Consensus principles for wound care research obtained using a Delphi process

Thomas Serena, MD[1]; Barbara Bates-Jensen, PhD[2]; Marissa J. Carter, PhD[3]; Renee Cordrey, PT, MPH[4]; Vickie Driver, MS, DPM[5]; Caroline E. Fife, MD[6]; Paul B. Haser, MD[7]; Diane Krasner, PhD[8]; Marcia Nusgart, RPh[9]; Adrianne P. S. Smith, MD[10]; Robert J. Snyder, DPM[11]

1. Wound and Hyperbaric Centers, The Serena Group, Cambridge, Massachusetts,
2. School of Nursing & David Geffen School of Medicine, Division of Geriatrics, University of California, Los Angeles, California,
3. Strategic Solutions, Inc., Cody, Wyoming,
4. Program in Physical Therapy, The George Washington University, Washington, District of Columbia,
5. Department of Surgery, Boston University School of Medicine, Boston, Massachusetts,
6. Intellicure, Inc., The Woodlands, Texas,
7. Division of Vascular Surgery, University of Medicine & Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, New Jersey,
8. Wound & Skin Care Consultant, York, Pennsylvania,
9. Alliance of Wound Care Stakeholders, Bethesda, Maryland,
10. Chief Medical Consultant, Day & Zimmerman, Inc., San Antonio, Texas, and
11. Wound Healing Center, University Hospital and Medical Center, Tamarac, Florida

Reprint requests:
Dr. T. Serena, Serena Group, 90 Sherman St., Cambridge, MA 02140, USA.

For the Alliance of Wound Care Stakeholder's Panel on Wound Care Evidence-Based Research (POWER™).

Manuscript received: September 16, 2011
Accepted in final form: January 27, 2012

DOI:10.1111/j.1524-475X.2012.00790.x

ABSTRACT

Too many wound care research studies are poorly designed, badly executed, and missing crucial data. The objective of this study is to create a series of principles for all stakeholders involved in clinical or comparative effectiveness research in wound healing. The Delphi approach was used to reach consensus, using a web-based survey for survey participants and face-to-face conferences for expert panel members. Expert panel (11 members) and 115 wound care researchers (respondents) drawn from 15 different organizations. Principles were rated for validity using 5-point Likert scales and comments. A 66% response rate was achieved in the first Delphi round from the 173 invited survey participants. The response rate for the second Delphi round was 46%. The most common wound care researcher profile was age 46–55 years, a wound care clinic setting, and >10 years' wound care research and clinical experience. Of the initial 17 principles created by the panel, only four principles were not endorsed in Delphi round 1 with another four not requiring revision. Of the 14 principles assessed by respondents in the second Delphi round, only one principle was not endorsed and it was revised; four other principles also needed revision based on the use of specific words or contextual use. Of the 19 final principles, three included detailed numbered lists. With the wide variation in design, conduct, and reporting of wound care research studies, it is hoped that these principles will improve the standard and practice of care in this field.

INTRODUCTION

The incidence of new wounds is greater than the incidence of cancer that develops each year in the USA with an estimated 2.8–5.1 million pressure, venous, and diabetic foot ulcers[1–4] vs. 1.5 million new cases of cancer forecast for 2010.[5] About 6.5 million patients have a pressure, venous, or diabetic foot ulcer at any given time in the USA, which represents about 2% of the general population,[4–6] and the cost of treating such ulcers annually in the USA is estimated at $38 billion, $11 billion, and $3 billion, respectively.[3,6–8] These are the conservative costs for wound care; they do not include the cost of traumatic wounds, surgical wounds, or wounds of other etiologies. Yet despite these impressive statistics, wound care receives moderately little attention compared with other medical conditions. For example, in its list of the 100 initial priority topics for comparative effectiveness research, the Institute of Medicine had only one topic on wound care research—comparing the effectiveness of topical treatments and systemic therapies in managing chronic lower extremity wounds—and it was ranked last in the third quartile.[9]

The rigor of wound care research is also challenging.[10–12] In particular, the European Wound Management Association has highlighted methodological inconsistencies in the primary research, citing as an illustration the poor level of evidence for modern dressings vs. traditional (typically gauze-based dressings).[12] There are many reasons for this situation.

First, randomized controlled trials (RCTs) can be difficult to properly execute in wound care research because of lack of funding, difficult or complex study designs, narrow focus, extensive inclusion/exclusion criteria, and the problem with endpoints.[13] The gold standard for endpoints

in wound care is complete wound healing according to the US Food and Drug Administration,[14,15] but this requirement can necessitate long follow-up times and may be inappropriate for testing certain medical devices, drugs, or treatment procedures.

Second, while testing under controlled conditions is desirable to initially ascertain efficacy, the results may not be generalizable to "real world" wound care patients because a high proportion have many comorbidities or come from highly vulnerable populations that are typically excluded from controlled trials.[16,17] Therefore, such results do not help patients and clinicians who need to know in practice which treatment is the best choice for a *particular patient*.

