Findings

In general, findings from non-randomized and observational research report that laser spine surgery is effective in reducing pain in patients with herniated disc and/or nerve root entrapment. Two randomized controlled trials (RCTs) concluded that there were no significant differences in short-term post-operative back pain or functional disability between patients who underwent surgery using laser versus conventional techniques. However, the authors of one RCT reported significantly higher levels of lumbar back pain at one-year follow up in patients who underwent laser spine surgery as compared to those who underwent conventional, open surgery, and; significantly higher levels of radicular pain were observed at 14 days, 2 months and one-year post-surgery in patients who underwent the laser surgical procedure. Authors of a second RCT reported no difference in functional disability between patients who underwent laser versus conventional surgical procedures; however, at one-year follow up, a significantly higher proportion of patients in the laser spine surgery group had required re-operation with conventional, open surgery.

No relevant economic studies regarding the cost effectiveness of laser spine surgery in patients with herniated disc and/or nerve root entrapment were identified.

One eligible guideline from the United States did not state any recommendation with regard to percutaneous lumbar laser disc decompression due to a lack of high-quality evidence.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and March 28, 2017.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened all citations returned from the literature searches, and selected eligible studies and guidelines. In the first phase of screening, titles and abstracts were reviewed for relevance. Titles and abstracts deemed to be potentially relevant were then retrieved and assessed for eligibility using full-text. The inclusion of sources at all levels of screening was based on the eligibility criteria outlined in Table 1.

Table 1: Selection Criteria

Population	Adult patients with herniated discs and/or nerve root entrapment
Intervention	Laser spine/back surgery
Comparator	Q1-2: Current standard of surgical care in Canada (e.g., including but not limited to: discectomy open surgery, less invasive surgery; i.e., none using lasers); No treatment/sham
Outcomes	Q1: Clinical effectiveness (e.g., reduction in pain) , safety (e.g., patient benefits and harms) Q2: Cost-effectiveness outcomes (e.g., cost per increase in quality-adjusted life years (QALY), cost per pain/disability avoidance) Q3: Evidence-based guidelines specific to laser spine surgery, including recommended indications.
Study Designs	Health techonology assessments/systematic reviews/meta-analyses, randomized controlled trials, economic evaluations, evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, were included and described within systematic reviews that were included in this review, or were published prior to 2012.

Critical Appraisal of Individual Studies

Included systematic reviews were critically appraised using the AMSTAR tool;[18] clinical studies were critically appraised using the Downs and Black checklist,[19] and; clinical guidelines were assessed using the AGREE II instrument.[20] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations assessed in each included study and guideline were described.

Summary of Evidence

Quantity of Research Available

A total of 83 citations were identified in the electronic database search. Following the screening of titles and abstracts, 48 citations were excluded and 35 potentially relevant reports were selected for full-text review. In addition, the grey literature search identified two potentially relevant publications. Full-text review of the resulting 37 potentially relevant sources identified 32 that were ineligible for various reasons and excluded from this review. Five reports met the review's inclusion criteria and are described in this report. Appendix 1 outlines study selection using a PRISMA diagram.

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

One eligible health technology assessment (HTA) (in the form of a rapid HTA report); two randomized controlled trials (RCTs) and; one evidence-based guideline were eligible for inclusion in this review. No studies of cost-effectiveness were identified. Additional details describing the characteristics of included studies are reported in Appendix 2.

HTA

One relevant HTA report was identified from the Emergency Care Research Institute (ECRI) in the United States (i.e., a 'Hotline Response' report).[14] The authors sought evidence informing the use of percutaneous laser disc decompression (PLDD) in patients with herniated lumbar disc.[14] The report describes a search of PubMed, the Cochrane Library and grey literature sources between January 1, 2011 and August 19, 2016, followed by full-text retrieval of eligible systematic reviews only (all other included study designs underwent an abstract review only).

The rapid HTA report identified nine clinical studies and four eligible guidelines. Of the guidelines, one overlapped with the guideline identified in the current review.[15] The clinical studies included in the rapid HTA were two reviews (one systematic review and one literature review that did not employ a systematic methodology), one RCT and six non-randomized/observational studies. Two of these nine clinical studies overlapped with those identified as eligible studies within the current review (one systematic review[8] and one RCT[7]). Because the overlapping systematic review[8] was described by the authors of the rapid HTA, we excluded it from this review. Conversely, the overlapping guideline[15] and RCT[7] were both retained in this review to allow for full-text retrieval and data abstraction.

Randomized Controlled Trials

Two RCTs were identified: one conducted in Iran[12] and the other in the Netherlands.[7] Both trials describe a non-inferiority design to compare laser with conventional, open surgical approaches. Abrishamkar and colleagues studied plasma-laser nucleoplasty in 200 patients with herniated lumbar disc in one centre;[12] while Brouwer and colleagues studied PLDD in 115 patients with sciatica due to herniated disc across eight centres.[7] The comparator in both trials was conventional, open surgery. Block randomization was used in both trials; however, blinding to treatment allocation was not possible in either study due to the nature of the intervention (e.g., visible scar).

