Effective Health Care

Treatment of Painful Peripheral Neuropathy

Results of Topic Selection Process & Next Steps

The nominator, American College of Physicians (ACP) is interested in a new evidence review on Treatment of Painful Peripheral Neuropathy to develop new clinical practice guideline.

Topic didn't pass duplication. We identified twenty-five (n=25) systematic reviews and sixteen (n=16) Cochrane systematic reviews covering the scope of the nomination, therefore, a new review would be duplicative of an existing product. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Number and Name #: 0774 Treatment of Painful Peripheral Neuropathy

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Authors
Aysegul Gozu
Rose Relevo
Christine Chang

Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Background

Peripheral neuropathy (PN) is a common neurological disorder caused by damaged to the peripheral nerve system (apart from the brain and spinal cord). PN is a general term and can result from variety of diseases and conditions. More than 100 types of peripheral neuropathy have been identified, each with its own symptoms and prognosis[5]. The most common reasons are diabetes mellitus (DM), toxins, chemotherapy, alcohol, infections and injury. PN symptoms vary depending on the type of nerves—motor, sensory, or autonomic—that are damaged. Most neuropathies affect all three types of nerve fibers to varying degrees; others primarily affect one or two types.

Damaged to sensory nerves may impair sensation and may cause variety of sensation related symptoms from numbness or mild pain to severe unbearable pain to the affected patient. PN pain is usually chronic and cause a significant detrimental impact on patients' quality of life, functional status, society, and healthcare systems. The prevalence of neuropathic pain in the general population has been estimated at 8–10% and expected to be increase more[5].

Nominator and Stakeholder Engagement
The nominator is interested in using a rigorous systematic review process to develop American College of Physicians (ACP) clinical practice guideline (CPG) on the benefits and harms of the pharmacologic and non-pharmacologic therapies in adults with painful peripheral neuropathy. The nominator would also like to know if the benefits and harms of therapies for peripheral neuropathy vary according to the cause of the neuropathy, patient characteristics, baseline severity of pain, kidney function, or other factors The nominator will use the results of a systematic review to develop CPG and publish a summary evidence report alongside CPG in a peer-reviewed journal. The guideline will also be disseminated via ACP guidelines app, presentation at ACP annual internal medicine meeting, and inclusion in guideline database.

Key Questions and PICOS
The key questions for this nomination are:

Key Question 1. In adults with painful peripheral neuropathy, what is the effectiveness and comparative effectiveness of different pharmacologic and non-pharmacologic therapies on intermediate and long-term pain and health outcomes?

Key Question 2. In adults with painful peripheral neuropathy, what are the harms and the comparative harms of different pharmacologic and non-pharmacologic therapies?

Key Question 3. Do the benefits and harms of therapies for peripheral neuropathy vary according to the cause of the neuropathy, patient characteristics, baseline severity of pain, kidney function, or other factors?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, outcomes, and setting (PICOS) of interest (Table 1).

Table 1. Key Questions and PICOS

Key Questions	In adults with painful peripheral neuropathy, what is the effectiveness and comparative effectiveness of different pharmacologic and non-pharmacologic therapies on intermediate and long-term pain and health outcomes?	In adults with painful peripheral neuropathy, what are the harms and the comparative harms of different pharmacologic and non-pharmacologic therapies?	In adults with painful peripheral neuropathy, do the benefits and harms of therapies for peripheral neuropathy vary according to the cause of the neuropathy, patient characteristics, baseline severity of pain, kidney function, or other factors?
Population	Adults (>=18) with painful peripheral neuropathy	Adults (>=18) with painful peripheral neuropathy	Adults (>=18) with painful peripheral neuropathy
Interventions	Pharmacotherapies (oral and topical) or non-pharmacologic treatments	Pharmacotherapies (oral and topical) or non-pharmacologic treatments	Pharmacotherapies (oral and topical) or non-pharmacologic treatments

Comparators	Placebo, other pharmacotherapies, non-pharmacologic therapy	Placebo, other pharmacotherapies, non-pharmacologic therapy	Placebo, other pharmacotherapies, non-pharmacologic therapy
Outcomes	Pain intermediate or long-term , functional status, quality of life, employment, ulcers/amputations, harms including falls, fractures	Pain intermediate or long-term , functional status, quality of life, employment, ulcers/amputations, harms including falls, fractures	Pain intermediate or long-term , functional status, quality of life, employment, ulcers/amputations, harms including falls, fractures
Setting	Outpatient	Outpatient	Outpatient

Methods

We assessed nomination "Treatment of Painful Peripheral Neuropathy" for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a literature search in PubMed from January 1, 2013 and August 24, 2018. We reviewed 236 titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review.
See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search.
We reviewed all identified titles and abstracts for inclusion and classified identified studies by key question and study design to assess the size and scope of a potential evidence review.