Third, a wound typically receives many different treatments from inception to healing, in part because of the many phases of wound healing, and therefore identifying a suitable comparator group in any comparative trial, especially an RCT, can be problematic. Consequently, many wound care trials are small observational studies that add little to the treatment evidence base. Unfortunately, even when the evidence base is reasonably strong, e.g., adequate compression for venous ulcers, and sufficient offloading in neuropathic diabetic foot ulcers,[18] it is often ignored by treatment providers.

In order to address these and other problems in wound care research, the Alliance of Wound Care Stakeholders created an expert panel in wound care research from its participating organizations (Panel On Wound Care Evidence-based Research; POWER™). (The Alliance of Wound Care Stakeholders [http://www.woundcarestakeholders.org] is a multidisciplinary consortium of 19 physician, clinician, provider, manufacturer, and patient organizations whose mission is to promote quality care and patient access to wound care products and services through effective advocacy and educational outreach in regulatory, legislative and public arenas.) POWER members decided to define a set of principles to provide direction to all stakeholders involved in clinical or comparative effectiveness research in wound healing. Specifically, these principles are aimed at developers and users of new or existing products or devices or interventions, such as wound assessment techniques, mobility/exercise, nutrition, treatment "bundles," or prevention regimens that are being used or will be used in the treatment of wounds, whether acute or chronic.

METHODS

The POWER panel of 11 experts in the field of wound care convened in a round-table format to discuss and generate a preliminary consensus document, consisting of 17 principles with supporting background.

A modified Delphi approach was used to reach consensus on the 17 principles. The Delphi method involves using input from experts to reach consensus on a particular subject,[19] and consisted of two separate web-based survey questionnaires for consensus building with conferences of the POWER panel following each round of the Delphi to review analyses and generate revisions as indicated.

Subjects and setting

The expert panel included one medical researcher, two nurse researchers, one pharmacist, one physical therapist, four physicians, and two podiatrists. Delphi respondents were drawn from a variety of professionals throughout the US. POWER contacted the leadership of 19 professional organizations having an interest in wound care to invite their members to participate in the Delphi process. Persons interested in participating contacted POWER directly or had their contact information passed on through their affiliated organization. Participating organizations decided on their method of participation. Fifteen organizations participated in the process: American Association of Wound Care Management, American College of Certified Wound Specialists, American College of Hyperbaric Medicine, American College of Foot & Ankle Surgeons, American Diabetes Association Foot Council, American Dietetic Association, American Physical Therapy Association, American Podiatric Medical Association, American Professional Wound Care Association, Association for Advancement of Wound Care, Coalition of Wound Care Manufacturers, Society for Vascular Medicine, Society for Vascular Surgery, Undersea & Hyperbaric Medical Society, and Wound Healing Society. One hundred seventy-three persons responded to the initial request for participation in the Delphi, of whom 115 completed the first Delphi questionnaire (66% response rate) and 80 completed the second Delphi questionnaire (46% response rate).

Delphi questionnaires

The initial questionnaire consisted of the 17 principles each with a brief explanation of the concept, rated on a 4-point scale (1 = strongly disagree; 4 = strongly agree) addressing endorsement, clarity, and need for revision. Open-ended questions allowed for comments. Basic demographic questions and questions addressing wound research background and experience were also included. The *a priori* criterion for endorsement of a principle was greater than or equal to 90% of participants responding with "agree" or "strongly agree" to the principle. Principles with less than 90% agreement were considered for revision by the POWER panel. Principles that received $\geq$15% affirmative responses by participants to the question, "Does the statement require revision?" were also reviewed and considered for revision by the POWER panel.

The second questionnaire consisted of those principles not receiving endorsement in the first Delphi round. Fourteen revised principles, each with a brief rationale for the revision, were rated using the same scale, and open-ended questions were employed in the first round. During the revision process, the panel split principles 5 and 8 into four separate principles for the second questionnaire. The second Delphi questionnaire included the descriptive statistics from the first questionnaire for all principles.

Delphi participants were sent an individual electronic link to the questionnaire. Each respondent was assigned an individual code to assure only one response per participant. Participants were given 3 weeks to respond. Electronic mail reminders and phone calls were sent and made to participants at the end of weeks 1 and 2. After the third week, initial questionnaire responses were analyzed, and aggregate results were sent electronically to POWER members prior to their conference meeting. The second Delphi questionnaire was available for participants 2 weeks following the POWER conference meeting. The same process was used in administration of the second questionnaire and convening of the POWER conference meeting.

Statistical analyses

The proportion of panelists endorsing each item (responding to statements with "agree" or "strongly agree") was calculated for responses to both questionnaires. Open-ended comments to the first questionnaire were content analyzed for general themes, and the compilation was sent to panelists as part of the second questionnaire.

