Decision Memo for Percutaneous Image-guided Lumbar Decompression for Lumbar Spinal Stenosis (CAG-00433R)

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Decision Summary

After considering public comments as required by section 1862(l) of the Social Security Act, CMS will finalize its proposal to continue CED and expand the January 2014 NCD. CMS will cover through a prospective longitudinal study PILD procedures using an FDA-approved/cleared device that successfully completed a CMS-approved RCT that met the criteria listed in Section 150.13 of the NCD manual.

In addition, the CMS-approved prospective longitudinal study must answer at least one of the following questions:

1. *Does PILD provide a clinically meaningful improvement of function (e.g., reduced acute and post-acute hospitalizations, nursing home care or inpatient rehabilitation services) and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?*
2. *Does PILD provide a clinically meaningful reduction in pain (e.g., as measured by class, dose, duration of prescription pain medication use) in Medicare beneficiaries with LSS compared to other treatments?*
3. *Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services (e.g., repeat PILD procedures, other interventions and surgical treatments), compared to other treatments?*

The prospective longitudinal study must also meet the following criteria:

1. The protocol must specify a statistical analysis and a minimum length of patient follow-up time that evaluates the effect of beneficiary characteristics on patient health outcomes as well as the duration of the benefit.
2. The eligibility requirements, both inclusion and exclusion criteria that were specified in the CMS-approved RCT protocol, must be maintained in the new prospective longitudinal study.
3. All study sites and study results must be listed in the ClinicalTrials.gov database.

All CMS-approved clinical research studies must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Research & Quality (AHRQ) Registry of Patient Registries (RoPR).
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

All clinical research study protocols must be reviewed and approved by CMS. The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator's contact information, to the address below.

Director, Coverage and Analysis Group
Re: PILD CED

Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850

Email address for protocol submissions: clinicalstudynotification@cms.hhs.gov
Email subject line: "CED [NCD topic (i.e. PILD)] [name of sponsor/primary investigator]"

The information will be reviewed, and approved studies will be identified on the CMS website - https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html.

See Appendix B for our proposed manual language.

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Decision Memo

TO: Administrative File: CAG-00433R

FROM: Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group

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Tara Hall, LGSW
Analyst

SUBJECT: National Coverage Determination for Percutaneous Image-Guided Lumbar Decompression (PILD) for Lumbar Spinal Ste

DATE: December 7, 2016

I. Decision

After considering public comments as required by section 1862(l) of the Social Security Act, CMS will finalize its proposal to continue CED and expand the January 2014 NCD. CMS will cover through a prospective longitudinal study PILD procedures using an FDA-approved/cleared device that successfully completed a CMS-approved RCT that met the criteria listed in Section 150.13 of the NCD manual.

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See Appendix B for our proposed manual language.

II. Background

Throughout this document we use numerous acronyms, some of which are not defined as they are presented in direct quotations. Please find below a list of these acronyms and corresponding full terminology:

AAOS - American Association of Orthopaedic Surgeons
ASA -American Society of Anesthesiologists
BMI - body mass index
CED - Coverage with Evidence Development
CI - confidence interval
CMS - Centers for Medicare & Medicaid Services
CT - computed tomography
ECRI - Emergency Care Research Institute
ESI - epidural steroid injection
FDA - Food and Drug Administration
LF - ligamentum flavum
LSS- lumbar spinal stenosis
MIC - minimal important change
MILD® - minimally invasive lumbar decompression
MRI - magnetic resonance imaging
NASS - North American Spine Society
NC - neurogenic claudication
NCA - National Coverage Analysis
NCD - National Coverage Determination
NIH- National Institutes of Health
NPRS - numeric pain rating scale
NRS - numeric rating scale
ODI - Oswestry Disability Index
PDI - Pain Disability Index
PE - pulmonary embolism
PILD - percutaneous image-guided lumbar decompression
PROMIS - Patient-Reported Outcomes Measurement Information System
RCT - randomized controlled trial
US - United States
VAS - Visual Analog Scale
ZCQ - Zurich Claudication Questionnaire

The scope of this national coverage analysis (NCA) includes a review of the evidence on whether PILD improves health outcomes in Medicare beneficiaries with LSS.

Most people will experience low back pain at some point in their lives. Pain complaints are the leading reason for medical visits. The most common pain complaints are musculoskeletal, and back pain is the most common of these, and the prevalence and impact of back pain have led to an expanding array of tests and treatments, including injections, surgical procedures, implantable devices, and medications. (Deyo et al. 2009)

Spinal stenosis is the most common reason for lumbar spine surgery in adults over the age of 65 years. (Weinstein et al. 2008) Spinal stenosis often results from the aging process. Surgery for spinal stenosis was reported to be the fastest- growing type of lumbar surgery in the United States from 1980 to 2000. Rates of surgery for lumbar stenosis declined slightly from 2002-2007, but use of more complex procedures has increased substantially. (Deyo et al. 2010)

A 1995 population study in Sweden reported spinal stenosis incidence of 50 per 100,000; an incidence of 25 per 100,000 inhabitants for spinal stenosis associated claudication; and, an incidence of 1 per 100,000 for cauda equina syndrome. (ECRI Health Technology Assessment Group 2001)

Lumbar spinal stenosis (LSS) is defined as the reduction of the cross sectional area, i.e. narrowing, of the lumbar spinal canal. It is usually caused by spinal degenerative conditions and is commonly found to be asymptomatic. (Kovacs et al. 2011) LSS is sub-classified into three broad categories, specifically central stenosis, lateral stenosis, and spondylolisthesis. Central stenosis refers to a narrowing of the spinal canal across the anterioposterior diameter, the transverse diameter, or both". (ECRI 2001)

Symptomatic patients typically present with symptoms of radicular leg pain or with neurogenic claudication (pain in the buttocks or legs on walking or standing that resolves with sitting down or lumbar flexion). Indications for surgery appear to vary widely, and rates of procedures vary five-fold or more across geographic areas. (Weinstein et al. 2008)

The geographic variation in treatment of LSS, the lack of a definitive diagnostic tool, and the absence of reliable evidence about the natural history of the condition bring up issues on how to best approach the treatment of LSS. The North American Spine Society (NASS) evidence-based clinical guideline identified an absence of reliable evidence about the natural history of degenerative lumbar stenosis. (NASS 2011) The ECRI technology assessment reported, "… the presence of apparent stenosis in the asymptomatic population raises a question about whether stenosis per se causes symptoms, those with more severe symptoms are more likely to have stenosis. …The presence of stenosis and slippage in spinal images of asymptomatic people indicates that treatment must be based on the convergence of symptoms and image evidence rather than on either type of evidence alone." (ECRI 2001)

Haig reported, "Some clinicians use the term stenosis to describe statistical deviation from average size of the spinal canal or neural foramen regardless of the symptoms, while others use it to describe a clinical syndrome that presents classically with neurogenic claudication-pain in the back or legs with ambulation." (Haig et al. 2006) There are no standard criteria for the clinical diagnosis of stenosis. Anatomic measures can be obtained via

imaging tests such as magnetic resonance imaging (MRI), which have become a standard for diagnosis. However no clear relation between the severity of symptoms and the extent of stenosis on imaging exists; and surgical outcomes do not clearly relate to the results of imaging measures. In addition, no cutoff for canal size measurement to diagnose the clinical syndrome has been widely accepted. (Haig et al. 2006)

Little is known about the diagnostic accuracy of the different tests available in detecting LSS. (de Graaf et al. 2006) De Graaf talked about an ideal situation with a "clear diagnostic entity with an agreed gold standard to prove its existence as well as knowledge about the natural course and effectiveness of treatments." However, there is no consensus about the gold standard. After a systematic review of the accuracy of diagnostic tests for the diagnosis of LSS, de Graaf could not "draw any firm conclusions about the diagnostic accuracy of imaging, clinical, and other tests in diagnosing lumbar spinal stenosis." (de Graaf et al. 2006)

It appears consensus concerning the definition of spinal stenosis has not been reached among experts. There is no "gold standard" for diagnosis and treatment of stenosis because of variable signs and symptoms, physicians' history-taking and physical methods and diagnostic tests. (Sandella et al. 2013)

LSS is a pathological condition causing a compression of the contents of the canal, particularly the neural structures. In 2003, Gunzburg and Szpalski opined that if compression does not occur, the canal should be described as narrow but not stenotic. Degenerative disc disease is the most common cause of LSS. A bulging degenerated intervertebral disc anteriorly, combined with thickened infolding of ligamenta flava and hypertrophy of the facet joints posteriorly result in narrowing of the spinal canal. The site of compression may be central, lateral or a combination of the two. "When a canal size is too narrow for the dural sac size that it contains, stenosis occurs. An identical canal size can therefore be stenotic for one person while not being stenotic for another who happens to have a smaller dural sac size. LSS is therefore a clinical condition and not a radiological finding or diagnosis." (Gunzburg and Szpalski 2003)

The utility of diagnostic imaging studies should be to confirm the information gathered from a thorough history and physical exam. In 1996, Boden warned, "Excessive reliance on diagnostic studies without precise clinical correlation can lead to erroneous or unindicated treatment of degenerative disorders of the lumbar spine." (Boden 1996) The clinical syndrome for stenosis does not always present with classic complaints on examination, and similar symptoms occur in a wide variety of disorders ranging from vascular disease to polyneuropathy to mechanical back pain. According to Haig (2006), further confusion can come into play when a radiologist's report of stenosis influences the clinician's impression.

"Because other causes of back pain are both common and difficult to prove, it is possible that mechanical backache, perhaps in conjunction with coincident neuropathy or other unrelated leg complaint, might lead to inappropriate treatment including surgery. Thus accurate diagnosis of the clinical syndrome of spinal stenosis is of critical importance." (Haig et al. 2006)

"When a patient presents with LSS symptoms and confirmatory imaging, unless they have an absolute indication for surgery (rapidly progressive neurologic decline, clinically relevant motor deficits, or cauda equina syndrome), the treatment algorithm begins with nonoperative management." (Kurd et al. 2012)

Unfortunately, there remains a lack of consensus among clinicians about the indications for surgical intervention for LSS. (Kurd et al. 2012) Non-surgical or conservative care for LSS may include physical therapy, epidural injections, chiropractic manipulation, acupuncture, lumbar corset, the use of anti-inflammatory drugs, and the use of opioid analgesics.

Treatment options for LSS, historically, have varied from conservative management on the one hand and invasive surgical decompression on the other hand. There is a gap for patients failing the former but not severe enough or not ready for the latter. (Mekhail et al. 2012) "While conservative measures, such as physical therapy with/without epidural steroid injections, may be adequate for mild cases, they fail to provide long-term relief to the moderate-to-severe LSS patient and, thus the progression to the next treatment option of surgery. The goal of surgical treatment for symptomatic lumbar canal stenosis is to achieve relief of symptoms by adequate neural decompression while preserving as much of the anatomy and not disrupting the biomechanics of the lumbar spine as possible." (Mekhail et al. 2012)

The AAOS website provided the following information about surgical options for LSS.

"Surgery for lumbar spinal stenosis is generally reserved for patients who have poor quality of life due to pain and weakness." In the past there have been two main surgical options to treat LSS – laminectomy and spinal fusion when there is spinal instability. The laminectomy procedure involves removing the bone and ligaments that are compressing the nerves. The traditional laminectomy procedure has been performed as an open procedure however a laminectomy can also be done using a minimally invasive method. These newer, minimally invasive decompression procedures are performed using smaller incisions and surgeons rely more on microscopes to see the area of surgery. Another minimally invasive procedure is the placement of an interspinous process device which involves placing a spacer between the spinous process in the back of the spine to keep the space for the nerves open by spreading the vertebrae apart." (AAOS 2013)

The focus of this national coverage analysis is on a newer technique - percutaneous image-guided lumbar decompression (PILD) which is a posterior decompression of the lumbar spine performed under indirect image guidance without any direct visualization of the surgical area. The use of a cannula and trocar provides a portal that allows access to the anatomic area for instruments used for resection. This is a procedure proposed as a treatment for symptomatic LSS unresponsive to conservative therapy. This procedure is generally described as a relatively non-invasive (compared to open surgery) procedure using specially designed instruments to percutaneously remove a portion of the lamina and debulk the ligamentum flavum. (The terms non-invasive, minimally invasive and percutaneous are used interchangeably in the literature.) In addition to providing durable symptomatic relief, another important goal of PILD is to avoid the need of invasive spinal surgery and to reduce patient harms The procedure is performed under x-ray guidance (e.g., fluoroscopic, CT) with the assistance of contrast media to identify and monitor the compressed area via epiduragram. The procedure that most closely falls under this description is commercially known as the MILD® procedure. (Vertos Medical) "The MILD® procedure offers a minimally invasive alternative to a standard laminotomy-laminectomy." (Deer et al. 2011)

Endoscopically assisted laminotomy/laminectomy, which requires open and direct visualization, as well as other open lumbar decompression procedures for LSS are not within the scope of this NCA.

