**Public Comments and Responses for HBO and DFU CPG**

| Commenter | Comment | Response | Changes to Manuscript? |
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| Commenter 1 | The major problem that I have that is kind of addressed but is still really just wrong involves the Wagner system. This system is likely useful up to Grade 2 (probes to bone) but them becomes less descriptive and predictive when infection and ischemia are both mixed. Plus, everyone still gets it wrong. This is hugely frustrating, since there have now been several systems that build on this that are far more descriptive and predictive. WIFI is the most recent example, which has now been validated by SVS and already includes the IDSA and SVS ischemia grading systems. That said, I understand that reimbursement seems to be tied into Wagner-- but using a system that is non-descriptive and adding descriptors just to make it so (thereby making it unintelligible) is just dumb, no? | As mentioned in the manuscript, we would have preferred a better clinical evaluation and scoring system than Wagner, but no studies of the use of adjunctive hyperbaric oxygen for the treatment of DFUs utilized any such score. | None added |
| | I definitely have a suggestion on how to implement: Eliminate what currently exists and apply validated systems to the current CPG. This is completely doable and will be a major-league shift toward relevance. My point is that you can retrospectively apply these highly descriptive systems like the University of Texas or Wi-Fi or the international working group on two previous studies. It will, paradoxically, give you even more predictive potential because you are using something that is much more specific | We have created a table that shows our attempt to re-classify each of the 5 RCTs using alternative wound classifications systems (University of Texas, IDSA, IWGDF, Strauss Wound Score, and WIfI) and why we were unable to do so. | Table 14 added |
| Commenter 2 | Have a look at WIfI. Surely you have ABI, TP or TcPO2 measurements on each patient. If the ABI is noncompressible or unreliable, the default for ischemia is toe pressure (or TcPO2). | We have created a table that shows our attempt to re-classify each of the 5 RCTs using alternative wound classifications systems (University of Texas, IDSA, IWGDF, Strauss Wound Score, and WIfI) and why we were unable to do so. | Table 14 added |
| Commenter 3 | The guidelines are very well written however the last sentence under the paragraph " Conclusions" which states that "Future research should be directed at raising the quality of evidence through improved study methodology etc.., should be removed ,as it diminishes the cited studies which are in defense of using HBO in diabetic foot ulcers.That sentence diminishes the case for using HBO in diabetic foot ulcers. | The Moderate GRADE of evidence that was found correlates with the recommendation that "Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate of effect," so we certainly cannot just remove the recommendation that future research should be done. We also want to stress that there were methodologic shortcomings in all of the studies that were included, and despite these shortcomings we still had moderate level of evidence. We will work on re-wording the sentence to acknowledge the studies that have been done to date, while still calling for studies that have stronger design in the future. | Rewording added |
| Commenter 4 | 1) The recommendations use the Wagner classification. How the committee defined Wagner classifications needs to be clarified. In two different locations the committee acknowledged the differences in the "classic" Wagner classification, and how it is generally currently accepted in the HBO literature. After reading the paper I'm still slightly unclear what the committee is recommending. Does the committee include tendon involvement as part of their definition of Wagner 3, or is that a Wagner 2? A clear definition of terms would be very helpful. | We state that we recommend using the "classic" Wagner definition, which is provided in Figure 12. This would include tendon involvement if there is infection. We have also added tables describing the characteristics of the other classification systems. | Table 1 added |
| | 2) The committee recommends the use of adjunctive hyperbaric oxygen therapy treatments in Wagner grade 3 ulcerations that have persisted for greater than 30 days. What is the research rational for the 30 day wait? Did the studies cited use this rational? If the studies did not (eligibility merely being presence of an ulceration at the specified depth) persistence at the depth should not be included in the CPG. | The use of 30 days was based on the existing requirements of some reimbursement policies.There is no scientific rationale for using 30 days, which is the reason that the last recommendation looked at the immediate use of hyperbaric oxygen. | None added |
| | 3) The notation of the use of transcutaneous oximetry for risk stratification but no mention of it in the CPG clouds the issue. The brief summary of the current state of the TCOM is excellent, but is dropped (appropriately) in the practice guidelines due to a lack of supporting data. The mention of it earlier weakens the recommendations of the CPG. If it is to be excluded it may be superior to ignore it in the discussion, rather than leave an opening for users of the CPG (payors) to re-insert TCOM as a requirement for the use of HBOT. | We feel that it is important to mention TCOM, as to omit it would perhaps lead to questions of why we ignored this aspect of DFU care. We will more clearly state that we could not incorporate TCOM into our CPG recommendations. | Text Clarified |
| Commenter 5 | 1) greatest respect for all who tackled this difficult task | Thank you | None added |
