A Discourse on the Contributions of Evidence-based Medicine to Wound Care

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Abstract

Although a healthcare system crippled by lack of resources cannot perform effectively, spending more money in an ineffective system may not lead to better outcomes. To ensure systemwide resource maximization, evidence-based medicine and guidelines that consider treatment cost-effectiveness and recommend treatment for persons with the most to gain are required. To demonstrate that increasing use of evidence-based medicine can improve wound care, the effect of informed treatment decisions on improving patient care was reviewed. A Medline and OvidSP literature search was conducted of English-language literature using the MESH terms evidence-based practice and wounds and injuries. The adoption of evidence-based medicine by individual healthcare professionals can help ensure the limited resources available are used efficiently, enhancing confidence that additional funds will translate into more people receiving better wound care and having better health. Wound care professionals are encouraged to participate in conducting well-designed and controlled clinical studies of wound dressings and to resist the routine use of new, usually more expensive, dressings in the absence of good quality clinical evidence for their benefit over existing products.

Key Words: review, wound care, evidence, treatments, cost-effectiveness

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Results of a 2009 market research study show that wound care is one of the most costly components of the world healthcare system. Wound care is also one of the most rapidly expanding medical device market segments for manufacturers and providers — recent worldwide industry reports estimate the $14 billion market in 2008 will grow 7% per year. In 2008, more than 89 million patients in the US alone were treated annually for wound conditions at costs in excess of $25 billion.

A healthcare system crippled by a lack of resources cannot perform effectively; pouring more money into an ineffective system may not lead to better outcomes. However, in the context of a healthcare system with a fixed budget, it is not enough to consider the risk-benefit trade-offs of treatment. To ensure maximization of system resources, evidence-based medicine and better guidelines that consider treatment cost-effectiveness and recommend treatment for persons with the most to gain — ie, treatment for person with high risk-benefit — are required.

To demonstrate that increasing use of evidence-based medicine can contribute to a more efficient system of wound care, a Medline and OvidSP literature search of English-language publications was conducted for the MESH terms evidence-based practice (MESH H02.249) and wounds and injuries (MESH C21.866).

Inadequate Wound Care Management

Worldwide, healthcare professionals caring for patients with wounds are faced with the challenge of continuously improving the quality of their services and safeguarding high standards of care. All patients with a wound have the right to expect a good minimum standard of care regardless of wound etiology or geographic/clinical setting or provider. However, qualitative studies have shown that a high proportion of chronic wounds has been found to remain unhealed for long periods and/or for longer than necessary. Ineffective management can result not only in prolonged patient suffering, but also in increased cost to...
healthcare organizations.4,5 Also, although excellent healthcare practitioners may be delivering high quality, cost-effective care, provision of care may not be consistent because wound management worldwide is generally not organized or delivered in a uniform fashion against measurable standards of care and with clear referral pathways.6

Currently, access to some therapies is restricted depending on where the patient lives, where and by whom care is provided, or insurance coverage criteria.7-10 The US has one of the most sophisticated and advanced medical care systems in the world, attracting people from around the globe for treatment of complex and difficult health conditions.7 Yet the extent to which individuals living in this country benefit from this care depends to a great degree on whether they have health adequate insurance.7-10 Studies8-10 consistently show that persons without health insurance are far less likely to use health services than those with health insurance. In addition, the number of people without health insurance is on the rise, providing more cause for concern. More than 42 million Americans under the age of 65 years were completely uninsured in 1999.10 This may be related to the complexity and cost of products or equipment as well as to local protocol and service provision. Unfortunately, decision makers have not always understood the importance of wound healing8; once this was recognized, industry understood it to have demonstrated evidence that wound care products, both new and already produced, heal wounds rather than provide treatment per tradition.

Wound care has three main aims: prevention, care (healing), and the provision of symptomatic relief. Many healthcare professionals continue to treat and dress wounds according to traditional practices despite the fact that new research shows this may not be the best for the patient.12 Therapy choice still is largely a factor of marketing, expert opinion, and gut feeling rather than scientific evidence.12,13 For example, given their widespread use and higher cost, it is not unreasonable to expect that all modern wound dressings would have clinical evidence of benefit over conventional dressings in terms of wound healing. However, two systematic reviews14,15 of wound care dressing clinical trials have shown this is not the case. The first review14 included 99 studies, none of which were high-quality (level 1) studies; findings of note were that for chronic wounds hydrocolloid dressings were better than saline gauze or paraffin gauze for complete healing and that alginates, alone or in sequential treatment with hydrocolloid dressings, were better than other modern dressings for debriding necrotic wounds and reducing wound area. For acute wounds, hydrofiber and foam dressings reduced time to healing in comparison with other traditional dressings and with modern silver-coated dressings. The second review15 considered 42 studies of dressings for treating venous leg ulcers. Most studies were small (range 13 to 200 subjects, median 70), only five stated the method of randomization and blinding of allocation, and only one reported blinding of assessment. A meta-analysis of nine trials15 (n = 792) found no significant difference in healing between hydrocolloids and simple low-adherent dressings when applied beneath compression (relative risk 1.09, 95% CI 0.89–1.34). Evidence was insufficient to draw conclusions for other comparisons between dressings.

