Knowledge Development And Research Utilization In Evidence-Based Wound Care

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Knowledge Development And Research Utilization In Evidence-Based Wound Care

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CONTENTS

Chapter 1	General introduction and outline of the thesis	7
Chapter 2	What is the most commonly used treatment for donor site wounds after split-skin grafting? A survey of national policies and current reviews *Nederlands Tijdschrift voor Heelkunde 2011; 20(2):66-9.*	13
Chapter 3	Is the red-yellow-black scheme suitable to classify donor site wounds? An inter-observer analysis *Burns. 2011; 37(5):823-7.*	23
Chapter 4	The effectiveness of six common dressings for donor site wounds after split-skin grafting. A systematic review *Submitted.*	33
Chapter 5	Fundamentals of randomized clinical trials in wound care: Design and conduct. *Wound Repair and Regeneration 2012; 20(4):449-55.*	49
Chapter 6	Which dressings do donor site wounds need? Study protocol for a randomized controlled trial (Rembrandt Trial) *Trials. 2011; 12(1):229.*	65
Chapter 7	Which dressing do donor site wounds need? The results of a randomized controlled trial (Rembrandt Trial) *Submitted.*	77
Chapter 8	Values of patients and caregivers for donor site scars: An inter-observer analysis between patients and caregivers and prediction of cosmetic satisfaction *Burns. 2012; 38(6):796-801.*	91
Chapter 9	Do stakeholders in wound care prefer evidence-based wound care products? A survey in the Netherlands *International Wound Journal. 2012.*	103
Chapter 10	Competencies of specialized wound care nurses: A European Delphi study *Submitted.*	119
Chapter 11	General discussion	141
Chapter 12	Summary in English	149
Chapter 13	Summary in Dutch	155
Appendices		
	Curriculum vitae	161
	PhD portfolio	165
	List of publications	171
	Dankwoord (Acknowledgments)	175

Chapter 1

General introduction and outline of the thesis

GENERAL INTRODUCTION

Patients visiting health care institutions (e.g., hospitals, outpatient clinics, or wound expertise centers) deserve a good quality of care. Therefore, the decisions that caregivers make should be of the best possible quality, because these directly influence the health of patients. This may seem logical, but it is unclear what exactly constitutes good quality in daily practice.

Variety hampers quality of care

This is especially true in the realm of wound care. Here, quality of care is confounded by a large variation in wound types, physicians' and nurses' preferences, and the competencies of the caregivers involved. In addition, the number of types of available wound dressing materials is overwhelming and the availability of high-quality evidence and evidence-based guidelines is disappointing[1]. Moreover, a variety of stakeholders with different interests play a role in wound care, such as general physicians, clinical specialists, (wound care) nurses, dressing manufacturers, buying departments, and insurance companies.

This situation is likely to result in suboptimal care for the many patients suffering from wounds, and it is a challenge for evidence-based decision-making[1]. Only recently some national interdisciplinary initiatives have started to survey and counteract this variety[2;3]. However, if the variety of wound types is an important factor in causing the variations in wound care, then less variation should be expected in the care of 'standard' wounds. For this purpose we chose a seemingly uniform type of wound that should be simple to classify and treat, i.e., donor site wounds after split-skin grafting.

Sources available to decrease variation

Many ways of decreasing the variation in care have been described, of which many refer to research utilization in daily clinical practice during the treatment phase as well as to education. In this thesis we will focus on a few of these sources.

A first-stage method of reducing variation is to use or develop valid and reliable classification instruments. These measures of (wound care) outcomes are essential in clinical practice as well as in scientific research[4]. The aim of such assessments should be to arrive at an unambiguous classification in order to make a suitable treatment decision.

To further reduce variation in care and to facilitate evidence-based clinical decision-making, well-designed and well-conducted studies are needed. In particular, a higher methodological quality of randomized clinical trials (RCTs) will also increase the value of what are often derogatorily called "unhelpful Cochrane systematic reviews of wound care." For this purpose, a standard framework for wound care studies, focusing on

design and reporting, may help to improve the standard of research and transparency about the methodology of research.

On the other hand, some wound care systematic reviews are available that can be considered as high-quality evidence as they provide helpful results, which does make evidence-based treatment decisions in wound care possible[5-8]. In this situation the newly generated evidence should be implemented in practice and in education. This would enable caregivers to keep abreast of current professional knowledge, and to apply research evidence in their daily practice in order to deliver the highest possible quality of care.

Overall, this thesis is a compilation of interdisciplinary efforts to contribute to the body of knowledge on wound care, and it aims to promote evidence-based decision-making in order to reduce unnecessary variation in wound care. Therefore, we investigated (1) the extent of treatment variation; (2) the niches in available evidence; (3) and strategies to decrease this variation in the care of donor site wounds. We aimed to collaborate with as many stakeholders as possible (e.g., doctors, wound care nurses, educators, and manufacturers), as stakeholders are pivotal in promoting knowledge development and in the utilization of research into evidence-based wound care.

OUTLINE OF THE THESIS

To appreciate the variation in the current care of donor site wounds after split-skin grafting and to identify the most commonly used dressing materials we first conducted a national survey (**Chapter 2**). Several reasons may be advanced which explain why current wound-dressing policies are not standardized, for instance, the absence of a useful and reliable classification tool. Therefore, in **Chapter 3** an inter-observer analysis is described, in which the usefulness of the well-known Red-Yellow-Black scheme for classifying donor site wounds is evaluated.

Another reason for the variations in practice could be a lack of convincing evidence of the effectiveness of different dressing materials. We conducted a Cochrane systematic review (SR) to find the available evidence on the effectiveness and adverse effects (healing, pain, infections, itching, and cosmetic appearance) of the dressing materials most frequently used for the treatment of donor site wounds (**Chapter 4**). Because the design and conduct of RCTs in wound care are considered a challenge given the variety of wound types, dressings, and patients[9], we set out to formulate minimum requirements for proper clinical trials in wound care and designed a framework to deal with methodological problems; this is described in **Chapter 5**.

Based on the large variation in the practice of dressing usage and the paucity of evidence revealed in the SR, a new randomized clinical trial (RCT) appeared expedient.

The trial protocol and the results of this RCT, called "the Rembrandt trial", are described in detail in **Chapter 6** and **Chapter 7**.

Caregivers mostly focus on wound healing. However, scars also have a psychological impact and can affect the patient's quality of life[10]. Therefore, in **Chapter 8** we have described an inter-observer and patient analysis carried out to investigate the agreement between caregivers and patients on the cosmetic outcomes of the scar caused by the donor site wound using the Patient Observer Scar Assessment Scale (POSAS). In addition, we investigated which POSAS items best correlate with overall cosmetic satisfaction with the scar, which can be important for clinical decision-making in terms of what to focus on when pursuing scar satisfaction.

Not only should new evidence be generated where it is lacking, but already available evidence, particularly if it is compelling, should also be internalized by all stakeholders in wound care. This is a prerequisite for eventual evidence-based patient care. In **Chapter 9** we have described how we carried out a national survey to investigate the awareness and use of available evidence on wound dressings among the stakeholders.

When looking into the near future, the boundaries of the responsibility of nurses will change and task substitution is likely to occur. Furthermore, the competencies of wound care nurses and the ideas about the ideal competencies differ widely. We therefore undertook a Delphi study among healthcare professionals in several European countries (**Chapter 10**) to reach a consensus about the desired competencies of specialized wound care nurses.

Finally, **Chapter 11** presents a general discussion that puts the results of the studies in this thesis into a broader context.

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Chapter 2

What is the most commonly used treatment for donor site wounds after split-skin grafting: A survey of national policies and current reviews

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Adapted from Nederlands Tijdschrift voor Heelkunde 2011; 20(2):66-9.

ABSTRACT

Aim: To investigate current treatment policies for donor site wounds (DSW) in medical centers in the Netherlands, to assess extent of treatment variation and most common local treatment options presently in use, and to create recommendations for uniform treatment of DSWs.

Methods: Dutch medical centers with a surgical department were selected from the internet site www.kiesbeter.nl. Doctors and specialized wound care nurses at these centers were contacted by telephone and email and asked two questions; a) "Does your institution have a DSW treatment protocol?" and b) "Which dressings do you use to cover DSWs?"

We retrieved systematic reviews to formulate evidence-based recommendations from relevant literature databases (Cochrane Wounds Group Specialized Register, CENTRAL and Medline).

Results: A high response rate 92% (78/85) was achieved. Thirty-two percent of the responding centers had a wound dressing protocol. In total, 23 different types of dressing were reported. The five most-used dressing groups were films (45/78 centers; 58%), alginates (36/78; 46%), hydrofibers (25/78; 32%), silicone dressings (20/78; 26%), and paraffin gauze (15/78; 19%). Alginates were mostly used for primary dressings (46%). Films were the most popular secondary dressing material (21/78; 27%), covering a wide range of primary dressings.

Based on four systematic reviews, moist dressings seem preferable over non-moist dressings in the management of DSWs.

Conclusion: This national survey revealed a large variation in the dressing materials currently in use to cover DSWs. These findings call for an evidence-based guideline on the treatment of DSWs. We recommend the use of dressings that create a moist wound environment in the management of DSWs.

BACKGROUND

Wound care, particularly of wounds with an extended healing time, is a large and challenging problem worldwide[1]. Large because almost 50% of all inpatients have a wound which involves high costs[2], and challenging because of the large number of treatment options available.

There are many different wound dressings available and it is possible that the great variety of wound dressings causes variation in wound care, in some cases resulting in suboptimal care. The correct choice of dressing is not only essential for wound healing, but also has consequences for patients and the cost of health care[3]. Although choice of treatment and responsibility for wound care primarily rests with physicians, in practice it is often specialized wound care nurses and surgical nurses who carry out local wound care and who have some freedom in choosing wound care products[4].

Research in the Netherlands has shown a large variation in dressings used for the local treatment of open surgical wounds[5]. There are several reasons for non-standardized dressing management: the large variation in types of wound and wound dressings, personal opinions, and the absence of convincing evidence for the effectiveness of individual dressing materials all make optimum care difficult[4]. If variety of wounds is really an important factor for the variation of wound care, then less variation is to be expected in the care of 'standard' wounds.

One wound that could be described as 'standard' is a donor site wound (DSW) following harvesting of the upper layer of the skin, known as split-skin grafting (SSG)[6]. This technique is commonly used to cover skin defects, such as burn wounds, traumatic wounds, and chronic ulcers. In 2008, 702 SSG operations were recorded by the Dutch National Medical Registration Office. The skin is harvested in a relatively uniform manner using a dermatome, and involves harvesting only the epidermal layer and part of the dermis[7;8]. The donor site too is fairly uniform, being mostly located on the upper leg[9]. The SSG procedure leaves a superficial wound which, depending on its thickness, generally fully re-re-epithelializes in 7 to 21 days[7].

In the Netherlands there are known variations in the approach to treating these standard wounds and it is unclear which of these treatments is most effective. The aim of this national survey was to explore the extent of treatment variation and the local treatment options presently in use.

METHODS

National survey

Between April and July 2009, we contacted 85 hospitals over a period of 11 weeks. Hospitals with surgical departments were selected via www.kiesbeter.nl. All kinds of hospitals were contacted, i.e. university, general, and burn centers.

In addition, the network of wound-care nurses which is part of the Dutch Union of Nursing Professionals (*V&VN; "Verpleegkundigen & Verzorgenden Nederland*", a professional society for nurses and nursing assistants) was contacted by email. These nurses are specialized in wound care and work in a range of health care institutions where they determine wound care policy. Due to this, they have insight into the availability of protocols, the variation in wound treatment, and choice of dressings. In the absence of a specialized wound care nurse we contacted doctors (e.g. surgeons). If there was no response, a second attempt was made to improve the response rate by telephoning.

Doctors and specialized wound care nurses at these centers were asked two questions:

1) "Do you have a DSW treatment protocol?"
2) "Which dressings do you use to cover DSWs?"

Formulating evidence-based recommendations

To formulate evidence-based recommendations we retrieved all systematic reviews (SR) evaluating the effectiveness of dressings for DSWs of SSGs from the relevant literature databases (Cochrane Wounds Group Specialized Register, CENTRAL, and Medline). The search terms used were 'skin graft donor site' and combinations of the words 'skin grafts', 'donor' and 'dressings'. In order to take all considerations into account recommendations were formulated in accordance with the Dutch evidence-based guideline development methods (www.cbo.nl).

Analysis

Descriptive analysis was applied to the questionnaire data and percentages were calculated. Dressings were categorized by generic name and as either a primary dressing (in direct contact with a wound) or a secondary dressing (used as fixation material for a primary dressing). SRs were also presented descriptively.

RESULTS

The first attempt by email yielded little response (19%), even after four reminder emails. The second attempt by means of telephone calls resulted in a response from 78 out of 85 hospitals, i.e. a response rate of 92%. Of these 78 hospitals, 8 were university clinics, 23 STZ ("Association of tertiary medical teaching hospitals"), 3 burn centers, and 44 general hospitals.

Local treatment protocol

Twenty-five of 78 hospitals (32%) claimed to have a protocol on local treatment of DSWs. These protocols gave different recommendations on primary and secondary dressings. Fifteen of 25 protocols (60%) recommended alginates as the primary dressing after skin harvesting. Eight of 15 protocols (53%) advised covering these alginates with gauze, 5 out of 15 (33%) advised covering with film, one (7%) with foam, and one (7%) with a silicone dressing (Figure 1).

In 4 out of 25 protocols (16%), films were prescribed as the primary dressing. Combination products, such as foam with silicones (3/25; 12%), hydrofibers (2/25; 8%) and paraffin gauze (1/15; 4%) were less often used as a primary dressing.

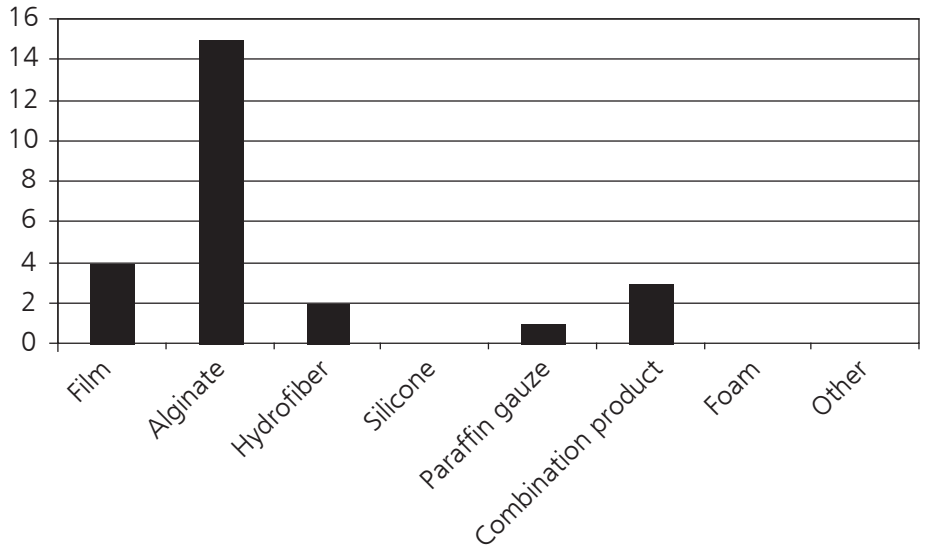

Figure 1. Recommendations based on protocols for primary dressing of donor site wounds

Usage of DSW dressings in local practice

In total, 23 types of dressing were mentioned (Figure 2). Some hospitals used more than one type of dressing for donor site wounds. The five most frequently used

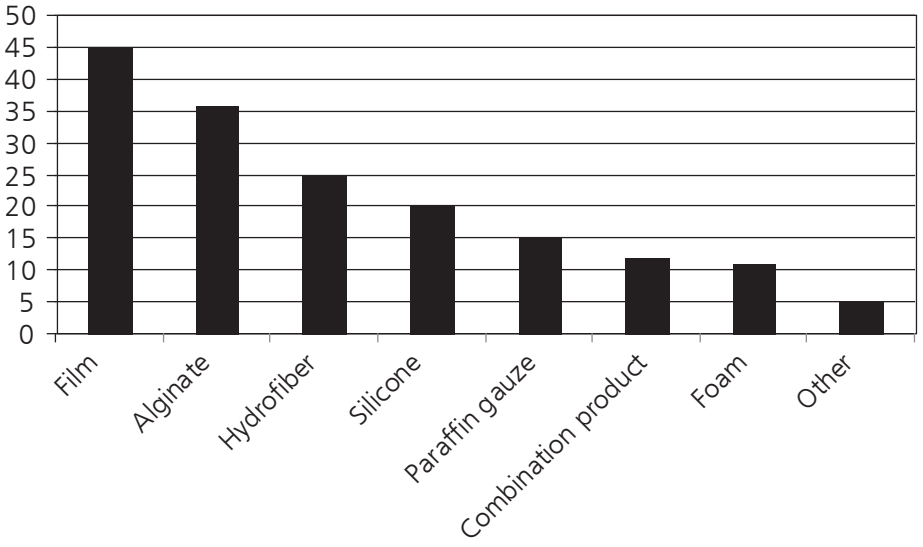

Figure 2. Types of dressing used for the treatment of donor site wounds

dressing groups were films (45/78 centers; 58%), alginates (36/78; 46%), hydrofibers (25/78; 32%), silicone dressings (20/78; 26%), and paraffin gauzes (15/78; 19%). Combination products (12/78; 15%) and foams (11/78; 14%) were mentioned less frequently.