RESULTS

Demographics of respondents

The most common age group for the respondents was 46–55 years, with geographic location evenly spread throughout the U.S.A. (Table 1). The most common primary work-related settings were wound care clinics (23.9%) followed by hospitals (18.6%) with physician as the most common role (27.0%). More than half of the respondents had >10 years' wound care research experience and almost 65% had the same number of years of wound care clinical practice.

Delphi round 1

Of the 17 principles assessed by the correspondents in Delphi round 1, only four principles were not endorsed (8, 9, 15, and 16) but only four principles did not require revision (6, 7, 12, and 17) (Table 2). Principles 4, 8, 15, and 16 attracted the most comments. Comments were mostly focused on application of the principle (i.e., use in different situations), objection to specific words or phrases or content (i.e., lack of clarity), or disconnects (i.e., more than one principle embedded in the statement). Some respondents were especially concerned that some principles had too broad a scope and needed better defined or narrower application.

Delphi round 2

Of the 14 principles assessed by respondents in the second Delphi round, only one (principle 9) was not endorsed and it was revised, although four other principles (4, 5a, 8b, 11) also needed revision (Table 3). These principles needed revision are largely based on the use of specific words or contextual use of the principle. Of the 19 final principles (Table 4), three principles (principles 7, 15, and 16) had additional detail in the form of numbered lists that specifically described embodiments of the principles to illustrate their application (Table 5).

DISCUSSION

While some principles seemed obvious to respondents ("This is Wound Care 101."), other principles elicited considerable controversy. Principle 4 is concerned with the many new products and devices entering the wound care market that are derivations of previously marketed products. The Code of Federal Regulations, Title 21, Parts 800 to 898, governs the marketing and utilization of these products,[20] and the Food and Drug Administration (FDA) Modernization Act (section 501 K) allows exemptions based on how the product is intended to be used. Thus, the FDA may designate a product

Table 1. Demographics of the respondents

Demographic	*n* (%)
Gender	
Male	54 (47.8)
Age (y)	
18–25	2 (1.8)
26–35	7 (6.3)
36–45	22 (19.6)
46–55	46 (41.1)
56–65	29 (25.9)
>65	6 (5.4)
Location (region)	
New England	11 (9.9)
Mid-Atlantic	18 (16.2)
East North Central	14 (12.6)
West North Central	5 (4.5)
South Atlantic	24 (21.6)
East South Central	4 (3.6)
West South Central	16 (14.4)
Mountain	11 (9.9)
Pacific	8 (7.2)
Primary wound-related work setting	
Wound care clinic	27 (23.9)
Other outpatient setting	8 (7.1)
Home health agency	1 (0.9)
Long-term care	6 (5.3)
Hospital	21 (18.6)
Long-term acute care/subacute facility	3 (2.7)
Academic	18 (15.9)
Industry/manufacturer	16 (14.2)
Other	13 (11.5)
Role	
Administration/management	9 (7.8)
Educator	9 (7.8)
Licensed practical/vocational nurse	1 (0.9)
Marketing/sales	0 (0)
Physical therapist	5 (4.3)
Physician	31 (27.0)
Podiatrist	19 (16.5)
Registered nurse	11 (9.6)
Researcher/scientist	17 (14.8)
Other	13 (11.3)
Years involved in wound care research	
≤2	6 (5.3)
3–5	16 (14.2)
6–10	18 (15.9)
11–20	32 (28.3)
>20	26 (23.0)
Not in involved in wound care research	15 (13.3)
Years involved in wound care clinical practice	
≤2	2 (1.8)
3–5	6 (5.3)
6–10	19 (16.8)
11–20	44 (38.9)
>20	29 (25.7)
Not in wound care clinical practice	13 (11.5)