III. History of Medicare Coverage

On January 9, 2014, CMS posted its final decision memorandum for National Coverage Determination (NCD 150.13), (https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=269), covering PILD for beneficiaries with LSS when provided in a randomized controlled clinical trial (RCT) meeting certain conditions under section 1862(a)(1)(E) through Coverage with Evidence Development (CED). The RCTs must be designed using current validated and reliable measurement instruments and clinically appropriate comparator treatments, including appropriate medical or surgical interventions or a sham controlled arm, for patients randomized to the non-PILD group.

Two studies have been approved:

Study Title: MILD® Percutaneous Image-Guided Lumbar Decompression versus Epidural Steroid Injections in Patients Diagnosed with Lumbar Spinal Stenosis Exhibiting Neurogenic Claudication.
Sponsor: Vertos Medical
Clinicaltrials.gov Number: NCT02093520
CMS Approval Date: 05/06/2014

Study Title: A Prospective, Multi-center, Randomized Controlled Double-Blind Trial Evaluating the VertiFlex® Totalis™ Direct Decompression System versus a Sham Surgical Procedure in Patients with Lumbar Spinal Stenosis
Sponsor: VertiFlex®, Inc.
Clinicaltrials.gov Number: NCT02079038
CMS Approval Date: 05/22/2014

A. Current Request

CMS received a complete formal request for a reconsideration of the January 9, 2014, NCD which limits coverage of PILD for LSS to RCTs. The formal request letter can be viewed via the tracking sheet for this NCA on the CMS website at https://www.cms.gov/medicare-coverage-database/details/nca-tracking-sheet.aspx?NCAId=284.

B. Benefit Category

Medicare is a defined benefit program. For an item or service to be covered by the Medicare program, it must fall

within one of the statutorily defined benefit categories outlined in the Social Security Act. PILD may be considered to be within the benefits described under sections;

- 1861(b) as an inpatient hospital service,
- 1861(s)(2)(B) as a hospital service incident to physicians' services rendered to outpatients, and
- 1861(s)(1) as a physician service.

Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

Date	Action
04/13/2016	CMS opens an NCA for Initial 30-day public comment period begins.
05/13/2016	First public comment period ends. CMS receives 36 comments
09/08/2016	CMS posted proposed decision memorandum. Second 30-day public comment period begins.
10/25/2016	Vertos Medical presentation to CMS.
10/08/2016	Second public comment period ends. CMS received 116 comments

V. Food and Drug Administration (FDA) Status

Various devices implanted during spine surgery may fall under FDA regulatory oversight. The focus of our review is for the PILD procedure and no devices are implanted during this procedure, however there are specialized instruments that are used which are under the oversight of the FDA.

The MILD® tool kit (Vertos Medical) initially received 510(k) clearance as the X-Sten MILD Tool KIT (X-Stern Corp.) in 2006. The indications for use are identified as, "The X-Sten MILD Tool Kit is a set of specialized surgical instruments intended to be used to perform percutaneous lumbar decompressive procedures for the treatment of various spinal conditions." (http://www.accessdata.fda.gov/cdrh_docs/pdf6/K062038.pdf)

The VertiFlex® Totalis ™ Direct Decompression System received 510(k) clearance in 2012. The indications for use are identified as, "The VertiFlex® Direct Decompression System is a set of specialized surgical instruments intended to be used to perform lumbar decompressive procedures for the treatment of various spinal conditions." (http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122662.pdf)

VI. General Methodological Principles

When making national coverage determinations, CMS generally evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member under section 1862(a)(1)(A) of the Social Security Act. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the Agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A.

Public comments sometimes cite published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS responds in detail to the public comments on a proposed national coverage determination when issuing the final national coverage determination.

VII. Evidence

A. Introduction

Neurogenic claudication and various back and leg pains are symptoms of LSS. Sustained improvement in these symptoms of pain perception and a reduction in the pain-related functional restrictions are appropriate outcomes of clinical trials. It is challenging to attribute symptom changes to treatment because the natural history of degenerative lumbar spinal stenosis is unclear. (Issack 2012) Additionally, pain perception is subject to regression to the mean and placebo effect. Therefore, clinical trials with appropriate controls utilizing

independently assessed validated instruments are most heavily weighted.

Patient reported outcomes reflecting symptoms and function are often used to measure the effects of treatment for symptomatic degenerative lumbar spinal stenosis. Standardizing the measures facilitates study comparison. The most commonly used instruments are the Oswestry Disability Index (ODI) and the Visual Analog Scale (VAS). The ODI is used to measure a patient's functional disability on a scale of 1 to 100. VAS measures pain intensity on a scale of 0 to 10. The Zurich Claudication Questionnaire (ZCQ) is a less commonly used assessment tool for patient function and has several domains. The Pain Disability Index (PDI) and the Roland-Morris Disability Questionnaire (RMQ) are also tools for measuring disability. The SF-36 and shorter version, SF-12, are measures of general health status. A recent study in patients with LSS revealed that subjective measures of pain and disability had little correlation to actual patient activity, calling into question the current use of these measures without other performance or non-pathology specific outcomes. (Pryce, et al. 2012) CMS attributes more evidentiary weight to those studies reporting reliable, validated outcomes that reflect true patient activity and quality of life.

With the use of any of these instruments, consideration must be given to the clinical meaning of a change in the reported score. How well, if at all, does a score change of some increment reflect a meaningful change in symptom or function experienced by the patient? Other considerations include the error of measurement of the instrument used and the clinical importance of a statistically significant score change. In a 2003 study by Hagg of 29 patients treated surgically or non-surgically in a randomized controlled trial, the standard error of measurement of the ODI was four units, with a 95% tolerance interval of 10, and the minimum difference that appeared clinically important was 10 units. The minimal clinically important difference of VAS back pain was 18-19 units [on a 100 point scale] with a 95% tolerance interval of 1.5. (Hagg, et al. 2003) These recommendations are similar to those by Ostelo who also noted that when baseline was taking into account, a 30% improvement when comparing before and after measures for individual patients—should be the guide for the minimal important change (MIC). (Ostelo, et al. 2008) Ostelo, in an aim towards international consensus regarding minimal important change, noted that workshop participants (during the Low Back Pain Forum VII) stressed that proposed MIC values were for individual rather than group changes. (Ostelo, et al. 2008) The clinically important change is based on an individual, but is often misused to compare the difference in mean scores between two groups, but this is not a clinically important difference. (MEDCAC 2006)

Determining the true clinical impact of interventions that treat pain and improve pain-related functional difficulties is challenging. Well-designed clinical trials can provide the strongest evidence for treatment effect. Well-constructed randomization protects against bias and inclusion of an appropriate comparator facilitates study interpretation. In pain treatment trials, the natural history of the disease, regression toward the mean and the placebo response are important considerations. For these reasons, an appropriate comparator is necessary for accurate interpretation. Accurate interpretation of pain treatment trials also necessitates reporting of concomitant pain treatments, most importantly analgesic use. In the case of research in the area of pain treatment, more evidentiary weight is accorded to studies designed to mitigate the bias of placebo response and that account for the natural history of the disease and regression toward the mean.

B. Literature Search

The 2014 PILD NCD final decision memorandum considered literature published before November 29, 2013. Section VII, the Evidence Section, of the 2014 decision memorandum includes an explanation of the evidence we

considered. We are incorporating the entirety of the previous NCD record as part of this reconsideration record. We performed a literature search utilizing PubMed for randomized controlled trials (RCTs) and nonrandomized controlled trials, cohort or case-control studies, case series studies, and systemic reviews for "percutaneous image-guided lumbar decompression for lumbar spinal stenosis." CMS limited the search to English language articles specific to the human population. But CMS considered English-language studies conducted outside—as well as inside—the United States.

In this decision memorandum, CMS discusses all new human, English language articles related to PILD that have been published since November 29, 2013. We use a number of sources to identify articles in the medical literature that addressed the use of PILD in patients with LSS. These sources included PubMed, Embase, and Cochrane Collaborative Library.

We searched the above mentioned three databases for the following terms:

- Lumbar Stenosis
- Lumbar Spinal Stenosis (LSS)
- Minimally Invasive Lumbar Decompression (MILD®) Percutaneous Decompression
- Percutaneous Image-Guided Lumbar Decompression (PILD)

After performing these searches, CMS then excluded non-English language articles, studies with fewer than ten (10 patients), and those not including human subjects.

We found six articles that met the above criteria. They include the following:

1. One systematic review (Kreiner et al. 2013)
2. Two articles evaluating the same randomized controlled trial (Staats 2016 and Benyamin 2016)
3. One single-site case series study (Basu 2012)
4. One retrospective observation cohort study (Durkin et al. 2013)
5. One case-series study (Wang et al. 2013)

In our proposed NCD, we invited the public to submit any additional studies or comments for our consideration. Although we received additional studies via the public comments, all the studies submitted were duplicative of what has been reviewed in this NCA, the January 2014 NCD, or were beyond the scope of this NCA.

C. Discussion of Evidence

1. Evidence Question(s)

The question of interest for this NCA:

Is the evidence sufficient to conclude that PILD improves health outcomes in Medicare beneficiaries with LSS?

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue.

3. Internal Technology Assessment

Below is a summary of the all of the studies we reviewed for this NCA. Our analysis of each of the below studies or articles is in Section VIII, CMS Analysis.

Basu S. MILD® Procedure Single-Site Prospective IRB Study. Clin Journal of Pain. 2012;28:254-258.

This small, single center case series study described six (6) month safety and efficacy results of the MILD® procedure in twenty-seven (27) patients treated in two phases from November 2009 through June 2010. All 27 patients had neurogenic claudication with radiographic confirmation of hypertrophy of ligmentum flavum. They previously had failed conservative treatment. Endpoints of the study included:

1. VAS—to provide a measure of the patient's back and leg pain;
2. ODI –to measure functional disability; and
3. ZCQ—to measure physical function, symptom severity, and patient satisfaction

The study participants were composed of 52% females and 48% males with a mean age of 63.3 years (range 37 to 83) and totaled 44 levels of decompression.

No significant intraoperative or postoperative complications were reported. Also, no subsequent surgical decompression procedures were performed during the six (6)-month follow-up period.

Subjects experienced a statistically significant improvement in VAS pain scores compared to their baseline VAS score (9.1 at baseline to an average of 3.9 at six months; $P < 0.001$). The baseline average ODI score of 55.1 showed statistically significant improvement at six months with a score of 31.1 ($P < 0.004$). At the six (6)-month follow up, all ZCQ domains, including physical function, symptom severity, and patient satisfaction, showed statistically significant improvements.

Durkin B, Romeiser J, Shroyer L. et al. Report from a Quality Assurance Program on Patients Undergoing the MILD® Procedure. Pain Med. 2013 May;14(5):650-6.

Durkin and associates performed an uncontrolled retrospective observational cohort study to characterize trends in pain and functional outcomes. They looked to identify risk factors in patients with LSS and neurogenic claudication who underwent the MILD® procedure.

In 2010, the Stony Brook Medical Center for Pain Management established a program that offered the MILD® procedure to LSS patients. The Medical Center included a quality assurance registry (Surgical Quality Improvement Program) as part of the program. The registry prospectively gathered safety and outcomes data on all MILD® patients. It collected information on preoperative medical characteristics, MRI and CT evidence of lumbar stenosis and LF hypertrophy, intraoperative course, postoperative pain status, and functional outcomes.

Fifty (50) patients undergoing the MILD® procedure from October 2010 to May 2012 were included in the study. Follow-up visits extended for an additional six (6)-month period. Clinical information was collected prospectively prior to and during follow-up visits at one (1), three (3), and six (6) months following surgery. Specific inclusion and exclusion criteria were established, and all patients underwent the MILD® procedure on one (1) to three (3) lumbar regions.