When a distinction between primary and secondary dressings was made, different usage rates for films, silicones, paraffin gauzes and foams were observed (Figure 3). Alginates were most often used as primary dressings (36/78; 46%), followed by films (29/78; 37%) and hydrofibers (24/78; 31%). The most used secondary dressings were films (21/78; 27%). Silicones (2/78; 2%) and foams (2/78; 2%) were also used as secondary dressings.

Systematic literature search

Four systematic reviews comparing the effectiveness of different dressings to cover DSWs after split-skin grafting were found. These SRs were published between 1998 and 2009[8;10-12]. The number of studies included in these SRs ranged from 33 to 75[10;11]. One of the SRs included non-randomized studies[11]. Three out of four SRs concluded that strong evidence about the effectiveness of various types of donor site dressing is lacking, particularly concerning the use of alginates[8;10;12].

Nevertheless, all SRs concluded that a moist wound environment seems to be most effective in treating DSW in terms of time to complete wound healing. Dressing materials to create a moist wound environment are not gauze-based, but comprise

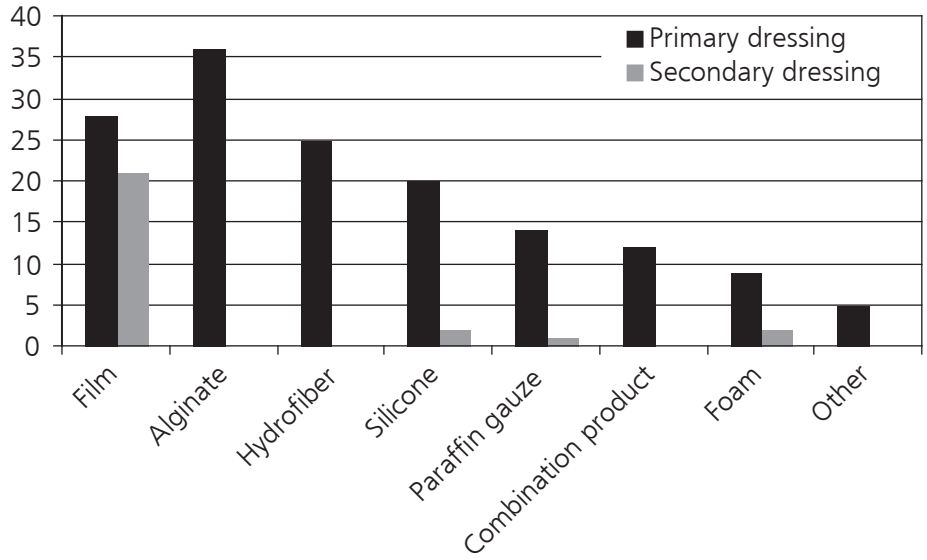

Figure 3. Types of primary and secondary dressing used in the treatment of donor site wounds

films, alginates and hydrocolloid[4;8;11]. This prevents the formation of a scab which could otherwise delay wound healing, and it simultaneously closes the wound to external bacterial penetration[4].

Wiechula concluded that a moist wound environment decreases pain and infection rates[8]. Only Rakel et al. concluded that film seems to be most cost-effective in treating DSWs in terms of wound healing, pain and infection[11]. However, their conclusions were only based on the price of films.

DISCUSSION

This national survey showed that there was a large variation in the dressing materials currently in use to cover DSWs. The uniformity of this wound does not go hand-in -hand with a uniform choice of dressing. It seems that the variety of wound etiologies is not a predictive factor for the large variation in wound dressings. In the Netherlands, films and alginates were found to be the most frequently used products for the treatment of DSWs. These materials create a moist wound environment. The available literature indicates that a moist wound environment seems most effective in treating DSWs[8;10;12]. However, there is still no guideline or strong evidence for a specific dressing which could improve the uniformity of dressing choice[8;10-12].

The Netherlands is not unique

Our results are in accordance with two other national surveys carried out in Australia and Great Britain[9;13]. These surveys also found variation in the local treatment of DSWs after split-skin grafting. Furthermore, in both countries, alginates were the most frequently used product. Notably, evidence for the effectiveness of alginates on wound healing is still lacking[8;10-12]. This preference could be connected with its supposed additional haemostatic capacity[14;15].

Film is less popular in the other surveys than it is in the Netherlands. Remarkably, 10% of the respondents in the British survey did not want to use film as a local treatment option for the treatment of DSWs[9]. In the Australian survey, only 13% used film. However, after alginates film is the most frequently used product in the Netherlands. Although films have practical disadvantages, such as the accumulation of fluids below the film in the acute phase of the wound, it seems that films decrease pain rates more than other materials[11].

Another international survey which included burn centers, also found a large variation in dressing choice[16]. In the burn centers conventional, gauze-based materials were used most frequently for the treatment of DSWs. The reason they gave was that they prefer tried and tested dressing materials to the as yet unproven modern dressings. This differs remarkably from the results of our survey.

Lack of evidence and underestimation

The explanation for variation could be that the variation exists as a consequence of the lack of evidence. This is probably an important reason why there are many dressing materials in use.

Our national survey may be underestimating the real variation in practice. Only specialized wound care nurses and a few doctors were contacted, thus not all doctors and nurses who are involved in the treatment of DSWs. However, more than half of the respondents said they used dressing materials which create a moist wound environment. The available literature supports this[8;10-12].

The fact is that most of the hospitals contacted do not have a protocol for the treatment of DSWs, which increases the chance of variation. Doctors and nurses could possibly be treating wounds in a different way than specialized wound care nurses. Specialized wound care nurses have often more knowledge of the different materials.

Generalizability of available literature for the Netherlands

Modern dressings are used on a regular basis in the Netherlands and are generally available in each health care institution. However, the cost-effectiveness of different dressings and health care professionals available should be taken into account by making dressing choices. The cost price of dressing materials ranges from €0.46 to €10.23 per item (size 10x10cm)[17]. However, the total cost of the local wound treatment

is strongly dependent on the combinations of products used and the frequency of dressing changes[8]. The risk of major complications due to a moist environment in DSWs is low. The depth of harvesting of the skin is important for the cosmetic result, but also influences the time to complete wound healing[7]. It is not known if the use of some dressings leads to a poor cosmetic result, such as keloid, hypo- or hypertrophic scarring.

Wound treatment can have side effects (e.g. itching and eczema) due to oversensitivity of the skin to specific components of the dressing materials, particularly hydrogels and hydrocolloids[18;19]. However, taking into account the frequency with which these dressing materials are used, allergic reactions can be considered uncommon[19].

Other complications such as infections, occur only in 5% or fewer of all DSWs[11]. However, health care professionals should take precautions to prevent infection which could increase costs and lengthen hospital stay.

The future

Despite the lack of strong evidence a Cochrane Systematic Review is necessary. The protocol for such a Cochrane SR has already been published[20]. Furthermore, a randomized clinical trial to investigate the effectiveness of various dressing materials is ongoing in the Netherlands (www.rembrandt-trial.nl, NTR 1849). Although guidelines on the treatment of DSWs are lacking, these findings call for an evidence-based guideline on the treatment of acute wounds, including DSWs. This guideline, coupled with an implementation project, should decrease the variation in wound care and increase the quality of care for such wounds in the future. Other recommendations are desirable in the sphere of pain- and itching treatment and haemostatic- and skin harvesting methods.

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Chapter 3

Is the red-yellow-black scheme suitable to classify donor site wounds? An inter-observer analysis

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Hester Vermeulen,
Dirk T Ubbink.

Burns. 2011; 37(5):823-7.

ABSTRACT

Background: The red-yellow-black-scheme (RYB) is a well-known and validated scheme to classify chronic and acute wounds, based on wound color and moistness. We investigated whether this RYB-scheme is also useful to classify donor site wounds uniformly (DSW).

Methods: Twenty-three digital photographs of DSWs in various stages of wound healing were presented to internationally renowned wound scientists (n = 11), surgical doctors (n = 31), specialized wound nurses (n = 55), and surgical nurses (n = 28). These observers classified the color and moistness of the wound according to the RYB-scheme, yielding seven wound categories. Inter-observer agreement (IOA) was expressed as a kappa (k) value.

Results: IOA's among specialized wound nurses were moderate when based on wound color and moistness (k = 0.41, 95% CI 0.33 to 0.49), wound color only (k = 0.41, 95% CI 0.29 to 0.53), or moistness only (k = 0.54, 95% CI 0.45 to 0.64). However, these IOA's tended to be better than those among the scientists, doctors and nurses. Scientists showed the lowest agreement (k-values between 0.17 and 0.25). Doctors scored slightly better than nurses.

Conclusion: Clinicians and scientists have difficulty with classifying DSWs by means of the RYB-scheme. Therefore, this scheme does not appear useful to classify donor site wounds in a uniform manner.

BACKGROUND

Classification of wounds is important to help clinical decision-making. The present-day variation in wound types, the huge number of dressing products available, and a myriad of opinions among doctors and nurses involved calls for uniformity in wound classification and subsequent dressing choice to optimize quality of care[1].

Available classification schemes are the RYB (red-yellow-black) scheme[2], TIME (tissue, infection, moisture, edge) scheme[3], MEASURE (measure, exudate, appearance, under-mining, reevaluate)[4], and PUSH (Pressure Ulcer Scale for Healing)[5]. Only the first two are well described in scientific journals. These schemes are used to assist clinical judgment and to get insight in the progression of wound healing in a uniform way.

The RYB-scheme appears particularly useful because it is simply based on the color and moistness of the wound and is capable of guiding the appropriate choice of wound care interventions[2;6-8]. The color 'red' indicates granulation tissue, which merely requires protection and is usually indicative of proper healing. 'Yellow' indicates yellow necrosis (slough) requiring wound cleansing, while 'black' stands for black necrosis, for which debridement is necessary[2;8].

Previous research on the RYB-scheme shows that it can be helpful in chronic and acute wounds[9-12]. This suggests usefulness in donor site wounds (DSWs) after split skin grafting (SSG). These are acute wounds created under standard conditions. SSGs are used to repair skin defects (e.g. burns, chronic, and traumatic wounds) and involves the harvesting of only the epidermal layer and part of the dermis[13;14]. Depending on the thickness of the SSG and an uneventful healing period, a DSW fully re-reepithelializes in 7–21 days[13]. Categorizing DSWs might help choosing an appropriate wound dressing, particularly because a large variation exists among health care professionals regarding their choice for wound dressing materials or topical agents to treat DSWs[15-17].

The value of the RYB-scheme has not been studied in DSWs. This should be done because they differ from the previously studied acute wounds as to depth of the wound and healing time. We therefore investigated whether the RYB-scheme helps professionals involved in wound care to uniformly judge DSWs in order to improve the care for patients with these wounds.

METHODS

Digital photographs

To assess inter-observer agreement using the RYB-scheme, we obtained digital photographs of DSWs from Dutch hospitals via a national wound care network. We used photographs rather than in vivo observations to avoid observers judging the

same wounds at different moments during the healing process, which could affect the reliability of the study[18]. Furthermore, using photographs was obviously the only way to get an international group of observers to judge the same wounds.

A first selection of high-quality and representative photos was made by our hospital's Wounds and Pressure Ulcer Committee, consisting of experienced plastic and general surgeons and specialized wound care nurses. Representative photographs were defined as those demonstrating wounds in various stages of wound healing and reflecting the six possible combinations of color (red, yellow, and black) and moistness (dry or wet).

We used these two mutually exclusive categories for moistness because photographs hardly allow discernment of the three levels of wound moistness (dry, moist, or wet) according to the RYB-scheme. In addition, we created an extra category, i.e. ''completely healed'' DSWs. This was defined as complete re-epithelization of the skin without defects or scabs.

Finally, a set of 23 representative photographs was converted into a slide presentation.

Observers

The 23 slides were judged by a selected group of internationally renowned scientists in wound care, as well as groups of doctors (surgeons, plastic surgeons, trauma surgeons, residents and research fellows), surgical nurses, and specialized wound care nurses of the Dutch wound care network and employed by different Dutch hospitals or community care. These latter groups were considered a representative sample of those who clinically judge DSWs in real life.

Judgment procedures

Judgment of the slides took place during a national meeting of specialized wound care nurses and during a presentation to our local department of surgery, using electronic voting devices: ResponseCard^{TM} keypads linked to TurningPoint for Microsoft® PowerPoint® (Turning technologies, Ohio, USA, version: 4.1.0.9020). Each wound slide was presented for 15 seconds to be judged. During these sessions we emphasized the observers should enter their judgments independently and without discussion during the presentation.

Secondly, we distributed 35 CDROMs with the slide presentation (also programmed to show each slide for 15 seconds) and a scoring form to doctors and nurses of 12 Dutch medical centers and the international group of scientists.

Before viewing the DSW slides all observers were given the same instructions about the RYB-scheme and definitions used by means of a few introductory slides.

All observers were blinded to additional information about wound and patient characteristics.

We also collected basic demographic data from the various observer groups, including their age and educational level.

Data analysis

Inter-observer agreement (IOA) according to the RYB-scheme among scientists, doctors, specialized wound care nurses, and nurses involved in DSW care was expressed as group kappa (k) values. These were calculated using AGREE for Windows version 7.002 (Science plus Group, Groningen, The Netherlands). K-values lie between 0 and 1. A k-value above 0.8 is interpreted as 'very good', between 0.8 and 0.6 is 'good', between 0.6 and 0.4 'moderate' and below 0.4 'poor'[19]. We calculated group k-values including 95% confidence intervals to assess the IOA in the groups of scientists, doctors, specialized nurses and surgical nurses. We imputed missing values by the median value (i.e. the most common answer for each slide) of the judgment of a slide to assess the effect of any missing value on the resulting k-values. If more than 50% of the answers were missing, the data of this observer were excluded from the analysis.

Next to the overall IOA as to wound color and moistness, we also calculated the group k-values using wound color or moistness or complete healing separately, to see whether one of these characteristics were easier to assess. For wound color agreement four categories were used (i.e. completely healed wounds and red, yellow, and black wounds), while for the agreement on moistness two categories were used (i.e. dry and wet).

RESULTS

Eventually, 11 international wound care scientists (from Canada, Australia, UK, USA, Switzerland, New Zealand, and the Netherlands), 31 doctors from five Dutch hospitals, 55 Dutch specialized wound care nurses and, 28 surgical nurses from 12 Dutch hospitals contributed. The characteristics of the four groups are shown in Table 1.

Completeness of data

None of the observers had to be excluded from the analysis due to >50% missing answers. In total, 45 out of 2875 (1.5%) answers were missing and were therefore imputed. Most of the answers missing were found among the specialized wound care nurses (32/1265; 2.5%), followed by nurses (7/644; 1.1%), and doctors (6/713; 0.8%). No missing answers were found among the scientists.

Table 1. Characteristics of doctors and nurses; professional background

Group	n	Median age category	Professional background		
Scientists	11	41-50			
Doctors	31	>31-40	Surgeon	Plastic surgeon	Vascular surgeon
Number			1	3	2
Spec. nurses	55	41-50	Nurse practioner	Wound consultant	Wound and decubitus nurse
Number			3	38	8
Nurses	28	<30	Ward manager	Senior staff nurse	Nurse (RN)
Number			1	3	16

Inter-observer agreement

An overview of the IOA among the different observer groups is shown in Figure 1. Overall agreement regarding the classification of DSWs was moderate at best. IOA among specialized wound care nurses (k = 0.41, 95% CI 0.33 to 0.49) tended to be higher than those among scientists, doctors, and surgical nurses, who showed a poor agreement. Conversely, IOA among the scientists were always lower than those among the other observer groups. These observations were also true for the IOAs based on ''color'' only, ''moistness'' only, and ''complete healing'' only IOA for all four observer groups were best when judging moistness and complete healing. Surgical doctors generally scored higher IOAs than surgical nurses.

