COALITION OF

Wound
Care
Manufacturers

COALITION OF WOUND CARE MANUFACTURERS' COMMENTS ON THE AHRQ DRAFT TA ON "NEGATIVE PRESSURE WOUND CARE TECHNOLOGIES"- JULY 16, 2014

General

The Coalition of Wound Care Manufacturers ("Coalition") is submitting the following comments in response to the AHRQ draft report entitled, "Negative Pressure Wound Therapy Technologies." The Coalition represents leading manufacturers of wound care products used by Medicare beneficiaries for the treatment of wounds including those products that are subject to this draft policy. Since our members have a vested interest in the coverage of these products, this draft policy is of concern to us. The Coalition appreciates the opportunity to offer our comments.

While we appreciate the opportunity to offer our comments, we are very disappointed in the short amount of time that the AHRQ allowed for a deadline to respond to this very dense document that is so critical to wound care stakeholders. It is our understanding that the Technology Assessment Program provides 2 weeks for public review of its draft reports. However, releasing the report on July 1 and then extending the due date one day to July 16th does not take into consideration the holiday during which with many take vacations during this time and thus does not constitute a meaningful public comment period. This is the second time in the past few years during which AHRQ has released its draft during a major holiday—the first was during New Years and Martin Luther King's birthday in 2011 for "Skin Substitutes for Treating Chronic Wounds. We would respectfully request that in the future that AHRQ and its contractors plan more carefully and not release a draft TA during a holiday.

The Coalition members take writing our comments to this draft very seriously, and has convened conversations and emails to ensure that our members' input will be included. Since we still do not believe there is enough time to give this important document the careful consideration that it needs, we are submitting these comments, but intend to supplement our filing as we receive more information from our members.

We have many concerns regarding this draft TA in that the authors demonstrate a fundamental lack of understanding in regard to NPWT and wound care, the settings in which NPWT is used in regard to study inclusion, and many methodological issues, which we have addressed in the various sections.

Introduction/Background

The authors seem to demonstrate a fundamental lack of understanding of the use of NPWT, as well as its mechanisms of action. We submit that as stated below, if the

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authors had read and included more recent publications regarding this issue, then their outlook and knowledge base and conclusions might have been quite different.

1. In the Introduction the authors state that *"The exact mechanism by which these devices may promote wound healing is not known. Hypotheses for the healing effect include the removal of excess fluid while improving circulation to the wound bed,[11], reducing bacterial load on wound surface, or the presence of a mechanical effect that aids wound healing.[12]"* The authors cite amongst other references the original Wake Forest publication (Morykwas, Argenta, Shelton-Brown, & McGuirt, 1997). This seems to imply to a non-specialist reader that the therapy is poorly understood and relatively uninvestigated, whereas on the contrary, there has been rather a lot of progress and understanding developed over the NPWT mechanisms of action: see Glass & Nanchahal for an independent recent review (J Plast Reconstr Aesthet Surg 2012;65(8):989-1001.). In particular the reduction of bacterial bioburden in contaminated clinical wounds under NPWT has been extensively investigated and now widely accepted as not to be a major mechanism of action; hence the increasing interest in the use of antimicrobials, of one sort or another, in combination with NPWT (Siegel HJ, et al., Clin Orthop Relat Res 2014;472(3):830-5; Kim PJ, et al., Plast Reconstr Surg 2013;132(6):1569-79.

   It is likely that several mechanisms are responsible for the benefit of NPWT, including: fluid removal, drawing the wound together, micro-deformation, and moist wound healing (Orgill DP, Bayer LR. Plast Reconstr Surg 2011;127 Suppl 1:105S-115S); systemic mobilization of endothelial progenitor cells (EPCs) during NPWT (Seo SG, et al., Exp Mol Med 2013;45:e62); and support [of] (neo-) angiogenesis and transformation of chronic non-healing wounds in a physiological wound healing process when combined with surgical debridement (Malsiner CC. et al., Int Wound J 2013 Sep 13. [Epub ahead of print]). In summary, the authors could have done a much better job of describing the mechanism of action of NPWT by reviewing more recent references in the literature.

2. It should be noted that the goal of NPWT is to improve wound healing to the point where application of traditional dressings that maintain a moist wound environment can be applied to finish the process. NPWT is ideal for chronic wounds that are "stuck" and unable to progress. NPWT is cost effective by helping certain wounds progress through the healing process which in turn reduces the hospital readmission rates and overall healthcare expenditures. We believe that this point was missed by the authors.

3. Although NPWT is often initiated in the hospital and patients' transition to the home, it is not a straight path to home care. Patients can transition to the home, long term care, or long term acute care facilities. Their wounds can also be treated in a hospital affiliated or independent wound clinic, physician office, or visiting nurse association in the home settings. Each of these settings has different

standards of care and delivery methods and thus makes it difficult to define control groups and monitor study protocols.