Durkin and associates collected information on: age, gender, body mass index (BMI), preoperative usage of opioid medications, and lumbar spine pathology defined by MRI or CT. The authors looked at severity of canal stenosis and LF hypertrophy [>4 mm] prior to the procedure.

Durkin and associates compared the change in pre-MILD® patient data with follow-up outcomes. They assessed clinical outcomes using a variety of metrics including:

1. Adverse events (e.g., bleeding, nerve injury, dural tears);
2. Improvement, no change, or worsening based on psychometric tools (11-point numerical rating scale [NRS];
3. Pain interference scores from the National Institutes of Health [NIH] Patient-Reported Outcomes Measurement Information System [PROMIS];
4. Patient-completed freehand drawings of their pain distribution patterns related to lower back and/or lower extremities); and
5. Change in functional status as evaluated by the ODI, ZCQ, and NIH PROMIS.

Pain and functional data were collected by a trained clinical team member at baseline prior to the procedure and at one (1), three (3), and six (6) months post-op. Opioid use was tracked,

Frequency tables and basic descriptive statistics were generated for all categorical variables, and continuous variables, respectively. Pre and post-procedure change scores were calculated for each pain and functional status measurement instrument. For the univariable analyses, chi-square, Fisher's exact, paired t, and Wilcoxon Signed Rank tests were performed to assess for statistically significant differences. Given the small sample size of 50 patients, the authors could not evaluate the impact of risk factors on postoperative outcomes using multivariable analytical approaches.

In the study, 50 patients underwent MILD® procedures (the average age of participants was 73.3 ± 9.4 years; 52.0% of subjects were female patients; mean BMI of 31.2 ± 7.0 and 48% were obese with BMI ≥ 30). Based on the physical status classification system of the American Society of Anesthesiologists (ASA), 68% of patients had a class 3 grade (severe systemic disease), while 24% and 8% were graded as class 2 (mild systemic disease) and class 4 (life threatening systemic disease), respectively.

All of the patients had previously undergone low back pain interventions such as epidural lumbar blockade (74%), medial nerve branch blockade (24%), and/or radio-frequency ablation of medial nerve branches (30%). All patients complained of neurogenic claudication with varying degree of pain distribution patterns (buttocks and/or legs) elicited by walking or standing, and the most common lower extremity dermatomes affected were S1 and S2. Almost all patients indicated "low back" pain corresponding to truncal dermatomes L3-L5. Gait instability was present in 68% of the patients; 55.1% of the patients used a walking assistance device.

Psychometric testing revealed that the average pre-operative NRS pain score averaged 7.5 (95% confidence interval [CI] 7.0, 8.0). Pain on to the ZCQ symptom severity scale averaged 3.2 (95% CI 3.0, 3.4). Pain interference score by the NIH PROMIS (N = 39) at baseline was 63.5 ± 7.7 indicating worse than average impact of pain on daily living compared with the general U.S. population (NRS pain scores and corresponding NIH PROMIS pain interference scores captured different aspects of the patient's pain experience). Functional status by the ODI at baseline averaged 40.6 (95% CI 36.1, 45.1). The NIH PROMIS physical function scores averaged 34.1 ± 7.2, which indicated a moderate-to-severe impact on daily life in comparison with the general U.S. population

norms matched by age and gender.

During the study, none of the MILD® participants incurred any procedure-related complications. NRS scores decreased post-operatively; 64.3% of patient reported less pain after 3 months. One quarter of the patients reported clinically meaningful improvements in functional ODI scores at 6 months.

While the authors concluded that overall pain was reduced and functional status improved in LSS patients following the MILD® procedure at 3 months and 6 months as measured by several scales, there was only a 2% net reduction in use of opioids. In addition, 10% of patients who did not previously use opioids began use after the procedure. Although gait instability and use of a walking assistance device was reported at baseline, the authors did not report post-procedure changes in either factor. And given the small sample size, it was not yet possible to identify patient subgroups at risk for "no improvement." They also noted that continued follow-up of longer-term outcomes appears warranted to develop evidence-based patient selection criteria.

Kreiner D, MacVicar J, Duszynski B, Nampiaparampil DE. The MILD® procedure: a systematic review of the current literature. Pain Med. 2014 Feb;15(2):196-205. doi: 10.1111/pme.12305. Epub 2013 Dec 5.

Kreiner and associates performed a systematic review of the medical literature to determine if the minimally invasive lumbar decompression (MILD®) procedure reduces pain in patients suffering with symptomatic LSS. The authors retrieved articles from PubMed, Embase, and the Cochrane Library. Search terms included lumbar stenosis, percutaneous decompression and MILD® procedure. They reviewed full length articles written in any language up through May 2013.

The authors only considered articles that met the following criteria:

1. Study participants had lower extremity claudication—confirmed with CT or MRI due to LSS
2. Participants had to be older than 18 years
3. Patients assigned to treatment with MILD®
4. Patients were assessed for lower extremity pain relief by using the visual analog scale (VAS)

Secondary outcome measures included ODI—to measure functional benefit—and ZCQ—to measure pain and patient satisfaction. Kreiner and associates monitored complications, adverse events, and co-interventions.

The authors serially assessed intervals of 30 days, 6 weeks, 3 months, 6 months, and 1 year and longer. The study did not specify how long beyond 1 year. Study quality was assessed using an instrument developed by the

International Spine Intervention Society Standards Division.

Three of the authors reviewed all of the articles that met the inclusion criteria and resolved disagreements through discussion. GradePro software (GRADE Working Group) was used to consolidate the data from the different studies into workable follow-up periods of short (4–6 weeks), medium (3–6 months), and long term (1 year and more).

The investigators identified one (1) randomized controlled trial (RCT) (Brown et al. 2012), seven (7) prospective cohort studies (Basu 2012; Chopko 2011; Chopko 2013; Chopko and Caraway 2010; Deer et al. 2012; Mekhail et al. 2012; Wilkinson and Fourney 2012), four (4) retrospective cohort studies (Deer and Kapura 2010; Durkin et al. 2013; Lingreen and Grider 2010; Wang et al. 2013), and one (1) case series (Wong 2012).

Each of the reviewed articles showed statistically significant improvement in pain relief post-MILD® procedure than pre- procedure. Patients had statistically significant pain relief in the short, medium, and long terms. Functional outcome measures similarly showed statistically significant improvement from the MILD® procedure.

While all the studies considered met the inclusion criteria, a few of them had notable deficiencies. The single RCT by Brown et al., a comparison between MILD® and a single ESI treatment, which was reviewed in the original NCD, only reported short term outcomes and was essentially unrandomized at 6 weeks. The other studies in this systematic review have also been individually reviewed in the original NCD and in this one. All were either case series or retrospective studies. Two (2) of the articles considered in the review Wilkinson and Fourney 2012 and Brown, et al 2012—had missing data. In one study (Mekhail et al. 2012), thirteen (13) patients were not available for follow-up and at least two (2) proceeded to lumbar surgery after one (1) year. No substantial direct procedure-related complications were identified in any of the studies.

In the five (5) studies that evaluated patient satisfaction, ZCQ scores ranged from 1.86 to 2.20 (95% CI ± 0.26). The satisfaction scale ranged from 1.0 to 4.0, with values of less than 2.5 indicating some degree of satisfaction, although a score of 2.0 or lower is typically considered "satisfied." Three (3) studies evaluated medication usage among patients receiving MILD®. The results are mixed. The Chopko study showed that half of the patients were able to decrease or stop opioid medication use post-procedure, but the study by Wilkinson and Fourney reported a small post-procedure increase in opioid analgesic usage.

The authors concluded that the MILD® procedure was a relatively safe procedure for the treatment of symptomatic LSS and that the MILD® procedure resulted in statistically significant reductions in pain intensity and intermediate improvements in function in the short term. However, the data did not support a long term assessment of the effectiveness of the procedure; and the improvements in the mean pain scores were only slightly greater than the accepted minimal clinically important change for chronic lower back pain and lumbar radicular pain.

Staats PS, Benyamin RM. MiDAS ENCORE: Randomized Controlled Clinical Trial Report of 6-Month Results. Pain Physician 2016; 19:25-37.

Benyamin RM, Staats PS. MILD® is an Effective Treatment for Lumbar Spinal Stenosis with Neurogenic Claudication: MiDAS ENCORE Randomized Controlled Trial. Pain Physician 2016; 19:229-242.

Staats and Benyamin conducted a prospective, randomized controlled, unblinded trial comparing MILD® to lumbar interlaminar epidural steroid injections (ESIs) in patients with lumbar spinal stenosis (LSS) assessing both six (6)-month and twelve (12)-month Oswestry Disability Index, Numeric Pain Rating Scale, and Zurich Claudication Questionnaire differences. A total of 302 patients were enrolled in the study from 26 US international pain management centers.

Inclusion criteria included all of the following:

1. Medicare beneficiaries 65 years and older;
2. Patients experiencing neurogenic claudication symptoms for at least three (3) months that had failed to respond or poorly responded to physical therapy, home exercise programs, and oral analgesics;
3. Patients that had LSS with neurogenic claudication diagnosed via symptomatic diagnosis and radiologic evidence of LSS. Radiological criteria required unilateral or bilateral ligamentum flavum > 2.5 mm confirmed by a pre-operative MRI or CT performed within twelve (12) months of the baseline visit;
4. Patients with comorbid conditions commonly associated with spinal stenosis; and
5. Patients willing to complete six (6)-month and one (1)-year follow-up visits

Exclusion criteria included:

1. ODI Score < 31 (0-100 ODI Scale)
2. NPRS Score < 5 (0-10 NPRS Scale)
3. Prior surgery at any treatment level
4. History of spinal fractures with current related pain symptoms
5. Grade III or higher spondylolisthesis
6. Motor deficit or disabling back and/or leg pain from causes other than LSS with neurogenic claudication
7. Inability to walk ≥ 10 feet unaided before being limited by pain
8. Previously randomized and/or treated in this clinical study
9. Previously received the MILD® procedure
10. Received epidural steroid injections (ESI) eight (8) weeks prior to study enrollment
11. Epidural lipomatosis (if deemed to be a significant contributor of canal narrowing by the physician)
12. Being on (or pending) Workman's Compensation or known to be considering litigation associated with back pain

Patients were randomized in an allocation ratio of 1-to-1 to the MILD® procedure or epidural ESI study cohorts (149 patients were randomized to the MILD® and 153 patients were randomized to ESI as active control).

Neither the investigators nor the patients were blinded. Following randomization, six (6) MILD® patients and 22 ESI patients voluntarily withdrew prior to the study treatment, leaving 143 and 131 patients in the MILD® and ESI cohorts, respectively. Of these, two (2) ESI patients missed their six (6)-month follow-up visit. Accordingly, the six (6)-month data analysis included 143 MILD® patients and 129 ESI patients.

Between the six (6)-month and one (1)-year follow-ups, two (2) patients in the MILD® cohort died of unrelated causes (one cardiopulmonary arrest and one cardiac arrest). Two (2) patients in the ESI arm withdrew for unrelated health reasons. Per the statistical plan, these four (4) patients were included in the one (1)-year analysis using their six (6)- month follow-up data that was carried forward. Two (2) additional patients in the ESI arm missed both the six (6)- month and one (1)-year follow-ups and were not included in this analysis. Therefore, outcomes for 143 patients who received MILD® and 129 patients who received ESI were included in the one (1)-year report.

The mean age in the MILD® group was 75.6 years, while the mean age of the ESI group was 75.0 years. There was a significant difference in gender between the two groups. When considering males, a larger proportion was in the MILD® group (49.7%) compared to the ESI group (37.9%).

Both groups presented with similar adverse events. For the most part, patients reported the same rate and type of adverse events in both groups. The ESI group, however, had significantly more patients presenting with facet arthropathy than found in the MILD® group.

Baseline values for ODI, NPRS, and ZCQ domains showed no significant differences between the groups. The ESI group had a significantly higher pre-operative rate of aquatic therapy than the ESI group. Procedure times, procedure settings, and anesthesia type were all significantly different due to the nature of the two (2) treatments. ESI patients received an average of 1.7 ESI treatments during the first six (6) months with a range of one (1) to four (4) and a median of one (1).