The primary outcome in the Abrishamkar trial was pain measured using a numeric pain scale rating (i.e., no elaboration or reference was provided regarding this measure). In the Brouwer trial, the primary outcomes were self-reported functional disability measured using the Roland-Morris Disability Questionnaire (RDQ); back and leg pain using the Visual Analog Scale (VAS) and self-reported, perceived recovery using a 7-point Likert scale. The non-inferiority margin in the Abrishamkar et al. trial was reported as a minimally important difference of 0.8 on the pain scale; however, no rationale for this threshold was provided. In the Brouwer et al. trial, the non-inferiority margin was specified as 4 on the RDQ, based on the assertion that this is the commonly recognized minimally important difference (though, no citation is provided in support of this). Both trials also reported on secondary outcomes, including measures of function, surgical complications and the proportion of patients requiring re-operation. Brouwer and colleagues specified that secondary outcomes were analyzed for superiority, rather than non-inferiority (as with the primary outcomes). Finally, both studies used a repeated-measure ANOVA to analyze data on the primary outcome at various time points, ending at one-year of follow-up.

Evidence-based Guideline

One eligible evidence-based guideline was identified from the American Society of Interventional Pain Physicians (ASIPP) in the United States.[15] The guideline is comprised of two published reports: one is a background document which also describes methodological

detail,[21] and the other focuses on a presentation of evidence in support of guidance and recommendations.[15]

While the guideline was expansive, broadly considering chronic spinal pain and multiple interventions that are not relevant to the current review, one subsection of the guideline specifically addressed PLDD as a surgical intervention for herniated disc and/or nerve root entrapment.[15] As part of the evidence reviewed, the ASIPP guideline detailed the findings of the systematic review reported by Singh and colleagues[8] that was earlier excluded from this review due to its duplicate inclusion in the rapid HTA[14] described in this report, as above.

Summary of Critical Appraisal

Strengths of the rapid HTA by ECRI[14] include a comprehensive search of more than one electronic database, supplemented by a search of selected grey literature sources. As well, included studies were described in some detail, and a complementary list of additional, relevant sources was included in the report's appendix.

Several methodological limitations were noted of the rapid HTA. For instance, neither a protocol, nor *a priori* methods were referenced and no description of source selection or explicit rationale for the exclusion of studies was reported.

The RCTs by Abrishamkar et al.[12] and Brouwer et al.[7] featured some strengths, including clear study objectives, patient eligibility criteria and outcomes of interest. Both described study power calculations — including an explanation of the expected variability in the primary outcome. Treatment assignment was randomized in both studies; though, the Brouwer et al. report provided details describing the randomization procedures whereas the Abrishamkar et al. report did not. Length of follow-up was consistent for all patients in each arm of the trial, and some findings were described clearly in both reports — including observed surgical complications. Additional strengths specific to the Brouwer study included: a detailed description of the surgical interventions under study, and a report of loss to follow-up.

Several limitations of the included RCTs were also noted; for instance, several results were reported inconsistently within each paper e.g., between the abstract and table(s)/narrative (see Appendix 4; Table A8 for details). As well, neither study addressed the possibility of potentially confounding variables. Abrishamkar and colleagues neither described the surgical interventions, nor the primary outcome measure in detail, and; a lack of clarity was noted with regard to the description of the design as a non-inferiority trial (as opposed to the report of findings which describes comparative effectiveness) and, the number of patients included in the study. In addition, Abrishamkar et al. did not describe loss-to-follow-up.

Importantly, neither RCT clearly reported or addressed some of the important considerations that non-inferiority trial designs impose on the interpretation of study findings. Abrishamkar et al. did not describe a rationale for the selection of their non-inferiority margin, and did not report confidence interval values in their results, preventing validation of their conclusion regarding non-inferiority. Further, the authors of the Abrishamkar et al. study conclude that the laser procedure was as effective as conventional surgery; however, this conclusion must be interpreted with caution, as details of the non-inferiority analyses (specifically the confidence intervals describing between-group comparisons) were not provided.

Similarly, while Brouwer and colleagues were transparent about a protocol revision from an efficacy to a non-inferiority trial design (based on lower-than-expected recruitment), important features of the limitations of non-inferiority trials were likewise not described in sufficient detail. Most notably, Brouwer et al. described the experimental intervention as PLDD in their methods, but concluded that PLDD plus follow-up surgery when needed was shown to be non-inferior to conventional, open surgery. It must be emphasized that this apparent post-hoc revision to the definition of the experimental intervention represents a significant risk of bias to the results and conclusions of the study and therefore must also be interpreted cautiously.