Table 2. Responses for Delphi round 1

Principle	Principle response *n* (%)				Number of comments (%)	Revision? (Yes) *n* (%)
	Strongly agree	Agree	Disagree	Strongly disagree		
1. There is a need for a guidance document in the field of wound care research.	69 (62.2)	36 (32.4)	6 (5.4)	0 (0)	28 (25.2)	24 (21.6)
2. Wound care researchers, product developers, manufacturers, policymakers, payers, clinicians, and consumers should be educated on wound care research guidelines.	75 (67.6)	34 (30.6)	2 (1.8)	0 (0)	28 (25.2)	20 (18.0)
3. All human wound care research should follow good clinical practice.	85 (76.6)	18 (16.2)	6 (5.4)	2 (1.8)	16 (15.8)	20 (18.0)
4. A wound care study design should be matched to its purpose.	65 (59.6)	34 (31.2)	9 (8.3)	1 (0.9)	39 (36.1)	34 (31.5)
5. Research should include interprofessional studies evaluating multiple interventions (simultaneous and/or sequential interventions).	58 (55.2)	40 (38.1)	7 (6.7)	0 (0)	31 (29.5)	30 (28.6)
6. Research design should include parameters that are appropriate for the type of the study.	70 (67.3)	33 (31.7)	1 (1.0)	0 (0)	16 (15.4)	15 (14.4)
7. Primary endpoints in wound care research need to be matched with both the function of the intervention and clinical practice.	75 (72.8)	23 (22.3)	4 (3.9)	1 (1.0)	23 (22.3)	14 (13.6)
8. Study design should be independently reviewed and open for amendment or modification.	55 (53.4)	37 (35.9)	9 (8.7)	2 (1.9)	37 (35.9)	22 (21.4)
9. Quantitative wound care studies should include a run-in period as part of the initial assessment.	32 (31.1)	47 (45.6)	22 (21.4)	2 (4.9)	31 (30.1)	27 (26.2)
10. The rationale for inclusion and exclusion criteria in wound care research should be reasonable.	67 (65.0)	28 (27.2)	8 (7.8)	0 (0)	24 (23.3)	17 (16.5)
11. Vulnerable populations are underrepresented in clinical wound care research practice and should be included.	66 (64.7)	30 (29.4)	5 (4.9)	1 (1.0)	28 (27.5)	18 (17.6)
12. The definitions for intervention(s) provided to the comparator groups in any clinical study, typically defined as "moist wound care" or "usual care" need to be explicit.	84 (82.4)	18 (17.6)	0 (0)	0 (0)	18 (17.6)	8 (7.8)
13. An appropriate but comprehensive dataset should be included in the research design to describe the participants.	62 (60.8)	40 (39.2)	0 (0)	0 (0)	28 (27.5)	20 (19.6)
14. An appropriate but comprehensive dataset should be included in the research design for any study that involves wound evaluation.	74 (72.5)	25 (24.5)	2 (2.0)	1 (1.0)	18 (17.6)	17 (16.7)
15. Wound care research should include appropriate follow-up to determine rates of recurrence.	60 (58.8)	29 (28.4)	10 (9.8)	3 (2.9)	35 (34.3)	26 (25.5)
16. National or formal wound registries should be developed with practice-based evidence data collection, which may be made possible by the mandated use of electronic health records.	52 (51.0)	37 (36.3)	8 (7.8)	5 (4.9)	34 (33.3)	19 (18.6)
17. Cooperative groups, composed of multiple researchers working in concert, should be formed in order to facilitate and optimize wound care research.	67 (65.7)	30 (29.4)	4 (3.9)	1 (1.0)	15 (14.7)	13 (12.7)

Table 3. Responses for Delphi round 2

Principle	Principle response *n* (%)				Revision? (Yes) *n* (%)
	Strongly agree	Agree	Disagree	Strongly disagree	
3. All human wound care research conducted in the USA should follow the principles of good clinical practice in accordance with Food and Drug Administration regulations.	63 (75)	19 (23)	2 (2)	0 (0)	7 (8)
4. The study design of research conducted in wound care should be matched to its purpose.	51 (61)	28 (33)	5 (6)	0 (0)	23 (27)
5a. Wound care research should include evaluation of simultaneous and/or sequential interventions when appropriate.	54 (65)	25 (30)	3 (4)	1 (1)	18 (22)
5b. Wound care research should incorporate a multidisciplinary approach whenever possible.	58 (71)	21(25)	3 (4)	0 (0)	11 (13)
7. Primary endpoints in wound care research need to be matched with both the function of the intervention and clinical practice.	62 (77)	13 (16)	5 (6)	1 (1)	14 (17)
8a. Study design should be reviewed.	51 (64)	26 (33)	2 (2)	1 (1)	13 (16)
8b. Study design should be open to amendment.	49 (61)	25 (31)	4 (5)	2 (3)	20 (25)
9. Quantitative wound care studies should include a run-in period as part of the initial assessment when it is appropriate.	36 (45)	35 (44)	7 (9)	2 (2)	19 (24)
10. The rationale for inclusion and exclusion criteria in wound care research should match the goals of the study, but the generalizability of the results to wound care populations should also be spelled out.	48 (60)	30 (38)	2 (2)	0 (0)	10 (13)
11. Ultra-vulnerable populations are underrepresented in clinical wound care research practice and should be included where feasible.	52 (65)	22 (28)	5 (6)	1 (1)	18 (23)
13. An appropriate but comprehensive dataset should be included in the research design to describe the participants.	53 (66)	23 (29)	3 (4)	1 (1)	14 (18)
14. An appropriate but comprehensive dataset should be included in the research design for any study that involves wound evaluation.	59 (74)	19 (24)	1 (1)	1 (1)	9 (11)
15. Clinical wound care research should include rates of recurrence where feasible.	51 (64)	23 (29)	6 (7)	0 (0)	13 (16)
16. National or formal wound registries should be developed with real-world data collection.	49 (65)	28 (35)	1 (1)	2 (3)	9 (11)

status as "substantially equivalent" to the predicate product based on preclinical data or a product may be required to undergo more substantial testing for clearance under the premarketing application process.