Methods/Results

We found several issues in regard to the methodology of this TA, some of which are very serious flaws:

1. We find that the authors may not really understand that wound care in the home does initially begin in the hospital setting. Thus we question why aren't hospital/inpatient/LTC studies results applicable to the home setting? There is no delineation between hospital use and home use. Patients are not followed in the inpatient setting long enough to make determinations that hospital-based NPWT is insufficient. Patients are often started inpatient then transferred to LTC or home use. The decision just to look at studies that exclusively had home settings is flawed because the use of NPWT does not change between settings and such a strategy excluded many valuable studies.

2. Patient compliance with wound therapies, nutrition, psychosocial concerns, management of comorbidities and environment are all critical components in wound management. Management of the above can be closely monitored and documented in an acute care setting. The home environment presents greater challenges in ensuring the above variables are appropriately managed. Therefore, the home care environment presents many barriers to obtaining quality study data and it may be unrealistic to expect outcomes of the type proposed in the TA. We believe that having a clinician on the team who is well versed in the practice of NPWT at home would have made this TA much more useful.

3. Evidence was also downgraded because complete healing was not defined according to the FDA's definition of healing. For observational trials and non-pivotal trials this is often inappropriate as most of these studies would not use such a definition in practice or pragmatic trials. Moreover, NPWT is often used to partially close a wound to prepare a wound for further surgery (e.g., flap closure). The authors knew this because one of their planned outcomes was "Time to surgical readiness of the wound bed." We would submit that then to downgrade evidence just because outcomes did not meet the FDA's definition of healing is illogical and arbitrary.

4. Studies were excluded if they did not have a comparison group. While we understand this is reasonable for determination of efficacy/effectiveness, less common safety issues are usually reported in large case series. Excluding these can miss valuable data.

5. Sometimes NWPT devices are used in heavily exudating wounds in which the patient is not a surgical candidate due to co-morbidities and attempts at alternative wound care has been attempted and has been unsuccessful. NWPT can allow for fewer dressing changes and decreases nursing utilization. It also increases patient comfort and quality of life. This was not included as an outcome.

6. Table 3. Manufacturer/Company – Mendela is incorrect. It should instead be "Medela."

Discussion/Conclusion

We disagree with many of the conclusions in this TA:

1. The level of data in the literature (over 5,000 citations) is enough for AHRQ to make some sufficient declarative statement on the efficacy and safety of NPWT. Even the study conducted by Fife et al shows this. For the authors to state that Lavery et al's 2007 study on DFUs is insufficient, tells us that the authors were too stringent on the guidelines for clinical data.

2. Based on data analysis, to dismiss the observational studies as being too inconclusive is unfair given that carriers have adopted less stringent guidelines for acceptance of data that is in real-time. If observational and retrospective studies are acceptable for cellular and/or tissue-based therapies then they should be acceptable for NPWT. We question whether the authors really understand some of the observational studies: "…larger studies were retrospective and based on administrative databases." For example, the study conducted by Fife et al (Int Wound J 2008;5 Suppl 2:17-22.) is based on electronic health records and is NOT an administrative database.

3. A further concern is the omission of a number of randomized controlled trials (RCTs) from study inclusion because they were not entirely conducted in the home setting (Armstrong DG & Lavery LA, Lancet 2005;366(9498):1704-10.; Blume PA, et al., Diabetes Care 2008;31(4):631-6.). The study by Armstrong and Lavery was subjected to an economic analysis published by Apelquist et al in 2008 (Am J Surg 2008;195(6):782-8), which details where care was given: A total of 24.4% of all dressing changes were performed in the hospital, 18.3% in the outpatient clinic, and 42.1% during home care. In terms of the 10,908 days of total therapy, 9,719 (89.1%) and 1,189 (10.9%) were in the home care and inpatient settings respectively. Similarly, in the randomized study in 342 diabetic foot ulcer patients conducted by Blume et al., which was carried out in 37 centers, the proportion of home care therapy days to total therapy days was 9,471 of 10,579 (89.5%) for NPWT and 12,210 of 12,810 (95.3%) for AMWT (the controls). Given that this is a population consisting of diabetic foot ulcers or patients receiving amputations for foot ulcers, some inpatient care is absolutely necessary (i.e., this is "real life."). Moreover, in regard to inpatient vs. outpatient NPWT, the data are quite clear that this has evolved to a "bridge to outpatient"

technology. Thus, we question the decision to exclude such studies as not being "sufficiently" homecare based. Could the authors have not conducted an analysis of these kinds of trials in terms of subpopulations?