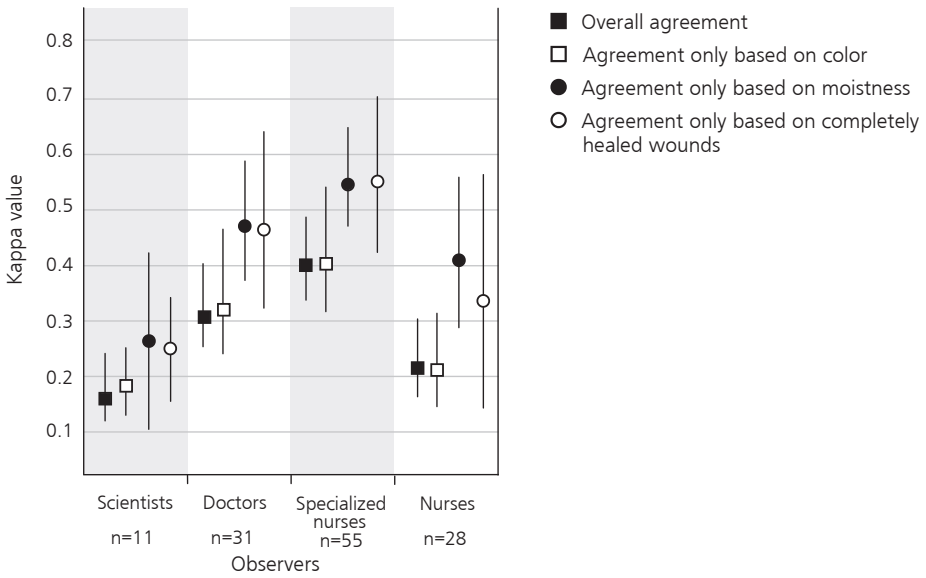

Figure 1. Inter-observer agreement among the four observer groups

Trauma surgeon	Gastro intestinal surgeon	Surgical resident	Plastic surgical resident	Trainees	Research
1	3	5	5	2	9
Wound nurse	Nurse (RN)	Nursing assistant specialized in wound care	Other		
1	2	1	2		
Student nurse	Other				
5	3				

DISCUSSION

This inter-observer study showed that the RYB-scheme, based on wound color and moistness, does not appear useful to uniformly classify donor site wounds. The inter-observer agreement was moderate at best when assessed by specialized wound care nurses. Judging only wound color, moistness, or complete wound healing only slightly improves judgment agreement among each of the four groups of professionals.

Present findings are in contrast with previous studies which are performed regarding the classification of (open) surgical -and chronic wounds according to the RYB-scheme[9-12]. These studies found a moderate to good agreement. Agreement in judgment as found here about whether a DSW is completely healed is in accordance with the study of Margolis et al[20]. They found a good agreement in chronic wounds based on the definition of wound healing according to the Wound Healing Society[20]. We also strictly predefined the definition of completely healed wounds because wound healing is frequently based on subjective assessments of wound closure by care providers and scientists[20].

Although DSWs of SSGs are surgical wounds, the variation in the appearance of DSWs is probably too small to make a proper distinction based on the RYB-scheme. Indeed, the majority of DSWs are red wounds, in which infection (with yellow slough) is rare, and which virtually never lead to black necrosis. When variation is small, agreement is supposed to be larger and this is taken into account when kappa values are calculated. This may be the reason why our kappa values may be an underestimation and are therefore in contrast with previous studies[21]. Additionally, our kappa values could be underestimation of the truth in daily wound care practice, because in real life situations many more elements can be taken into account, including patient characteristics. The difference in IOA between in vivo and in vitro situations for health care workers is difficult to assess. Doctors and nurses are not

able to classify DSWs simultaneously, but after a certain time lapse, in which wound characteristics could have changed. Furthermore, even if photographs are harder or easier to judge than in vivo, our results do not differ substantially. However, it may also overestimate the true values for agreement. The observers were instructed about the definitions of the categories used in the RYB-scheme before assessing the slide presentation. There are some limitations to this inter-observer agreement study. First, the photographs we used for assessment of DSWs were taken with different digital cameras. This is not the same as clinically judging DSWs in real life. However, there is evidence that selected photographs can be assessed in a reliable way based on studies with different classification schemes[9;22]. Second, wound and patient characteristics, such as age, comorbidity, time interval after graft take, presence of odor or pain, were not available. Awareness of clinical information provides indirect knowledge and may influence the observer's decision[18]. For example, it is easier to make a distinction between dried blood and black necrosis if it is known how many days after graft take the photograph is taken. Third, determination of validity is usually accomplished by comparing the measurement against a reference standard. In this study a reference standard was lacking, so the correctness of the judgments as made by the four groups of professionals could not be verified.

Present day reality is that there is no reliable scheme for the assessment of DSWs, although a lot of classification schemes are used in clinical practice (e.g. RYB, TIME, and MEASURE) for acute and chronic wounds. Most chronic wounds are seldom uniform in color[7]. However, this does not appear to be the case for DSWs, which are usually red, well granulating and quickly healing wounds. Despite this uniformity, based on national surveys, large variation was found among health care workers regarding the dressing materials currently in use to cover DSWs[15;16]. Apparently, a uniform 'standard' wound is not associated with a uniform assessment and dressing choice for DSWs.

We conclude that the RYB-scheme appears to be unreliable in daily clinical practice to classify DSWs and to guide treatment decisions. These findings call for a new evidence-based classification scheme to assess DSWs in a uniform manner.

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Chapter 4

The effectiveness of six common dressings for donor site wounds after split-skin grafting. A systematic review

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Adapted from: Cochrane Database of Systematic Reviews (submitted)
Abridged version of Cochrane Systematic Review

ABSTRACT

Background: To cover donor site wounds (DSWs) after split-skin grafting, a variety of wound dressings is available. However, the best choice to support the quick and uneventful healing of DSWs is still unclear. Therefore, the available evidence on the effectiveness of six commercially available dressings to treat DSWs was studied.

Methods: A systematic review was performed of trials comparing the effectiveness of at least two of the following dressings in adult patients with DSWs after split-skin grafting for any indication: alginates, films, gauzes, hydrocolloids, hydrofibers and silicones. The outcomes assessed were wound healing, pain, infection rates, itching, costs and scarring. Five databases were searched for randomized clinical trials (RCTs) up to September 2011. Trial selection, quality assessment, data extraction and synthesis were conducted by two authors independently.

Results: Of the 635 citations identified, 18 RCTs met the inclusion criteria. Sample sizes ranged from 8 to 60, totaling 560 patients. Trials reported on gauzes (n = 14), hydrocolloids (n = 8), films (n = 7), alginates (n = 3), and hydrofibers (n = 3).

Based on trials of mediocre quality, hydrocolloids and films seemed the most beneficial with regards to wound healing (up to 8 days quicker) and pain (up to 3 points lower on a 10-point scale) as opposed to gauze dressings. Infections rarely occurred among all groups. No significant differences were found in itching scores.

Conclusion: It appears that dressings which create a moist environment (such as hydrocolloids and films), should be incorporated in wound care protocols. However, a large, well–designed trial is warranted to corroborate this recommendation.

BACKGROUND

Split-skin grafting is a widely used reconstructive technique for traumatic, chronic and burn wounds[1;2]. Harvesting the skin leaves a donor site wound (DSW). The optimum local care for DSWs should promote wound healing, while preventing complications, such as pain, infection and scarring.

At present, a large number of dressings and topical agents for DSWs are available. Alginates are most commonly used to cover DSWs[3-6], probably due to their additional haemostatic properties[7;8]. Other popular dressings include gauzes, films, hydrofibers and silicones[3-6].

Up to now, three reviews showed a lack of strong evidence for the effectiveness of different dressings for the treatment of DSWs[1;2;9]. These reviews tentatively concluded that dressings which promote a moist wound environment, in particular hydrocolloids and films, are preferable in terms of wound healing. Films seemed to decrease pain more than other dressings[1], although they were also found to have practical disadvantages, such as the accumulation of fluids underneath the film in the acute phase of wound healing. Hydrocolloids appeared to be the most widely studied dressing and led to faster wound healing than wound products which promoted a non-moist wound environment[2]. However, these were less popular in daily practice[7], possibly due to the more frequent dressing changes required because of wound leakage[1].

The need for the present systematic review of the treatment options for DSWs is based firstly on the belief that evidence-based decision making should preferably be based on studies with the least risk of bias, i.e. randomized clinical trials (RCTs)[1;9], which was not the case in the previous reviews[1;2;9]. Second, the latest review only included studies prior to 2008[9]. The continual updating of systematic reviews by adding recent trials helps to find the true effect of an intervention[10]. Third, Voineskos et al. compared dressings that do with those that do not promote a moist wound environment for the treatment of donor sites, whereas the clinical effectiveness of the dressings within the moist dressing group is also relevant. Lastly, given the large variation in treatment options for DSWs, a new systematic review could offer more uniform recommendations for daily practice. As a result, this practical advice may promote behavioral changes among caregivers and the implementation of research findings.

Therefore, a relevant systematic review was carried out, focusing on six dressing materials, including five commonly used dressings as well as hydrocolloid, which is a promising dressing material identified from the literature. The effectiveness of these six dressings for the treatment of patients with DSWs after split-skin grafting was assessed, in terms of wound healing, pain, infection rates, itching, costs and scarring.

METHODS

The methods and results in this systematic review are summarized according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct of meta-analyses and intervention studies[11;12].

Eligibility criteria

RCTs were eligible if they compared at least two of the following dressings with each other for the treatment of DSWs: alginates, gauzes, films, hydrocolloids, hydrofibers and silicones. Moreover, they had to address at least one of the following outcomes: complete wound healing (i.e. complete re-epithelization), pain (using a Visual Analogue Scale), infection rates, itching, costs and scarring (using the scores of the Vancouver Scar Scale (VSS) or the Patient Observer Scar Assessment Scale (POSAS)). No restrictions on the follow-up period, publication data, language, or publication status were used.

Information sources

RCTs were identified by searching the Cochrane Wounds Group Specialized Register, Ovid Medline, Ovid Embase, and EBSCO Cinahl up to September 2011, as well as the Cochrane Central Register of Controlled Trials (CENTRAL) up to issue 3, 2011. Furthermore, the authors screened the reference lists of all included articles to identify additional relevant trials.

Study selection

Two review authors independently selected potentially relevant trials based on the titles and abstracts of the articles identified by the search.

Full-text versions of the articles were obtained if they matched the eligibility criteria or if further scrutiny was needed regarding eligibility. The final trial selection was made independently by the same review authors. A third review author was involved in case of any discrepancies.

Data collection process

Two authors independently extracted and summarized characteristics and data from the included trials using a predefined data extraction sheet. Disagreements were resolved by discussion, and a third author made the final decision if needed. Data from trials published in duplicate were included only once.

Risk of bias in individual studies

The methodological quality of each trial was determined by two authors independently. The Cochrane Collaboration appraisal tool was used to assess risk of bias[13]. Again, a third review author arbitrated any discrepancies.

Data items

The data extracted were: (1) characteristics of the trial (e.g. study design, method of randomization); (2) number of participants per intervention group (3) types of intervention compared; (4) estimated effects of primary and secondary outcomes; and (5) funding resource.

Summary measures and methods of analysis

Quantitative data were entered and analyzed in RevMan 5.1.4 (Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2011) by one author, and checked by another. Summary estimates of the treatment effects (with 95% Confidence Intervals [CI]) were calculated for every comparison. For continuous outcome parameters, mean differences (MD) were calculated, and risk ratios (RR) were determined for dichotomous outcome parameters. If it was not possible to calculate these summary estimates, P-values were presented as stated in the original article. In this review, the authors presented quantitative data using a vote-counting table, presenting a simple count of the number of studies significantly in favor of a dressing material (+), the number of studies against (-) it, and those with indifferent results (0).

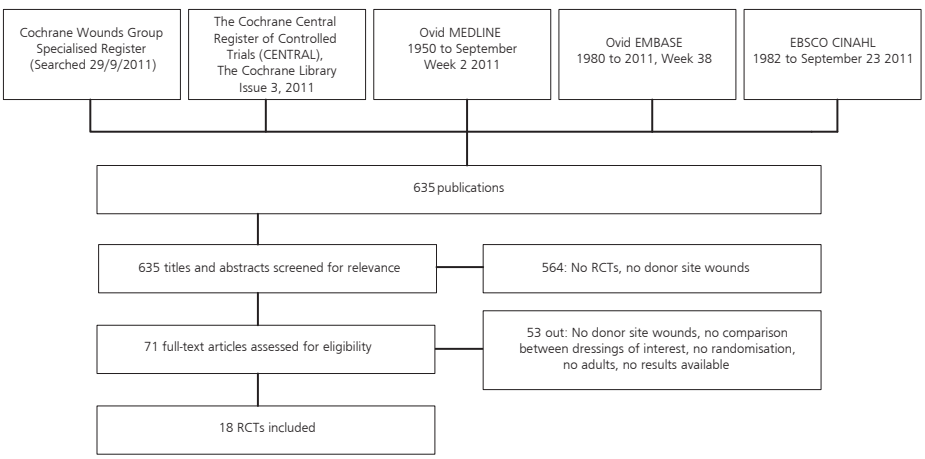

Figure 1. Flow of information through the various phases of a systematic review

Table 1. Characteristics and methodological quality of included studies

Author	Country	N*	Intervention	Comparison
Barnea[15]	Israel	46	Hydrofiber (Aquacel®) (n=23)	Gauze (paraffin gauze) (n=23)
Barnett[26]	USA	60	Film (Tegaderm®; Opsite®) (n=46)	Gauze (fine mesh gauze) (n=14)
Cadier[27]	England	21	Hydrocolloid (Dermasorb®) (n=21)	Gauze (Jelonet®) (n=21)
Cihantimur[24]	Turkey	80	Alginate (Kaltostat®) (n=40)	Gauze (Jelonet®) (n=40)
Demetriades[18]	South-Africa	20	Hydrocolloid (Granuflex E®) (n=10)	Gauze dressing (n=10)
Dornseifer[17]	Germany	50	Film (Opsite®) (n=unclear)	Hydrofiber (Aquacel®) (n=unclear)
Feldman[28]	USA	30	Hydrocolloid (Duoderm®) (n=10)	Gauze (Xeroform®) (n=13)
Hickerson[29]	USA	76	Hydrocolloid (WCL®) (n=38)	Gauze (Xeroform®) (n=38)
Iregbulem[14]	Nigeria	92	Film (Opsite®) (n=46)	Gauze (Sofratulle®) (n=46)
Leicht[19]	Denmark	16	Hydrocolloid (Duoderm E®) (n=8)	Film (Omniderm®) (n=8)
Loshiriwat[31]	Thailand	20	Ionic silver-containing hydrofiber (n= unclear)	Gauze (paraffin gauze) (n=unclear)
O'Donoghue[20]	Ireland	51	Alginate (Kaltostat®) with 0.25% bupivacine (n=30)	Gauze (Jelonet®) (n=21)
Persson[16]	Sweden	60	Tulle (Jelonet®) (n=20)	Film (Steridrape®, Tegaderm®) (n=40)
Porter[22]	Scotland	65	Hydrocolloid (Granuflex E®) (n=31)	Alginate (Kaltostat®) (n=34)
Rohrig[25]	USA	19	Hydrocolloid (Duoderm CGF®) (n=9)	Film (Opsite®) (n=10)
Smith[30]	USA	30	Hydrocolloid (n=14)	Gauze (fine mesh gauze) (n=16)
Steenfos[23]	Denmark	44	Alginate (Comfeel Seasorb®) (n=22)	Gauze (Jelonet®) (n=22)
Tan Baser[21]	Turkey	40	Film (Omniderm®) (n=20)	Gauze (fine mesh gauze) (n=40)

* = number of study subjects included (e.g. patients, wounds, or wound halves). 1, random sequence; 2, allocation concealment; 3, blinding care provider; 4, blinding patient; 5, blinding outcome assessor; 6, drop-out rate acceptable (i.e. <20% for short-term follow-up and <30% for long-term follow-up) ; 7, intention to treat analysis; 8, selective reporting (e.g. all pre-specified outcomes in the methods are reported in the results, trial reported on key outcomes that would be expected); 9, risk of other bias, including baseline comparability, similar co-interventions, financial support

RESULTS

Study selection

The search provided a total of 635 possibly relevant titles, of which 18 fulfilled the eligibility criteria. The study inclusion process is shown in figure 1.