While RCTs are conducted to analyze the *efficacy* of treatments under controlled conditions (how well a modality or procedure works relative to some standard control modality or procedure), observational studies are designed to quantify *effectiveness* (the ability to elicit an effect in real world practice).[16] Because some wound healing phenomena may be best studied initially by qualitative, descriptive, or other designs, as opposed to RCTs, the POWER panel suggests that initial research could be based on observational studies to fulfill the requirement of effectiveness in products or devices that are modifications of existing products or devices; other trials could then use RCTs to answer specific questions of efficacy. Examples of "derivative" products might include surgical dressings and some topical therapies, while biologically based products and drugs, whether novel or not, are likely to need more sophisticated study designs for acceptability because of issues of unpredictability, possibility of adverse events, and demonstration of efficacy under controlled situations.[16]

The premise behind Principle 5 is that most experimental designs focus on a single intervention of interest. However, wounds heal via a series of sequential and overlapping phases and may have multiple contributory factors. Chronic wounds, therefore, often require multiple interventions or episodes of treatment.[21] As an example, to prevent the possibility of amputation, a patient with an ischemic, neuropathic, diabetic foot wound might receive debridements, topical antimicrobial treatments and/or systemic antibiotics, hyperbaric oxygen treatments, offloading, specific biological products, physical therapy, nutritional counseling, diabetes education, and

Table 4. The final 19 principles

Principle	Content
1	There is a need for a guidance document in the field of wound care research.
2	Wound care researchers, product developers, manufacturers, policymakers, payers, clinicians, and consumers should be educated on wound care research guidelines.
3	All human wound care research conducted in the USA should follow the principles of good clinical practice in accordance with Food and Drug Administration regulations.
4	The study design of research conducted in wound care should be matched to its purpose.
5	Wound care clinical research should include evaluation of simultaneous and/or sequential interventions when appropriate.
6	Wound care research should incorporate a multidisciplinary approach whenever possible.
7	Research design should include parameters that are appropriate for the type of the study.
8	Primary endpoints in wound care research need to reflect both the goals of the intervention and clinical practice.
9	Study design should be reviewed.
10	Study design should be open to amendment.
11	Quantitative wound care studies should include a run-in period as part of the initial assessment when it is appropriate.
12	The rationale for inclusion and exclusion criteria in wound care research should match the goals of the study, but the generalizability of the results to wound care populations should also be spelled out.
13	Highly vulnerable populations are underrepresented in clinical wound care research practice and should be included where feasible.
14	The definitions for intervention(s) provided to the comparator groups in any clinical study, typically defined as "moist wound care" or "usual care" need to be explicit.
15	An appropriate but comprehensive dataset should be included in the research design to describe the participants.
16	An appropriate but comprehensive dataset should be included in the research design for any study that involves wound evaluation.
17	Clinical wound care research should include rates of recurrence where feasible.
18	National or formal wound registries should be developed with real-world data collection.
19	Cooperative groups, composed of multiple researchers working in concert, should be formed in order to facilitate and optimize wound care research.

perhaps a skin graft at the end, among other possibilities. Although "usual care" can equate to just offloading in the simple example of a well-perfused uncomplicated diabetic foot ulcer, many chronic wounds require more sophisticated approaches. Because the RCT design is so narrowly focused, it is not always the best approach to study multiple interventions that occur simultaneously or sequentially, unless the collection of interventions is examined as a "bundle" or an outlined protocol for progression.

Principle 7 is associated with the issue that wound care studies are often lacking crucial parameters in regard to design, execution, and reporting. Some useful reference works include the FDA's *Guidance for Industry: Chronic Cutaneous Ulcer and Burn Wounds – Developing Products for Treatment*,[22] and the CONSORT and STROBE criteria for RCTs,[23] and observational studies,[24] respectively. We propose a series of criteria for both RCTs and observations studies that we consider a "minimum set" with appropriate reporting in any publication (Table 5).

The concept embodied in Principle 8 emphasizes that primary endpoints in wound care are often diverse and do not always reflect complete wound healing, which may be an inappropriate endpoint for the type of intervention being evaluated.[25] For example, the goal to treat contaminated wounds is to create an infection-free wound so that subsequent treatments can be successfully applied for the next phase of wound healing. In palliative care, ultimate wound healing may not always be possible nor a goal; comfort, pain relief, and odor reduction may be desirable goals. Another example is debridement, the endpoint of which is a clean and granulating wound, whatever the method of debridement used. Under these circumstances, surrogate endpoints such as biological wound markers or physical parameters such as wound size and appearance at designated weeks of follow-up may be appropriate.[26,27]

The run-in period (Principle 11) is a way to normalize or equalize all subjects, making them comparable at the start of the test phase where appropriate.[22] In many quantitative wound care studies, patients often drop out during the first few weeks of a trial because of incompatibility problems with the intervention or unforeseen issues. To obviate these situations, a run-in period can be instituted, defined as a period of