Wound care clinicians are encouraged to insist on evidence before adopting new treatment regimens and to participate in well-designed controlled clinical studies to evaluate the clinical and cost-effectiveness of modern wound dressings.

Evidence-based Medicine: Efficacy and Effectiveness

Levels of evidence. Evidence-based medicine is the “conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.”17 The practice of evidence-based medicine integrates individual clinical expertise with the best available external clinical evidence from systematic research.17 Advocates of evidence-based medicine classify studies according to levels of evidence on the basis of the research design.18-20 (see Table 1). In the hierarchy of research design, the results of randomized, controlled trials and meta-analyses of randomized controlled trials are considered to be evidence of the highest grade for the majority of clinical or interventional questions; whereas, observational studies fall at intermediate levels because they reportedly overestimate treatment effects and descriptive studies (eg, case series) and expert opinion receive the lowest levels.18-20 Although study quality is sometimes evaluated within each level, each...
and/or international interprofessional consensus panels.24-29 Literature, such as Cochrane reviews, and consulting national lines based on the strongest evidence, which includes review of these working groups use rigorous processes to develop guide lines.22 Curative use of dressings — eg, four-layer bandages to treat venous leg ulcers — provide other examples of prescribing based on Level 1 evidence.23

Failure to base therapeutic decisions on good evidence may deprive patients of a chance to benefit and will waste resources, limiting what can be spent on other aspects of health.7 Interdisciplinary working groups have been formed to develop best-practice recommendations relevant to wound care;24-28 these working groups use rigorous processes to develop guidelines based on the strongest evidence, which includes review of existing wound care recommendations and research literature, such as Cochrane reviews, and consulting national and/or international interprofessional consensus panels.24-28

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Table 1. Levels of evidence rating scale for therapeutic studies

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study type</th>
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<tbody>
<tr>
<td>1</td>
<td>High-quality, multicenter or single-center, randomized controlled trial with adequate power; or systematic review of these studies</td>
</tr>
<tr>
<td>2</td>
<td>Lesser-quality, randomized controlled trial; prospective cohort study; or systematic review of these studies</td>
</tr>
<tr>
<td>3</td>
<td>Retrospective comparative study; case-control study; or systematic review of these studies</td>
</tr>
<tr>
<td>4</td>
<td>Case series</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion; case report or clinical example; or evidence based on physiology, bench research or “first principles”</td>
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Category is considered methodologically superior to those below it.18 This hierarchical approach to study design has been promoted widely in individual reports, meta-analyses, consensus statements, and educational materials for healthcare professionals.18-20

Information from randomized, controlled clinical trials and their systematic evaluation by meta-analysis and other techniques is based, at least in part, on scientific evidence. For example, the use of artificial skin grafts to promote wound closure in patients with chronic diabetic foot ulcers is grounded in firm Level 1 evidence,21 as is the use of moist wound management to improve healing.22

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The popularity of many old remedies derived, in part, from spontaneous resolution of wounds following their use. When the UK Committee on the Review of Medicines began its work in 1975, 39,000 medicines were available on the UK market; by 1990, only 10,000 or so remained because many manufacturers were either unable to demonstrate the efficacy of their products or were unwilling to undertake the necessary expenditure to prove their effectiveness.24 The importance of randomized, double-blind, controlled clinical trials was not generally recognized until after World War II.31

Several considerations established the importance of this research method.23 The vagaries of human disease dictate that only in rare cases is the outcome so clearly foreseeable that the effectiveness of treatment can be deduced without a comparison group; plus, the suggestibility of patients and their physicians is generally sufficient to frustrate any attempts to fairly compare nonblinded treatments.20 Biases in choosing patients for experimental treatment also conspire to invalidate comparisons unless the treatment allocation is made randomly.20

In addition, determining the effectiveness of medical interventions from clinical research data is not an easy task, especially if studies addressing the same therapeutic problem produce conflicting results. Assessment of the validity of the primary studies has been identified as one of the most important steps of the peer-review process31 and as one of the key components of systematic reviews.34-35