Outcomes	Follow up	1	2	3	4	5	6	7	8	9
Healing, pain, infection, scarring	One year after surgery	?	?	-	-	+	?	?	-	-
Healing, pain, infection	Until healing	?	?	-	-	?	?	?	+	-
Healing, infection	Until healing	+	?	-	-	?	+	?	+	-
Healing, pain, infection	Until healing	?	?	-	-	?	+	-	-	?
Healing, infection	14 days	?	?	-	-	?	+	+	+	?
Healing, scarring, costs	10 days	?	?	-	-	+	+	-	-	?
Healing, pain, infection, costs	Until healing	+	?	-	-	?	?	?	+	-
Healing, pain, infection	Maximum 14 days	?	?	-	-	?	+	-	+	-
Healing, infection	Maximum 28 days	?	?	-	-	?	+	-	+	?
Healing, infection, itching	Until healing	?	?	-	-	?	+	+	-	-
Healing, pain, infection	Until healing	?	?	-	-	?	?	?	+	?
Healing, infection	10 days	?	?	-	-	?	+	+	+	-
Healing, pain, infection	14 days	+	?	-	-	+	+	+	+	+
Healing, infection	Until healing	+	?	-	-	?	+	?	-	+
Healing, pain, infection	Until healing	+	?	-	-	?	+	?	+	?
Healing, infection	17 days	?	?	-	-	?	+	-	+	?
Healing	8 days	?	?	-	-	?	?	?	+	-
Healing, pain, infection, scarring	6 months	?	?	-	-	?	+	+	+	-
Total of +		5	0	0	0	3	13	5	13	2

Characteristics of included studies

Table 1 shows the characteristics and methodological quality of the included trials. Trial sizes ranged from 8 to 60 patients, totaling 570 patients. All trials were published between 1983 and 2011. The RCTs contained patients undergoing a split-skin operation as a treatment for different indications, i.e. burns (n = 6), chronic wounds (n = 1), various reasons (n = 9), not specified (n = 2). A few studies randomized different wounds within the same patients. The study by Iregbulem et al. included only dark-skinned patients[14]. The 18 included trials compared gauzes (n = 14), hydrocolloids (n = 8), films (n = 7), alginates (n = 3), and hydrofibers (n = 3). Intervention and comparator dressings differed among the trials. None of the included trials studied silicone dressings. Most trials reported on wound healing and infection, although these outcomes were assessed in various ways. Only one trial investigated itching.

Risk of bias within the studies

The 18 RCTs varied in methodological quality (Table 1). The method of randomization was not stated in 13 trials (72%), and concealment of allocation was not ensured in any of the trials. The nature of the intervention made blinding impossible for patients and caregivers. In three trials (17%) it was stated that the outcome assessors were blinded for the intervention[15-17], but only five trials (28%) mentioned the use of an intention-to-treat (ITT) analysis[16;18-21].

Heterogeneity

The trials varied markedly in terms of comparator treatments and outcomes. As a result, clinical heterogeneity was substantial, which prohibited meta-analysis. Because meta-analysis was not feasible, the authors constructed a vote-counting table (Table 2).

Descriptive synthesis of results

The results are presented descriptively, in alphabetical order of the dressing, per outcome reported.

Wound healing

Overall, wound healing was reported in all of the 18 trials, but was measured in different ways, such as time to complete healing, and the proportion of wounds healed within the follow-up period. Table 2 summarizes the results of the comparisons between various dressings. Not one dressing seemed to be superior compared to all others, although gauze appeared to be disadvantageous in terms of wound healing.

Alginate dressings vs. hydrocolloid dressings

One trial compared alginates with hydrocolloids[22]. No significant differences were found in the number of patients reaching complete wound healing between alginates (14 out of 28) and hydrocolloids (20 out 30) at the first inspection (exact time point not mentioned) (RR 0.75, 95% CI 0.48 to 1.17).

Alginate dressings vs. gauze dressings

Three trials compared alginates with gauzes[20;23;24]. Two trials found a significant difference in complete wound healing in favor of alginates measured at days eight or ten (RR 1.98, 95% CI 1.45 to 2.69 and 2.22, 95% CI 1.19 to 4.15, respectively)[20;24]. However, Steenfos et al.[23] found no significant differences in complete healing at day six (RR 3.00, 95% CI 0.37 to 24.17).

Film dressings vs. hydrocolloid dressings

Two trials compared films with hydrocolloids[19;25]. Leicht et al.[19] found a significantly longer healing time for films (mean 10.63 days, SD 1.3) than for hydrocolloids (mean 7.63 days, SD 1.06) (MD 3.00, 95% CI 1.84 to 4.16). This is in contrast with the results of Rohrig et al.[25], who found no significant difference in days to complete wound healing (MD -0.92, 95% CI -4.27 to 2.43).

Film dressings vs. hydrofiber dressings

Only one trial compared films with hydrofibers, and reported a significant difference in the proportion of completely healed wounds in favor of film compared to hydrofibers at postoperative day 10 (reported P-value < 0.001)[17].

Film dressings vs. gauze dressings

Four trials compared films with gauzes[14;16;21;26]. Three of these trials found a significant difference in days to complete wound healing in favor of films (MD ranging from 3.70 to 7.74 days)[14;21;26]. Conversely, Persson et al. reported no differences in percentage healed wound area (reported P-value = 0.3)[16].

Hydrocolloid dressings vs. gauze dressings

Five trials compared hydrocolloids with gauzes[18;27-30]. Two of these trials reported a significantly shorter wound healing time in favor of the hydrocolloid dressings (P-values of 0.003 and <0.002, respectively)[27;30]. Cadier et al. also found a significant difference at the final assessment (exact time not stated) in a proportion of completely healed wounds (RR 0.45, 95% CI 0.27 to 0.74). These results are in contrast with Feldman et al.[28], who found a significant delay in wound healing in the hydrocolloid group (15.3 days) compared to 10.5 days in the gauze dressing group (P-value <0.002)[28]. Demetriades et al.[18] reported a significant difference in the proportion of completely healed wounds at day 8 in favor of hydrocolloids (5 out of 10) compared to gauzes (1 out of 10). However, when recalculating their reported data, a significant result was not found (RR 0.20, 95% CI 0.03 to 1.42). Furthermore, one trial found no significant differences in the number of patients with complete healing at the end of the study (although it was not clear what the follow-up duration was) (RR 1.20; 95% CI 0.95 to 1.50)[29].

Hydrofiber dressings vs. gauze dressings

Two trials compared hydrofibers with gauzes[15;31], and both trials found a significant difference in wound healing in favor of hydrofibers (P-values 0.016 and 0.027, respectively). In the trial of Barnea et al.[15], the time to complete wound healing ranged

from 7 to 10 days in the hydrofiber group compared with 10 to 14 days in the gauze group. Lohsiriwat et al.[31] found a mean healing rate of 7.90 days (SD 2.47) in the hydrofiber group compared to 11.20 days (SD 5.32) in the gauze group. It was not possible to calculate mean differences because it was unclear how many donor sites in each group were included.

Pain

Overall, pain was reported in eight trials, but it was measured at different time points. None of the studies investigated pain when using alginate dressings (Table 2). In 7 out of 8 studies, gauzes turned out to cause more pain. Only pain in-between dressing changes are presented in the vote-counting table.

Film dressings vs. hydrocolloid dressings

Only one trial compared pain rates between films and hydrocolloids[25]. Patients treated with films had significantly higher pain rates (P-value <0.001).

Film dressings vs. gauze dressings

Three trials compared pain rates between films and gauzes[16;21;26], and two found a significant difference in pain scores in favor of films (MD 3.10 [95% CI 1.92 to 4.28] and 1.30 [95% CI 0.66 to 1.94], respectively)[21;26]. Persson et al.[16] found no significant differences assessed one to two days postoperatively (P-value = 0.08), whereas VAS scores 14 days postoperatively were significantly lower in favor of film dressings (P-value = 0.014).

Hydrocolloid dressings vs. gauze dressings

Two trials compared pain rates between hydrocolloids and gauzes[28;29]. Both reported significantly lower VAS scores for patients treated with hydrocolloid dressings (average pain scores of 0.53 and 2.94, respectively) compared to gauze dressings (average pain scores of 2.41 and 4.64 with P-values of 0.01 and <0.001, respectively).

Hydrofiber dressings vs. gauze dressings

Two trials compared pain rates between hydrofibers and gauzes[15;31]. One of these trials found a significant difference in pain in favor of hydrofiber measured at different time points postoperatively[15]. Lohsiriwat et al.[31] found no significant differences at rest, with a rate of 0.74 in the hydrofiber group compared to 0.80 in the gauze dressing group (P-value = 0.894). However, they found lower mean pain scores at

Table 2. Overview of results using vote-counting

	Alginate vs. other dressings	**Film vs. other dressings**	**Gauze vs. other dressings**	**Hydrocolloid vs. other dressings**	**Hydrofiber vs. other dressings**
	4 trials	7 trials	14 trials	8 trials	3 trials
Outcome					
Healing	+ + 0 0	+ + + + 0 0 -	+ 0 0 0 0 - - - - - - - - - -	+ + + 0 0 0 0 –	+ + -
Pain		+ + + -	0	+ + +	0
Infection	0 0 0	0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0
Itching		0		0	
Costs		+	+	-	-
Scarring		0	- -		0

dressing removal in favor of the hydrofiber dressing group (3.12) compared with the gauze dressing group (4.70) (P-value = 0.027).

Other endpoints

Overall, infection was reported in 16 trials. Infections rarely occurred in the trials and none of the studies found a significant difference related to one of the six treatment arms. In addition, no significant difference was found for itching (Table 2). Only Leicht et al. reported on itching[19]. However, in their study none of the patients complained about itching.

Two trials reported on costs[17;28]. One of these trials reported that gauzes are less expensive compared to hydrocolloids, with average dressing costs per patient of 1.16 dollars in the gauze-treated group compared to 54.88 dollars in the hydrocolloid-treated group[28]. The other trial found that using hydrofibers turned out to be approximately four times more expensive compared to films. However, these amounts seem to refer to direct costs only.

Three trials reported on scarring using the VSS[17;21] or a modified VSS[15]. Only Dornseifer et al.[17] stated that there were no differences in scarring (no data given). Tan Baser et al.[21] found a significantly better score in the film dressing group compared to gauzes (pigmentation: MD 0.85; 95% CI 0.37 to 1.33; vascularity: 0.85; 95% CI 0.37 to 1.33), but no significant difference was found in the pliability score (MD 0.39; 95% -0.02 to 0.80). Barnea et al.[15] reported a significantly better score in the hydrofiber dressing group compared to the gauze group at one year postoperatively (P-value = 0.0091).

DISCUSSION

Evidence from currently available mediocre-quality RCTs shows that gauze dressings have been studied most often, but should be avoided in the local treatment of DSWs in patients after split-skin grafting, as these dressings lead to longer healing times and higher pain scores. Also, hydrocolloids and films have been well-studied and appear to be effective in terms of wound healing and pain relief. Other dressings, like alginates and hydrofibers, also seem to perform better than gauzes, and although silicone dressings are commonly used to cover DSWs, no trials were identified in this review to support this practice.

The findings of this study corroborate the conclusions of the already available reviews[1;2;9]. These reviews also included other study designs apart from RCTs. The current review only included studies with a higher internal validity, which could therefore be considered as more robust evidence. One of the strengths of this review is that it focused on the dressings most commonly used in daily practice. Despite a varying methodological quality, the available evidence suggests the use of dressings that support a moist wound environment. This may prevent tissue dehydration and cell death, thereby accelerating angiogenesis, increasing the breakdown of dead tissue, and potentiating the interaction of growth factors with their target cells[32].

Vote-counting was used to present the results in an understandable and pragmatic way. However, this method is open for debate, as it assumes equal weight being given to each study and effect, regardless of their size. As a result, this review also reported summary estimates of the treatment effects to allow the reader to better appreciate the size and precision of the positive, negative and indifferent findings. Second, the included studies were published over a period of 28 years, in which techniques and indications may have changed. However, the technique of split-skin grafting seems not to have changed largely over the years. Therefore, we do not think that this time interval affected our conclusions. Third, this review does not offer evidence for other clinically relevant questions related to the treatment of the DSW.

Apart from the type of dressing used, other factors also influence the treatment results, for example the harvest site (mostly located on the upper leg[4]), the thickness of the harvested skin (and thus the depth of the donor site wound)[33], the age of the patient, the use of pertinent medication, such as steroids[34], and pre-existing diseases, such as diabetes. Another factor may be the use of various haemostatic agents to limit intra-operative blood loss[35]. According to the best available evidence, epinephrine and fibrin sealant appear to be superior for achieving haemostasis when substantial topical blood loss is anticipated, particularly in cases of (larger) split-skin grafts[35]. However, it is unclear what the effects of these haemostatic agents are on wound healing. This question deserves further investigation. Furthermore, the general outcome of split-skin grafting may be less favorable when applied to severely ill or multi-morbid patients.

Although most of the included trials measured patient-related and clinically relevant outcomes, endpoints like adverse effects, scarring and cost-effectiveness were underreported. This may be explained by the fact that DSWs, being clean, superficial wounds, normally heal without any large problems and generally fully reepithelialize in 7 to 21 days[33]. Itching was described in only one trial[19], so it remains unclear whether itching is a major problem in DSWs. From previous studies regarding burns and linear scars, itching has a serious impact on patient satisfaction[36-38]. Within this review, only three trials measured scarring[15;17;21]. Scarring may have a psychological impact and could affect the patient's quality of life, particularly if scars are located in visible areas[39]. Therefore, evaluating scars is important to balance the pros and cons of wound care options and make well-informed clinical decisions for the treatment of wounds and prevention of scars. There are two reasons why the evaluation of scars is of interest. First, caregivers and patients do not agree in their judgment of the donor site scar, and second, they value different aspects of the scar[40]. Furthermore, cost-effectiveness was not investigated. Only the cost of dressings was given, which gives an incomplete estimation. However, the total cost of the local wound treatment is strongly dependent on the combinations of products used and the frequency of dressing changes. The latter is a proxy for staff costs, which has a prominent role in the summary of costs when plotted against effectiveness.

Further evaluation through well-designed and well-conducted RCTs is needed to corroborate the clinically relevant effects of dressing options for DSWs, preferably in multicenter studies, as the results of single-center studies may show larger effects or are contradicted when tested in multicenter settings[41].

In conclusion, an evidence-based choice of a wound dressing in the treatment of donor site wounds after split-skin grafting does make a difference, particularly in terms of wound healing and pain. With some caution the use of dressings that promote a moist wound environment, such as hydrocolloid and film dressings, can be advocated.

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Chapter 5

Fundamentals of randomized clinical trials in wound care: Design and conduct

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ABSTRACT

The care for chronic and acute wounds is a substantial problem around the world. This has led to a plethora of products to accelerate healing. Unfortunately, the quality of studies evaluating the effcacy of such wound care products is frequently low. Randomized clinical trials are universally acknowledged as the study design of choice for comparing treatment effects, as they eliminate several sources of bias. We propose a framework for the design and conduct of future randomized clinical trials that will offer strong scientific evidence for the effectiveness of wound care interventions. While randomization is a necessary feature of a robust comparative study, it is not suffcient to ensure a study at low risk of bias. Randomized clinical trials should also ensure adequate allocation concealment and blinding of outcome assessors, apply intention-to-treat analysis, and use patient-oriented outcomes. This article proposes strategies for improving the evidence base for wound care decision-making.

INTRODUCTION

Evaluation of wound care procedures and products is a challenge for researchers and clinicians alike. Unfortunately, only few articles are based on randomized clinical trials (RCTs). This article provides a guide for designing and conducting high-quality research focusing on, and relevant to, clinical practice. Based on a clinical scenario we will lead you through various issues related to RCTs.

CLINICAL SCENARIO

You, a vascular surgeon, performed a below-knee amputation in a 70-year-old man suffering from an acute Charcot foot with an extensive infection of the plantar fascia originating from a neuropathic foot ulcer. Although you administered prophylactic antibiotics, the patient develops an infection at the amputation stump. Hence, you remove most of the stitches to drain the wound.

The wound care nurse discusses with you whether or not to apply an iodine dressing or another antiseptic agent locally. As an evidence-based surgeon, you search the evidence that would support a choice. Three comparative trials come close to the problem you are facing with this patient, but these do not address amputation wounds and show contradicting evidence about which antiseptic is to be preferred[1-3]!

OPTIMUM STUDY DESIGN

While treating your patient according to local best practice, you realize there is a need for an RCT to answer this clinical quandary. The first dilemma that immediately arises is: Which study design is preferable and feasible at the same time? RCTs are acknowledged by some as the methodologically preferable design for investigating treatment effects because they eradicate important sources of bias, such as selection and confounding bias[4-6]. Any positive treatment effect found in an RCT generally provides more confidence about the efficacy of an intervention than in non-comparative studies or registries because possible confounders are equally distributed over the study groups, while known prognostic factors can be dealt with by stratification. This is advantageous particularly in wound care, where there is a large variety in types of wound, different wound etiologies, multiple comorbidities, and a wide range of treatment options (e.g., for local and systemic wound care). A pragmatic, real-life study design, e.g., through liberal patient inclusion from various settings and accepting relevant co-interventions or common comorbidities, would yield information about effectiveness rather than mere efficacy of wound treatments.