The ASIPP clinical guideline stated a clear objective, research questions, target population and intended users.[15,21] The authors report compliance with recommended guideline development practices outlined by the Institute of Medicine (IOM). Specifically, they employed a series of systematic reviews of the literature and included sufficient detail when describing the methods used to search and identify relevant evidence. An expert working group was assembled, and levels of evidence were assigned to sources included in the development of recommendations. Finally, conflicts of interest for the guideline authors were reported.

Noted limitations of the ASIPP clinical guideline include no description of consultation with patients and/or members of the public, lack of any grading and/or quantifiable strength of recommendation accompanying specific guidance statements, and no explicit description of the guideline's applicability.

Summary of Findings

1. *What is the clinical effectiveness of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?*

All sources included in this review addressed outcomes of relevance to the clinical effectiveness of laser spine surgery in patients with herniated disc and/or nerve root entrapment. Relevant and common measures of clinical effectiveness included pain, function and proportions of patients requiring re-operation.[7,12,14,15]

Studies in this review generally reported that laser spine surgery is an effective intervention for improving pain in patients with herniated disc and/or nerve root entrapment.[7,12,14,15] The rapid HTA by ECRI[14] identified two reviews that both made conservative but favourable conclusions with regard to improvement in pain for patients who undergo PLDD. One review reported 60% to 84% pain relief in herniated disc patients at greater-than 12 months follow-up.[8] Although both reviews summarized in the ECRI rapid HTA emphasized the lack of high-quality evidence. In their own summary of included primary, non-randomized and observational studies, the authors of the ECRI rapid HTA indicate that outcomes — including pain — were generally favourable for most patients who underwent PLDD (Appendix 4; Table A7).

Pain was a primary outcome in both of the RCTs included in this review,[7,12] however, both trials sought to establish non-inferiority of the experimental laser surgical approach compared with conventional, open surgery. Consequently, the comparative clinical effectiveness of laser spine surgery versus conventional surgery with regard to pain in herniated disc and/or nerve root entrapment patients could not be established by these trials.

In the Abrishamkar et al. trial, there were no between-group differences in post-operative lumbar pain scores at 14 days, 1-, 2- and 3-months follow-up; however, at one-year follow-up, lumbar pain scores were statistically significantly higher in the plasma-laser nucleoplasty group as compared to patients who had undergone conventional, open surgery.[12] Radicular pain scores were statistically significantly higher in patients who had undergone conventional open surgery at 14 days post-surgery compared to the plasma-laser nucleoplasty group. However, at 3-months and one-year follow up, radicular pain scores were statistically significantly higher in patients who had undergone plasma-laser nucleoplasty as compared to those who underwent conventional, open surgery.

The Brouwer et al. trial showed similar short-term follow-up results with no difference in leg and back VAS pain scores at eight weeks post-intervention.[7] Unlike Abrishamkar and colleagues, Brouwer et al. found no between-group difference in pain scores at one-year of follow-up; however, the results of their repeated-measures analyses did identify a statistically significantly higher VAS leg pain score in patients who underwent PLDD as compared to those who underwent conventional surgery. Finally, the authors emphasized a significantly higher proportion of patients who required re-operation in the PLDD group compared to the conventional surgery group.

As it concerns self-reported functional disability, the Brouwer et al. trial[7] reported non-inferiority of PLDD, in combination with follow up surgery as needed, compared with conventional, open surgery (i.e., a similar degree of functional improvement was observed in both groups of patients) (Appendix 4; Table A8). The investigators also measured function as a secondary outcome using the Prolo and SF-36 Scales, reporting no significant difference in patient function between groups at all time points throughout study follow-up.

With regard to surgical complications, Abrishamkar and colleagues reported no cases of infection or discitis in either the plasma-laser nucleoplasty or conventional, open surgery groups.[12] On the other hand, Brouwer et al. describe complications in 5% of patients who underwent PLDD and 11% in patients who underwent conventional, open surgery.[7] (Appendix 4; Table A8) Specifically, transient nerve root injury occurred in three patients (5%) in the PLDD group and in one patient (2%) in the conventional surgery group. Further surgical complications reported by Brouwer and colleagues all occurred in the conventional surgery group: three patients (5%) experienced a dural tear with cerebrospinal fluid leak; one patient (2%) experienced micturition requiring catheterization, and; one patient (2%) was operated on at the wrong level. Further to these complications, Brouwer and colleagues reported technical failure of PLDD in five patients (9%).

Re-operation was a clinical outcome described by the ECRI rapid HTA,[14] which summarized the results of an observational study that reported 12.7% of 197 patients who underwent PLDD required a follow-up procedure using open, conventional surgery. Abrishamkar and colleagues reported a smaller proportion of re-operations in their study sample, with seven occurring in the plasma-laser nucleoplasty group (7%) and eight in the conventional surgical group (8%) — demonstrating no significant difference between groups.[12] On the other hand, Brouwer and colleagues emphasized a significantly higher proportion of patients in the PLDD group (44%) who required re-operation with conventional, open surgery, as compared to the conventional surgery group, in which only 16% of patients required re-operation.[7] (Appendix 4; Table A8)

Finally, the guideline addressed pain relief in patients who underwent PLDD for herniated disc and/or nerve root entrapment by summarizing the results of a systematic review of observational studies.[15,8] Their report concluded that, on average, patients who underwent

the procedure experienced 75% pain relief at greater-than 12 months follow-up (Appendix 4; Table A9).