Compilation of Findings
We constructed a table with the selection criteria and our assessments (Appendix A).

Value
We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

Results
See Appendix A for detailed assessments of all EPC selection criteria.

Appropriateness and Importance
This is an appropriate and important topic.

Desirability of a New Review/Duplication
A new evidence review would be duplicative of an existing evidence review. We found twenty-five (n=25) systematic reviews relevant to KQs on pharmacologic and other treatments for painful NPs (one completed review and two planned reviews from AHRQ; 16 by Cochrane; and 8 found in PubMed). These SRs covered common NPs and broad range of pharmacologic interventions though most reviews provided limited information on non-pharmacological interventions and comparative effectiveness (CE) of different interventions due to limited number of underlying CE studies.

AHRQ completed a systematic review in 2017 on treatments for diabetic peripheral neuropathy. Types of treatments included pharmacologic treatments and non-pharmacologic treatments. AHRQ has a request for task order for two systematic reviews on chronic pain: one on opioid treatment for chronic pain, including neuropathic pain; and another on non-pharmacologic treatment for chronic pain, including neuropathic pain.

We identified sixteen Cochrane systematic reviews. One Cochrane SR was on Treatment for IgG and IgA paraproteinaemic neuropathy[6] and one on Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies [7]. The other 14 SRs included variety of pharmacologic interventions for mixed PNs such as oxcarbazepine, topical clonidine, capsaicin, gabapentin, morphine, oxycodone, buprenorphine, paracetamol, methadone, venlafaxine, fentanyl, hydromorphone, nortriptyline and tramadol.[8-21]

Of the SR identified through pubmed, one SR included patients with chemotherapy induced peripheral neuropathy (CIPN) treated by lafutidine, acupuncture and sweet bee venom[22]. Four SRs focused on patients with DM-PN treated with pregabalin, tapentalol, and variety of pharmacologic interventions [3, 23-25]. Of these, one SR focused on harms of pregabalin treatment[25]. Four SRs included patients with mixed PNs treated with variety of pharmacologic agents.[26-29]

These reviews focused on different underlying disease conditions (eg: DM-PN, CIPN, mixed NPs.) and included wide range of interventions of interest to the partner (ACP).

A new evidence review would be duplicative of an existing evidence reviews since variety of pharmacologic agents reviewed by multiple SRs. However this evidence has been synthesized by a large number of systematic reviews, and a single review of these many conditions and treatments may be of benefit to the nominator.
See Table 2, Duplication column.

Impact of a New Evidence Review
A new systematic review may have unclear level of impact.

Feasibility of New Evidence Review
A new evidence review is feasible. See Table 2, Feasibility column.

We identified a total of 47 studies across the three KQs. Forty-three of the studies were relevant to KQ-1 and likely KQ-2; and four studies were relevant to KQ-3.

We identified 26 RCTs, 13 pre/post studies, 4 cohort studies and 4 data base studies. The majority of the studies included patients with DM-PN (n=28) and CIPN (n=12). Five studies included mixed group of PN patients, and 3 included patients with less common diseases. The studies assessed a variety of interventions; pharmacotherapy with duloxetine and pregabalin were the most common interventions followed by surgical decompression, gabapentin, and tricyclic antidepressants (TCAs, such as amitriptyline, nortriptyline). There were few studies of non-pharmacologic interventions or CAM.

We found 10 active, recruiting or recently completed RCTs on ClinicalTrials.gov relevant to three KQs. See Table 2 for breakdown by KQ and Appendix C for hyperlinks.

Table 2. Key Questions from Nomination, Results of Duplication Search, and Results of Feasibility Search

Key Question	Duplication (Completed or In-Process Evidence Reviews, 1/1/2015-8/24/2018)	Feasibility (Published and Ongoing Research, 1/1/2013-8/24/2018); Yield=236)
KQ-1 In adults with painful peripheral neuropathy, what is the effectiveness and comparative effectiveness of different pharmacologic and non-pharmacologic therapies on intermediate and long-term pain and health outcomes?	Total number of identified systematic reviews: # 25 • AHRQ #1[3] (plus 2 new TOs on Chronic pain) • Cochrane #16[6-21] • PubMed #8[22-24, 26-29]	Size/scope of review Relevant Studies Identified: # 43 • RCT #26[30-54] • Pre-post #13 [55-67] • Cohort#4[68-71] Clinicaltrials.gov (from 1/2013 to 8/30/2018) #10 • Recruiting: # 2 • Active: # 2 • Recently completed/unknown # 6
KQ-2 In adults with painful peripheral neuropathy, what are the harms and the comparative harms of different pharmacologic and non-pharmacologic therapies?	Total number of identified systematic reviews: # 1 • Cochrane #1[25]	Size/scope of review Relevant Studies Identified: see KQ-1 Clinicaltrials.gov: 0 None specific to harms but likely overlaps with above trials