Some argue that there is no sound reason for wound care researchers to choose a design other than an RCT to evaluate wound care strategies[7]. Yet, RCTs are inappropriate in situations such as in case of rare, life-threatening diseases, such as toxic epidermal necrolysis[8], and when randomization would be unethical. It can be considered immoral to conduct an RCT to determine if primary amputation is as effective as a surgical or radiological intervention to treat critical leg ischemia. In such circumstances, data from observational studies may be more appropriate and sufficient.

A general, internationally accepted guideline on how to report RCTs has been formulated in the recently updated Consolidated Standards of Reporting Trials (CONSORT) statement[9]. This statement is also, albeit indirectly, useful for the preparation and conduct of RCTs. In this article, we will elaborate on issues particularly relevant for the internal validity of RCTs in wound care.

STUDY PREPARATION

In the clinical scenario presented above, an RCT to investigate the effectiveness of interventions seems possible and preferable. The next step is to consider several criteria that are considered essential components of intervention research (see Table 1). Formulating the exact research question helps define the patients needed for the study, the intervention under study, the standard policy as comparator, and the most clinically relevant outcomes.

Patients for whom the intervention is intended determine the setting from which eligible patients are to be selected, e.g., home care, general hospital, trauma or emergency ward, specialized wound clinic, nursing home, or university center. The same holds true for the patient characteristics. To ensure the appropriate spectrum of patients, consider whether vulnerable patients due to the presence of comorbidities (e.g., diabetes, kidney failure requiring dialysis) or certain types of medication (e.g., steroids) should be excluded. These factors may reduce the clinical success rate and/or increase the rate of complications; on the other hand, the question arises whether the clinical success under these different conditions is of particular interest because it reflects real life. In amputees, diabetics may be an important patient group to include, whereas the use of steroids is a likely exclusion criterion as it seriously hampers the normal immune response.

Exclusion criteria will reduce the number of eligible patients. Keep in mind that narrow inclusion criteria, which should demonstrate more powerful treatment effects, lead to further difficulties in the recruitment of patients and the generalization of the results (external validity). Eligible patients should be fully informed about the treatment options and, if they decide to take part in the trial, they have to give written informed

Table 1. Checklist of criteria to be defined and completed for an optimum design in wound care trials

		Yes	No
Setting	The trial setting (e.g. home care, general hospital, nursing home, or specialized (university) clinic) is defined		
Patients	Eligibility criteria for patients are described (inclusion and exclusion criteria)		
	Written informed consent will be obtained from every patient included		
Interventions	The treatment to apply in each trial arm is standardized		
	Co-interventions are allowed but prespecified (the same in both trial groups)		
Outcomes	Primary and secondary outcomes are prespecified		
	It is described when and how outcomes are assessed		
Sample size	Sample size is calculated (calculation based on expected clinical relevant difference in primary endpoint)		
Randomization	The unit of randomization defined (e.g., the wound or the patient)		
	The allocation sequence is randomly generated		
	The treatment allocation is adequately concealed		
Blinding	It is defined who is blinded after assignment to the intervention and how, including:		
	o Patients (recommend)		
	o Caregivers (recommend)		
	o Outcome assessors (strongly recommended)		
Intention-to-treat	All randomized patients are to be analyzed in the group to which they were allocated		
Funding	Funding through unrestricted grants only		
Follow-up	Duration of follow-up is defined		
Ethics	Ethics review board approval Trial registration		

consent[10]. Hence, it is advisable to perform an a priori sample size calculation (for more details, see section "Predefined plan for data analysis") to achieve sufficient power to detect clinically relevant differences. Furthermore, this sample size provides a realistic estimate of the length of time needed to recruit patients.

To be able to include a sufficient number of patients within a reasonable time interval, one should consider increasing the number of recruiting centers. A multicenter trial is preferable, not only to accelerate recruitment but also to enhance the generalizability of the results[11]. Admittedly, an (multicenter) RCT in wound care may be more time-consuming than a pharmaceutical study, at least in terms of the attending clinician's time, and may subsequently interfere or disrupt daily practice routines. In addition, involving clinicians from different specialties in the trial will likely improve the implementation of the result of the trial by all invited specialties. Tissue viability nurses or specialized wound care nurses tend to be zealous in contributing to studies in their area of expertise and can therefore play an invaluable role. A drawback

can be that multicenter RCTs are more expensive and pose logistic challenges, so financial support is a necessity to conduct a proper trial.

Generally, clinicians have had to rely ostensibly on financial support from commerce to extend the boundaries of our knowledge. In addition, the Food and Drug Administration (FDA) formulated some relevant patient outcomes for wound care (e.g., healing rate and pain relief) as the result of pharmaceutical interaction. Conversely, legislation in many countries does not consider wound care products as pharmaceutical agents, which may simplify the legal and safety requirements of such a trial. Ideally, first-choice funding should be obtained from independent (inter)national institutions. A second option is commercial funding from manufacturers to magnify valorization of the knowledge obtained. Many of these manufacturers are relatively small and cannot afford lengthy and/or expensive studies, which calls for a joint effort by several stakeholders (e.g., wound care researchers, clinicians, manufacturers). To avoid any conflict of interest, analysis and reporting of the trial should remain the domain of the researchers. A legal agreement helps to ensure the grant is unrestricted. Unfortunately, there is a trend to publish only studies with positive results that favor the sponsoring industry[12-14]. An "unrestricted grant" or a combination of sponsorships will assist in minimizing publication bias[15].

To demonstrate and document good clinical practice and patient safety, one should clearly describe the design of the RCT in sufficient detail in a research protocol. This protocol will need to undergo scrutiny by the local Ethics Review Board(s) before the study can start. In addition, one should register the research protocol in a publicly accessible database (http://www.isrctn.org or ClinicalTrials.gov) to announce the RCT is planned, ongoing, or completed. For many major medical journals this is a prerequisite for publication to reduce publication bias[16;17]. Availability of a protocol can help to restrict post hoc changes to the methods during the inclusion period[9]. Finally, a run-in period (e.g., pilot-inclusion of a few patients) can be useful to check the feasibility, logistics, and final success of the trial.

MAIN METHODOLOGICAL ISSUES OF DESIGN IN RCT

Randomization and allocation concealment

Randomization evenly distributes both known and unknown prognostic factors between comparison groups[18]. In addition, one may stratify patients by factors known to influence treatment outcomes, for example, age, wound size, and comorbidity, to disperse these demographic and prognostic factors evenly between the treatment groups[19]. This even distribution ensures that detected differences are attributable only to the intervention under investigation and not to confounding variables. To detect

any between-group differences, the collection and reporting of relevant patient and wound characteristics is essential (e.g., age, comorbidities, co-interventions, wound characteristics).

A concealed allocation process helps to reduce the risk of selection bias when comparison groups are not created in a truly random fashion. Examples are allocation by the person's date of birth, by the day of the week, by a person's medical record number, or just allocating every alternate person. These quasi-random methods do not offer patients an equal chance to receive either treatment. Furthermore, caregivers may easily become aware of the treatment the next patient will receive, which can cause (un)intentional inclusion or exclusion of the patient[20]. Therefore, it is best to assign a person unrelated to the study to perform the randomization, or to use a central randomization institute (particularly in case of a multicenter trial), or a web-based randomization service. The crux is to conceal the randomization schedule to prevent manipulation of allocation to the different treatment arms. It is preferable to randomize as shortly before the intervention as possible. This prevents dropouts after randomization, for example, when a surgical treatment is inadvertently cancelled.

Blinding patients and caregivers

Blinding of patients and caregivers regarding the allocated treatment is recommended. This is the Achilles' heel of most RCTs in wound care. Whenever possible, the test agents should be masked. This has been successfully performed when testing the effects of zinc oxide[21] and ibuprofen[22]. Blinding is obviously impossible when comparing, for example, negative pressure wound therapy (NPWT) with conventional wound dressing materials. This may introduce performance bias, i.e., patients and caregivers may act differently if they are aware of the treatment given (e.g., patients in the control group may be more likely to use additional care, and patients who know they are in the intervention group may experience placebo effects). Unequally applied co-interventions generally diminish the contrast between the treatment effects, for example, when the amount of antibiotics or analgesics given or the frequency of visits or follow-up intervals differs between the groups. Therefore, these should also be recorded. Some wounds may require a number of unavoidable procedural interventions to promote healing, e.g., regular episodes of debridement. This is acceptable when applied and recorded commensurately in both treatment groups.

Blinding outcome assessors

An independent outcome assessor who is unaware of the treatment given can conquer the challenge of blinding in wound care. It can be helpful to give patients instructions not to tell the independent outcome assessor to which intervention they were allocated. This is particularly relevant in studies in which it is difficult for patients

not to discuss the intervention, for instance, when their wounds are treated with NPWT or debrided with maggots.

Blinding of the outcome assessors is important, particularly in wound care, because most of the outcomes (see the section "Study outcomes") are subjective and open to overestimation in favor of the new intervention (e.g., wound healing)[23]. Only if the outcome parameters are objective, such as death, does this become less imperative. Some outcomes are difficult to measure objectively (e.g., patient comfort), while others (e.g., pain) can prove time-consuming and/or expensive.

Intention-to-treat principle

In wound care, some patients may switch from one intervention to the other due to side effects, apparent lack of effect, lack of treatment compliance, or simply a change in preferences. Despite these switches, one should analyze every patient in the group to which they were originally allocated, even if they did not receive the treatment as defined by the protocol or they withdrew from the study. The reason for this intention-to-treat principle is that it maintains treatment groups that are similar (apart from random variation). It therefore validates the use of randomization, and allows for handling of protocol deviations, further protecting the randomization process[24]. If some patients would have been excluded who did not complete their treatment because it was too burdensome (e.g., the use of sheepskin as they developed skin irritation[25]) or because they responded poorly, only the responders will contribute to the—obviously overestimated— treatment effect. Comparing the treatments the patients actually receive (also known as "per protocol" analysis), rather than to which they are allocated (e.g., after crossing over to the other treatment group), confounds the initially equal distribution of patients at randomization.

MAIN CLINICAL ISSUES

Comparability of study treatments

The comparator treatment should be current best practice rather than placebo. Particularly in acute wound care, there may be little consensus about what constitutes standard policy, making the comparator choice difficult. Another consideration regarding the interventions in the trial groups is their uniform application. Factors such as dressing change frequency, leg elevation, adequate compression, pressure relief, moment of applying an antiseptic or drainage device, cleansing procedure, antibiotics, and treatment duration are important procedures to standardize. Those who will perform the intervention or apply the device, dressing, or topical agent will benefit from training and instructions on how to use the intervention before the start of the

trial. It is also essential to define the indication for, and use of, additional treatments ("co-interventions") such as wound bed preparation, debridement, pain management, additional medication, nutritional supplements, antiseptics or antibiotics, and surgical procedures to avoid differential application. If the latter occurs, the groups are not treated equally and the effect found cannot be attributed only to the intervention under investigation. This flaws the validity of the trial.

Study outcomes

One should choose primary and secondary outcomes carefully and beforehand, as well as how, through which (valid) methods, and after which time interval(s) these outcomes will be assessed.

Primary outcome(s)

This outcome should represent the main effect of the intervention and is used for the sample size calculation (see section Predefined Plan for Data Analysis). The clinical effect of any intervention should be based on outcomes that are meaningful to patients. One may choose a valid intermediate or surrogate outcome if complete wound healing is not the primary aim (e.g., suitability for secondary surgical closure in the case of vacuum assisted closure [VAC] treatment). Then, goals shift toward maintaining or enhancing functional status, optimizing wound condition, or relieving suffering, for example, pain relief in patients with chronic leg ulcers. One should not settle for such end points just to shorten the follow-up period. For example, a 50% reduction in bacterial count might seem an impressive result to the researcher, but the patient still suffers from having a colonized wound. The follow-up should be long enough to measure all predefined outcomes. By defintion, chronic wounds are due to an underlying etiology (e.g., venous hypertension in venous leg ulceration). Consequently, if the etiology is not resolved, the risk of the lesion recurring over time has to be considered. This eventuality demands months or years of follow-up. Similarly, a study on quality of healing (e.g., hypertrophy, keloid) would also require an extended follow-up period. Moreover, many patients with chronic ulcers are subjected to polypharmacy, thus increasing the risk of drug-associated delays of wound healing. Unfortunately, sometimes less clinically relevant end points substitute primary outcomes when the latter were not as good as expected.

Secondary outcomes

In a study regarding preferences on ideal wound dressing characteristics, a short wound healing time, minimal pain during dressing changes, and short duration of hospital stay were valued most[26]. Meticulous wound pain assessment, preferably using standardized Visual Analog Scale, and proper documentation of pain and

analgesics usage is essential to appreciate an important aspect of wound care[27]. In addition, any complications or adverse effects should be recorded, such as toxic or allergic responses to dressing materials, blistering, infection, malodor, leakage, unexpected need for redressing, or wound recurrence. If there is a non-negligible risk of serious adverse effects, a data safety monitoring board is required to monitor these events. Adverse effects are usually underreported in publications, but are important to be aware of to weigh the benefits against the possible harms of an intervention. Examples of this are the underestimated adverse effects of silver sulfadiazine for burns and the overestimated ones of iodine as antiseptic agent[28-30].

It is of value to also consider assessing quality of life, functional status, and patient satisfaction because it provides valuable information on the patient-perceived burden of illness[31]. Both generic questionnaires, e.g., the Medical Outcomes Study Short Form-36[32] or Nottingham Health Profile[33], and wound type specific questionnaires[34] may be combined. In chronic wounds, these measurements should be repeated after larger intervals to determine the long-term effects of the interventions[35]. For the purpose of comparability among studies, uniform time points for clinical follow-up are highly desirable. Furthermore, the cosmetic result after complete wound healing is an outcome often appreciated by patients[36].

In today's economically constrained health services, the costs of treatment are an indispensable outcome parameter[37]. Therefore, one should try to measure cost-effectiveness from a societal perspective, including all relevant medical costs and nonmedical costs[38]. Analysis of medical costs should include the unit costs of all (dressing) materials used, costs of personnel involved in wound care, and inpatient treatment period required; costs of immediate and long-term complications; and costs of long-term outpatient monitoring and care. Additionally, the nonmedical costs may be calculated based on costs due to incapacity for work, transportation to the hospital, home adjustments, cleaning of soiled clothing, and so on.

The Cochrane Wounds Group also strongly advocates using only valid, objective outcomes. The proportion of wounds completely healed at a particular time, rates of healing, and incidence of new wounds or infection are considered suitable as primary outcomes[39]. The FDA guidance formulated definitions of outcomes that can be used to measure efficacy in wound care research. It helps to define outcomes for chronic and burn wounds, as well as for acute wounds[40].

Finally, it is mandatory to store the study database securely and ensure it is available for audit and access. Furthermore, these data may be also valuable for future meta-analysis.

PREDEFINED PLAN FOR DATA ANALYSIS

A comprehensive study protocol includes a predefined plan for statistical data analysis, which underpins the formulated hypothesis and helps to answer the research question. A meaningful comparison between treatment groups is possible only if an RCT is adequately powered to detect a predefined, clinically relevant difference in the primary outcome, should such a difference exist. For this purpose, one can make a calculation of the required number of patients to be included before the start of the trial. A power (1 – b) of at least 0.80 is considered acceptable, which indicates that there is a 20% risk that a true difference in treatment effect remains undetected, should such a difference exist. In addition, a significance level (a) of usually 0.05 is considered appropriate, meaning that it is accepted that there remains a 5% risk that a difference found is not a true treatment effect, but merely based on chance. We strongly recommend consulting a biostatistician or clinical epidemiologist for the study design and statistical analysis before designing the protocol.

When analyzing the data, remember to use the intention-to-treat principle for the reasons explained above. Subgroup analysis may also be considered to examine the treatment effect in a specific group of patients or wounds in the trial, in which the treatment is expected to be more effective. It is important to define such analysis before starting the RCT to avoid the suspicion of "data dredging." Moreover, such a comparison with less than the initial, complete set of patients is always underpowered and any differences found may be coincidental.

DISCUSSION

The scale of the worldwide wound care problem seems to match the high volume of publications, with at least 150,000 hits in Medline related to wound care. These PubMed-indexed studies include opinion-based reports, epidemiological studies, and studies of diagnosis, prognosis, and therapy. A strikingly small proportion of the publications on therapeutic interventions are comparative or randomized studies, and even fewer are (Cochrane) systematic reviews. Most of these Cochrane reviews end by concluding that the volume and quality of the existing research is low, the consistency of study design is lacking regarding study outcomes, few replication studies exist, meta-analysis is mainly impossible due to heterogeneity of the studies, and most studies are at high risk of bias[7].