Table 5. Additional details of principles 7, 15, and 16

Principle	Additional details
7	For randomized controlled trials, the following criteria should be considered a minimum set with appropriate reporting in any publication: 1. Properly define inclusion and exclusion criteria and methods of participant selection. 2. Use an appropriate randomization algorithm, including adaptive techniques for equal representation of particular groups or parameters where appropriate and avoidance of simple block designs to prevent breaking of allocation concealment. 3. Use a foolproof allocation concealment scheme. 4. Properly define allocation of treatment. 5. Define primary and secondary outcomes, including any composite or surrogate outcomes. 6. Blind patients, clinical assessors, and analysts where possible. 7. Define guideline of care, including any differences when more than one center is involved. 8. Define how missing data will be handled (i.e., patients lost to follow-up, etc.). 9. Include intent to treat (ITT) as well as per protocol analysis (raw data and results after any adjustments). 10. Follow-up (length, type of follow-up) must be appropriate to the goals of the study. 11. Measure drop-out rates in each arm of the study, and report causes. 12. Provide sufficiently detailed baseline data for all groups that each population is well characterized; baseline data should account for all known confounders. 13. Consider alternative designs for trial conduct if appropriate. 14. Select capable and skilled investigators/analysts for study. 15. Select capable research sites for study that have the capacity to complete the task. 16. Use validated tools where possible 17. Appropriate comparator groups should be utilized as a means of comparison against experimental treatment/intervention groups.
7	For observational studies, the following criteria should be considered a minimum set with appropriate reporting in any publication: 1. In cohort studies, define the eligibility criteria for each group as well as sources and methods for selection of participants. 2. In case-control studies, define the eligibility criteria for each group as well as sources and methods for case and control selection. 3. For cross-sectional studies, define the eligibility criteria as well as sources and methods for selection of participants. 4. In matched studies, define matching criteria, exposed and unexposed cases, and case : control ratio. 5. Properly define allocation of treatment if relevant to study. 6. Define primary and secondary outcomes, including any composite or surrogate outcomes if relevant to study. 7. Define guideline of care, including any differences when more than one center is involved if relevant to study. 8. Define how missing data will be handled (i.e., patients lost to follow-up, etc.) if relevant to study. 9. Follow-up must be appropriate to the goals of the study if it is relevant. 10. Measure drop-out rates in each arm of the study, and report causes if relevant to study. 11. Provide sufficiently detailed baseline data for all groups that each population is well characterized. 12. Select experienced and skilled investigators/analysts for study. 13. Select experienced and skilled research sites for study. 14. Use validated tools where possible.
15	The following are suggested as a guideline to include in any research design: 1. Age; 2. Gender; 3. Social status (as appropriate, e.g., socioeconomic status, education level, married vs. single, rural vs. urban, lives alone or with others); 4. Acuity score (if appropriate and available); 5. Ethnicity/race; 6. Comorbid medical conditions (as appropriate); 7. Activities of daily living (ADLs) and functional measures; 8. Health habits (e.g., nutritional status, exercise, tobacco, alcohol, and drug abuse); and 9. Additional measures as appropriate.

Table 5. Continued.

Principle	Additional details
16	The following are suggested as a guideline, depending on the type(s) of wounds involved in the investigation: 1. Wound etiology; 2. Wound duration (prior to assessment/treatment); 3. Compression (for venous leg ulcers); 4. Off-loading (for pressure and diabetic ulcers); 5. Debridement (frequency, types of debridement); 6. Moist wound healing (type of treatment); 7. Vascular assessment (how accomplished); 8. Surface area measurement (e.g., length × width, and method of measurement); 9. Evaluation of tissue depth (how measured; whether measured in size or involvement of tissue); 10. Location of the wound; 11. Tissue types; 12. Bacteriology as appropriate; 13. Use of validated tools; 14. Research-based standard wound assessment; and 15. Other criteria as appropriate.

time before a clinical trial in which prospective subjects are screened for potential adverse effects or problems that might interfere with participation. For example, if a new product is going to be tested for efficacy in venous leg ulcers using an RCT, all eligible subjects might be screened and placed on the control treatment (including compression bandaging) for a week before being randomized to the new treatment or remaining on the control treatment.

Principles 12 and 13 underscore the issue that the inclusion/exclusion criteria for many wound care studies are often overly restrictive, and therefore results can be limited in terms of generalizability to "real world" wound care populations, especially vulnerable or priority populations.[16] Although all wound care populations are vulnerable in a sense, some populations are highly vulnerable and include females, the elderly (various definitions exist: Medicare population ≥65 years, ≥70 years, and ≥85 years), racial and ethnic minorities, patients with disabilities, patient with multiple comorbidities, and those requiring palliative care.[28–31] For example, patients with renal failure or frail patients under long-term care could be considered highly vulnerable. While highly vulnerable populations are almost never represented in RCTs that test new interventions, products, or strategies, this is often acceptable if the first RCT is used to show whether the new intervention, product, or strategy works at all. However, subsequent RCTs should include highly vulnerable populations where feasible. In addition, for other types of studies, whether biobehavioral, observational, or basic science, investigators should also consider including highly vulnerable populations to acquire additional data where relevant.

