Venous Care Partnership

Working collaboratively to ensure appropriate care for our patients

August 3, 2016

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5600 Fishers Lane
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RE: **Treatment Strategies for Patients with Lower Extremity Chronic Venous Disease (LECVD)**

Submitted electronically to epc@ahrq.hhs.gov.

Dear Dr. Gozu & Dr. Berliner,

On behalf of the representatives of the Venous Care Partnership ("Partnership"), we appreciate the opportunity to comment on the June 28, 2016 AHRQ Technology Assessment (TA), "Treatment Strategies for Patients with Lower Extremity Chronic Venous Disease (LECVD). The Partnership is comprised of appointed representatives from ten specialty societies and associations representing over 100,000 physicians who care for patients with venous disease. It is these representatives who have contributed to this letter.

We want to recognize the authors of the AHRQ technology Assessment as they have put substantial effort into this document. However, we have both general and specific concerns that we would like to bring to your attention.

1. Most importantly, in conducting this review the authors' were restricted to reviewing the literature published since the year 2000. When questioned by the panel, the authors acknowledged this limitation, but did not adequately emphasize that this could lead to misleading conclusions. The diagnosis and treatment of venous diseases has a long history. Much of the evidence supporting the diagnosis and treatment of superficial

venous disease was established before the limited time period covered by this review. For example, duplex ultrasound is currently recognized as the standard of care for the diagnosis of acute deep venous thrombosis, yet studies validating its accuracy in comparison to contrast venography were performed well before the year 2000. Given the results of previous rigorously conducted studies, it expected that there is little recent evidence evaluating the accuracy of duplex ultrasound. Similarly, compression therapy has been validated as an effective therapy in the treatment of chronic venous disease. Two systematic Cochrane reviews ("Effects of compression on venous ulcer healing", O'Meara et al and "Compression for preventing recurrence of venous ulcers", Nelson et al.) demonstrated the effectiveness of compression therapy. Unfortunately, both of these were listed in the references of the AHRQ document but not cited in the text. Both sclerotherapy and the surgical removal of the incompetent saphenous veins were established as effective by clinical trials published prior to 2000. Accordingly, as the long term value of superficial venous intervention was well established before 2000, evidence acquisition shifted to focusing on the improved early outcomes in comparison to standard interventions (e.g. high ligation of stripping) rather than comparison to conservative therapy alone. Several well-done randomized clinical trials (Rasmussen et. al, JVS 2010 2, Brittenden et. al, NEJM 2014) have confirmed that the newer technologies have equivalent outcomes in comparison to traditional surgery, but are associated with less post-operative discomfort, improved early quality of life, and more rapid return to productive activity. Limiting the systematic review of the literature to the period after 2000 eliminated the evidence base on which the more recent technology rests. In a comparable example, we no longer test the value of aspirin in acute myocardial infarction when discussing the value of antiplatelet therapy, for it was well-established decades ago; now we focus on therapeutic advances. Limiting the conclusions to the literature published after 2000 removes the foundational base upon which this work has been done.

2. Another significant concern is that the abstract inclusion criterion for the second question, KQ2, was too rigorous. Randomized controlled trials were preferred and observational trials were only considered if the sample size was greater than 500 subjects, excluding adequately powered but smaller clinical trials. Of the 10,201 abstract reviewed only 88 studies met the inclusion criteria for KQ2. We believe that the strict size criteria resulted in an incomplete appraisal of the evidence. Indeed, the report's authors noted that the therapies did provide benefit, but that the evidence was insufficient to estimate at what time point, in what population and at what severity that benefit exists. Our position is supported by the panelists who noted that The National

Institute for Health and Care Excellence (NICE) guidelines, which were largely based on a randomized trial funded by the NHS Health Technology Assessment Program (Michaels, BR J Surg 2006), may be more representative of the current state of the evidence. We recognize that the authors were given a very specific task with a specific methodology, but we would encourage the authors to acknowledge these limitations of the study design and the effect on the report's conclusions.