2. *What is the cost-effectiveness of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?*

No studies addressing the cost-effectiveness of laser spine surgery in patients with herniated disc and/or nerve root entrapment were identified.

3. *What are the evidence-based guidelines associated with the use of laser spine surgery for adult patients with herniated discs and/or nerve root entrapment?*

The guideline included in this review did not make any recommendation with regard to the use of PLDD, other than to state that the evidence informing its use is limited.[15] Specifically, the guideline detailed the findings of a systematic review of observational studies,[8] and concluded the section describing PLDD by implying that the findings from double-blind RCTs are needed. Importantly however, this guideline was published in 2013, prior to the publication of the two RCTs described within this report.[12,7]

Limitations

The main limitation of this report is a persistent lack of high-quality evidence informing the use of laser spine surgery in patients with herniated disc and/or nerve root entrapment — as was concluded by both the rapid HTA[14] and clinical guideline[15] included in this review. While the relatively recent publication of two RCTs contributes toward narrowing the clinical evidence gap in this area, neither trial was designed to establish the comparative clinical effectiveness of laser spine surgical approaches against conventional surgical approaches; rather, both studies concluded that the laser spine surgical approaches under study were non-inferior to open, conventional surgery.[12,7] Further, there was no evidence identified in either the peer-reviewed or grey literature explicitly addressing the cost-effectiveness of laser spine surgical approaches. Finally, the guideline that was included in this review was unable to establish any recommendation regarding PLDD based on a lack of high-quality evidence.[15] Given that the evidence identified and summarized within this report was generated outside of Canada, its applicability to the Canadian context and health systems may be limited.

Conclusions and Implications for Decision or Policy Making

This report identified clinical evidence and a guideline addressing the use of laser spine surgery in patients with herniated disc and/or nerve root entrapment.

In general, a broad consensus in the literature emphasizes the lack of high-quality evidence addressing the use of lasers in spine surgical procedures.[15,6,14] Evidence from observational and non-randomized studies to-date suggest that laser spine surgery is an effective surgical approach for reducing pain in patients with herniated disc and/or nerve root entrapment.[14,15] While non-inferiority of laser spine surgical techniques compared to conventional, open surgery was investigated in two RCTs, it could not be confirmed by the data presented in one of the trials.[12] In the other RCT, the authors concluded that percutaneous laser disc decompression plus follow-up surgery when needed was non-inferior to conventional, open surgery — however, the addition of follow-up surgery to the experimental intervention was not clearly part of the planned analyses, representing an important risk of bias.[7]

Importantly, the superiority of laser spine surgery as compared to conventional surgery for patients with herniated disc and/or nerve root entrapment has not been demonstrated. Further, evidence from one RCT suggests that at one-year follow-up, a significantly higher proportion of patients who undergo percutaneous laser disc decompression may require re-operation as compared to conventional, open surgery patients;[7] though, the evidence with regard to this outcome is inconsistent across the two RCTs identified in this review.[12]

No evidence was identified that addressed the cost-effectiveness of laser spine surgical techniques; though, one RCT made a cursory mention of ongoing research investigating the cost-effectiveness of PLDD.[7] Given that the non-inferiority of laser spine surgery has been concluded by the authors of two RCTs additional evidence concerning cost-effectiveness will be particularly salient to clinical and health policy decision makers as it becomes available.

Finally, the authors of a clinical guideline that addressed the use of PLDD were unable to establish a specific recommendation based on a cited lack of high-quality evidence. However, this guideline was published prior to the publication of the two RCTs described herein.

In conclusion, despite the relatively recent emergence of two randomized trials investigating the non-inferiority of laser surgical techniques versus conventional, open surgery in the treatment of herniated disc, superiority of laser spine surgery for patients with herniated disc and/or nerve root entrapment has not been established. Thus, high-quality RCTs are yet needed to support evidence-informed clinical and health policy decision-making.[7]