To enhance the depth and validity of newly generated evidence needed to support clinical decision-making in wound care, we propose this comprehensive framework for wound care researchers to undertake properly designed and executed RCTs. Timely contemplation of methodological rigor is pivotal to achieve the desired scientific

knowledge. Many barriers and issues of RCTs can be overcome by proper design and conduct. Understanding the rationale for this comprehensive framework is also important for policymakers to help with decision-making with regard to the plethora of wound care products and the limited financial resources.

A more consistent approach as to the design and conduct of RCTs will facilitate meta-analysis of original studies. Many researchers and clinicians plead for more consistency in the choice of comparators and outcomes to be measured and reported in future research[37;41;42]. We hope the recommendations given here will help contribute to uniform, high-level research in this realm. Thus, the framework should ultimately help caregivers in decision-making for their patients with wounds. We do realize that this framework does not address the reporting of a trial, which is another essential aspect besides appropriately designing and conducting a trial[43].

The obstacles we face when initiating and performing RCTs in wound care are also shared by other clinical areas such as surgery[44;45]. Indeed, Farrokhyar et al. identified several factors that influence the internal validity of surgical trials. Nevertheless, many of these challenges can be overcome, and in most cases, these issues do not restrict the conduct of an RCT[45]. This seems to be in contrast with the European Wound Management Association position document[37], which also supports the use of cohort studies in wound care. According to Bell-Syer et al., the use of observational studies for evaluating treatment effects is only recommended in very specific circumstances, such as studying rates of diseases or harmful effects[7].

Another reason for the seemingly reluctant attitude toward rigorous trials may be the fact that commercially available wound care products, such as dressings and topical agents, do not (yet) need to undergo the scrutiny that pharmaceuticals do before being marketed because they are not subjected to the same rigor by FDA or good clinical practice regulations. Therefore, this does not force manufacturers to perform extensive research on their products. Nevertheless, evidence-based practice has become necessary in an area where clinicians increasingly have to justify their decisions toward patients, insurance companies, and government, and liability issues have become too common.

Given the worldwide magnitude of the wounds problem, health care professionals as well as manufacturers of wound care products should take every effort to improve the quality of care for patients with wounds. The recommended standards presented here for optimum trial design in wound care research are an earnest attempt toward achieving this goal while recognizing that their implementation is not without its own particular challenges.

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Chapter 6

Which dressing do donor site wounds need?
A study protocol for a randomized controlled trial (Rembrandt Trial)

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ABSTRACT

Background: Donor site wounds after split-skin grafting are rather 'standard' wounds. At present, lots of dressings and topical agents for donor site wounds are commercially available. This causes large variation in the local care of these wounds, while the optimum 'standard' dressing for local wound care is unclear. This protocol describes a trial in which we investigate the effectiveness of various treatment options for these donor site wounds.

Methods: A 14-center, six-armed randomized clinical trial is being carried out in the Netherlands. An a-priori power analysis and an anticipated dropout rate of 15% indicates that 50 patients per group are necessary, totaling 300 patients, to be able to detect a 25% quicker mean time to complete wound healing. Randomization has been computerized to ensure allocation concealment. Adult patients who need a split-skin grafting operation for any reason, leaving a donor site wound of at least 10 cm^2 are included and receive one of the following dressings: hydrocolloid, alginate, film, hydrofiber, silicone dressing, or paraffin gauze. No combinations of products from other intervention groups in this trial are allowed. Optimum application and changes of these dressings are pursued according to the protocol as supplied by the dressing manufacturers. Primary outcomes are days to complete wound healing and pain (using a Visual Analogue Scale). Secondary outcomes are adverse effects, scarring, patient satisfaction, and costs. Outcome assessors unaware of the treatment allocation will assess whether or not an outcome has occurred. Results will be analyzed according to the intention to treat principle. The first patient was randomized October 1, 2009.

Discussion: This study will provide comprehensive data on the effectiveness of different treatment options for donor site wounds. The dressing(s) that will prevail in effectiveness, satisfaction and costs will be promoted among clinicians dealing with such patients. Thus, we aim to contribute a well-designed trial, relevant to all clinicians involved in the care for donor site wounds, which will help enhance uniformity and quality of care for these patients.

Trial registration: http://www.trialregister.nl, NTR1849. Date registered: June 9, 2009

BACKGROUND

Split-skin grafting (SSG) is a widely used reconstructive technique to repair skin defects (e.g. burns, chronic, and traumatic wounds)[1;2], including those that cannot be covered by a skin flap or are not likely to heal by secondary intention[3]. The wound created after harvesting the skin is called the donor site wound (DSW). Depending on the thickness of the SSG, the DSW should re-epithelialize completely in 7 to 21 days[3]. Optimum local care for these DSWs should promote wound healing and be cost-effective, while it should prevent complications, such as pain, discomfort, infection, and scarring. Particularly pain and discomfort are reported to occur more frequently from DSWs than at the recipient site[3-5].

Clinical practice shows a large number of dressings and topical agents for DSWs, while the optimum dressing choice for local wound care is unclear[1;2;6;7]. Consequently, large variation exists among health care professionals regarding their choice for wound dressing materials or topical agents to treat DSWs[8-10]. Based on national surveys, alginates appear to be the most commonly used primary dressing[8-10], probably due to their additional haemostatic properties[11;12]. They are followed by films, hydrofibers, silicone dressings and paraffin gauzes[8].

Available evidence comprises four systematic reviews (SRs), presenting a lack of strong evidence for the effectiveness of the different dressings for the treatment of DSWs, especially for alginates[1;2;6;7]. These SRs tentatively conclude that moist dressings are preferable over non-moist dressings in terms of wound healing. Hydrocolloid and films seem better than nearly all other materials (e.g. alginates, paraffin gauzes, hydrofibers, and foams) as to healing and pain[7]. Hydrofibers in turn seem to outperform tulle dressings in terms of wound healing and pain[13;14]. Although tulle dressings seem to be least suitable for the local treatment of DSWs, recent evidence shows that gauze-based dressings still have a place in wound care[15]. Some centers still adhere, or have returned to, these gauze-based dressings[16]. Silicone-based dressings have the advantage of being non-adhesive, although they tend to dislocate easily and do not seem to outperform alginates[17]. These conclusions are formulated cautiously as most authors state that more well designed and rigorous studies are needed.

We therefore conceived a trial to compare the six most promising dressing groups, based on common usage and available evidence. In this paper we will report on the design of our 14-center six-armed randomized clinical trial (RCT). This trial received the acronym "Rembrandt" trial, which stands for Recognizing Effective Materials By Randomizing & Assessing New Donorsite Treatments. In this trial we aim to answer the following question: Which of the following dressing materials for DSW of SSGs stand out in effectiveness: hydrocolloids, alginates, films, hydrofibers, silicone dressings, or paraffin gauzes, in terms of wound healing, adverse effects (e.g. pain and scarring), and costs?

METHODS

Protocol and registration

The methods applied in our 14-center RCT were specified in advance, documented in a protocol, and registered (http://www.trialregister.nl, NTR 1849). The study was approved by the local medical ethics committee and by the institutional review boards of each participating hospital or burns centre. The methods used are summarized here according to the revised CONSORT Statement[18].

Design and setting

We designed a national, 14-center RCT with six treatment groups in the Netherlands (Figure 1). The coordinating center (Academic Medical Center at the University of Amsterdam) invited hospitals (i.e. departments of surgery, plastic surgery and otorhinolaryngology) and burns centers to participate in the trial, resulting in 13 contributing hospitals (4 university hospitals, 5 teaching clinics and 4 general hospitals) and 1 burns center.

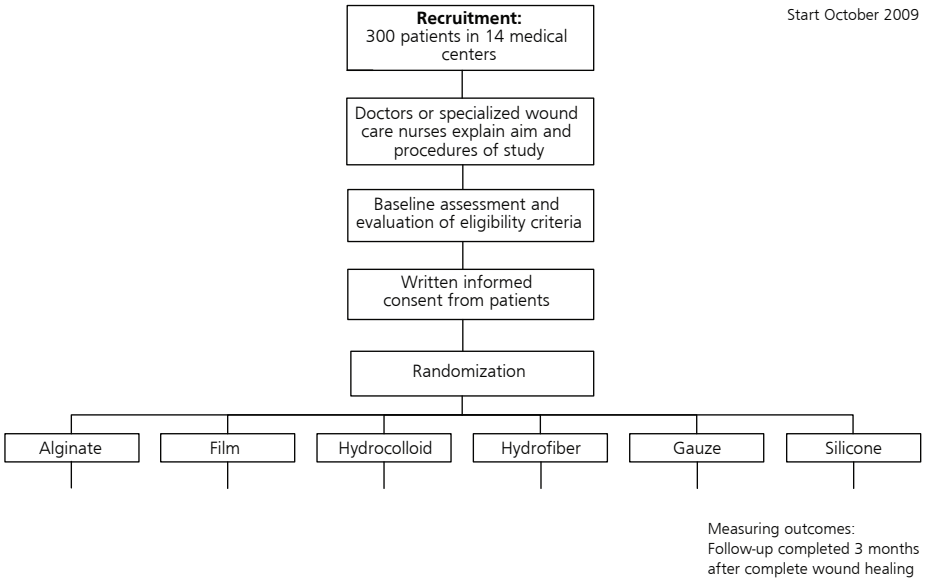

Figure 1. Flowchart of the Rembrandt Trial

Eligibility criteria for patients

In this trial we include all adult patients, either hospitalized or under treatment in the outpatient clinic in one of the contributing hospitals or burns centre, who need a SSG-operation for any reason. The DSW should have a minimum size of 10 cm^2 (to

allow proper application and investigation of the study dressings) and be suitable for all treatment options in the trial. Patients are included after full, understandable and neutral explanation by the treating physician or coordinating investigators and after giving written informed consent. Patients are excluded when they receive a treatment known to seriously impair normal wound healing (e.g. chemotherapy, corticosteroids, or local irradiation therapy) or if patients are not physically or mentally able to consent.

Interventions

Before starting the trial, manufactures of the products involved were invited to develop a protocol how best to apply their wound materials for DSWs, to ensure correct and uniform application of the six different dressing groups:

1. A paraffin gauze-based material (e.g. Jelonet®, Adaptic®);
2. A hydrocolloid (e.g. DuoDERM® E);
3. An alginate (e.g. Kaltostat®, Algisite®, Melgisorb®);
4. A semi-permeable film (e.g. Tegaderm®, Opsite®);
5. A silicone dressing (e.g. Mepitel®);
6. A hydrofiber (e.g. Aquacel®).

The coordinating investigators (FEB and AME) or dressing manufactures orally instructed medical and nursing staff on the wards and out-patient clinics of the contributing centers at the beginning of the trial. Furthermore, they received written application advices as reminders for a uniform treatment protocol, e.g. regarding change frequency and treatment duration. Posters and pocket charts were also distributed to inform about inclusion criteria and contact persons.

Surgical procedure

A SSG operation is to be performed with an electric or pneumatic dermatome or free hand-knife, according to local best practice. The SSG should preferably be between 0.20 and 0.30 mm to achieve a reasonably uniform depth of the DSW and should be taken from thighs, arms or buttocks. Method of haemostasis of the DSW is at the discretion of the surgeon (e.g. adrenaline-soaked gauze). However, the decision to use haemostasis must be made before randomization and will be recorded.

Wound treatment

Local wound care according to the assigned dressing group starts directly after randomization (see heading Randomization). The brand of the dressing will be recorded. No combinations of products from other dressing groups in this trial are allowed to ensure that the effect found after completion of the trial can be attributed only to the dressing to which the patient was allocated. The optimum changing frequency will be pursued as advised for each dressing material. This may differ

from no dressing changes (e.g. hydrofiber) to daily changes in case of leakage (e.g. hydrocolloid or paraffin gauze). We allow coverage of the primary dressings with cotton gauzes and bandages. The type of secondary dressings used will be recorded. Furthermore, we will record any crossovers and make sure the patient returns to the initially allotted dressing.

Co-interventions

Additional wound debridement, cleaning or protection may be indicated during a dressing change and is allowed in all treatment arms, as this reflects real life. In case of an (impending) wound infection, the wound may be treated with iodine (Povidone- or Cadexomer iodine), to be applied beneath the allotted dressing material[19]. The type of iodine used will be recorded.

Study outcomes

Primary endpoints

The primary endpoint with respect to the effectiveness of wound dressings in the treatment of DSWs is time to complete wound healing. We define wound healing as re-epithelialization of the total wound surface. We decided this is not the case until all crusts have come off. This end-point is to be assessed by an independent investigator who is not aware of the treatment given. The second primary outcome is pain from the donor site area. It is documented by the patient on a Visual Analogue Scale (VAS), varying from 0 (no pain) to 10 (intolerable pain). This is scored daily for the first two weeks postoperatively and twice a week during the third and fourth week, in a patient-held diary. Both primary endpoints are meaningful and relevant to patients and were therefore used for the sample size calculation[20].

Secondary endpoints

As secondary endpoints we assess the occurrence of local complications, e.g. wound infections, based on clinical symptoms of infection, scarring at 12 weeks postoperatively (using Patient and Observer Scar Assessment Scale (POSAS) assessed by the patients themselves and researchers, treating physicians or specialized wound nurses)[21], patient satisfaction (varying from 1 (absolutely dissatisfied) to 10 (absolutely satisfied), and costs (material and nursing costs). Itching scores are also collected by using a VAS, ranging from 0 (no itching) to 10 (intolerable itching) and obtained through the patient-held diary.

Randomization

Patients are to be randomized in the operation theatre, just after the skin harvest and haemostasis, and before the DSW is to be dressed. In each contributing center

an appointed officer performs the randomization using an online computer software program (ALEA NKI-AVL, Amsterdam, The Netherlands, Release: 2.2.) to ensure allocation concealment. The trial is stratified by center, with a balanced allocation ratio for each treatment arm using a biased coin[22]. The biased coin method pre-serves most of the unpredictability associated with simple randomization[22].

Blinding

Blinding of patients and careproviders (e.g. doctors and nurses) is not possible because the treatment options cannot be masked. To overcome this possible source of performance bias, independent doctors and nurses of the outpatient clinic, who are unaware of the treatment allocation, will assess whether or not an endpoint has occurred[23].

Sample size

The study size calculation (using nQuery Advisor version 7.0, Statistical Solutions Ltd, Cork, Ireland) was based on two primary outcomes using a one-way analysis of variance. To detect a 25% quicker mean wound healing, which is in agreement with the study of Wiechula[2], and with a 5% significance level, a power of 90%, and a standard deviation (SD) of 3 days, a sample size of 50 patients per group is necessary, given an anticipated dropout rate of 15%. This number also allows detection of a minimum difference in pain scores of 2.0 or greater (with a SD of 2) on the VAS and discernment of a cost difference of €2 per day. To recruit this number of patients an 18-month inclusion period is anticipated based on the performed number of SSGs as estimated by each of the 14 co-operating hospitals.

Data collection

The coordination center designed a standardized case record form (CRF) and distributes this in a paper-based or electronic version. The latter one is made available through a secured website, http://www.rembrandt-trial.nl (using Joomla, an open-source website software package), which also facilitates remote patient randomization and data entry. We collect copies of all completed forms from the co-operating hospitals and maintain the data-base using SPSS software (PASW statistics version 18.0, IBM, Armonk, NY, USA). Data are collected on baseline demographic and clinical patient characteristics of each group, whether the patients receive the allotted treatment and complete the study protocol, and are analyzed for the primary outcomes. Patients whose treatment deviates from the initial allocation will be described together with the reasons for this. Data on all important adverse events or side effects in each intervention group are recorded as well. Data from the patient-held diaries will be returned to the coordinating center. Double data entry will be conducted by FEB and

AME, and compared using the SPSS Data Entry Builder program (Release 4.0.2). We will resolve any discrepancies by discussion and by re-checking the data.

Data monitoring

Data completeness is reviewed weekly, and reminders or queries are sent timely. FEB and AME visit the cooperating hospitals on a regular basis to promote the trial and to be closely associated with the data collection. Thus, an accurate and complete data set is ensured. Because no (serious) adverse effects were expected from the commercially available dressings that would require interim analysis, we refrained from installing a data safety monitoring board.

Data analysis

Data coding and analysis will be carried out using SPSS software (PASW statistics version 18.0, IBM, Armonk, NY, USA). Differences in outcome variables will be analyzed on an intention-to-treat basis. A general linear model will be used to analyze the differences between the treatment arms for the various endpoints measured repeatedly, as the data are likely to be unequally distributed. Differences in wound healing time between the dressing groups will be examined using the Kaplan-Meier method and the Mantel-Cox log-rank test. Data analysis will be conducted by the authors and replicated by the Clinical Research Unit of the coordinating hospital. We will record any crossovers and make sure the patient returns to the initially allotted dressing. Missing data are dealt with by using the Generalized Estimating Equations model in our statistical analysis.