| | 2) public comment period rather short | We wanted to balance a period of public comment with the need to publish this CPG and submit to guidelines.gov. We appreciate the effort you put in to submit comments before the deadline. | None added |
| | 3) allusion to CMS concurrence with a more loose interpretation of Wagner grading system- would very much like to see references that support that assertion. | We refer you to Strauss, M.B., The Wagner Wound Grading System. Wound Care & Hyperbaric Medicine, 2012. 3(4): p. 38-45. | None added |
| | 4) several statements RE: Wagner grading system seem either inaccurate or misleading, e.g.: that it is based on a single observation, that "it first addresses perfusion, then grades the wound on single markedly different observations...etc, etc". To me, this suggests perhaps incomplete understanding of the Wagner grading system. First, it does not address perfusion, per se. It describes the continuum/natural progression of the process, i.e., the neuropathic foot at risk due to deformity &/or callus through superficial ulcer to deep but uninfected ulcer, then complicated infection/abscess to necrotizing soft tissue infection with gangrene due to thrombosis of the digital &/or plantar arch vessels. [This progression & especially the pathophysiology of the septic arteritis/gangrene, is detailed in the Levin & O'Neal 'Diabetic Foot', 7th edition, pp 377-386.] Thus, when he states, "Foot lesions are divided into six grades. The determination of grade is based on the depth of the skin lesion and the presence or absence of infection and gangrene.", in most cases, the gangrene is due to necrotizing infection in the setting of abnormal microvasculature, not simply due to advanced arterial insufficiency. He doesn't exclude 'dry gangrene', but clearly focuses on the progression as noted above. | The comments expressed by the commenter reflect the confusion between Wagner's Grading System and his management algorithms based off of those grades. Wagner's Grading System does not include vascular status in defining the grade of the DFU, however his treatment algorithm does address perfusion using an ABI cutoff of 0.45 in diabetic patients for clinical decision making purposes. The management strategy proposed by Wagner is based on the status of a wound at the time of initial decision making, not as a matter of monitoring the DFU over time (*i.e.*, Given that the wound is a Grade 3 DFU with an ABI > 0.45, one would initiate his treatment algorithm based on the assessment at that time). It would be inaccurate to describe the progression of the DFU as a continuum, as a Wagner 1 DFU does not always progress to a Wagner 5 DFU. Wagner does not make a distinction between wet or dry gangrene, which have different levels of seriousness. We still feel that the Wagner grade is less than ideal when it comes to clinically grading DFUs. | Text Clarified |
| | In your final paragraph of the introduction, you note that. "A Wagner grade is assigned from the appearance of the wound at a single observation." There is no reason that a wound cannot be re-graded if its status has changed & in fact, Wagner notes that with the exception of a grade 5 lesion, that everything else can theoretically return to a grade zero foot. It follows that since the grading system describes a progression of events, that a grade 2 can progress to a grade 3, which can progress to a grade 4 lesion & from there, to a grade 5. | The Wagner Grade can be assigned at any point at which the patient is evaluated, and Wagner Grades can certainly worsen or improve as noted by the commenter. We meant to note that Wagner's management algorithm is determined by the appearance of a wound at a single observation, which is different than the Wagner Grade at any point in time. | Text clarified |
| | 5) in question 3, the wording is subtly different than the CMS coverage determination & might foster confusion. The CMS policy reads "no measurable signs of healing", further defined as "a decrease in surface area or volume" (among other parameters) with no qualifiers, e.g., 40% decrease in 30 days, or whatever. Your question states, "...that has not healed in 30 days". So, say the wound is 99% smaller, but not completely closed- you still want to add HBO? I think that CMS & other carriers would find this wording a bit concerning. I do realize that you are not married to the CMS coverage determination, but I think that whoever authored it expressed it very carefully to try to limit inappropriate use of HBO. The investor-owned centers would be on this like a duck on a June bug. | The overuse of HBO is a very valid concern, and our language will be modified to avoid the appearance that practitioners should use HBO indiscriminately | Text modified |
| | 6) 3rd paragraph of 'Discussion'- how exactly has The Hyperbaric Community interpreted the Wagner classification system & how exactly has CMS endorsed the misinterpretation? Those in my hyperbaric medicine community follow CMS treatment criteria carefully & literally- what is everyone else doing? Who in & how has CMS endorsed it? | CMS and third party payers do not follow the classic Wagner classification recommendations with regard to management of Wagner 3 DFUs, and a review of the Margolis results shows that many facilities out there do not even follow the CMS recommendations. Faglia showed that immediate use of HBO resulted in decreased morbidity, however in a patient who has a septic, suppurative foot (Wagner 3), CMS and third party payers require a 30 day delay in treatment. | Text Clarified |
| | 7) recommendation 2: same concern with phrase, "that have not healed in 30 days" as in point #5 above | The overuse of HBO is a very valid concern, and our language will be modified to avoid the appearance that practitioners should use HBO indiscriminately | Text Clarified |