Key Question	Duplication (Completed or In-Process Evidence Reviews, 1/1/2015-8/24/2018)	Feasibility (Published and Ongoing Research, 1/1/2013-8/24/2018); Yield=236)
KQ-3 In adults with painful peripheral neuropathy, do the benefits and harms of therapies for peripheral neuropathy vary according to the cause of the neuropathy, patient characteristics, baseline severity of pain, kidney function, or other factors?	Total number of identified systematic reviews: # 0	Size/scope of review Relevant Studies Identified: # 4 #3 [72-74] used previous RCTs and cohort studies data #1 [75] looked at medical record data to identify patient characteristics. Clinicaltrials.gov: 0 • None specific to harms but likely overlaps with above trials

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question

Value

The potential for value is limited. Treatment of peripheral neuropathies are of interest to clinicians, and clinical practice guidelines developed by ACP can influence practice.

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would be duplicative of an existing product. We found multiple systematic reviews that are relevant but do not fully address the pertinent KQs.
- Impact: A new systematic review would have unclear impact because it is unlikely that help resolve current controversies and lead to a clinical practice guideline that will promote better patient outcomes and reduce unnecessary healthcare expenditure.
- Feasibility: A new review is feasible. The evidence base is likely medium.
- Value: The potential for value is limited. Treatment of peripheral neuropathies are of interest to clinicians, and clinical practice guidelines developed by ACP can influence practice.

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Appendix A. Selection Criteria Summary

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on both effectiveness and comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible and it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. Approximately 8 to 10% of population have peripheral neuropathy.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects heath care decisions for a large, vulnerable population.
2c. Represents important uncertainty for decision makers	The topic represents some uncertainty for decision makers. Since the available evidence is not strong for variety of proposed pharmacologic and non-pharmacologic agents by variety of SRs and CPGs
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both benefits and potential harms of prevention interventions, pharmacological interventions, and non-pharmacological interventions for painful peripheral neuropathy.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, the condition is common and chronic. Long term use of medications can be costly.

Selection Criteria	Supporting Data
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A new review could potentially duplicate other systematic reviews on the topic. However the evidence is synthesized in a number of systematic reviews, and it would benefit the nominator to have a single review that examines the literature for the variety of types of neuropathies and treatments of interest. We found 25 systematic reviews relevant to the nomination. AHRQ completed a relevant SR in 2017 on the treatment of DM-NP. AHRQ review did not include other types of NPs. AHRQ plans to start two systematic reviews on chronic pain, including neuropathic pain. One will focus on opioid compared to other pharmacologic treatment and another on non-pharmacologic treatments. Because these reviews have not yet started it is not known whether the results will be reported by type of peripheral neuropathy. Cochrane completed multiple SRs (#16) in the last 3 years on treatment of mostly mixed NPs. We found 8 additional SR in Pubmed: • One focused on chemotherapy induced peripheral neuropathy (CIPN) treated by lafutidine, acupuncture and sweet bee venom • Four on patients with DM-PN treated with pregabalin, tapentalol, and variety of pharmacologic interventions; one looked only at harms of pregabalin • Four SRs included patients with mixed PNs treated with variety of pharmacologic agents
4. Impact of a New Evidence Review	

Selection Criteria	Supporting Data
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	The standard of care is not very clear. There is some inconsistencies between CPGs and SRs. Treatment options recommended for painful NPs by AAFP, AAN, NICE CPGs and evidence from AHRQ -SR showed that most treatment options for painful NPs are similar. However we found differences between the findings of SRs and CPGs. This may be it is due to population differences; the NICE review included all painful PNs (though mostly Diabetic PN) whereas the AAN guideline, AAFP guideline and AHRQ SR included only diabetic PN patients. • Recently published NICE CPG on the treatment of painful PNs (mixed), AAN and AAFP recommends use of gabapentin as first line but 2017- AHRQ-SR found that gabapentin is not more effective than placebo (low SOE) (for more detail info on the comparison of CPGs are attached as supplementary doc) • AAFP and AAN are currently in the process of updating their CPGs for treatment of painful diabetic NPs. AAFP will update its guideline on diabetic neuropathy with the 2017 AHRQ-SR on treatments for diabetic neuropathy A new systematic review likely may not help to resolve these controversies and lead to guidelines that may improve patient outcomes.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	There is some practice variations likely due to differences between current clinical practice guidelines.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	We estimate that the total size of the relevant literature (August 2013 – present) may be approximately 47 studies across key questions. Scope of the review is likely small/medium if the review updates the 2017 AHRQ SR But if the new review considers to include all painful neuropathies the review might be medium to large size. ClinicalTrials.gov: We found 10 recruiting, ongoing or recently completed RCTs relevant to KQs.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Treatment of peripheral neuropathies are of interest to clinicians, and clinical practice guidelines developed by ACP can influence practice.