There were no statistical significant differences in pain medication use 6 months and at one year between the MILD and ESI groups. At baseline, 90.6% of MILD® patients and 83.0% of ESI patients reported using medication for their neurogenic claudication. At six (6) months and one (1) year, the percent of patients using these medications in the MILD® arm was 89.5% and 88.2%, respectively and in the ESI arm was 85.3% and 84.2%, respectively.

Both groups had high non-responder rates. For primary efficacy, at six months, the proportion of ODI responders in the MILD group (62.2%) was statistically significantly higher than for the ESI group (35.7%). At one (1) year, the 58.0% ODI responder rate in the MILD® group was statistically significantly higher than the 27.1% responder rate in the ESI group.

The studies looked at ODI, NPRS, and ZCQ. The primary efficacy measure is the proportion of ODI responders. The study defined ODI responders as patients achieving the validated Minimal Important Change (MIC) of ≥10 point improvement in ODI from baseline to follow-up. Secondary efficacy measures include the proportion of NPRS and ZCQ responders using validated MIC thresholds. The primary safety measure was the incidence of device or procedure- related adverse events in each group. At both six (6)-month and one (1)-year follow-ups, all primary and secondary efficacy results provided statistically significant evidence that MILD® is superior to the active control. Further, all secondary efficacy parameters demonstrated statistical superiority of MILD® versus the active control. The primary safety endpoint was achieved, demonstrating that there was no difference in safety measures between MILD® and ESIs for both six (6) months and 12 months.

The authors concluded that both six (6)-month and one (1)-year results demonstrate that MILD® is statistically superior to ESIs in the treatment of LSS patients with neurogenic claudication and verified central stenosis due to ligamentum flavum hypertrophy. Although the authors point out that patients status post the MILD® procedure showed statistically significantly improvement in function even after one (1) year, there was no concomitant decrease in use of pain medication.

Wang J, MD, Bowden K, Pang G, Cipta A. Decrease in Health Care Resource Utilization with MILD®. Pain Medicine 2013; 14: 657–661.

Wang and associates conducted a single-center, single-armed case series of 22 Veteran's Administration (VA) Hospital patients undergoing minimally invasive lumbar decompression (MILD®) to assess the short-term improvement in observed pre- to one to two weeks post-operative MILD® visual analog scores (VAS) and patient satisfaction in addition to a follow up assessing time spent in specialty care and reductions in interventional pain procedures with follow-up durations ranging from 2-15 months.

All 22 MILD® patients who were identified over a 13-month period (July 2011 to August 2012) had pre-operatively presented with symptoms consistent with LSS and had radiographic evidence of central canal stenosis caused by ligamentum flavum hypertrophy by either lumbar computed tomography or magnetic resonance imaging.

Patients were 51 to 91 years of age (mean of 74.2 years) and mostly male (95.5%). Though two patients had aborted MILD® procedures and one was lost to follow-up, they were still included in the data analysis. At the time of the chart review, each participant had at least two (2) months of post-MILD® follow-up. When looking at pre-MILD® chronic pain management resource usage (days from initial clinic consultation to the MILD® procedure date), there was a mean of 9.33 and median of 5.625 months between initial consultation and receiving MILD®. During that time, each patient received an average of 3.68 and a median of two (2) chronic pain procedures. Three (3) patients (13.6%), however, did not receive any interventional pain procedures before MILD.

The average VAS score before MILD® was 7.0, and 4.82 one to two weeks post-MILD®, with an average VAS

reduction of 2.27 per patient. Post-MILD® duration is the difference between day of the MILD® procedure and either the date the chart review was conducted or the date of discharge from the chronic pain or spine surgery clinic. Patients spent a longer duration in pre-MILD® care (9.33 months) than post-MILD® specialty care (5.11 months). The entire study cohort received an average of 0.395 pain procedures per month. Patients spent 53.6% of post-MILD® months in post-MILD® specialty care. Post-MILD®, over half the patients (54.5%), no longer required chronic pain management to treat their LSS symptoms. The other ten (10) patients continued their care with chronic pain management for their LSS, and three of those patients were eventually referred to spine surgery for surgical decompression.

1. Medicare Evidence Development & Coverage Advisory Committee (MEDCAC)

A MEDCAC meeting was not convened on this issue.

2. Evidence-Based Guidelines

No evidence-based guidelines were found.

3. Professional Society Recommendations / Consensus Statements / Other Expert Opinion

No professional society recommendations were found. We received comments from State and National societies. All comments were reviewed.

4. Public Comment

Public comments sometimes cite the published clinical evidence and give CMS useful information. CMS finds that public comments that give information on unpublished evidence, such as the results of individual practitioners or patients, to be less rigorous and therefore less useful for making a coverage determination.

CMS uses comments submitted during the initial comment period to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision (*i.e.*, submitted during the second comment period) when issuing the final decision memorandum. All comments that were submitted without personal health information may be viewed in their entirety by using the following link - https://www.cms.gov/medicare-coverage-database/details/nca-view-public-comments.aspx?NCAId=284.

Initial Comment Period: 04/13/2016 – 05/13/2016

During the initial 30-day public comment period, CMS received a total of 36 comments. We reviewed the comments in their entirety, including reviewing all referenced literature submitted in part as comments from professional organizations.

We redacted five (5) comments (13.9%) because they contained personal health information. Medical doctors submitted 24 of the comments (66.7%). Directors/Presidents (12/33.3%) of medical centers submitted the majority of comments. Other commenters included universities or medical colleges (5/13.9%), pain management centers or specialists (10/27.8%), and pain societies (7/19.4%). One manufacturing company (2.8%) submitted a comment.

Three comments (8.3%) were neutral. They sought assistance in locating study sites participating in the approved CED studies and shared their perspective of various study techniques. Three (8.3%) commenters cautioned against Medicare coverage for the PILD procedure. They had skepticism about PILD's associated health outcomes or benefits.

Thirty (83.3%) commenters were in favor of expanding Medicare coverage to include PILD. Five (13.9 %) of these favorable commenters belong to different sectors of the Society of Interventional Pain Physicians. All of the favorable commenters believed PILD to be cost effective, safe, and essential in relieving pain and improving quality of life.

Second Comment Period: 10/08/2016 – 11/08/2016

During the 30-day public comment period following our proposed decision, we received a total of 116 comments. Three (2.6%) commenters favored conducting additional research so that more evidence could be generated to better understand the procedure's outcomes.

The majority of comments were submitted by physicians 86 (74.1%) or directors/presidents 26 (22.4%). Thirteen (11.2%) of the commenters were MILD® trial investigators, 1 (0.9%) was an investor and 46 (39.7%) performed the MILD® procedure. Pain management/specialists comprised 27 (23.3%) of the commenters as well as 4 (3.4%) pain physicians and 7 (6.0%) sectors of different Pain Societies. One (0.9%) State Representative commented. Other commenters represented universities 8 (6.9%), pain centers 9 (7.8%), and 5 (4.3%) spine services.

We reviewed the comments in their entirety, including reviewing all referenced literature submitted. Nine additional references were submitted during the second comment period. Seven of the references submitted were articles that discussed studies conducted before 2013 and were reviewed in the original NCD decision memorandum published in January 2014. The two remaining articles were reviewed as part of this NCA but were duplicative—only the order of authors' names were switched. The other studies submitted were not directly related to PILD and therefore outside the scope of this decision.

Our responses to the comments are grouped below:

CED Public Comments

Comment: Some commenters favored our proposal to conduct additional research using CED so that more evidence could be generated to better understand the procedure's outcomes. One commenter stated there is minimal risk and sustained benefit for pain and function, but still may not prevent the need for subsequent surgical intervention in some patients. Another commenter agreed that the current literature on this procedure at this time appears discordant. Some industry-sponsored trials have demonstrated clinical efficacy while others have shown limited clinical efficacy requiring reoperation.

Response: We agree. Although we acknowledge that one prospective, randomized controlled trial under CED has been completed, we discussed in detail our concerns with the results in the analysis section of this memorandum. It is generally acknowledged that long term outcomes are important for the PILD procedure since the goal of the procedure is sustained pain relief and avoidance of surgery. As stated in the original NCD decision memorandum published in January 2014:

"*CMS believes that durability of benefit is an important evidentiary question. A beneficiary's preferences are informed by the ability to consider potential benefits and harms among the available therapeutic options. This consideration is significantly limited if the likely duration of benefit is unclear."*

The reason it is important to demonstrate longer term outcomes is because lumbar spinal stenosis is often a chronic, progressive disease, and a minimally invasive intervention that produces durable improvements in health outcomes has been sought to avoid the need for invasive spinal surgery. It is important that PILD be considered in this context. In addition, as noted in the RCT publication, there were two deaths in the MILD® treatment group. Since PILD is designed to be minimally invasive, these deaths were unexpected and not adequately addressed by the investigators. A prospective longitudinal study will answer these questions while allowing continued patient access and support for innovation.

Despite these continued evidentiary concerns, we do not believe it would be appropriate to issue a national non-coverage decision at this time. As discussed in detail in the analysis, the results remain inconclusive. We still await the results of the second CED sham-controlled blinded RCT approved under the current NCD. Moreover, our proposed decision to continue CED reflected our goal to facilitate the collection of important evidence concerning longer term outcomes, such as subsequent invasive spinal procedures (e.g., surgery), potential harms of the procedure and pain medication usage which are key to answering the CED questions we asked in the 2014 NCD and today to get us to a decision about whether or not PILD is reasonable and necessary to treat LSS. Since the RCTs approved under our earlier NCD have now been completed, and no patients have access to Medicare coverage of PILD, CED will provide coverage again. We believe access to this potentially promising procedure remains important even though the evidence does not yet support full coverage under 1862(a)(1)(A).

Comment: Many commenters stated that the practice of medicine depends on innovation.

Response: CMS supports innovation with CED and covered two CMS approved randomized controlled trials. If CMS were to issue a national non-coverage determination, manufacturers would need to bear more cost of evidence development for this procedure. CED, therefore, supports studies so that evidence required for a coverage determination can be generated.

Comment: Some commenters were unclear on what this new prospective study would accomplish.

Response: CED will permit appropriate patient access to the PILD procedure and support innovation and evidence development. The longitudinal prospective study will help answer the questions on long term health outcomes, such as whether patients have subsequent invasive procedures (e.g., surgery), whether there are other potential harms of the procedure, and whether the procedure reduces pain medication usage. This data is key to answering the question we asked in the 2014 NCD and, again today, to get us to a decision about whether PILD reasonable and necessary under 1862(a)(1)(A) for beneficiaries with LSS.

Comment: Some commenters further noted that the research questions and criteria to achieve this definitive resolution must be transparent, well-defined, predictable and achievable.

Response: We agree. As noted in the CED Guidance Document (https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27) all decisions to require CED are made using the NCD process.

The NCD process is fully described in the August 7, 2013 *Federal Register Notice* (Vol 78, No 152). The NCD process, in general, is a transparent one. Requesters may meet with CMS and frequent, informal contact is possible. A tracking sheet is posted on the CMS website that allows interested individuals to participate in and monitor the progress of the review. The proposed decision includes details of CED study design, including the research questions for stakeholders to comment. Consistent with section 1862(l)(3)(B) of the Act, we provide 30 days for public comment on the proposal. Not later than 60 days after the close of the 30-day public comment period, we issue a final NCD.

Comment: Many commenters expressed that an additional prospective cohort study as described in our proposed decision will be costly. Commenters also stated that IRB fees could discourage most sites from participating. Some assert that a prospective cohort study would also require more time to conduct and further delay patient access to the PILD procedure. Commenters claim that patients may not want to participate in studies due to the extra effort, paperwork, and time involved.

Response: We appreciate the comments. With the public comments in mind, we reconsidered our proposal to require a prospective cohort study. CMS understands that research studies take time and effort. Based on the public comments and conversations with the manufacturers, CMS has modified the study design requirements. We believe the new study design allows quick, broad, and appropriate patient access during the time that additional evidence is generated. We believe that a prospective longitudinal study will be able to answer our CED questions, show duration of benefit and avoidance of harms and determine whether the results reported in the first completed RCT are actualized in general clinical practice. This NCD increases appropriate patient access. Further, since the study design has been revised to reduce burden, there should be minimal effort, perhaps no extra effort, on the part of the patients. Research costs such as IRB fees are outside the scope of this decision.