Data storage

Data are stored at the coordinating center in a Trial Master File and at the co-operating hospital sites, where an Investigator File is kept. After finishing the trial, data will be saved for at least 5 years, in accordance with the recommendations as to low risk studies of the Dutch Federation of University Medical Centers.

DISCUSSION

In current clinical practice, a 'standard' wound such as a DSW does not appear to be associated with a uniform dressing choice.[8] Also the systematic reviews of available literature report a large clinical heterogeneity among the available trials[1;2;6;7]. To date, available evidence allows the tentative conclusion that dressings creating a moist environment seem to be preferable over gauze-based dressings in the management of DSWs. This recommendation is tentatively formulated because strong recommendations for clinical practice are hard to draw, mainly due to the poor quality

and small sample sizes of the available trials. Therefore, most systematic reviews recommend new and large randomized clinical trials[2;6;7].

However, doing research in the realm of wound care involves much more than simply comparing wound care products in eligible patients. It poses many methodological and practical challenges in the design and execution of trials[24].

The first challenge is the design of our, intentionally pragmatic, RCT. To enhance the applicability and generalizability of the results of this trial, we chose a multicenter trial design and recruited patients from low- and high-volume centers like teaching hospitals and burns centers. We realize that for many surgical procedures, patients have better outcomes in high-volume centers[25-29]. However, split-skin grafting is a rather common procedure, also in smaller hospitals. Second, we are forbearing regarding local clinical care, for example by allowing several brands within each dressing group, different depths of skin grafting, and different methods of haemostasis. This helps mimicking 'real life', at the cost of losing some contrast between the six treatment arms.

Although we are liberal and pragmatic at some points, we feel we need to and can be strict in others. We urge the contributing centers to adhere to the same dressing type until complete wound healing is reached. This allows us to appreciate the true effects of each of the dressing types studied. Some argue this is not reflecting common practice[30], in which the dressing type is changed in response to any change in the clinical condition of the wound during the healing process. We do not think this will be a frequently occurring issue since these superficial DSWs usually have fairly short healing times. The protocol does allow for an antiseptic agent to be added in case of an (impending) wound infection.

Another frequent methodological challenge in wound care research is the use of subjective or surrogate outcome variables. In this trial we aim to measure our endpoints in a reliable and valid way. We strictly predefined our primary endpoint, time to complete wound healing. In a previous study it was shown that, by using this strict definition, specialized nurses had a better inter-observer agreement than doctors or nurses regarding the assessment of complete wound healing[31]. Therefore, in this trial predominantly specialized nurses will assess our primary endpoint. Our second primary outcome variable, pain, is measured using VAS scores. This is a reliable and acknowledged scale for general clinical use[32;33].

Today, financial support is a necessity to properly conduct a (multicenter) trial. For this purpose, we obtained funding from an independent institution, i.e. the Dutch Burns Foundation, which is to be preferred over subvention from one or more dressing manufacturers to avoid any publication bias. To avoid any conflict of interest, analysis and reporting of the trial stays the domain of the investigators.

The strengths of this trial are firstly the fruitful collaboration with manufacturers, who developed a dedicated protocol for the treatment of the DSW with their product. This greatly supports the uniform application of each dressing type under

study. Second, using this six-armed, multicenter trial we investigate the effectiveness of the dressings most commonly used in the Netherlands and most promising from the available literature. This will facilitate implementation of the results. We expect to present the results of this trial in the course of 2012.

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Chapter 7

Which dressing do donor site wounds need? The results of a randomized controlled trial (Rembrandt Trial)

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ABSTRACT

Objective: To study which dressing material for donor site wounds (DSWs) after split-skin grafting is best for a quick and uneventful wound healing.

Background: Large variation exists in the local treatment of DSWs, ranging from classic gauze dressings to modern silicone dressings.

Methods: A 14-center, six-armed randomized clinical trial (stratified per center) was conducted comparing six wound dressing materials in adult patients with DSWs larger than 10cm^2 for any indication. Primary outcomes were complete re-epithelization and pain using a Visual Analogue Scale (VAS; 4 weeks). Secondary outcomes included itching (VAS; 4 weeks), adverse events and scarring after 12 weeks using the Patient Observer Scar Assessment Scale (POSAS).

Results: Between October 2009 and December 2011, 289 patients were randomized (of whom 288 were analyzed) to either alginate (n = 45), film (n = 49), gauze (n = 50), hydrocolloid (n = 47), hydrofiber (n = 47) or silicone (n = 48). Time to complete re-epithelization using hydrocolloid dressings (median 16 days) was seven days shorter than using any other dressing (median 23 days) (P-value < 0.001, log-rank test). Overall pain scores were low and slightly lower using film dressings (P-value = 0.038, type-III test of fixed effects). Infection rate among patients treated with gauzes was twice as high as in those receiving other dressings (18% vs. 9%, risk ratio 2.39, 95% confidence interval 1.14 to 5.01). Patients receiving films were least satisfied about overall scar quality.

Conclusion: This trial shows that hydrocolloid dressings lead to the shortest healing time of DSWs among the dressings investigated, while gauzes should be avoided due to increased risk of infection.

BACKGROUND

Split-skin grafting (SSG) is frequently used by general, trauma and plastic surgeons to close skin defects like traumatic injuries, chronic ulcers, abdominal wall defects or deep burns[1;2]. This split-skin harvest technique involves excision of the epidermis and part of the dermis and leaves a so-called donor site wound (DSW). Although such wounds are created under controlled, sterile conditions, they can be a considerable burden to patients during and after the healing process in terms of itching, pain, infection and cosmetic inconvenience[3-5].

Surgeons largely agree that local treatment of DSWs should aim at creating an environment that allows rapid and uneventful re-epithelialization with a minimum of pain, discomfort and length of hospital stay[3;6;7]. Based on available evidence, several dressings seem suitable for this purpose, ranging from classic gauzes to modern silicone dressings, alginates, films and hydrofibers[8-11]. However, treatment regimes vary considerably among centers, disciplines and individual surgical specialists[5;6;12;13].

Available aggregate evidence comprises four systematic reviews based on mainly small trials, from which it is hard to distil the optimum local treatment for DSWs[1;6;7;14]. Films and hydrocolloids seem most effective in terms of pain relief and patient comfort[1;6;15]. All SRs conclude that more convincing evidence is needed.

This study was conducted to detect which dressing material for DSWs after SSG stands out in terms of wound healing, pain, complications, itching, costs and scarring.

METHODS

Trial design and study setting

A stratified, parallel group, multicenter randomized clinical trial (RCT) was designed comparing alginates, films, gauzes, hydrocolloids, hydrofibers or silicone dressings in patients undergoing SSG (the Rembrandt Trial; Recognizing Effective Materials By Randomizing & Assessing New Donorsite Treatments). This trial was registered as NTR1849 (www.trialregister.nl). The 14 recruiting centers included Dutch university centers and general hospitals as well as one of the national burn centers.

The institutional review boards of each contributing center approved the study protocol, which has been published in detail elsewhere[16]. Contrary to this protocol, the group "paraffin gauzes" was renamed to "gauzes", since Adaptic® was used in all but three cases (where Jelonet® was applied) in this group. Furthermore, the present Methods section only highlights the most important issues according to the revised CONSORT statement[17].

Participants and data collection

Eligible patients should have a DSW with a surface area larger than 10 cm^2 after SSG for any indication. Patients under treatment known to seriously impair wound healing or those who could not provide written informed consent were excluded. The flow of patient inclusion and follow-up is shown in Figure 1.

Contributing centers provided baseline and peri-operative characteristics and outcome data of all included patients through the trial website (www.rembrandt-trial.nl). One of the trial coordinators stored the data in the trial database, which were checked for correctness independently by another (FEB and AME).

Dressing materials and nursing time involved in caring for the DSWs were recorded on case record forms by each contributing center. Patients also noted materials and nursing time in patient diaries during their follow-up period to facilitate precise registration of these data, particularly in the outpatient setting. Despite repeated efforts, we were confronted with a large amount of missing data. Given these unreliable data, it was decided not to report on the costs outcome.

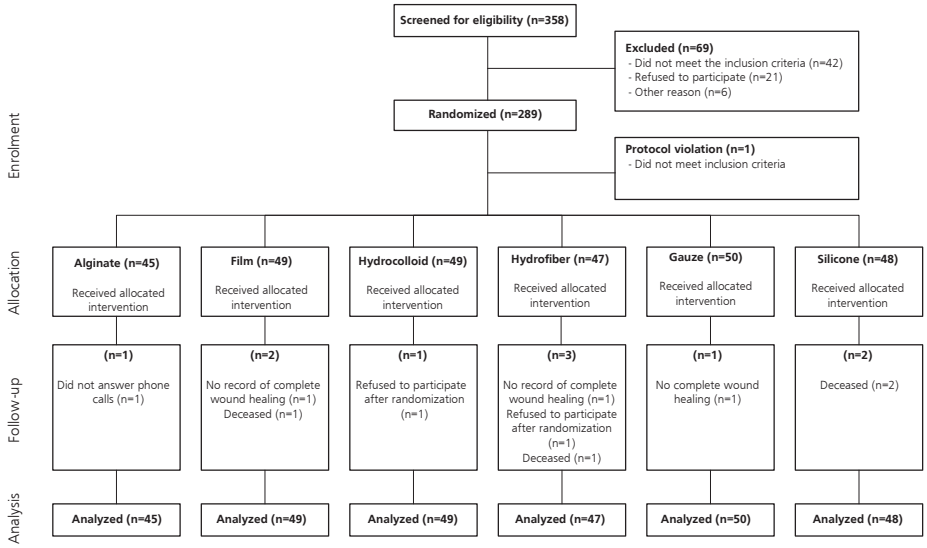

Figure 1. Flow of participants during the study

Treatment and interventions

The methods of harvesting, local haemostasis and desired thickness of the graft were to the surgeons' discretion. These variables were recorded for possible sub-group analyses. After the skin harvest and local haemostasis , if any, the patient was randomized using a computer program (ALEA v. 2.2, NKI-AVL, Amsterdam, The Netherlands) by an appointed officer in each center or by calling the trial coordinators

(FEB and AME) to be treated with a dressing material from one of the following dressing groups:

1. A gauze-based material (Jelonet®, Adaptic®);
2. A hydrocolloid (DuoDERM® E);
3. An alginate (Kaltostat®, Algisite®, Melgisorb®);
4. A semi-permeable film (Tegaderm®, Opsite®);
5. A silicone dressing (Mepitel®);
6. A hydrofiber (Aquacel®).

The brand names indicate the products actually used in this trial. In three dressing groups the centers were allowed to choose from more than one dressing type to accommodate their local practice and to reflect "real life". Caregivers applied and changed the allotted dressings according to the instruction protocol provided before the start of the trial by the different manufacturers of the dressings used. During the follow-up period caregivers were to apply the same dressing type until complete wound healing.

To ensure equal treatment in all groups, only cotton gauzes and bandages were allowed as secondary dressing. When a DSW infection was suspected, caregivers were allowed to add an iodine-containing product to a fresh primary dressing. In case of a Pseudomonas infection acetic acid was to be applied. Additional cleansing or protection during dressing changes was allowed in all treatment groups.

Blinding of patients and care providers was obviously not possible. However, to avoid performance bias, patients were only instructed about how to use their wound dressing and care for their wound without expressing any expectations regarding the effectiveness of the dressings in the trial.

Outcomes

Primary endpoints were: days to complete wound healing (defined as full re-epithelialization of the donor site without any remaining scabs) and pain using a 10-cm Visual Analogue Scale (VAS). Wound healing was assessed by patients, caregivers or investigators. Secondary outcomes included adverse events (i.e. clinical signs of DSW infection, hypergranulation, or allergic reactions), itching (VAS), and scarring, assessed 12 weeks after complete healing of the DSW by the caregivers (observers) and the patients, using the Patient Observer Scar Assessment Scale (POSAS)[18]. The range of the scar assessment varies between 6, indicating normal skin, and 60, indicating the worst possible result. Pain and itching were assessed and recorded in diaries by the patients once a day, approximately at noon, during the first two weeks of follow-up and twice a week thereafter until complete wound healing.

Sample Size

With a 5% significance level and a power of 90%, a sample size of 43 patients per group, i.e. a minimum total of 258 patients if no dropouts would occur, was needed to detect either a 25% quicker wound healing time or a 2-point difference on a 10-point VAS scale in one dressing group as compared to the other five groups combined.

Statistical methods

SPSS software (PASW statistics version 18.0, IBM, Armonk, NY, USA) was used for coding and analysis. The intention-to-treat principle was applied to analyze the outcome data. To analyze differences in wound healing time we used the Kaplan-Meier method and the Mantel-Cox log-rank test. Furthermore, a Chi-square test was used to examine differences in number of local adverse events and a general linear mixed model to analyze the differences in pain and itching over time. This model assumes a continuous outcome variable (VAS), which is linearly related to a set of explanatory variables (i.e. dressing material used). After the residuals were checked for normality and model-fitting was performed, the auto-regressive of order one (AR-1) model was applied. The AR-1 model is one of a group of linear prediction formulas and allows specifying the covariance structure for the random-effects model. For dichotomous outcome parameters the risk ratio (RR) was calculated with 95% Confidence Intervals (CI) and Numbers Needed to Treat or Harm (NNT, NNH). Differences in scar assessment scores were analyzed using the Mann-Whitney U test due to their non-normal distribution.

RESULTS

Participant flow

From October 2009 to December 2011, 358 patients were screened for inclusion, of whom 289 were eligible to be randomized (Figure 1). Follow-up was completed in April 2012.

During the trial ten patients dropped out; thus follow-up was complete for 279 patients (96.5%). Crossover to another dressing group occurred in 37 out of the 289 patients (13%). Crossover varied from thrice in the hydrocolloid group up to ten times in the hydrofiber group, due to unfamiliarity with the product (n = 14), preference of the patient (n = 12), infection (n = 6), leakage (n = 3), or logistic reasons (n = 2). By means of the ITT-analysis we avoided the effects of these drop-outs and crossovers. The response rate of the patient diaries returned was over 75 percent, equally divided over the six groups.

Baseline data

Patients' baseline demographic and peri-operative characteristics were similar among the dressing groups (Table 1), except for the use of haemostasis, which was applied in

Table 1. Baseline and peri-operative characteristics by treatment allocation

	Alginate (n=45)	Film (n=49)	Gauze (n=50)	Hydrocolloid (n=49)	Hydrofiber (n=47)	Silicone (n=48)
Mean age ± SD, years	60 ± 17.8	61 ± 17.9	62 ± 17.7	61 ± 17.1	60 ± 16.1	62 ± 17.2
Males, n (%)	36 (80)	37 (74)	30 (60)	32 (65)	27 (57)	36 (75)
DM, n (%)	11 (24.4)	10 (20.0)	11 (22.0)	13 (26.5)	8 (17.0)	11 (22.9)
Smokers, n (%)	11 (24.4)	15 (30.0)	10 (20.0)	13 (26.5)	12 (25.5)	13 (27.1)
Weight loss, n (%)						
>5% in 1 month	6 (13.3)	7 (14.0)	5 (10.0)	2 (4.1)	2 (4.3)	2 (4.2)
>10% in last 6 moths	4 (8.9)	5 (10.0)	5 (10.0)	3 (6.1)	2 (4.3)	1 (2.1)
BMI, n (%)						
BMI < 18.5	1 (2.2)	1 (2.0)	2 (4.0)	1 (2.0)	2 (4.3)	4 (8.3)
BMI > 30	12 (26.7)	14 (28.0)	10 (20.0)	12 (24.5)	15 (31.9)	6 (12.5)
Antibiotics, n (%)						
- for DSW	-	2 (4.0)	-	-	1 (2.1)	-
- not for DSW	11 (24.4)	14 (28.0)	15 (30.0)	17 (34.7)	13 (27.7)	10 (20.8)
ASA classification, n (%)						
- ASA I	17 (37.8)	15 (30.0)	13 (26.0)	16 (32.7)	13(27.7)	18 (37.5)
- ASA II	18 (40.0)	21 (42.0)	22 (44.0)	17 (34.7)	16 (34.0)	15 (31.3)
- ASA III	10 (22.2)	13 (26.0)	14 (28.0)	14 (28.6)	16 (34.0)	12 (25.0)
Indication for SSG, n (%)						
- Chronic wound	10 (22.2)	8 (16.0)	10 (20.0)	13 (26.5)	6 (12.8)	12 (25.0)
- Burn wound	1 (2.2)	2 (4.0)	3 (6.0)	1 (2.0)	3 (6.4)	1 (2.1)
- Surgical/traumatic wound	29 (64.4)	28 (56.0)	27 (54.0)	30 (61.2)	27 (57,4)	25 (52.1)
- Tumor excision	5 (11.1)	10 (20.0)	8 (16.0)	4 (8.2)	10 (21.3)	9 (18.8)
- Other	-	1 (2.0)	1 (2.0)	-	-	-
Location of the DSW, n (%)						
- Thigh	44 (97.8)	44 (88.0)	46 (92.0)	47 (95.9)	44 (93.6)	45 (93.8)
- Other	1 (2.2)	5 (10.0)	3 (6.0)	1 (2.0)	2 (4.2)	2 (4.2)
Median DSW surface	50.0	49.0	50.0	49.0	37.5	40.0
area, cm^2 (range)	(10-240)	(10-600)	(10-450)	(10-800)	(10-750)	(10-760)
Median thickness	0.30	0.30	0.30	0.30	0.30	0.30
of graft, mm (range)	(0.1-0.6)	(0.10-0.6)	(0.1-0.8)	(0.11-0.7)	(0.11-0.6)	(0.1-0.7)
Haemostasis, n (%)	18 (40)	10 (20.0)	23 (46)	26 (53.1)	14 (29.8)	23 (47.9)

SD, Standard Deviation; DM, Diabetes Mellitus; BMI, Body Mass Index; DSW, Donor Site Wound; ASA, American Society of Anesthesiologists; SSG, Split-Skin Grafting.

fewer patients (19.6%) in the film dressing group. The majority of grafts (57.4%) was used to treat a surgical or traumatic wound and were mostly taken from the thigh (n = 270, 93.4%), with a mean thickness of 0.32 millimeters (SD 0.15) and a mean grafted area of 78.4 cm^2 (SD 109.2). Participating centers mainly used Kaltostat® in the alginate group and Adaptic® in the gauze group, while Tegaderm® and Opsite® were applied equally frequent in the semi-permeable film group.