"Usual care" has the potential for significant wound healing but varies considerably between wound care centers as several investigators have shown (Principle 14).[32–34] Usual care is also equated to moist wound care, but gold standard definitions for usual care for different types of wounds are absent. Thus, when clinical studies define the comparator group as usual care or moist wound care, this does not define what the care truly is. Consequently, definitions for any comparator group need to explicitly state in detail what type of care was given for each type of wound in the study.

Recurrence of wounds is common (Principle 17). Definition of recurrence is difficult in part because data regarding recurrence of specific types of wounds are limited. If a wound heals completely as defined in the study but a wound reoccurs in the same or an overlapping region at a later time, this might be regarded as a failure of treatment, a problem secondary due to a comorbid condition, or a *de novo* wound that had nothing to do with the first wound.[35,36] While it is not appropriate for all clinical trials to include recurrence of wounds as an outcome, nor is it feasible in many cases, where possible, investigators should give thought to including wound recurrence as an outcome where follow-up length of time is long enough, particularly longitudinal studies and RCTs.

Major strengths of our study included the number of wound care experts in the Delphi process, their representativeness of all aspects of wound care, the relatively high response rate in the first round, and the fact that we used a structured process to reach consensus to validate the principles elaborated here. Limitations of the study are the lower response in the second round, and the possibility that we overlooked certain aspects of wound care research, or were biased in our assessment of the comments received.

In conclusion, the Delphi approach used in this study substantiates the shortcomings of presently accepted protocols and fosters a new paradigm shift in wound research.

ACKNOWLEDGMENT

The POWER panel would like to thank several companies that supported the costs of the web-based survey, analysis, preparation of the manuscript, and travel expenses of the panel members: American Association of Wound Care Management, Celleration, Hartmann-Conco, Hollister, Inc., Kalypto Medical, Kinetic Concepts, Inc., Mölnlycke Health

Care, Ohio Medical Corporation, Prospera, Regenesis Biomedical, and Smith & Nephew.

The POWER panel would also like to thank Dr. Peter Shannon for managing the web-based Delphi process and providing the statistics.

TS conceived the study; MN oversaw acquisition of the data, while all authors analyzed and interpreted the data; MJC drafted the manuscript while other authors revised the manuscript critically for important intellectual content; TS supervised the study, while MN helped obtain funding and provided administrative and technical support. All authors had full access to all the data in the study and take responsibility for data integrity and accuracy of the analysis. The authors declare no conflicts of interest for this work.