Clinical trials. The two main types of clinical studies are experimental and observational.18-20,31-32 Experimental studies provide the strongest empirical evidence.18-20,32 In experimental studies, which include randomized, controlled clinical trials and randomized cross-over clinical trials, the investigator controls the assignment of the exposure or of the treatment; otherwise, symmetry of potential unknown confounders is maintained through randomization.32 Disadvantages of randomized, controlled trials include lack of generalizability of the results; the difficulty of performing randomized, controlled trials in wound care (eg, difficulty in blinding); the rapidity with which technology changes; and the length of follow-up required in some randomized, controlled trials. Experimental studies include within patient studies, where the patient serves as his or her own control and receives the drug under study and the comparator (placebo or another active drug) in random sequence; and cross-over studies, the more commonly used design, facilitated by between-patient comparison that randomly allocates patients to receive one or another of two or more treatments. Treatment efficacy is assessed according to predetermined objective or subjective criteria and the results are analyzed statistically to show whether benefits and/or adverse effects were likely to have arisen by chance.33 As an example, the latter design was used to assess the relative merits of four-layer and short-stretch compression bandages in patients with venous leg ulcers in the Level 1 evidence VenUS I study.36-37 Patients (N = 387) were randomized, without negative control, to receive either four-layer or short-stretch bandages to determine the effects of each treatment separately. Unadjusted analysis identified no statistically significant difference in median time to healing, which was 92 days for four-layer and 126
days for short-stretch bandages. However, when prognostic factors were included in a Cox proportional hazards regression model, ulcers treated with the short-stretch bandage had a lower probability of healing than those treated with the four-layer bandage: hazard ratio 0.72 (95% confidence interval 0.57 to 0.91).

Clinical trial methods have advanced medical knowledge substantially but concerns have emerged. Different trials of the same treatments in the same conditions have yielded different estimates of benefit, which sometimes have clinical importance but statistical uncertainty or may be statistically significant but of dubious clinical worth. This led to the realization that insufficient attention had been paid to the statistical power of many such studies. Inadequate numbers of patients or over-optimistic estimation of the likely benefits of a therapy or both failed to demonstrate benefit.

**Meta-analysis.** Meta-analysis seeks to formally combine all available evidence from clinical trials. This contrasts with the old-fashioned narrative review, in which an expert often used a partial set of all possible information to buttress personal views. An intermediate stage is the systematic review, in which attempts are made to find all the relevant published and unpublished work on a particular topic with no formal statistical analysis of trial results. Meta-analysis and systematic review depend heavily on identifying the relevant work; neither can compensate for the absence of good clinical trials in a particular field. However, reasonable evidence can be used to construct guidelines to help prescribers.

Statisticians then may conduct meta-analyses in which the results of all randomized controlled trials of a particular therapy are evaluated, including their 95% confidence interval, and an overall estimate made of the treatment effects and their statistical significance. This approach was used to assess the overall benefits of optimal compression therapy for venous leg ulcers, in which the results of eight randomized controlled trials were compared and combined. The overall analysis showed that leg compression with stockings is clearly better than compression with bandages, has a positive impact on pain, and is easier to use.

Efficacy and effectiveness relate to one of the most important questions in wound care: Does a particular intervention work or not? This also may be one of the most interesting questions in wound research, yet it provides an incomplete picture of the usefulness of a given treatment in daily practice. Of equal importance in the evaluation of therapeutic interventions are the issues of the safety and cost of treatment modalities. These aspects are intimately interconnected. Their proper assessment is aimed at ensuring a treatment does more good than harm. They are viewed as the most fundamental preconditions that ought to be met before considering the integration of any therapy into routine care.

**Safety**

Adverse effects of drug treatment fall into two main categories: type A, which are common and relate to the pharmacology of the therapy in question; and type B, which are idiosyncratic in nature, less common, unpredictable, and often serious. Examples of type A reactions are gastrointestinal disturbances in patients receiving the vasodilator drug pentoxifylline for treating venous leg ulcers.

Not all adverse reactions are recognized during the pre-marketing studies of a drug. Most type B reactions are uncommon, occurring at a frequency of one in every 5,000 patients treated or less, and may not be acknowledged until many thousands of patients have been treated. Examples of type B reactions are argyria and leucopenia in patients receiving silver sulfadiazine for wound care. The possibility of delayed and rare reactions means the safety of new medicines in relation to their efficacy cannot be established until they have been used for some time in many patients. During that time, a new medicine will be the subject of post-marketing surveillance, allowing a more accurate estimate of the incidence of adverse effects to be made. An example is acute renal failure due to medullary toxicity induced by topical silver sulfadiazine. Also, a wider patient population is likely to be exposed to the medicine, including persons with potentially complicating disease of the liver or kidneys as well as concomitant drug therapy.