Comment: A number of commenters believe that continuing CED and requesting more trials is a financial ploy to prevent this procedure from becoming mainstream. Lobbying by spine surgical companies is the only reason the MILD® procedure is being delayed full coverage. The commenters believe this decision blocks open access to the public because CMS dictates private payers behaviors as well as access of any therapy to the public.

Response: We strongly disagree. CMS makes evidence-based national coverage determinations for the Medicare population, which is a different population than private payers. CMS is covering PILD for LSS under CED to allow for patients to have sustained access to the PILD procedure during evidence generation. CMS will cover a prospective longitudinal study to collect evidence from clinical practice (some refer to this as real world evidence) on the evidence gaps we identified in the first NCD. Medicare does not have authority or control over private payers' coverage determinations.

Comment: A number of commenters expressed concerns that the proposed CED study was limited only to investigators from the CMS approved RCTs, which restricts the number of physicians that can offer the procedure.

Response: We appreciate the comment and have revised the required study design. This NCD allows for increased access and broad participation by appropriate providers.

Comment: A commenter claimed that multiple follow-up visits to collect low-quality data will not result in better patient care, better use of resources, or better outcomes.

Response: We disagree. The study requirement should not produce low-quality data. The required study is to determine if the results of the RCT are actualized in general practice settings (also referred to as real world evidence which provides important information that is not typically obtained in RCTs). We have described what types of studies designs would most likely answer the questions we posed in the 2014 NCD and this current NCD. If the prospective longitudinal study is done well the data should not be low quality.

Comment: Some commenters stated that for CED to be supported, there needs to be clear objective criteria and a viable exit from CED to gain full coverage. Imposing a new study requirement at this stage calls into question both the transparency and logic of the CED process.

Response: We agree that CMS must have a clear objective when requiring CED. CMS uses an evidence-based medicine approach in making national coverage determinations. CED provides coverage when the evidence is not complete. We believe the decision to continue CED for PILD is necessary because the single RCT did not fully answer the important questions we asked in the 2014 NCD as described in the Analysis section of this NCA. These elements are key to answering the question we asked in the 2014 NCD and today to get to a decision under section 1862(a)(1)(A). As we noted in our approval letter of the PILD RCTs, "though a CED study may demonstrate certain findings, it may not be sufficient for CMS to change our coverage policies." Consistent with an evidence-based medicine approach, the quality, strength and totality of evidence are important. We believe that a prospective longitudinal study will help answer our CED questions, show duration of benefit and avoidance of harms and determine whether the results reported in the first completed RCT are actualized in general clinical practice. CED will also provide broader access to patients and support innovation and evidence development. Under this decision, coverage for PILD continues until the CMS reconsiders this NCD.

Comment: A number of commenters stated that the level of scrutiny the PILD procedure is undergoing is unprecedented and unjustified. The commenters claim that the FDA does not require such additional studies after a successful RCT; instead, at most, the FDA may demand a limited post-approval study for a very specific issue.

Response: We disagree with the commenters. Our evidentiary standards are the same and have not changed as noted above. This was an externally requested NCD reconsideration, and we are following our normal standards for making coverage decisions based on published evidence. CMS has required an RCT study design (e.g., Pharmacogenomic Testing for Warfarin Response (NCD 90.1), Transcutaneous Electrical Nerve Stimulation for Chronic Low Back Pain (NCD 160.27) and Home Oxygen for Chronic Obstructive Pulmonary Disease (NCD 240.2.1)) as well as additional subsequent longitudinal analysis (Positron Emission Tomography (NaF-18) to Identify Bone Metastasis of Cancer (NCD 220.6.19)) in other CED decisions.

We recognize the strengths of randomized controlled trials but acknowledge that the controlled trial environment is different than the general clinical practice setting. Due to practical aspects of conducting RCTs, sample size may be limited. While the sample size may not be considered small for a RCT, the number of patients that were treated in the PILD RCT is relatively small compared to the large number of potentially eligible patients. In a similar context, for lung cancer screening with low dose computed tomography (NCD 210.14), the MEDCAC noted there were evidence gaps though the National Lung Screening Trial (NLST) was a very large RCT (sample size of 53,454 with 7,110 participants 65 years of age and older).

Comment: A commenter suggested that since Medicare coverage is contingent upon the collection of additional clinical or scientific evidence (beyond FDA requirements for safety and efficacy), CMS should: - Collaborate with stakeholders to clearly identify the data collection objectives
- Consider the minimum data necessary to achieve those objectives
- Clearly identify with input from interested stakeholders, scientifically supported study endpoints and the duration of data collection in advance.

Response: We agree that stakeholder input is important. The NCD process includes two public comment periods to ensure public input from all stakeholders. Per our CED guidance document, we only consider minimum data necessary to answer the CED questions. Additionally, we have clinicians and scientists at CMS that review every protocol for the quality of the endpoints and the duration of the data-collection. In response to comments and stakeholder presentation, we have modified our study design to require a prospective longitudinal study and believe this will be able to answer our CED questions, show duration of benefit and avoidance of harms and determine whether the results reported in the first completed RCT are actualized in general clinical practice.

Comment: A commenter raised points from the 'Guidance for the Public, Industry, and CMS Staff: Coverage with Evidence Development' policy (https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27), indicating that a CED cycle is completed when an NCD reconsideration is opened. Since the CED cycle was completed and the reconsideration was opened, CMS should not mandate study participation as a condition of coverage.

Response: We disagree with the commenter's assertions. As outlined in the CED guidance document, a CED cycle is considered completed when CMS completes a reconsideration of the CED coverage decision and removes the requirement for study participation as a condition of coverage. As with all NCDs, any member of the public may request reconsideration of the NCD that requires CED. The current reconsideration requests was submitted early, based on only 6 month data, even though the requester expressly recognized that additional data was required.

In this specific NCD, we do not consider the CED cycle to be completed as additional information is still required under the 2014 protocol. CMS relies on published evidence to make any coverage decision.

MiDAS-ENCORE Study Public Comments

Comment: A commenter claimed that MiDAS ENCORE was a well-designed study that produced level 1 data and was approved by CMS. They contend that the study's one-year timeline and defined endpoints have been met.

Response: We agree that CMS approved the MiDAS ENCORE study. We commend investigators for participating in CED and completing the procedures in the RCTs. We recognize the strengths of randomized controlled trials. While the sample size may not be considered small for the MiDAS ENCORE RCT, the number of patients that were treated in the PILD RCT is relatively small compared to the large number of potentially eligible patients. Before full clinical implementation is supportable, we believe PILD should be tested in general clinical practice to confirm and further the evidence base on whether these RCT findings will be actualized in broad practice.

We note that the MiDAS ENCORE study protocol approved by CMS requires 24-month results. Since lumbar spinal stenosis is a chronic, progressive disease, a minimally invasive intervention that produces lasting improvements in health outcomes has been sought to avoid the need for invasive spinal surgery. It is important that PILD be considered in this context. The MiDAS ENCORE 12 month study results do not allow a robust assessment of the duration of benefit, which limits the quality and broader applicability of the study results.

Because of the reasons above and more fully discussed in the CMS analysis section of this decision memorandum, we believe this NCD is needed to further develop the evidence base to get us to a decision about reasonable and necessary under 1862(a)(1)(A). We believe the NCD will add important evidence concerning longer term outcomes, such as subsequent invasive procedures (e.g., surgery), potential harms of the procedure and pain medication usage which are key to answering the question we asked in the 2014 NCD and today. Since the RCTs have been completed, but not all of the results are in, no patients have coverage of PILD at this time. We proposed CED to gather more data to facilitate appropriate coverage and allow broader appropriate patient access. We also believe this additional evidence along with the results of the RCTs will help inform physicians and beneficiaries in making evidence-based treatment decisions.

Comment: Several commenters stated that the proposed prospective cohort study as described in the proposed decision limits treatment options for patients. The commenters stated that the ability to take care of patients is markedly diminished if MILD® is limited only to clinical trials for Medicare coverage and it may cause patients to decide not participate and turn down treatment. This limited coverage will cause more patients to undergo damaging surgical treatments that are unnecessary.

Response: We appreciate the comments. In response, we have revised the required study design from a prospective cohort study to a broader prospective longitudinal study to increase patient access. With regard to this decision encouraging patients to undergo surgery, CMS has not found any evidence to support the comments. Further, there are a number of treatment options for patients with LSS, and we encourage active involvement of patients in treatment choice and that patients are made aware of the benefits as well as potential harms of these treatments.

Comment: The MiDAS ENCORE outcomes were statistically and clinically relevant, proving MILD® to be a superior treatment for LSS. Commenters claimed that MILD® has been proven to be an inexpensive, safe, and effective alternative to spine surgery and suggested that it should be covered by Medicare.

Response: We disagree. As noted in the analysis, CMS described why the MiDAS trial did not fully answer our CED questions. For example, potential benefits and harms of MILD® (e.g., duration of benefit, potential harms, and pain medication use among others) need further assessment. There also have been several AHRQ technology assessments and systematic reviews indicating that ESIs as a control group is challenging. Based on the RCT results and the publications we reviewed listed in the evidence section of this NCA, the currently available evidence does not support full coverage for PILD.

Comment: A commenter disagreed with the CMS assessment of the MiDAS ENCORE study that the "small sample size and short duration may limit quality and broader applicability of the study results." The commenter pointed out that pain medication use was not a confounder. Finally, the commenter pointed out that more patients in the control arm that were lost to follow up, suggesting that the patients were seeking non-study treatment.

Response: We appreciate the comments. However, we believe that the 12 month results were inadequate to determine the duration of benefit, avoidance of invasive spinal procedures, and broader applicability of the PILD procedure. While the sample size may not be small for a RCT, the number of patients that were treated with PILD is relatively small compared to the large number of potentially eligible patients with LSS.

A confounder is a statistical term that describes a situation in which the effect or association between a treatment and outcome is distorted by the presence of another variable. We modified our language in the analysis to reflect the comment that pain medication use may be a co-intervention. We consider change in pain medication to be a core endpoint in studies of pain management as recommended by IMMPACT (Comer et al.) and have changed the terminology. For this reason, we suggest that pain medication—and particularly, narcotic usage—be considered as an endpoint in subsequent studies in addition to more subjective measures, such as the VAS, which might be subject to the placebo effect.

We also saw no significant difference in the rates of loss to follow up in the treatment arm compared to the

control arm due to poor response to their study treatment.

Coverage of PILD Public Comments

Comment: Some commenters suggested that without PILD, patients that are not candidates for surgery may be forced to rely on pain medications such as opioids. After all, narcotics can lead to significant side-effects and complications.

Response: We appreciate the comment. Under this final decision, we expect that Medicare patients will have access to PILD in the new CED longitudinal study. Further, CMS agrees with the importance of appropriate selective use of pain medications. This is why further evidence must be developed. As noted above, one published study reported that the PILD procedure resulted in an increased use of narcotic pain medications. Another study shows no decrease in pain medication usage post-PILD procedure. CMS seeks to better understand whether the PILD procedure reduces the need for pain medication—and particularly, narcotic usage. CED allows appropriate access to patients and support innovation and evidence development. This is also key information for beneficiaries to have to make informed treatment decisions. A number of treatment options exist for patients with LSS, and we encourage active involvement of patients in treatment choice and that patients are made aware of the benefits as well as potential harms of these treatments.

Other

Comment: A commenter suggested a certain number of training hours should be considered for doctors interested in performing MILD® procedure

Response: It is expected that all doctors will have adequate training before conducting PILD procedures like any other procedure.

Comment: A number of commenters stated that patients prefer to be treated by their physicians in a general practice setting and be offered proven, safe treatment options by their trusted provider.

Response: To ensure the best outcomes possible, we believe PILD should be performed by appropriate providers

in appropriate settings.

VIII. CMS Analysis

A. Introduction

National coverage determinations are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1869(f)(1)(B) of the Act). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. See § 1862(a)(1)(A)of the Social Security Act.

In addition to § 1862(a)(1)(A) of the Act, a second statutory provision may permit Medicare payment for items and services in some circumstances. That statute, section 1862(a)(1)(E) of the Act, provides, in pertinent part, that:

(a) Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services—
. . .
(1)(E) in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section.

Section 1142 of the Act describes the authority of the Agency for Healthcare Research and Quality (AHRQ) to conduct and support research on outcomes, effectiveness, and appropriateness of services and procedures to identify the most effective and appropriate means to prevent, diagnose, treat, and manage diseases, disorders, and other health conditions. That section includes a requirement that the Secretary assure that AHRQ research priorities under Section 1142 appropriately reflect the needs and priorities of the Medicare program.