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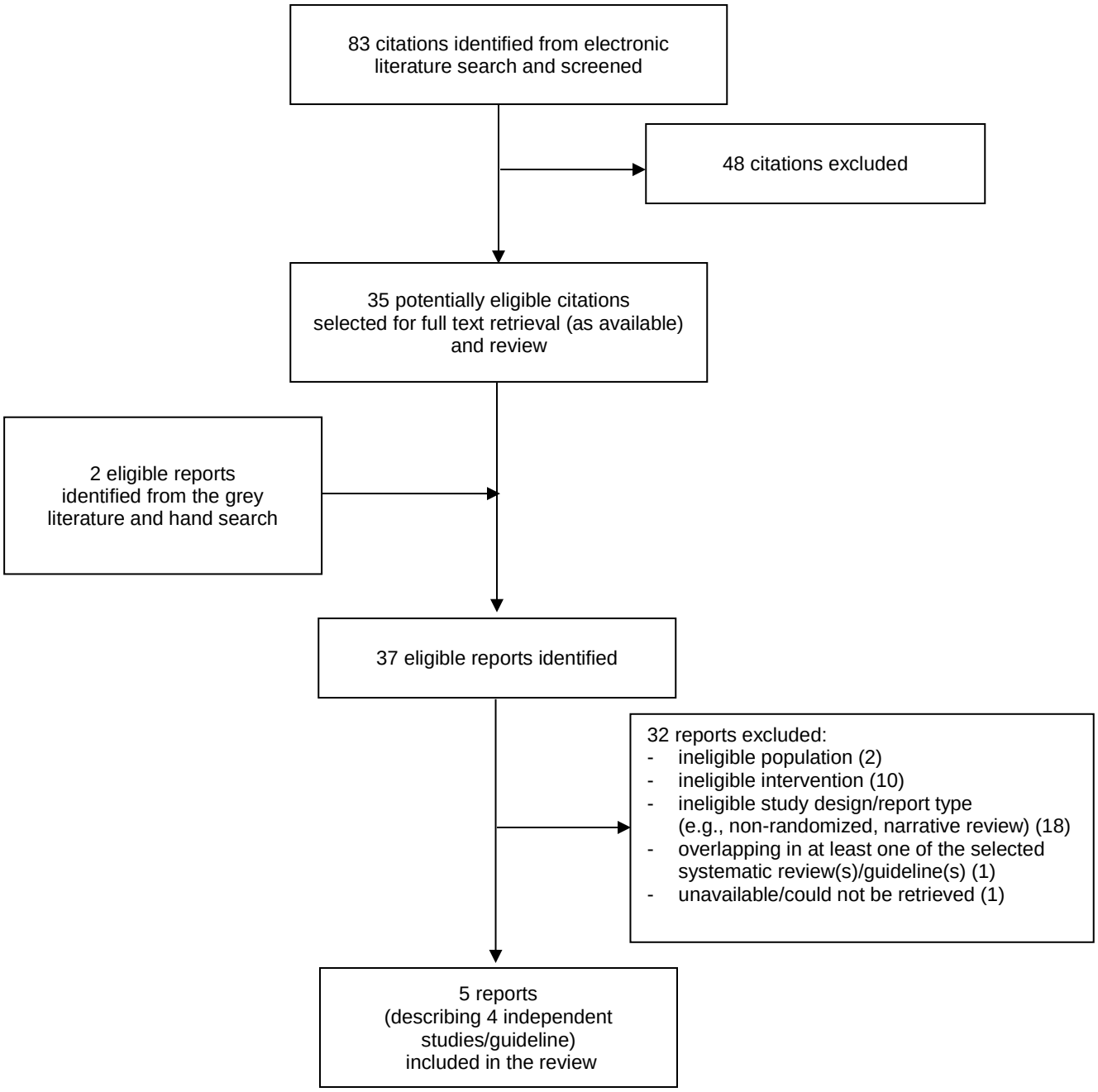
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table A1: Characteristics of the Included HTA

First Author, Publication Year, Country	Types and Numbers of Primary Studies Included	Population Characteristics	Intervention(s)	Comparator(s)	Clinical Outcomes, Length of Follow-up
ECRI 2016,[14] USA	**9 studies**: reviews (n=2); RCT (n=1); non-randomized/ observational (n=6);	Patients with herniated lumbar discs	Percutaneous laser disc decompression	Not specified	Not specified

HTA = Health Technology Assessment; ECRI = Emergency Care Research Institute; USA = United States of America; RCT = randomized controlled trial

Table A2: Characteristics of Included Randomized Controlled Trials

First Author, Publication Year, Country	Study Design	Patient Characteristics	Intervention(s)	Comparator(s)	Clinical Outcomes
Abrishamkar et al. 2015,[12] Iran	Non-inferiority RCT	Patients diagnosed with lumbar disc herniation and low back pain **N=200**	Plasma-laser nucleoplasty	Open surgical discectomy	Primary: lower back pain; lower limb pain Secondary: discitis, infection, surgical site hematoma, re-operation
Brouwer et al 2015,[7] Netherlands	Non-inferiority RCT	Adults aged 18-70 with sciatica associated with MRI-confirmed disc herniation **N=115**	Percutaneous laser disc decompression	Conventional surgical discectomy	Primary: self-reported functional disability; leg pain; back pain; self-reported recovery Secondary: function & economic (income) impact (Prolo scale); pain & physical function; sciatica symptoms; surgical complications re-operation