REFERENCES

1. Mohr DN, Silverstein MD, Heit JA, Petterson TM, O'Fallon WM, Melton LJ. The venous stasis syndrome after deep venous thrombosis or pulmonary embolism: a population-based study. *Mayo Clin Proc* 2000; 75: 1249–56.
2. National Pressure Ulcer Advisory Panel. Pressure ulcers in America: prevalence, incidence, and implications for the future. An executive summary of the National Pressure Ulcer Advisory Panel monograph. *Adv Skin Wound Care* 2001; 14: 208–15.
3. Kuhn BA, Coulter SJ. Balancing ulcer cost and quality equation. *Nurs Econ* 1992; 10: 353–9.
4. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA* 2005; 293: 217–28.
5. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* 2010; 60: 277–300.
6. Hess CT. Putting the squeeze on venous ulcers. *Nursing* 2004; 34 (Suppl. Travel): 8–13.
7. Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: the economic case for the limb salvage team. *J Am Podiatr Med Assoc* 2010; 100: 335–41.
8. Gordon MD, Gottschlich MM, Helvig EI, Marvin JA, Richard RL. Review of evidence-based practice for the prevention of pressure sores in burn patients. *J Burn Care Rehabil* 2004; 25: 388–410.
9. Institute of Medicine. *100 initial priority topics for comparative effectiveness research*. 2009. Available at http://www.iom.edu/~/media/Files/Report%20Files/2009/ComparativeEffectivenessResearchPriorities/Stand%20Alone%20List%20of%20100%20CER%20Priorities%20-%20for%20web.ashx (accessed September 24, 2010).
10. Flanagan M. Barriers to the implementation of best practice in wound care. *Wounds UK* 2005; 1: 74–82.
11. Baharestani MM. An overview of neonatal and pediatric wound care knowledge and considerations. *Ostomy Wound Manage* 2007; 53: 34–6. 38, 40, passim.
12. Gottrup F, Apelqvist J, Price P. Outcomes in controlled and comparative studies on non-healing wounds: recommendations to improve the quality of evidence in wound management. *J Wound Care* 2010; 19: 237–68.
13. Carter MJ, Warriner RA 3rd. Evidence-based medicine in wound care: time for a new paradigm. *Adv Skin Wound Care* 2009; 22: 12–6.
14. Stromberg K, Chapekar MS, Goldman BA, Chambers WA, Cavagnaro JA. Regulatory concerns in the development of topical recombinant ophthalmic and cutaneous wound healing biologics. *Wound Rep Reg* 1994; 2: 155–64.
15. Robson MC, Maggi SP, Smith PD, Wassermann RJ, Mosiello GC, Hill DP, Cooper DM. Original articles: ease of wound closure as an endpoint of treatment efficacy. *Wound Rep Reg* 1999; 7: 90–6.
16. Carter MJ, Fife CE, Thomson B, Walker D. Estimating the applicability of wound care randomized controlled trials to general wound-care populations by estimating the percentage of individuals excluded from a typical wound-care population in such trials. *Adv Skin Wound Care* 2009; 22: 316–24.
17. Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *JAMA* 2007; 297: 1233–40.
18. Fife CE, Carter MJ, Walker D. Why is it so hard to do the right thing in wound care? *Wound Rep Reg* 2010; 18: 154–8.
19. Adler M, Ziglio E, editors. *Gazing into the oracle: the Delphi method and its application to social policy and public health*. London: Jessica Kingsley Publishers, 1996.
20. U.S. Department of Health and Human Services Food and Drug Administration. *Title 21: food and drugs*. 2012. Available at http://www.access.gpo.gov/nara/cfr/waisidx_00/21cfrv8_00.html (accessed November 16, 2010).
21. Sussman C, Bates-Jensen B. *Wound care. A collaborative practice manual for health professionals*, 3rd ed. Philadelphia, PA: Lippincott, Williams & Wilkins, 2007: 500.
22. U.S. Department of Health and Human Services Food and Drug Administration. *Guidance for industry: chronic cutaneous ulcer and burn wounds—developing products for treatment*. 2006. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071324.pdf (accessed March 24, 2010).
23. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gøtzsche PC, Lang T; CONSORT GROUP (Consolidated Standards of Reporting Trials). The revised CONSORT statement for reporting randomized controlled trials: explanation and elaboration. *Ann Intern Med* 2001; 134: 663–94.
24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007; 4: e296.
25. Sibbald RG, Woo KY, Woodbury MG. Evidence-informed practice in a just-in-time format: Woundpedia and the World Union of Wound Healing Societies. *Ostomy Wound Manage* 2008; 54: 6, 8.
26. Margolis DJ, Gelfand JM, Hoffstad O, Berlin JA. Surrogate end points for the treatment of diabetic neuropathic foot ulcers. *Diabetes Care* 2003; 26: 1696–700.
27. Margolis DJ. Clinical trials: the use of surrogate endpoints. In: Kirsner R, Galiano R, section editors. In: *Advances in wound care*, Vol. 1. New Rochelle, NY: Mary Ann Liebert Inc., 2010: 197–201.
28. Pieper B. Vulnerable populations: considerations for wound care. *Ostomy Wound Manage* 2009; 55: 24–37.
29. LeBlanc TW, Wheeler JL, Abernethy AP. Research in end-of-life settings: an ethical inquiry. *J Pain Palliat Care Pharmacother* 2010; 24: 244–50.
30. Kilbourne AM, Switzer G, Hyman K, Crowley-Matoka M, Fine MJ. Advancing health disparities research within the health care system: a conceptual framework. *Am J Public Health* 2006; 96: 2113–21.

31. Centers for Medicare and Medicaid. *Health and Health Care of the Medicare Population*. Chapter 3. Vulnerable populations. 1995. Available at https://www.cms.gov/MCBS/Downloads/HHC_1995_chapter3.pdf (accessed November 16, 2010).
32. Walker N, Rodgers A, Birchall N, Norton R, MacMahon S. Leg ulcers in New Zealand: age at onset, recurrence and provision of care in an urban population. *N Z Med J* 2002; 12; 115: 159–62.
33. Kjaer ML, Mainz J, Soernsen LT, Karlsmark T, Gottrup F. Clinical quality indicators of venous leg ulcers: development, feasibility, and reliability. *Ostomy Wound Manage* 2005; 51: 64–6, 68–72, 74.
34. Department of Health and Human Services, Agency for Healthcare Research and Quality. *Usual care in the management of chronic wounds: a review of the recent literature*. March 8, 2005. Available at http://www.cms.gov/determinationprocess/downloads/id37TA.pdf (accessed November 16, 2010).
35. Kapp S, Sayers V. Preventing venous leg ulcer recurrence: a review. *Wound Pract Res* 2008; 16: 38–47.
36. Bates-Jensen BM, Guihan M, Garber SL, Chin AS, Burns SP. Characteristics of recurrent pressure ulcers in veterans with spinal cord injury. *J Spinal Cord Med* 2009; 32: 34–42.