CED is a paradigm whereby Medicare covers items and services on the condition that they are furnished in the context of approved clinical studies or with the collection of additional clinical data. In making coverage decisions involving CED, CMS decides after a formal review of the medical literature to cover an item or service only in the context of an approved clinical study or when additional clinical data are collected to assess the appropriateness of an item or service for use with a particular beneficiary.

The 2014 CED Guidance Document is available at https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27

In our analysis we seek answers to the below questions. We note that these questions are the same as set forth in the current NCD (see section 150.13 of the NCD Manual).

Is the evidence sufficient to conclude that PILD improves health outcomes in Medicare beneficiaries with LSS?

1. *Does PILD provide a clinically meaningful improvement of function (e.g., reduced acute and post-acute hospitaliztions, nursing home care or inpatient rehabilitation services) and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?*
2. *Does PILD provide a clinically meaningful reduction in pain (e.g., as measured by class, dose, duration of prescription pain medication use) in Medicare beneficiaries with LSS compared to other treatments?*
3. *Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services (e.g., repeat PILD procedures, other interventions and surgical treatments), compared to other treatments?*

B. Discussion

In our 2014 PILD NCD, CMS set forth CED criteria that required a randomized controlled trial (RCT) and noted a particular interest in improved beneficiary function and quality of life, specific characteristics that identify patients who may benefit from the procedure, and the duration of benefit. We recognize that PILD procedures performed prior to our 2014 decision may provide anecdotes but these were not systematically collected in a structured study. Since that time (January 2014), a single RCT has been completed, the MiDAS ENCORE study, and we received two published, peer-reviewed data articles based on that single RCT. (Staats 2016 and Benyamin 2016). In addition to the single RCT, we reviewed non-RCT articles published after November 2013. These articles include: a case series by Basu, a retrospective study by Durkin, and Wang's case review article. We reviewed a systematic review published by Kreiner and associates (Kreiner et. al. 2014). After reviewing the single RCT and the publications, we determined there are weaknesses in each of the studies or articles we reviewed, including methodology and design which erodes the confidence in the evidence presented. We explain below.

As stated in the evidence section of this decision memorandum, Staats and Benyamin concluded that MILD® is statistically superior to ESIs in the treatment of LSS patients with neurogenic claudication and central stenosis due to ligamentum flavum hypertrophy. The authors also found that the MILD® procedure showed statistically significantly improvement in function even after one (1) year. However, after closely reviewing the RCT data, several concerns were identified that need further study and explanation.

A concern was the occurrence of two deaths in the MILD® treatment group after the publication of the 6 month data. There were no deaths in the ESI group. While the authors stated that the patients "died of unrelated causes (one cardiopulmonary arrest and one cardiac arrest)", it is unclear how this determination was made since cardiopulmonary and cardiac arrest are non-specific and do not identify the underlying cause. Since these deaths were unexpected for a minimally invasive procedure, further detailed adjudication of these two deaths is needed. In addition, judgment about whether or not an outcome or harm was related may introduce bias. One of the strengths of comprehensive outcomes such as all-cause mortality is that these outcomes involve only ascertainment of the events and do not involve judgment. For example with CMS quality measures, mortality measures generally assess all-cause mortality; that is, they consider deaths for all reasons, not just due to the underlying principal diagnosis. There are reasons for this choice of outcome. First, from the patient perspective,

death from any cause is the key outcome. Second, it is often hard to exclude quality issues and accountability based on the documented cause of death (CMS, 2007).

Long term outcomes have not been reported. In the 2014 NCD we were explicit that we were interested in long term outcomes. In fact we stated in the 2014 NCD decision memorandum:

CMS believes that durability of benefit is an important evidentiary question. A beneficiary's preferences are informed by the ability to consider potential benefits and harms among the available therapeutic options. This consideration is significantly limited if the likely duration of benefit is unclear.

Durability of treatment effect: Since lumbar spinal stenosis is a chronic, progressive disease, a minimally invasive intervention that produces durable improvements in health outcomes has been sought to avoid the need for invasive spinal surgery. It is important that PILD be considered in this context. If benefits are only temporary or time limited, spinal surgery may not be avoided. Then these patients may be subject to multiple procedures and the burden of recovery from these procedures. The MiDAS ENCORE 12 month study results do not allow an assessment of the duration of benefit, which limits the quality and broader applicability of the study results.

Pain: Importantly, after review of the results of this trial it was noted that there were not any significant changes in the use of medication post-operatively. While several comments stated this was a positive outcome of the publications based on the MiDAS ENCORE study, we believe this is an objective measure of the effectiveness of PILD.

Comparator: There have been several AHRQ technology assessments and systematic reviews indicating that ESIs as a control group is challenging.

As explained above, we also reviewed non-RCT articles published after November 2013. Again, these articles include: a case series by Basu, a retrospective study by Durkin and a case review article by Wang.

All of the articles reviewed were non-RCTs and had major design flaws that preclude us from using them confidently as reliable evidence for full coverage of PILD procedures.

Durkin's retrospective study was not a randomized controlled study but rather a retrospective observational study that only characterized trends in pain and function after the MILD® procedure. The study did not look at hard endpoints. Retrospective observational studies are not high grade evidence because there is no control group, the sample size was small (n=50) and the study was not representative of the Medicare population.

Basu's case series study, similar to Durkin, had major design flaws. The study did not have a control group and it had an extremely small sample size (N=27). Further, follow up was short (6 months). The study endpoints only looked at safety and efficacy and not health outcomes such as quality of life or pain reduction. The small size of the study prevents us from generalizing the to Medicare beneficiaries.

Kreiner and associates did not perform a study but rather a systematic review (Kreiner et. al. 2014). CMS has reviewed all of the studies in the Kreiner review in the 2014 NCD. No new studies were identified.

Lastly, Wang and associates (2013) assessed change in pain score and patient satisfaction 1-2 weeks post-MILD® in addition to health care resource utilization in a select single-center Veteran's Administration (VA) chronic pain management clinic patient population. This study design did not have a control group, included a small number of participants (n=22), only measured pain and patient satisfaction 1-2 weeks post-MILD® procedure, and had variable follow-up (2– 15 months) over which reductions in interventional pain procedures and time spent in specialty care were assessed. Moreover, because Wang and associates reported on a single-centered select VA patient population, did not examine sustained patient satisfaction or visual analog scores, did not assess disability indices such as Oswestry Disability Index or medication usage for neurogenic claudication, and omitted emergency department and primary care visits for pain from health care utilization endpoint, the study is not reliable and not generalizable.

Coverage with Evidence Development

In our 2014 NCD, we established CED for PILD in beneficiaries with LSS and supported two RCTs because we recognized that LSS is a real and important source of pain and functional limitation for patients and that effective minimally invasive procedures could have a place in the treatment armamentarium.

CMS uses an evidence-based approach to determine whether an item or service improves health outcomes for the Medicare population. For PILD, two RCTs in a controlled research setting have been conducted and supported under CED. We recognize the strengths of randomized controlled trials but acknowledge that the controlled trial environment is different than the general clinical practice setting. Due to practical aspects of conducting RCTs, sample size may be limited. While the sample size may not be considered small for a RCT, the number of patients that were treated in the PILD RCT is relatively small compared to the large number of potentially eligible patients. Before full clinical implementation is supportable, we believe PILD should be tested in general clinical practice to further the evidence base and determine whether these RCT findings will be actualized in broad practice. This is consistent with widely accepted, long standing concepts in evidence development (also referred to as translation science defined by the National Institutes of Health as "the process of turning observations in the laboratory,

clinic and community into interventions that improve the health of individuals and the public — from diagnostics and therapeutics to medical procedures and behavioral changes" (see https://ncats.nih.gov/translation/spectrum).

For NCDs, CMS uses an evidence-based medicine approach and considers the quality, strength and totality of evidence for the Medicare population. Though CED clinical studies may demonstrate certain findings, the results themselves may not be sufficient for CMS to change coverage policies. We had proposed a prospective cohort study. In response to comments, we have revised the required study design from a prospective cohort study to a broader prospective longitudinal study to increase patient access. We believe that a prospective longitudinal study will be able to answer our CED questions, show duration of benefit and avoidance of harm, and provide evidence to support wide clinical implementation. The prospective longitudinal study design is consistent with the broader concept to incorporate real world evidence and data that provide important information for beneficiaries as they make treatment decisions.

CMS is also interested in evidence to address the use of prescription pain medications (e.g., as measured by class, dose and duration use), which has emerged as a potential co-intervention from the single published randomized trial reviewed in this NCD. To ensure confidence in the subsequent analysis results, the inclusion/exclusion criteria must be maintained in this second phase.

Prospective longitudinal studies may include prospective cohort studies using cohorts identified, followed and analyzed through administrative claims data. For claims-based studies, a methodically sound protocol and rigorous data plan to track patients and to determine subsequent outcomes are needed. For example in answering the CED questions, ascertainment of benefits and harms may include among others:

1. For functional status and quality of life, acute and post-acute hospitalizations, nursing home stays, inpatient rehabilitation facility stays, and others;
2. For reduction in pain, prescription pain medication use, type/class of pain medication, dosage, duration and others;
3. For other medical treatments and services, reoperations with PILD, invasive spinal surgery and other medical and surgical services.

CMS will carefully review prospective longitudinal study protocols and analysis plans to maximize the likelihood of obtaining high quality results to address the CED questions. Further, CMS will also be collaboratively reviewing methods with AHRQ to assist in addressing the CED questions.

We believe the decision to require CED will add evidence concerning longer term outcomes, such as subsequent invasive spinal procedures and potential harms of the procedure which are key to answering the question we asked in 2014 NCD, and again today, to enable us to reach a decision about coverage under section 1862(a)(1)(A) of the Social Security Act. Since the RCTs have been completed and no patients had coverage of PILD, we finalized this NCD to facilitate appropriate coverage and maintain patient access. We added a criterion about publishing results in the clinicaltrials.gov database because we believe it is important that the public is aware of the studies and any reported results.

In conclusion, based on the totality of the evidence reviewed, questions remain and there is not a clear picture of whether the promising observed improvements in the single RCT will also be seen when these procedures are broadly used in the general Medicare population outside the structured, controlled trial settings. For these reasons, we believe it is important to continue to support evidence development or as many refer to it, translational science, and believe that CED is the right evidentiary determination. CMS is not requiring another RCT or as we originally proposed, a prospective comparative study, but based on public comment, a prospective longitudinal study that will allow broader appropriate access and reduce burden.

C. Health Disparities

The current literature does not address general disparities, though gender, age, and some demographic information are reported in some studies. The studies fail to discuss matters related to race or ethnicity, socio-economic status, disability, geographic location or religious beliefs. In general, there is significant information in the literature regarding disparities in pain management, however, in the more recent studies reviewed in this analysis, CMS found no discussion regarding such disparities. Future studies involving the use of PILD in patients with LSS are encouraged to incorporate representative samples so that the findings may be more generalizable to the Medicare population.

IX. Decision (repeated from Section I)

After considering public comments as required by section 1862(l) of the Social Security Act, CMS will finalize its proposal to continue CED and expand the January 2014 NCD. CMS will cover through a prospective longitudinal study PILD procedures using an FDA-approved/cleared device that successfully completed a CMS-approved RCT that met the criteria listed in Section 150.13 of the NCD manual.

In addition, the CMS-approved prospective longitudinal study must answer at least one of the following questions:

1. *Does PILD provide a clinically meaningful improvement of function (e.g., reduced acute and post-acute hospitalizations, nursing home care or inpatient rehabilitation services) and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?*
2. *Does PILD provide a clinically meaningful reduction in pain (e.g., as measured by class, dose, duration of prescription pain medication use) in Medicare beneficiaries with LSS compared to other treatments?*
3. *Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services (e.g., repeat PILD procedures, other interventions and surgical treatments), compared to other treatments?*

The prospective longitudinal study must also meet the following criteria:

1. The protocol must specify a statistical analysis and a minimum length of patient follow-up time that evaluates the effect of beneficiary characteristics on patient health outcomes as well as the duration of the benefit.
2. The eligibility requirements, both inclusion and exclusion criteria that were specified in the CMS-approved RCT protocol, must be maintained in the new prospective longitudinal study.
3. All study sites and study results must be listed in the ClinicalTrials.gov database.