RCT = randomized controlled trial; MRI = magnetic resonance imagimg

Table A3: Characteristics of Included Guideline

Objectives			Methodology			
Target Population/ Intended Users	**Intervention & Practice Considered**	**Major Outcomes Considered**	**Evidence Collection, Selection & Synthesis**	**Evidence Quality Assessment**	**Development and Evaluation of Recommendations**	**Guideline Validation**
Manchikanti et al. 2013[15,21] USA						
Target population: Patients with chronic spinal pain (including from herniated disc and/or nerve root entrapment) **Intended users:** Interventional pain physicians in particular (or any specialty in general)	Interventions for the management of chronic spinal pain (including percutaneous lumbar laser disc decompression)	Primary: short- and long-term pain relief Secondary: functional improvement; psychological status; return to work; reduction/elimination of opioid/other drugs/interventions; complications	Electronic database and grey literature searches from 1966-2012 Two independent reviewers screened all citations with discrepancies addressed through discussion/consensus Meta-analyses performed where feasible	Critical appraisal performed on all included studies by two independent reviewers with discrepancies addressed through discussion and consensus/third-party review; levels of evidence assigned to each included source and described as a preamble to most recommendations	Followed the IOM approach i.e., based on a systematic review of the existing evidence; developed by a multidisciplinary panel of experts	External review was solicited by way of posting draft guidelines publicly; there is no description of whether feedback was received, nor how it was incorporated if received

USA = United States of America; IOM = Institute of Medicine

Appendix 3: Critical Appraisal of Included Publications

Table A4: Strengths and Limitations of included HTA using AMSTAR[18]

Strengths	Limitations
ECRI 2016[14]	
• Comprehensive search including grey literature • Included studies described in sufficient detail • List of potentially relevant sources not included in the review is presented	• No protocol nor reference to methods established *a priori* • No description of source selection • Rationale for exclusion of studies not described in detail • Critical appraisal not described

Table A5: Strengths and Limitations of Randomized Controlled Trials using the Down's & Black Checklist[19]

Strengths	Limitations
Abrishamkar, 2015[12]	
• Study objectives, outcomes (including potential variability) and patient characteristics are described in sufficient detail • Power calculation described • Study sample appeared to be representative of the population • Treatment assignment was randomized • Follow-up was consistent across patients • Main study findings are reported clearly • Surgical complications are described	• Non-inferiority design does not allow for the ascertainment of effectiveness • Study interventions not described in detail • Potentially confounding variables not described • Method of randomization not reported • No intention-to-treat analyses described • Loss to follow-up not reported • Confidence interval values not reported, prohibiting confirmation of the conclusion regarding non-inferiority
Brouwer, 2015[7]	
• Study objectives, outcomes (including potential variability), patient characteristics and interventions are described in sufficient detail • Power calculation described • Study sample appeared to be representative of the population • Treatment assignment was randomized • Method of randomization described in detail • Follow-up was consistent across patients • Main study findings are reported clearly • Loss to follow-up described • Intention-to-treat analyses described • Surgical complications are described	• Non-inferiority design does not allow for the ascertainment of effectiveness • Potentially confounding variables not described • *Post hoc* protocol amendment was necessary due to lower-than-expected recruitment • Concluding statement with regard to non-inferiority refers to a modified intervention (i.e., PLDD plus follow up surgery when needed) as compared to that described within the methods (i.e., PLDD)

Table A6: Strengths and Limitations of the Clinical Guideline using AGREE II20

Strengths	Limitations
Manchikanti et al. 2013,[15,21] U.S.A.	
• Guideline objectives, health questions and target population are clearly described • Methods for guideline development included systematic reviews of available evidence, an expert working group, external review and establishment of update procedures • Explicit links between the evidence and recommendations are made • Conflicts of interest among guideline authors are reported	• Consultation with patients/public in the development of the guideline is not described • Recommendations were not assigned a 'grade' or strength • Applicability of the guideline is not addressed in detail • Guideline authors state that no source of funding supported the development of the guidelines

Appendix 4: Main Study Findings and Authors' Conclusions

Table A7: Summary of Findings of Included Rapid HTA

Main Study Findings	Author's Conclusion
ECRI 2016[14]	

• Nine relevant clinical studies were included in the report
• Though studies addressing cost-effectiveness were sought, none were identified
• No clinical evidence was identified indicating superiority of percutaneous laser disc decompression compared with other treatments for herniated disc.
• Both reviews included observational studies only
  ○ Findings were suggestive of effectiveness of percutaneous laser disc decompression
  ○ Need for high-quality trials to demonstrate effectiveness definitively was emphasized
• Included RCT demonstrated non-inferiority of percutaneous laser disc decompression compared to conventional, open surgery
  ○ Re-operations were significantly higher in the laser disc decompression group
• Findings from included observational and non-randomized studies suggest favourable outcomes for 63% -92% of patients in the short-term, and 67%-87% of patients in the long-term
• Clinical guidelines included in the review either explicitly recommend against laser spine surgery, or emphasize the lack of evidence in support of establishing recommendations.
	• No conclusions were reported.