| | 8) I certainly hope that I have not wasted your time in this message; I am only trying to be helpful. I have also spotted a few typos & would be glad to help with that aspect of review if that would be of any value to you. | Thank you for your helpful comments in making this a more complete guideline. Identifying these typos is very helpful. | Text Clarified |
| Commenter 6 | 1. I think that it would be helpful to explain in a couple of sentences in the discussion why UHMS, a group that advocates for the use of HBOT, was able to conduct an unbiased review of this topic and found results that are somewhat different than previous Cochrane Reviews, Greer et al Ann I Med 2013; O Reilly Int J Tech Ass in Health Care 2013, etc. | The UHMS advocates for the responsible, evidence-based use of hyperbaric oxygen therapy. As experts in the field, we possess the experience to analyze the hyperbaric literature with clinical perspective. Non-hyperbaric physicians are included in the review committee to provide even more objectivity in the analysis. The results of this review, utilizing the same source material, differs from similar reviews conducted by Cochrane and the Canadian Program for Assessment of Technology in Health (PATH) because of differences in purpose and judgment. The Cochrane review is a summary of the evidence that does not seek to make clinical recommendations. The PATH review based their inferences on statistical significance (p-values) whereas we considered how precise were the estimates to support a particular decision. The GRADE methodology, and the transparency that is employed in this extensive statistical analysis, allows others to make their own judgments and compare them with the conclusions of this review committee. | Text Added |
| | 2. You mention four tenets of care in your introduction and that failure to use these tenets of care obviate the any discussion about the utility of HBO for DFU and you restate the need for aggressive revascularization in the beginning of the discussion section. Where these tenets of care utilized by the RCTs you use in your meta analysis? For example I am not really sure how patients in the Duzgun study were cared for. If my memory is correct Duzgun et al also used HBO more than once a day. | We will provide a table that showed how well each study adhered to these four tenets. We describe the hyperbaric treatment protocols in other tables. There were certainly differences in how hyperbaric oxygen therapy was delivered, which is accounted for by the Indirectness portion of the GRADE process. | Table 13 added |
| | 3. You redefine Wagner stage 3 in the executive summary. Did you use this redefinition for your study or did you use the classic Wagner definition in the rest of the study? | We used the Wagner definitions as they were reported by the original source documents. The older studies (Faglia and Doctor) used the "classic" definition and included patients that were inpatients, required surgery, and were presumably more acute. The more recent studies (Duzgun, Abidia, and Londahl) instituted a 30-day or longer waiting period before starting HBO2. We provided a table of all of the different classification systems. | Table 1 added |
| | 4.You used RevMan software. Is this a Cochrane study and will it be published by the Cochrane Wound Group? | This systematic review is not a Cochrane systematic review and will not be published in the Cochrane library. RevMan is statistical software developed by Cochrane but everyone uses it for free whether they are doing a Cochrane review or a non-Cochrane review. | None added |
| | 5. You studies span a 20 year period. Was standard therapy the same or has it evolved? Faglia et al hospitalized patients. It would seem to me that their standard therapy was very different then those who received out patient care. | Standard therapy has definitely changed over the span of the studies. We recognize that early studies admitted patients for the duration of their stay, while other studies used atypical hyperbaric treatment protocols. These all contributed to lowered ratings because of Indirectness with regard to the current clinical questions. We have added a table to address how each study addressed Standard Care. | Table 13 added |
| | 6. Did you use the GRADE software? Why was your GRADE analysis different than O'Reilly? | The GRADE software and Cochrane software are the same. O'Reilly did not use GRADE methodology and based their conclusions solely on p-value, not the estimate of effect. We used standard GRADE methods and the GRADE Working Group methods. Determining the domains of quality of evidence involves making judgements about how we view the evidence (regardless of the software). Our judgments were different from O'Reilly. We chose to rate the evidence up when we observed large and very large effects. Some may argue against rating up when there is a possibility of methodological limitations. This decision is explicit in the tables that describe our judgements and process. | Text Added |
| | 7. You mention that you could not assess for missing studies because there were not enough studies but this is often done anyway and is frequently done with as many studies as you found for analysis. For example there is a well known missing study from Canada. A funnel plot or another method would be nice to see. | Funnel plots and other methods of assessing for publication bias require 20 studies or more. People sometimes do such analyses with small number of studies but this is unreliable. This analysis only looks at the peer-reviewed and published literature. The "missing" Canadian study has not been published because of questions about methodological design. It will be included if it is published. | None added |
| | 8. In figure 1 you have a high level of heterogeneity based on I^2 | This is why we rated the study down based on inconsistency of results | None added |