All CMS-approved clinical research studies must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Research & Quality (AHRQ) Registry of Patient Registries (RoPR).
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion
m. criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
n. Thestudy protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

All clinical research study protocols must be reviewed and approved by CMS. The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator's contact information, to the address below.

Director, Coverage and Analysis Group
Re: PILD CED
Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850

Email address for protocol submissions: clinicalstudynotification@cms.hhs.gov
Email subject line: "CED [NCD topic (i.e. PILD)] [name of sponsor/primary investigator]"

The information will be reviewed, and approved studies will be identified on the CMS website - https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html.

See Appendix B for our proposed manual language.

APPENDIX A
General Methodological Principles of Study Design
(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

A. Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
B. Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
C. Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
D. Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
E. Masking (blinding) to ensure patients and investigators do not know to that group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is to the extent that differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well-designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of that have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials
Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e. g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in that confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent that the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co- interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention

than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

This information is representative of Medicare's national coverage determination (NCD) for comment purposes only. The information is subject to formal revisions as a result of public comments as well as formatting changes prior to the release of the final NCD contractor instructions and publication in the Medicare National Coverage Determinations Manual.

150.13 – Percutaneous Image-guided Lumbar Decompression (PILD) for Lumbar Spinal Stenosis (LSS)
(Rev.)

A. General

PILD is a posterior decompression of the lumbar spine performed under indirect image guidance without any direct visualization of the surgical area. This is a procedure proposed as a treatment for symptomatic LSS unresponsive to conservative therapy. This procedure is generally described as a non-invasive procedure using specially designed instruments to percutaneously remove a portion of the lamina and debulk the ligamentum flavum. The procedure is performed under x-ray guidance (e.g., fluoroscopic, CT) with the assistance of contrast media to identify and monitor the compressed area via epiduragram.

B. Nationally Covered Indications

Effective for dates of service specified below, the Centers for Medicare & Medicaid Services (CMS) has determined that PILD will be covered by Medicare when provided in a clinical study under section 1862(a)(1)(E) through Coverage with Evidence Development (CED) for beneficiaries with LSS who are enrolled in an approved clinical study that meets the criteria in section I or II below:

I. Effective for services performed on or after January 09, 2014, PILD will be covered by Medicare through CED for beneficiaries with LSS who are enrolled in an approved clinical study that meets the following criteria. CMS has a particular interest in improved beneficiary function and quality of life, specific characteristics that identify patients who may benefit from the procedure, and the duration of benefit. A clinical study seeking Medicare payment for PILD for LSS must address one or more aspects of the following questions in a prospective, randomized, controlled design using current validated and reliable measurement instruments and clinically appropriate comparator treatments, including appropriate medical or surgical interventions or a sham controlled arm, for patients randomized to the non-PILD group.

The study protocol must specify a statistical analysis and a minimum length of patient follow up time that evaluates the effect of beneficiary characteristics on patient health outcomes as well as the duration of benefit.

i. Does PILD provide a clinically meaningful improvement of function and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?

ii. Does PILD provide clinically meaningful reduction in pain in Medicare beneficiaries with LSS compared to other treatments?

iii. Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services, compared to other treatments?

These studies must be designed so that the contribution of treatments in addition to the procedure under study are either controlled for or analyzed in such a way as to determine their impact.

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for CED coverage.
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors

(http://www.icmje.org).
l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Social Security Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

II. Effective for services performed on or after the date of this final decision memo posting, CMS will cover through a prospective longitudinal study PILD procedures using an FDA-approved/cleared device that completed a CMS-approved RCT that met the criteria listed in section I above.

The CMS-approved prospective longitudinal study must answer at least one of the following questions:

1. *Does PILD provide a clinically meaningful improvement of function (e.g., reduced acute and post-acute hospitaliztions, nursing home care or inpatient rehabilitation services) and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?*
2. *Does PILD provide a clinically meaningful reduction in pain (e.g., as measured by class, dose, duration of prescription pain medication use) in Medicare beneficiaries with LSS compared to other treatments?*
3. *Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services (e.g., repeat PILD procedures, other interventions and surgical treatments), compared to other treatments?*

The prospective longitudinal study must also meet the following criteria:

1. The protocol must specify a statistical analysis and a minimum length of patient follow-up time that evaluates the effect of beneficiary characteristics on patient health outcomes as well as the duration of the benefit.
2. The eligibility requirements, both inclusion and exclusion criteria that were specified in the CMS-approved RCT protocol, must be maintained in the new prospective longitudinal study.
3. All study sites and study results must be listed in the ClinicalTrials.gov database.

All CMS-approved clinical research studies must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Research & Quality (AHRQ) Registry of Patient Registries (RoPR).
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

All clinical research study protocols must be reviewed and approved by CMS. The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator's contact information, to the address below:

Director, Coverage and Analysis Group
Re: PILD CED
Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850

Email address for protocol submissions: clinicalstudynotification@cms.hhs.gov
Email subject line: "CED [NCD topic (i.e. PILD)] [name of sponsor/primary investigator]"

The information will be reviewed, and approved studies will be identified on the CMS website - https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html.

C. Nationally Non-Covered Indications

Effective for services performed on or after January 09, 2014, CMS has determined that PILD for LSS is not reasonable and necessary under section 1862(a)(1)(A) of the Social Security Act.

D. Other

Endoscopically assisted laminotomy/laminectomy, which requires open and direct visualization, as well as other open lumbar decompression procedures for LSS are not within the scope of this NCD.

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Bibliography

AAOS – Lumbar Spinal Stenosis. American Academy of Orthopedic Surgeons web site. http://orthoinfo.aaos.org/topic.cfm?topic=a00329 Updated December 2013. Accessed July 2016.

Andreisek G, Hodler J, Steurer J. Uncertainties in the Diagnosis of Lumbar Spinal Stenosis. *Radiology* 2011; 261:681–684. doi:10.1148/radiol.11111086. PMID: 22095990

ASA – American Society of Anesthesiologists Physical Status Classification System [PDF] from web site. https://www.asahq.org/quality-and-practice-management/standards-and-guidelines Updated October 2014. Accessed August 2016.

Atlas SJ, Deyo RA, Keller RB, Chapin AM, Patrick DL, Long JM, Singer DE. The Maine lumbar spine study, part III: 1- year outcomes of surgical and nonsurgical management of lumbar spinal ste- nosis. Spine 1996; 21:1787-1794. PMID: 8855463

Atlas S, Keller R, Wu Y, et al. Long-Term Outcomes of Surgical and Nonsurgical Management of Lumbar Spinal Stenosis: 8 to 10 Year Results from the Maine Lumbar Spine Study. *Spine* 2005; 30(8): 936–943. PMID: 15834339

Basu S. MILD® procedure: single-site prospective IRB study. *Clin J Pain* 2012; 28(3):254-258. PMID: 21926907

Benyamin, R., et al. (2016), MILD® is an Effective Treatment for Lumbar Spinal Stenosis with Neurogenic Claudication: MiDAS ENCORE Randomized Controlled Trial, Pain Physician, 19: 229-242. PMID: 27228511

Benyamin RM, Staats PS. MiDAS ENCORE: randomized controlled clinical trial report of 6-month results. Pain Physician 2015; 18:307-316. PMID: 26815247

Boden S. Current Concepts: Review The Use of Radiographic Imaging Studies in the Evaluation of Patients Who Have Degenerative Disorders of the Lumbar Spine. *J Bone Joint Surg Am.* 1996; 78:114-24. PMID: 8550669

Brown L. A double-blind, randomized, prospective study of epidural steroid injection vs. the MILD® procedure in patients with symptomatic lumbar spinal stenosis. *Pain Practice* 2012; 12:333-34. PMID: 22272730

Bydon M, De la Garza-Ramos R, Macki M, Baker A, Gokaslan AK, Bydon A. Lumbar fusion versus nonoperative management for treatment of discogenic low back pain: A systematic review and metaanalysis of randomized controlled trials. J Spinal Disord Tech 2014; 27:297-304. PMID: 24346052

Carey T, Boden S. A Critical Guide to Case Series Reports. *Spine* 2003; 28(15): 1631–1634. PMID: 12897483

Centers for Medicare and Medicaid Services. Frequently Asked Questions (FAQs). Implementation and Maintenance of CMS Mortality Measures for AMI & HF. 2007. Available at: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/HospitalQualityInits/downloads/HospitalMortalityAboutAMI_HF.pdf

Chen H, Kelling J. MILD® Procedure for Lumbar Decompression: A Review. *Pain Practice* 2013; 13(2): 146-153. doi:10.1111/j.1533-2500.2012.00574. PMID: 22726247

Chopko B. A novel method for treatment of lumbar spinal stenosis in high-risk surgical candidates: pilot study experience with percutaneous remodeling of ligamentum flavum and lamina. *J Neurosug Spine* 2011; 14:46-50. PMID: 21142460

Chopko B, Caraway D. MIDAS 1 (MILD® decompression alternative to open surgery): a preliminary report of a prospective, multi-center clinical study. *Pain Physician* 2010; 13:369-378. PMID: 20648206

Chopko B. Long-term results of percutaneous lumbar decompression for LSS, two-year outcomes. *Clin J Pain* 2013; Feb 26. [Epub ahead of print]. PMID: 23446067

Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S, Brodt E. Noninvasive Treatments for Low Back Pain. Comparative Effectiveness Review No. 169. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 16-EHC004- EF. Rockville, MD: Agency for Healthcare Research and Quality; February 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Chou R, Hashimoto R, Friedly J, Fu Rochelle, Dana T, Sullivan S, Bougatsos C, Jarvik J. Pain Management Injection Therapies for Low Back Pain. Technology Assessment Report ESIB0813. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. HHSA 290-2012-00014-I.) Rockville, MD: Agency for Healthcare Research and Quality; July 2015 references.

Comer SD, Zacny JP, Dworkin RH, Turk DC, et al. Core outcome measures for opioid abuse liability laboratory assessment studies in humans: IMMPACT recommendations. Pain. 2012 Dec; 153(12):2315-24. doi: 10.1016/j.pain.2012.07.035. PMID: 22998781

de Graaf I, Prak A, Bierma-Zeinstra S, et al. Diagnosis of Lumbar Spinal Stenosis. A Systematic Review of the Accuracy of Diagnostic Tests. *Spine* 2006; 31:1168–1176. PMID: 16648755

Deer T, Kapural L. New Image-guided ultra-minimally invasive lumbar decompression method: the MILD® procedure. *Pain Physician* 2010; 13:35-4. PMID: 20119461

Deer T, Kim C, Bowman II R, et al. Study of percutaneous lumbar decompression and treatment algorithm for patients suffering from neurogenic claudication. *Pain Physician* 2012; 15:451-460. PMID: 23159960

Deer T, Mekhail N, Lopez G, Amirdelfan K. Minimally Invasive Lumbar Decompression for Spinal Stenosis. *JNR* 2011; 1(S1): 29-32.

Deer T. Minimally Invasive Lumbar Decompression for the Treatment of Spinal Stenosis of the Lumbar Spine. *Pain Management* 2012; 2(5): 457-465, ISSN 1758-1869. PMID: 24645862

Deyo R, Mirza S, Martin B, Kreuter W, Goodmand DC, Jarvik JG. Trends, Major Medical Complications, and Charges Associated with Surgery for Lumbar Spinal Stenosis in Older Adults. *JAMA* 2010; 303(13):1259-1265. doi:10.1001/jama.2010.338. PMID: 20371784

Deyo R, Mirza S, Turner J, Martin B. Over-treating Chronic Back Pain: Time to Back Off? *J Am Board Fam Med* 2009; 22:62-68. doi: 10.3122/jabfm.2009.01.080102. PMID: 19124635

Deyo RA. Walsh NE, Martin DC, Schoenfeld LS, el al. A controlled trial of transcutaneous electrical nerve stimulation (TENS) and exercise for chronic low back pain. N Engl J Med 1990; 322: 1627-1634. PMID: 2140432

Durkin B, Romeiser J, Shroyer AL, et al. Report from a quality assurance program on patients undergoing the MILD® procedure. *Pain Medicine* 2013; 14(5):650-6. PMID 23489390

ECRI Health Technology Assessment Group. *Treatment of Degenerative Lumbar Spinal Stenosis. Evidence Reports/Technology Assessment No. 32.* Rockville, MD: Agency for Healthcare Research and Quality; 2001 June. Available online at: http://www.ncbi.nlm.nih.gov/books/NBK33617/ Bookshelf ID: NBK33617, ISBN-10:1-58763-051-6. Accessed July 2016.