Selection Criteria	Supporting Data
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	The nominator will use the results of a systematic review to develop CPG and publish a summary evidence report alongside CPG in a peer-reviewed journal. The guideline will also be disseminated via ACP guidelines app, presentation at ACP annual internal medicine meeting, and inclusion in guideline database.

Appendix B: Search for Evidence Reviews (Duplication)

Between 01/01/2015 to 09/30/2018

Listed are the sources searched.

AHRQ: Evidence reports and technology assessments
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program
Cochrane Systematic Reviews and Protocols http://www.cochranelibrary.com/
PubMed
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/ York Center for Reviews and Dissemination (CRD)

Appendix C. Search Strategy Results (Feasibility)

MEDLINE(PubMed) Searched on August 24th, 2018	
peripheral neuropathy	peripheral neuropathy[Title/Abstract]
AND	
therapy	((("Drug Therapy"[Mesh] OR "drug therapy" [Subheading]) OR ("Therapeutics"[Mesh] OR "therapy" [Subheading])))
AND	
pain	"Pain"[Mesh] OR (pain[Title/Abstract] OR painful[Title/Abstract]))
AND	
Human English 5 years adult	Filters activated: published in the last 5 years, Humans, English, Adult: 19+ years
Systematic Reviews N=11	Systematic[sb]
	URL: https://www-ncbi-nlm-nih-gov.liboff.ohsu.edu/sites/myncbi/10EKwYd086dYyd/collections/56264405/public/
Randomized Controlled Trials (Cochrane's Sensitive Search Strategy for PubMed) N=176	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
	URL: https://www-ncbi-nlm-nih-gov.liboff.ohsu.edu/sites/myncbi/r.relevo.1/collections/56264425/public/
Other N=60	
	URL: https://www-ncbi-nlm-nih-gov.liboff.ohsu.edu/sites/myncbi/r.relevo.1/collections/56264433/public/

ClinicalTrials.gov

10 Studies found for: **Interventional Studies | Neuropathy, Painful | Adult, Older Adult | Phase 3, 4 | Start date from 01/01/2013 to 08/30/2018**

	Title	Status	Study Results	Conditions	Interventions
1	Phase 3 Gene Therapy for Painful Diabetic Neuropathy	Active, not recruiting	• Painful Diabetic Neuropathy • Diabetic Neuropathy, Painful	• Genetic: VM202 • Genetic: placebo	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment
2	Influence of OCT2 Inhibitor Cetirizine and Type 2 Diabetes on Gabapentin Kinetics Disposition in Patients With Neuropathic Pain	Enrolling by invitation	• Neuropathic Pain • Type 2 Diabetes Mellitus • Diabetic Neuropathy, Painful	• Procedure: Serial Blood Samples • Procedure: Serial Urine Samples • Drug: Gabapentin 300 mg • Drug: Cetirizine Hydrochloride 10 mg	Study Design: • Allocation: Non-Randomized • Intervention Model: Parallel Assignment • Masking: None (Open Label) • Primary Purpose: Treatment

	Title	Status	Study Results	Conditions	Interventions
3	A Study to Evaluate Efficacy and Safety of a Single Application of Capsaicin 8% Transdermal Delivery System Compared to Placebo in Reducing Pain Intensity in Subjects With Painful Diabetic Peripheral Neuropathy (PDPN)	Completed	• Diabetic Peripheral Neuropathy • Pain	• Drug: Capsaicin 8% • Drug: Placebo	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment
4	0.075% Capsaicin Lotion for the Treatment of Painful Diabetic Neuropathy	Completed No results yet	• Peripheral Diabetic Neuropathy	• Drug: 0.075% Capsaicin Lotion • Drug: placebo	Study Design: • Allocation: Randomized • Intervention Model: Crossover Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment

	Title	Status	Study Results	Conditions	Interventions
5	Evaluation of the Impact of Training on Outcome Measures in Subjects With Painful Diabetic Neuropathy	Unknown status	• Diabetes Mellitus • Painful Distal Symmetric Sensorimotor Polyneuropathy	• Drug: Pregabalin • Drug: placebo • Behavioral: Training Type A • Behavioral: Training Type B	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Double (Participant, Investigator) • Primary Purpose: Basic Science
6	Efficacy and Safety of KW21052 Compared to Lyrica in the Diabetic Patients With Neuropathic Pain	Unknown status	• Diabetic Neuropathy	• Drug: KW21052 • Drug: Lyrica • Drug: Lyrica (low dose) • Drug: Placebo of KW21052 • Drug: Placebo of Lyrica	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment
7	Long Term Outcome After Serial Lidocaine Infusion in Peripheral Neuropathic Pain	Completed recently No results yet	• Peripheral Neuropathy	• Drug: Lidocaine • Drug: Placebo	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment

	Title	Status	Study Results	Conditions	Interventions
8	A Study of Duloxetine (LY248686) in Participants With Diabetic Peripheral Neuropathic Pain (DPNP)	Completed Published in September 13, 2018 (after our lit review) This study demonstrated the noninferior efficacy of duloxetine compared with pregabalin in the treatment of adult patients with DPNP. The safety analyses showed an acceptable tolerability based on safety profiles of duloxetine and pregabalin.	• Diabetic Peripheral Neuropathic Pain	• Drug: Duloxetine • Drug: Pregabalin • Drug: Placebo	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Double (Participant, Investigator) • Primary Purpose: Treatment
9	Patient Assisted Intervention for Neuropathy: Comparison of Treatment in Real Life Situations	Completed	• Cryptogenic Sensory Polyneuropathy	• Drug: Nortriptyline • Drug: Duloxetine • Drug: Pregabalin • Drug: Mexiletine	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: None (Open Label) • Primary Purpose: Treatment

	Title	Status	Study Results	Conditions	Interventions
10	Treatment of Neuropathic Pain in Leprosy	Recruiting	• Pain, Neuropathic • Leprosy • Leprosy Neuropathy • Amitriptyline	• Drug: Amitriptyline • Drug: Placebo oral capsule • Drug: Tramadol	Study Design: • Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) • Primary Purpose: Treatment

Appendix D. Original Nomination

Topic Suggestion Description
Date submitted: March 1, 2018

Briefly describe a specific question, or set of related questions, about a health care test or treatment that this program should consider.

ACP Nomination for AHRQ-Sponsored Evidence Review: Treatment of Painful Peripheral Neuropathy
Key Questions:
1. In adults with painful peripheral neuropathy, what is the effectiveness and comparative effectiveness of different pharmacologic and non-pharmacologic therapies on intermediate and long-term pain and health outcomes?
2. In adults with painful peripheral neuropathy, what are the harms and the comparative harms of different pharmacologic and non-pharmacologic therapies?
3. Do the benefits and harms of therapies for peripheral neuropathy vary according to the cause of the neuropathy, patient characteristics, baseline severity of pain, kidney function, or other factors?

PICOTS:
Population: adults with chronic painful peripheral neuropathy (excluding acute neuropathy)
Intervention(s): pharmacotherapies (oral and topical) – licensed and off-label; non-pharmacologic treatments
Comparator(s): placebo, other pharmacotherapies, non-pharmacologic therapy
Outcomes: intermediate or long-term pain, functional status, quality of life, employment, ulcers/amputations, harms including falls, fractures, etc.
Timing: > 12 weeks
Setting: outpatient

Importance

Describe why this topic is important.

Pain related to a lesion or disease of the peripheral nervous system is very common and can have significant detrimental impact on patients' quality of life and functional status.

Potential Impact

How will an answer to your research question be used or help inform decisions for you or your group?

ACP would like to develop a guideline on this topic.
Neuropathic pain is usually conceptualized and treated differently than nocioceptive pain because the pathophysiology of the conditions differ, and the treatments to which they respond may be different. As with any treatment of a chronic condition, it is especially important for providers' and patients to understand both the benefits and long-term harms since treatment may be ongoing for many months to years.

Technical Experts and Stakeholders

Are there health care-focused, disease-focused, or patient-focused organizations or technical experts that you see as being relevant to this issue? Who do you think we should contact as we consider your nomination? This information will not influence the progress of your suggestion through the selection process, but it may be helpful to those considering your suggestion for further development?

American Academy of Family Physicians frequently endorses our guidelines, and we occasionally partner on developing joint guidelines with them.