4. The AHRQ TA included the issues related to the 2011 FDA safety communication regarding serious complications associated with NPWT devices used in the home. The Agency expressed concern that, although these devices can be used safely and effectively in that setting, greater risk mitigation is required to prevent patients using these devices from experiencing serious health problems. As stakeholders in the wound care community, the Coalition of Wound Care Manufacturers agreed with the FDA. The Coalition also took this very seriously performed the following activities in 2011:
   - Worked with FDA staff to educate them on how manufacturers inform the caregiver, patient and clinician on the correct use of NPWT in the home. This was accomplished by:
     - Marcia Nusgart spoke with Nada Hanafi of FDA on this issue
     - The Coalition gave input to FDA staff on the NPWT MedSun survey
     - Marcia Nusgart invited FDA staff Mary Brady and Diana Rivi (who has responsibility for MedSun survey) to speak on her panel at two SAWC meetings
   - Invited OIG staff (Christine Moundas) responsible for its NPWT report to speak on Marcia Nusgart' s panel at SAWC Spring meeting and met with her on this issue.

5. The authors are rather dismissive of the retrospective nature of the study that (Fife et al. performed in 2007 (published in 2008) which evaluated adverse events for the VAC. A point overlooked in the analysis in the TA is that every *prospective* RCT of NPWT *a priori* excluded patients on anticoagulants so as to reduce the risk of bleeding. All prospective trials of NPWT have also excluded patients with most major comorbidities (Carter MJ, et al. Adv Skin Wound Care 2009; 22:316-24.) What was unique about the 2008 Fife study is that it specifically looked for patients treated with NPWT in the home setting who were on coumadin, heparin or other medications associated with an increased risk of bleeding. Since patients taking these medications had been excluded from the prospective trials, the only way to analyze the safety of NPWT in the home setting for patients on these medications was via retrospective analysis of the data which had been prospectively obtained.

   The published study referenced in this AHRQ TA was a subset of a much larger analysis performed at the request of the FDA. The FDA requested that KCI provide data on the safety of the VAC in the home setting in relation to moist wound care. Nearly 10,000 wound care patients were analyzed, approximately 10% of whom underwent NPWT treatment with the VAC. We think that the FDA report is informative and that AHRQ would find it useful. In that analysis, 200 patients on anticoagulants were found among the roughly 900 patients undergoing

treatment with the VAC, none of whom had bleeding. Only one patient had VAC treatment discontinued due to blood-tinged drainage (not frank hemorrhage). That patient was on clopidogrel bisulfate and his wound was in the 99th percentile for size within this dataset.

The average number of major co-morbidities among patients treated with NPWT in this large data set was 8. As the 2009 Carter et al study showed, prospective trials have excluded patients with any serious diseases. So, while the AHRQ report is critical of studies utilizing retrospective data, *we submit that analysis of registry data is the ONLY way to assess the safety of NPWT. This is because prospective trials a priori exclude patients with significant co-morbid diseases and patients on medications which increase the risk of bleeding.*

In summary, it appears there is much bias against using registries as the best way to follow adverse events in the real world. For example, AHRQ would not even mention The U.S. Wound Registry in their upcoming edition of the AHRQ book on registries. It appears to us that AHRQ is unsupportive of efforts of the wound care industry to collect this type of data and make clinicians aware of its availability despite our efforts at education. This registry is now expanding its abilities to receive data as a result of the QCDR process.

6. Another key point is that these technologies require better operational definitions regarding when to start and stop. NPWT appears to be most helpful in reducing depth/complexity of wounds. It should then, generally speaking, be stopped in favor of less per-device expensive devices or just split thickness skin grafts when a suitable end point has been reached (Isaac et al, In: The Diabetic Foot: New York: Elsevier, 2013, 899-909).

7. Given that U.S. government agencies are unwilling to fund NPWT clinical studies, most of the cost of these trials must fall on the manufacturers. Adopting an unnecessarily narrow view point of the comparative clinical evidence does not encourage greater industry investment in clinical studies supporting innovations such as antimicrobials, instillation, or disposable NPWT devices. As all stakeholders have at heart the objectives of improving patient outcomes with the most cost efficient treatment protocols, we believe the conclusions of this TA, as it stands, does not serve patients.

8. Finally, we welcome the "characteristics of an ideal study" as outlined in Table 11 but question practically--what is the right wound study? Wounds are different by each co-morbidity, cause of wound and location of wound. Therefore a perfect clinical study is hard to define. Thus there are a variety of clinical study types. Total wound closure was one of the criteria used by AHRQ in their review, but not always a frequent endpoint for studies, i.e. percent closure etc.