In modern wound care provision, clinical practice needs to be refined in the light of emerging evidence of effectiveness as well as consider aspects of efficiency and safety from the perspective of the individual patient and carers in the wider community.

**Cost-effectiveness and Cost Utility**

A new therapy can be licensed if evidence determines pharmaceutical quality, efficacy (but not necessarily more so than comparators), and safety. The question of cost is explicitly excluded from consideration. However, almost all hospitals have a Drug, Technology and Therapeutics Committee, often serving not only the hospital(s) but also family physicians and their local communities. Cost-effectiveness is one of the parameters these committees will attempt to include in their decision regarding the inclusion or exclusion of a medicine in their local formulary, informed by work undertaken by drug information pharmacists and their nationwide network.

The issue of economic aspects of a therapy is complex because the boundaries to evaluating costs and benefits are artificial and the results are strongly dependent on where the boundaries are drawn. Modern therapies can be costly and yet still save money. One example is negative pressure wound therapy, which is more expensive than routine dressings in the treatment of diabetic foot ulcers and traumatic and postsurgical wounds, but randomized controlled trials suggest that appropriate usage can lead to savings through fewer surgical procedures, less-frequent monitoring, and fewer outpatient treatment visits.

Cost-effectiveness studies are the best examples of how efficacy and effectiveness studies differ in generalizability and
relevance to policy. Interventions with demonstrated benefit in efficacy studies need to be transported into the cost-effectiveness arena. Integrating cost-effectiveness models within efficacy studies yields results that are relevant both to policy and to clinical care. But even with such techniques, contextual and human factors, such as clinic prescribing practices and staff training, cannot affect care decisions.

Making Care Decisions
The prescription of any wound therapy represents a form of therapeutic experiment with the object of maximizing the benefit to the patient while minimizing risks. The decision, which must be made in partnership with the patient, first should take into account the severity and natural history of the condition from which the patient suffers, concurrent disease, and relative efficacy of alternative therapies. With that information, the evidence base can be applied. For example, a level 2 study demonstrated that most small traumatic lacerations in young people do not need antibiotics and level 5 evidence showed it would be unwise to give silver sulfadiazine to a pregnant patient for prophylaxis of infection in burn wounds. Provided the probable benefits of therapy are greater than those of alternatives and outweigh any potential risks, additional patient characteristics would need to be considered in the choice and length of administration of the therapy to be prescribed. The presence of disease affecting the metabolism or elimination of drugs and treatment with drugs that can interact are obvious problems.

Patient age is another important factor. Relatively few drugs have been adequately studied in children and some, such as silver sulfadiazine, have been found to be potentially dangerous. Older people have a reduced liver size and impaired renal function, which make them less able to eliminate many drugs; when treated with drugs that are eliminated unchanged by the kidney, people older than 75 years may require only one half or one third of the dosage used in young adults. Also, particular care needs to be taken with drugs with a narrow therapeutic index — eg, aminoglycosides, which can cause irreversible damage to hearing or balance when given to patients with infected wounds.

Conclusion
Driven by the development of technologically innovative products and rising incidences of chronic wounds as well as an increasing aging population, the wound care market is forecast to grow by 7.3% annually during 2008 through 2015 to reach $21.4 billion by 2015. Wound management products are costly to the world healthcare system. Like all therapeutic interventions, the choice of wound care products should be based on the evidence base for clinical safety, efficacy, cost, and patient suitability. Wound care professionals are encouraged to participate in conducting well-designed and controlled clinical studies of wound dressings and to resist the routine use of new dressings that are usually more expensive in the absence of good quality clinical evidence for their benefit over existing products.

In order to make an informed decision on wound management, wound care professionals need to have a good knowledge of the types of dressings available and the properties of individual dressings along with a sound understanding of wound healing. General factors such as safety, comfort, pain management, and convenience must be considered when deciding which dressing is the best for individual patients, given that dressings should be cost- as well as clinically effective.

Although high costs and widespread use would indicate that modern dressings have a clinical advantage over conventional ones, this is not always the case. Wound care professionals should consider whether the routine use of expensive modern wound dressings is justified on the basis of safety and patient preference. It is recommended that large-scale, local and individual health economies work together to develop local wound formularies to improve consistency in prescribing and maximize cost efficiency.

Increasing use of evidence-based medicine can contribute to a more efficient wound care system. The adoption of evidence-based medicine by individual healthcare professionals may help facilitate efficient distribution of resources, perhaps translating into more people receiving better wound care and having better health.

References