ECRI = Emergency Care Research Institute; RCT = randomized controlled trial

Table A8: Summary of Findings of Included Randomized Controlled Trials

Main Study Findings	Author's Conclusion
Abrishamkar, 2015[12]	

• 100 patients randomly assigned to each arm of the trial
  ○ Loss to follow-up not reported
• Lumbar pain scores at baseline and 3 months post-intervention:
  ○ Plasma-laser nucleoplasty group, mean (SD)
  ▪ 6.92 (±2.5) to 3.43* (±2.3)
  ○ Conventional, open surgery group, mean (SD)
  ▪ 7.5 (±2.2) to 3.04 (±1.6)
  ○ Between group difference non-significant at 3 months post-intervention (P=0.24)
  ○ At 1 year post-intervention, the between group difference in lumbar pain was significant i.e., increased pain in the plasma-laser nucleoplasty group (P=0.004)
• Radicular pain scores at baseline and 3 months post-intervention**
  ○ Plasma-laser nucleoplasty group
	Despite the study's stated interest in whether plasma-laser nucleoplasty is non-inferior to conventional surgery, the authors' conclusions address comparative effectiveness of nucleoplasty versus conventional surgery: "…nucleoplasty is as effective as open discectomy in the treatment of lumbar disc herniation…". (p. 1133)
	
	Further, the authors conclude that, because nucleoplasty involves less time during the surgical procedure; quicker patient recovery; higher patient compliance and; lower cost, it is more favourable than conventional surgery and thus "… can be considered as a first line method for treatment of patients with single

Table A8: Summary of Findings of Included Randomized Controlled Trials

Main Study Findings	Author's Conclusion
▪ 7.89 (±2.1) to 3.53 (±2.7) ○ Conventional, open surgery group ▪ 8.1 (±1.2) to 2.88 (±1.2) ○ Between group difference significant i.e., increased pain in the plasma-laser group (P=0.03) ○ At 1 year post-intervention, the between group difference in back pain was significant i.e., increased pain in the plasma-laser group (P=0.004) • Surgical complications ○ Infection/discitis ▪ None observed in either group at 6 months post-intervention • Re-operation required ○ 7 (7%) patients in the plasma-laser group ○ 8 (8%) patients in the conventional surgery group ○ Between-group difference non-significant (P=0.73) *While the abstract reports a post-surgical pain score of 3.43 in the plasma-laser nucleoplasty group at 3 months post-surgery, Table 2 indicates a score of 3.42 at the same time point; the conservative estimate is presented here. **The abstract and Table 2 report different radicular pain scores per group, as measured at 3 months post-intervention; the results from Table 2 are presented here.	level disc herniation." (p. 1136)
Brouwer, 2015[7]	
• 115 patients randomly assigned to each arm of the trial ○ Loss to follow-up: ▪ 1/57 from the percutaneous laser disc decompression arm (2%) ▪ 2/58 from the conventional microdiscectomy arm (4%) • Primary outcomes: ○ Roland-Morris Disability Questionnaire (RDQ) i.e., Δ from baseline (95% CI) ▪ At 8 weeks follow-up, between-group difference non-significant -0.1 (-2.3 to 2.1) ▪ At 52 weeks follow-up, between-group difference non-significant -0.2 (-1.6 to 1.2) ○ Visual Analog Scale (VAS) for leg pain i.e., Δ from baseline (95% CI) ▪ At 8 weeks follow-up, between-group difference non-significant -5.7 (-15.0 to 3.7) ▪ At 52 weeks follow-up, between-group difference significant -6.9 (-12.6 to -1.3) in favour of conventional surgery ○ Visual Analog Scale (VAS) for back pain i.e., Δ from baseline (95% CI) ▪ At 8 weeks follow-up, between-group difference non-significant -6.3 (-15.5 to 2.9) ▪ At 52 weeks follow-up, between-group difference non-significant -4.6 (-10.4 to 1.1)	The authors conclude that: "At 1 year, a strategy of PLDD, followed by surgery if needed, resulted in noninferior outcomes compared with surgery." (p. 858) The authors highlight concern over the proportion of re-operations in the percutaneous laser disc decompression group i.e., greater-than one-third, specifically citing potential cost as a key consideration

Table A8: Summary of Findings of Included Randomized Controlled Trials

Main Study Findings	Author's Conclusion
○ Perceived recovery (7-point Likert scale) i.e., time to first recovery (95% CI) ▪ Significantly longer perceived recovery time in the percutaneous laser disc decompression group i.e., 8 weeks (3.2 to 12.8) versus the conventional surgery group, 6 weeks (5.2 to 6.9) • Surgical complications ○ 5% in the percutaneous laser disc decompression group ○ 11% in the conventional surgery group • Re-operation required ○ 44% in the percutaneous laser disc decompression group* ○ 16% in the conventional surgery group *While the abstract reports that 38% of patients in the PLDD arm requiring re-operation, the results detail both the absolute number of patients requiring re-operation (i.e., 24/55 patients in the PLDD group) and the corresponding proportional value (i.e., 44%); thus, the latter value is presented here.	