Epstein NE. The frequency and etiology of intraoperative dural tears in 110 pre- dominantly geriatric patients undergo- ing multilevel laminectomy with non-instrumented fusions. J Spinal Disord Tech 2007; 20:380-386. PMID: 17607104

Gregg EW. Et al. Relationship of Changes in Physical Activity and Mortality Among Older Women. JAMA: Journal of the American Medical Association, 2003; 289(18)2379-2386. PMID: 12746361

Grider JS, Manchikanti L, Carayannopoulos A, Sharma ML, Balog CC, Harned ME, Grami V, Justiz R, Nouri KH, Hayek SM, Vallejo R, Christo PJ. Effectiveness of spinal cord stimulation in chronic spinal pain: A systematic review. Pain Physician 2016; 19:E33-E54. PMID: 26752493

Green CR, Anderson KO, Baker TA, et al. The Unequal Burden of Pain: Confronting Racial and Ethnic Disparities in Pain. *Pain Medicine* 2003; 4(5):277-294. PMID: 12974827

Gunzburg R, Szpalski M. The conservative surgical treatment of lumbar spinal stenosis in the elderly. *Eur Spine J* 2003; 12(2):S176–S180. doi: 10.1007/s00586-003-0611-2. PMID: 12961080

Hägg O, Fritzell P, Nordwall A. Swedish Lumbar Spine Study Group. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J*. 2003 Feb; 12(1):12-20. Epub 2002 Oct 24. doi: 10.1007/s00586-002-0464-0. PMID: 12592542

Haig A, Tong H, Yamakawa K, et al. Spinal Stenosis, Back Pain, or No Symptoms at All? A Masked Study Comparing Radiologic and Electrodiagnostic Diagnoses to the Clinical Impression. *Arch Phys Med Rehabil* 2006; 87:897-903. PMID: 16813774

IOM (Institute of Medicine) – Lo B and Field M. *Conflict of Interest in Medical Research, Education, and Practice.* Washington, DC: The National Academies Press. 2009. Available online at http://www.ncbi.nlm.nih.gov/books/NBK22942/. Bookshelf ID: NBK22942. doi: 10.17226/12598. PMID: 20662118. Accessed 7/14/2016.

Issack P, Cunningham M, Pumberger M, et al. Degenerative Lumbar Spinal Stenosis: Evaluation and Management. *J Am Acad Orthop Surg* 2012; 20:527-535. doi: 10.5435/JAAOS-20-08-527. PMID: 22855855

Khan MH, Rihn J, Steele G, Davis R, Don- aldson WF 3rd, Kang JD, Lee JY. Post- operative management protocol for incidental dural tears during degenerative lumbar spine surgery: A review of 3,183 consecutive degenerative lumbar cases. Spine (Phila Pa 1976). 2006; 15; 31:2609-2613. PMID: 17047553

Kovacs F, Urrutia G, Alacon J. Surgery versus Conservative Treatment for Symptomatic Lumbar Spinal Stenosis: a Systematic Review of Randomized Controlled Trials. *Spine* 2011; 36(20):E1335–E135. PMID: 21311394

Kreiner D, MacVicar J, Duszynski B, Nampiaparampil DE. The MILD® procedure: a systematic review of the current literature. *Pain Medicine* 2014; 15(2):196-205. doi: 10.1111/pme.12305. Epub 2013 Dec 5. PMID: 24308292

Kurd M, Lurie J, Zhao W, et al. Predictors of Treatment Choice in Lumbar Spinal Stenosis: a Spine Patient Outcomes Research Trial Study. *Spine* 2012; 37(19):1702–1707. PMID: 22426453

Levy R, Deer T. Systematic safety review and meta-analysis of procedural experience using percutaneous access

to treat symptomatic lumbar spinal stenosis. *Pain Medicine* 2012; 13:1554-1561. PMID: 23136978

Lingreen R, Grider J. Retrospective review of patient self-reported improvement and post-procedure findings for MILD® (minimally invasive lumbar decompression). *Pain Physician* 2010; 13:555-560. PMID: 21102968

Malmivaara A, Slätis P, Heliövaara M, Sainio P, Kinnunen H, Kankare J, Da- lin-Hirvonen N, Seitsalo S, Herno A, Kortekangas P, Niinimäki T, Rönty H, Tallroth K, Turunen V, Knekt P, Härkän- en T, Hurri H; Finnish Lumbar Spinal Research Group. Surgical or nonoperative treatment for lumbar spinal stenosis? A randomized controlled trial. Spine (Phi- la Pa 1976). 2007; 32:1-8. PMID: 17202885

Mamisch N, Brumann M, Holder J, et al. Radiologic Criteria for the Diagnosis of Spinal Stenosis: Results of a Delphi Survey. *Radiology* 2012; 264(1):174-179. PMID: 22550311

Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: A comparative systematic review and meta-analysis. Pain Physician 2016; E365-E410. PMID: 27008296

Manchikanti L, Kaye AD, Manchikanti KN, Boswell MV, Pampati V, Hirsch JA. Efficacy of epidural injections in the treatment of lumbar central spinal stenosis: A systematic review. Anesth Pain Med 2015; 5:e23139. PMID: 25789241

Manchikanti L, Staats PS, Nampiaparampil DE, Hirsch JA. What is the role of epidural injections in the treatment of lumbar discogenic pain: A systematic review of comparative analysis with fusion and disc arthroplasty. Korean J Pain 2015; 28:75-87. PMID: 25852828

Manini T et al. Daily Energy Expenditure and Mortality Among Older Adults, JAMA: Journal of the American Medical Association, 2006, 296(2):171-179. PMID: 16835422

Mattei T. A Gaze Beyond the Surface: Acknowledging the Little We Know About Radiographic Parameters for Evaluation of Lumbar Spinal Stenosis. *Neurosurgery* 2013; 72(1):E135 –E140. PMID: 23037829

MEDCAC. *Spinal Fusion for the Treatment of Low Back Pain Secondary to Lumbar Degenerative Disc Disease.* Medicare Evidence Development & Coverage Advisory (MEDCAC) Committee Meeting 11/30/2006 - http://www.cms.gov/medicare-coverage-database/details/medcac-meeting-details.aspx?MEDCACId=37 Accessed July 2016.

Mekhail N, Costandi S, Abraham B, Samuel S. Functional and patient-reported outcomes in symptomatic lumbar spinal stenosis following percutaneous decompression. *Pain Practice* 2012; 12:417-425. PMID: 22651852

Mekhail N, Vallejo R, Coleman M, Benyamin A. Long-term results of percutaneous lumbar decompression MILD® for spinal stenosis. *Pain Practice* 2012; 12(6):184-193. PMID: 21676166

Mills A, Edwards J, Shofer F, et al. Analgesia for Older Adults with Abdominal or Back Pain in Emergency Department. *West J Emerg Med* 2011; 12(1):43-50. PMID: 21691471

Nampiaparampil D, Nampiaparampil J, and Harden R. Pain and Prejudice. *Pain Medicine* 2009; 10(4):716-721. PMID: 19453964

NASS Evidence-Based Clinical Guidelines Committee. *North American Spine Society Clinical Guidelines for Multidisciplinary Spine Care Diagnosis: Treatment of Degenerative Lumbar Spinal Stenosis.* 2011; Available online at: https://www.spine.org/Documents/ResearchClinicalCare/Guidelines/LumbarStenosis.pdf Accessed July 2016.

Ostelo R, Deyo R, Stratford P, et al. Interpreting Change Scores for Pain and Functional Status in Low Back Pain: Towards International Consensus Regarding Minimal Important Change. *Spine* 2008; 33(1):90–94. PMID: 18165753

Pryce R, Johnson M, Goytan M, et al. Relationship between Ambulatory Performance and Self-Rated Disability in Patients with Lumbar Spinal Stenosis. *Spine* 2012; 37(15):1316–1323. PMID: 22261635

Phillips FM, Slosar PJ, Youssef JA, Andersson G, Papatheofanis F. Lumbar spine fusion for chronic low back pain due to degenerative disc disease: a systematic review. Spine (Phila Pa 1976) 2013; 38:E409- E422. PMID: 23334400

Quessy SN. Rowbotham MC. Placebo response in neuropathic pain trials. Pain 2008: 138:479-483. PMID: 18706762

Ragab AA, Fye MA, Bohlman HH. Surgery of the lumbar spine for spinal stenosis in 118 patients 70 years of age or older. Spine 2003; 28:348-353. PMID: 12590208

Saltychev M, Eskola M, Laimi K. Lumbar fusion compared with conservative treatment in patients with chronic low back pain: A meta-analysis. Int J Rehabil Res 2014; 37:2-8. PMID: 23820296

Sandella D, Haig A, Tomkins-Lane C, Yamakawa K. Defining the Clinical Syndrome of Lumbar Spinal Stenosis: A Recursive Specialist Survey Process. *PM R* 2013; 5:491-495. PMID: 23159240

Schomer D, Solsberg D, Wong W, Chopko B. MILD® Lumbar decompression for the treatment of lumbar spinal stenosis. *The Neuroradiology Journal* 2011; 24:620-626. PMID: 24059721

Shah R, Everett C, McKenzie-Brown A, Sehgal N. Discography as a Diagnostic Test for Spinal Pain: A Systematic and Narrative Review. *Pain Physician* 2005; 8:187-209. ISSN 1533-3159. PMID: 16850074

Siebert E, Prüss H, Klingebiel R, Failli V, Einhäupl K, Schwab J. Lumbar spinal stenosis: syndrome, diagnostics and treatment. *Nat Rev Neurol.* 2009; 5(7):392-403. doi: 10.1038/nrneurol.2009.90. PMID: 19578346

Staats P, Benyamin R, et al. MiDAS ENCORE: Randomized Controlled Clinical Trial Report of 6-Month Results. *Pain Physician* 2016. 19:25-38. ISSN 1533-3159. PMID: 26815247

Tafazal SI, Sell PH. Incidental durotomy in lumbar spine surgery: Incidence and management. Eur Spine J 2005; 14:287- 290. PMID: 15821921

Tumialan L. Regarding: Long-Term Results of Percutaneous Lumbar Decompression MILD® for Spinal Stenosis. *Pain Practice* 2012; 12(3):252–253. PMID: 22390527

Turner J, Deyo R, Loeser J, Von Kordd M, et al. The importance of placebo effects in pain treatment and research. JAMA 1994; 271:1609-14. PMID: 7880221

Udeh B, Constandi S, Dalton J, Ghosh R, Yousef H, Mekhail N. The 2-Year Cost-Effectiveness of three options to Treat Lumbar Spinal Stenosis Patients. *Pain Practice* 2015; 15(2):107-16. Epub 2014. doi: 10.1111/papr.12160. PMID: 24393198

Wang J, Bowden K, Pang G, Cipta A. Decrease in health care resource utilization with MILD®. *Pain Medicine* 2013; 14(5):657-61. PMID: 23578021

Weinstein J, Tosteson T, Lurie J, et al. Surgical versus Nonsurgical Therapy for Lumbar Spinal Stenosis. *N Engl J Med* 2008; 358:794-810. PMID: 18287602

Wilkinson J, Fourney D. Failure of Percutaneous Remodeling of the Ligamentum Flavum and Lamina for Neurogenic Claudication. *Neurosurgery* 2012; 71:86–92. doi: 10.1227/NEU.0b013e31825356f5. PMID: 22407072

Wong W. MILD® interlaminar decompression for the treatment of lumbar spinal stenosis, procedure description and case series with 1-year follow-up. *Clin J Pain* 2012; 28:534-538. PMID: 22673487

Zaina F, Tomkins-Lane C, Carragee E, Negrini S. Surgical versus non-surgical treatment for lumbar spinal stenosis. Cochrane Database Syst Rev 2016; (1):CD01026. PMID: 26824399

Zheng, H.; Ehrlich, F.; Amin, J. Quantifying the effect size of walking interventions to reduce the risk of coronary heart disease: meta-analysis. International Journal of Body Composition Research. 2010 Supplement, Vol. 8, p51 -59. 9p.

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