Similarly, the criteria used to exclude articles that relate to KQ3 on chronic venous obstruction resulted in a partial view of the overall body of evidence. Older compelling studies have demonstrated a strong correlation between iliac venous obstruction and a poor clinical outcome. Additionally, studies have demonstrated the correlation between relief of venous obstruction and improved clinical outcome. Some of this data is derived from RCTs, and the quality and consistency of this information has had a significant influence upon physician decision-making when they approach severely-affected patients with CVD and PTS.

3. We are concerned that the specificity of the questions posed for the MEDCAC may obscure the larger evidence base. KQ2 divided superficial venous disease into two broad categories; symptomatic and asymptomatic. The panelists seemed to be unclear as to the meaning of this stratification. Is a patient with a leg ulcer and no complaints an asymptomatic patient? Was a patient with spider veins and complaints of heaviness, achiness and throbbing a symptomatic patient? We recognize the difficulty associated with the nomenclature and look forward to helping define more precise definitions to facilitate specific conclusions. For now, we would encourage the authors to acknowledge these limitations and the effect on the report's conclusions.

4. We would like to express our concerns regarding potential inaccuracies and assumptions contained within the document. The authors state "There is substantial variation in how patients with LECVD are diagnosed and treated. In the past, vascular surgeons often diagnosed and treated patients with LECVD; now, however, primary care physicians, cardiologists, vascular medicine specialists, and radiologists also diagnose and manage these patients in the United States. In addition to physician specialty, other reasons for therapeutic variation include: patient characteristics and preferences, reimbursement rates for diagnostic tests and treatment modalities, and the clinical care location of these diagnostic tests and invasive procedures (as this dictates reimbursement, specifically when physicians own the office-based clinics or ambulatory

surgery centers where the procedures are performed)." The first portion of this statement is not accurate as ligation and stripping were often performed by general surgeons, sclerotherapy was performed by phlebologists, and endovascular venous procedures were developed and performed by interventional radiologists. Furthermore the paragraph implies that changes in outcomes were affected by a change in who (i.e., the specialty) and where the treatment was provided. We feel that this inference is without evidentiary support and recommend excluding this comment.

5. In the methods section, the authors describe the complications that are "typically seen" following venous treatments. We would encourage the word "typical" be changed as this implies that listed complications are expected or relatively frequent, which the data does not support.

6. Another point of needed clarification relates to a reference to a study by O'Sullivan G et al. in the discussion section for KQ3 on treatment of chronic venous obstruction. The patients reported in this paper were treated for ***acute*** thrombosis caused by right iliac artery compression of the left common iliac vein. Although some of the patients may have had a prior thrombosis of this segment, the thrombolytic was used to treat an acute deep venous thrombosis, and therefore the study is not relevant to patients with chronic obstructions.

7. Need for patient centered outcomes: We would submit that surrogate endpoints such as CEAP, patency and closure rates are not patient centered outcomes, dilute interpretation of the value of these therapies, and should not be used as a basis for policy decisions. Given that this disease is chronic and predominantly characterized by morbidity rather than mortality, patient centered benefit should be the primary outcomes of interest. This may include assessment of patient-relevant symptoms (e.g. pain, swelling), quality of life, and functional limitations. We would be happy to work with CMS and AHRQ to develop better standards for outcomes measurement. As this document presumably serves to inform policy decisions, we ask the authors to acknowledge this point and remove references to non-patient centered outcomes from the document.

In summary, although the authors have conducted an extensive review within the limitations required of them, this document may have hindered interpretation of the totality of the

evidence, thus diminishing its ability to effectively inform policy decisions. The exclusion of publications prior to the year 2000, the focus on patient conditions without description, broad and overlapping questions, and stringent study inclusion criteria have provided a subjective portrayal of the scientific evidence upon which modern venous treatment is based. We would be pleased to meet with AHRQ and CMS to discuss our concerns further and to serve as a resource to both entities in future endeavors related to venous disease.

Respectfully submitted, August 3, 2016

The listed representatives of the **Venous Care Partnership**, on behalf of the organizations they were appointed by, have endorsed this letter:

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