RCT = randomized controlled trial; PLDD = percutaneous laser disc decompression

Table A9: Summary of the Included Clinical Guideline

Relevant Findings and Recommendation
Manchikanti et al. 2013[15,21] U.S.A.
• Fifteen observational studies were included in the authors' review of available evidence to inform the use of PLDD. ○ **N.B.** the findings reported in the relevant subsection of the guideline are drawn from the systematic review by Singh et al.[8] that was excluded from this review due to overlap ○ The authors report that 3,171 patients who underwent PLDD were included in a synthesis of these 15 observational studies, which found that patients experienced, on average, 75% pain relief long-term (i.e., >12mos) • Guideline authors emphasize a lack of quality scientific evidence and the importance of high-quality RCTs to inform clinical decision-making around the use of lasers in percutaneous disc decompression surgery. • No explicit recommendation regarding PLDD is made, based on a lack of existing high-quality evidence i.e., ○ "The evidence, based on all available observational studies, is limited for percutaneous lumbar laser disc decompression in managing disc herniation. However, the results of a randomized, double-blind controlled trial have not been published yet." (p. S109)

U.S.A. = United States of America; PLDD = percutaneous laser disc decompression; RCT = randomized controlled trial

Appendix 5: Additional References of Potential Interest

Quirno M, Vira S, Errico TJ. Current Evidence of Minimally Invasive Spine Surgery in the Treatment of Lumbar Disc Herniations. Bull Hosp Jt Dis (2013). 2016 Mar;74(1):88-97.
N.B. Potentially relevant non-systematic review

Ong D, Chua NH, Vissers K. Percutaneous Disc Decompression for Lumbar Radicular Pain: A Review Article. Pain Pract. 2016 Jan;16(1):111-26.
N.B. Potentially relevant non-systematic review

Singh V, Manchikanti L, Calodney AK, Staats PS, Falco FJ, Caraway DL, et al. Percutaneous lumbar laser disc decompression: an update of current evidence. Pain Physician. 2013 Apr;16(2 Suppl):SE229-SE260.

N.B. Relevant systematic review excluded from the current review due to overlapping inclusion in sources that were included in the current review

UptoDate [Internet]. Waltham (MA): Wolters Kluwer. Subacute and chronic low back pain: surgical treatment; 2016 [cited 2017 Apr 4]. Available from: http://www.uptodate.com

N.B. Potentially relevant non-systematic review

Decompression of intervertebral discs using laser energy (laser discectomy) or radiofrequency energy (nucleoplasty) [Internet]. Portland (OR): The Regency Group (BlueCross BlueShield Association); 2016. Report No.: Medical Policy no. 131. [cited 2017 Apr 4]. Available from: http://blue.regence.com/trgmedpol/surgery/sur131.pdf

N.B. Potentially relevant policy document

Guideline summary: low back pain medical treatment guidelines. In: National Guideline Clearinghouse [Internet]. Bethesda (MD): Agency of Healthcare and Research Quality; 2014 [cited 2017 Apr 4]. Available from: https://guideline.gov/summaries/summary/49020

N.B. Non-specific condition(s) described that may bear some relevance to those of interest for this review

BlueCross & BlueShield of Mississippi [Internet]. Jackson (MS): BlueCross BlueShield of Mississippi; 2017. Decompression of the intervertebral disc using laser energy (laser discectomy) or radiofrequency coblation (nucleoplasty); 2017 [cited 2017 Apr 4]. Available from: http://www.bcbsms.com/medical-policies.html#/policy-detail?id=3c13eaa5-3578-419a-81ad-eadfd000f0a3

N.B. Potentially relevant policy document. Copy and paste link into browser.

Clyde BL. eBrainMD (blog) [Internet]. Bountiful (UT): eBrainMD.com; 2013. Laser discectomy; 2013 [cited 2017 Apr 4]. Available from: https://www.ebrainmd.com/blog.php?id=28

N.B. Potentially relevant non-systematic review

North American Spine Society. Clinical guidelines for diagnosis and treatment of lumbar disc herniation with radioculopathy [Internet]. NASS Evidence-Based Clinical Guidelines Committee, editor. Burr Ridge (IL): North American Spine Society; 2012. [cited 2017 Oct 4]. Available from: https://www.spine.org/Portals/0/Documents/ResearchClinicalCare/Guidelines/LumbarDiscHerniation.pdf

N.B. Non-specific intervention(s) described that may bear some relevance to those of interest for this review