Primary outcomes: Complete wound healing and pain

Time to complete re-epithelization was seven days (i.e. 30%) shorter using hydrocolloid dressings (median 16 days) than using any other dressing (median 23 days) (Figure 2; cumulative wound healing; P-value <0.001, log rank test). Median time to complete re-epithelization for each dressing group is shown in Table 2.

Overall, pain scores (10-cm VAS), as calculated from 3360 recordings, were low (median 0.4, Inter-quartile range [IQR] 0 to 1.4), although these were slightly but significantly lower in the semi-permeable film group (P-value = 0.038, type-III test of fixed effects) than in the other dressing groups combined.

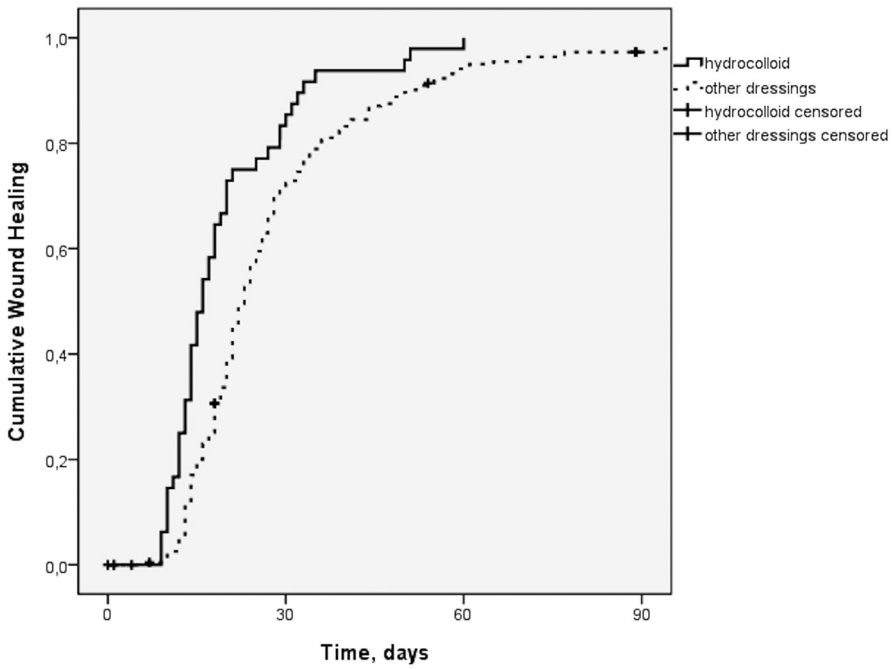

Figure 2. Kaplan-Meier cumulative wound healing curve comparing hydrocolloid dressing to the remaining dressings in donor site wounds. The difference in wound healing time between the two curves is significant (log-rank test P value < 0.001).

Table 2. Primary and secondary outcomes by treatment allocation group

Group	Alginate (n=45)	Film (n=49)	Gauze (n=50)	Hydrocolloid (n=49)	Hydrofiber (n=47)	Silicone (n=48)
Median time to wound healing, days (IQR)	22.0 (19-29)	23.0 (14-36)	22.0 (18-33)	16.0 (12-21)*	22.0 (15-27)	26.0 (18-33)
Pain, median (IQR)	0.4 (0.0-1.9)	0.3 (0.0-1.0)*	0.3 (0.0-1.5)	0.2 (0.0-1.1)	0.8 (0.0-1.5)	0.4 (0.1-1.1)
Itching, median (IQR)	0.2 (0.0-0.9)	0.3 (0.0-0.9)	0.2 (0.0-0.6)	0.2 (0.0-0.8)	0.3 (0.0-1.0)	0.2 (0.1-0.7)
Adverse events, n (%)						
- Clinical infection	0	8 (16.0)	9 (18.0)*	1 (2.0)	7 (14.9)	2 (4.2)
- Allergic reaction	0	0	0	0	0	0
- Hypergranulation	1 (2.2)	1 (2.0)	0	1 (2.0)	1 (2.1)	2 (4.2)
- Other	0	2 (4.1)	2 (4.0)	0	0	1 (2.1)

IQR, Inter-quartile range. *P- value < 0.05

Table 3. Patient and observer scar assessment results by treatment allocation groups

Group	Alginate	Film	Gauze	Hydrocolloid	Hydrofiber	Silicone
Patients (n)	24	20	22	21	21	22
POSAS, median (IQR)						
Observer	11 (8-14)	11 (10-15)	12 (8-14)	10 (8-14)	11 (9-15)	11 (8-13)
Patient	10 (7-13)	14 (11-15)	11 (8-14)	10 (8-12)	10 (7-15)	11 (9-14)
Overall scar rating observer, median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	2 (2-3)	2 (1-3)	2 (2-4)
Overall scar rating patient, median (IQR)	2 (2-5)	4 (1-4)	2 (2-5)	3 (2-5)	3 (2-5)	2.5 (1-4)
Dressing satisfaction patient, mean (range)	7.7 (4-10)	7.5 (1-10)	8.0 (5-10)	7.6 (1-10)	7.3 (4-10)	7.7 (2-10)

POSAS, Patient Observer Scar Assessment Scale; for Observer and Patient a score of 6 indicates normal skin, and 60 indicates the worst possible result. IQR, Inter-quartile range.

Secondary outcomes: Adverse events, itching and scarring

Infection rate was twice as high in patients treated with gauzes as in those receiving other dressings (18% vs. 9%, RR 2.39, 95% CI 1.14 to 5.01, NNH= 11). Allergic reactions were never reported and hypergranulation occurred rarely, as shown in Table 2.

Itching scores (10-cm VAS) were calculated from 3579 recordings and were lower (median 0.2, IQR 0 to 0.8) than the pain scores. No significant differences were found among the dressing groups.

POSAS data were collected in 137 patients from five contributing centers. Results and summary scores are shown in Table 3. Patients receiving semi-permeable films

were significantly less satisfied with their total score of the scar (P-value = 0.018, Wilcoxon rank sum test), especially regarding the item "wound relief" (P-value = 0.046, Mann-Whitney U test), as compared to those in the other dressing groups. Scar assessment by the observers did not show significant differences among the dressing groups.

DISCUSSION

This trial allowed the comparison of six commonly used wound dressing materials to cover donor sites after split-skin grafting. The evidence obtained shows that hydrocolloid dressings lead to a 7-day, i.e. a 30% shorter healing time than the other materials. The use of gauze dressings was found to increase the risk of infection.

This quicker wound healing when using hydrocolloid dressings might be explained by a differential wound angiogenesis associated with different degrees of occlusion[19]. Dressings promoting a moist wound environment, like hydrocolloids, have been shown to improve re-epithelialization, increase collagen synthesis and ultimately improve healing rates[1;20-23]. The shorter healing time of donor sites using dressings that promote moist wound healing was already suggested by previous aggregated evidence[1;6;7;14]. This trial now offers evidence for the effectiveness of a specific dressing type within this group of materials. Other occlusive or semi-occlusive dressings, such as foam dressings, might have similar healing effects, but these dressings were not included in this trial based on evidence from previous literature and a national inventory showing a lower eligibility[8;14]. The (moist) wound environment may also be influenced by the type of secondary wound dressings applied. In this trial the study protocol prescribed the uniform use of gauze-based secondary dressings. Hence, the effects of other secondary dressings (e.g. semi-permeable film) used in clinical practice could not be studied[8].

The time to complete healing we found in the hydrocolloid group exceeds the healing times reported in other studies, which varied from 10 to 12 days[5;12;13;24;25]. This is likely due to our strict definition of complete epithelialization stating that complete wound healing was not reached until any remaining scabs had fallen off. This is in contrast with a range of definitions applied in other studies, including epithelial coverage, absence of exudates, scarring appearance, and proportion of the wound healed[7]. Although our definition and, consequently, our healing time results may differ from other studies, it was chosen as an objective, uniform, easily assessable and patient-relevant outcome. Moreover, this definition had no influence on the differences in complete wound healing as found here.

The high risk of infection in patients treated with gauze dressings was also found for fine mesh gauze dressings with scarlet red, showing a 9.6% infection rate[26]. The

prescription of antibiotics may have influenced the infection rates recorded. In the present trial, patients in all dressing groups received systemic antibiotics in similar percentages from 20-30%, mostly subscribed for other indications than the DSW. This may have underestimated the infection rates found in our study. Still, despite the relatively high percentage of patients receiving antibiotics in this trial, gauze dressings were accompanied by a significantly higher infection rate of the donor sites, which will have prolonged the healing time. On the other hand, aggregated evidence of gauze dressings for donor site wounds and postoperative wounds did not find an increased risk of infection[1;6;7;14;27].

Haemostasis was applied in fewer patients in the film and hydrofiber groups than in other dressing groups. However, the surgeon's decision to perform haemostasis was not influenced by the dressing the patients were allocated to, as this was decided by randomization after the haemostatic intervention. In the gauze, hydrocolloid, and silicone groups, haemostasis was applied in about 50% of the patients, but time to wound healing differed considerably among these groups, indicating haemostasis does not seem to have a substantial effect on wound healing. Available literature also offers little evidence on the relation between haemostasis and wound healing[28].

Some possible limitations of this trial are the following. First, we accepted some variation regarding the thickness of the graft, method of harvesting, and the surgeons' preferences regarding haemostasis and treatment of infection. This was intentional, to allow for a pragmatic trial that would mimic daily clinical practice.

Second, cosmetic appearance of the scars was assessed after three months, even though actively remodeling and maturation of scars takes at least 12 months[29]. Nevertheless, the POSAS score is a reliable and valid instrument to identify a change of scar characteristics[18;30]. In our study protocol we were interested in differences in scar development related to the dressing materials investigated. Our assumption was that differences seen at three months would diminish in time, as shown in other studies[31;32].

Third, we were unable to accurately report on costs, which play a substantial part in the choice of wound treatment. Unit and total costs of hydrocolloid dressings are reported as costly[1;33]. However, investigators frequently report on unit costs but do not take into account dressing changes, nursing times, or rapid healing time and secondary wins as early mobilization. We were confronted with the same difficulty to accurately record and report the costs of such factors. However, the costs of local wound treatment should be put in perspective of other factors. The relatively high costs per dressing unit[1;4;33] are at least in part compensated by a low dressing change frequency of once in up to seven days, which causes little pain. Besides, patient preferences or priority for rapid healing may downplay the costs of a dressing material, e.g. in cases with extensive thermal injuries or severe comorbidity. In such scenarios

hydrocolloid dressings, which do not need frequent dressing changes, seem preferable to achieve a more rapid wound healing.

Comprehensive inclusion criteria (e.g. all adults requiring a split skin graft regardless of the presence of diabetes mellitus) are one of the strengths of this trial and allow application to a broad patient population with donor site wounds that may benefit from a hydrocolloid dressing. Also, these study results reflect local practice of 14 national centers that improve the generalizability and implementation[34]. Finally, in our trial set-up we put effort in minimizing the risk of bias due to incomplete outcome data, which resulted in a low percentage (3%) of dropouts.

The results of our study should decrease the current diversity in treatment choices of donor site wounds since treatment options can be made more evidence-based. Several practical considerations should be mentioned using hydrocolloid dressings. Before application of the dressing, the skin should be clean, i.e., fatty disinfectants may be avoided for better adherence. Especially with increasing wound size area, wound leakage can be a problem due to interaction of wound exudate with the dressing[35;36]. On the other hand, a moist interface between the dressing and the wound could reduce the postoperative discomfort and minimize tissue damage during dressing changes[23;35].

In conclusion, this randomized multicenter trial showed that hydrocolloid dressings lead to a seven-day shorter healing time than other commonly used dressing materials for donor sites. This result combined with other patient-relevant outcomes found, like infection rate, pain, and scarring, should contribute to a uniform and evidence-based treatment of donor site wounds.

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Chapter 8

Values of patients and caregivers for donor site scars: An inter-observer analysis between patients and caregivers and prediction of cosmetic satisfaction

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ABSTRACT

Background: The Patient and Observer Scar Assessment Scale (POSAS) is used to judge scars and involves patients and caregivers. Although the opinions of both are integrated, agreement between them is poorly investigated, especially in donor site scars (DSSs). Furthermore, it is unknown which POSAS-items are mostly associated with overall cosmetic satisfaction with the scar.

Methods: We included 106 DSS-patients. Twelve weeks after wound healing, patients and caregivers rated the DSS in vivo using the POSAS, comprising seven items. They were unaware of each other's judgment. Inter-observer reliability (IOR) was expressed as intra-class correlation coefficients (ICC). Items of the POSAS that best predicted patients' overall satisfaction were identified using multivariable regression analysis.

Results: Eleven caregivers from different medical centers judged the DSSs. IOR for the POSAS-items was 'moderate' at best regarding the item 'overall opinion' (ICC 0.44, 95% confidence interval 0.27 to 0.58). IORs regarding other POSAS-items were 'poor'. Itching and relief best predicted patients' overall satisfaction (total variance explained, R^2 = 0.174). For caregivers, pigmentation and pliability were most predictive (R^2 = 0.318).

Conclusion: Patients and caregivers appreciate different aspects of scar characteristics using the POSAS. This calls for shared decision-making, in which patient opinions are incorporated in the treatment choice.

BACKGROUND

Scars are undesired manifestations of the normal wound healing process. If located in visible areas, scars may have a psychological impact and could affect the patient's quality of life[1]. Evaluating scars is important to balance pros and cons of wound care options and make well-informed clinical decisions for treatment of wounds and prevention of scars.

To support the judgment of the eventual healing result, many scales are available to classify scars, such as the VSS (Vancouver Scare Scale)[2], POSAS (Patient and Observer Scar Assessment Scale)[3], MAPS (matching assessment of scars and photographs)[4], and the Manchester scar scale[5]. None of these scales really stands out or is generally accepted, though the VSS and POSAS are mostly used in daily practice[6;7]. The POSAS is unique in that it takes the opinion of the patients into account and consists of two scales: the Patient and Observer Scar Assessment Scale[3;8]. Patients and observers, i.e. their caregivers, score slightly different items related to the scar characteristics, e.g. color, thickness, relief, pliability, and more subjective factors, such as pain and itching[3]. In burn scars the POSAS is considered superior to other assessment scales[9].

Nowadays, incorporating patient's values and opinions in the decision process is promoted to ensure high-quality patient-centered care[10;11]. However, caregivers still tend to overlook or misrepresent the patients' opinion about their scars[12], which may lead to external decision-making about treatment choices[13]. Hence, clinicians should be aware of the scar characteristics patients value most. Previous research regarding the POSAS in patients with scars outside the realm of DSS, showed a good agreement among caregivers[3;14;15]. This scale has already been validated to classify burn- and linear scars, which suggests its usefulness in DSS after split-skin grafting, as these are acutely created and have a linear shape.

However, up to now it is unknown if patients and their caregivers differ in their perspectives regarding the desired result of the donor site scar (DSS). Furthermore, it is unclear which item (e.g. color, thickness, or pain) or combinations of items best predicts the overall opinion of patients and caregivers about the scar.

Therefore, the aim of this study was to investigate the extent to which patients and their caregivers agree in their appreciation of the scar using the POSAS and which scar characteristics contribute most to their judgments.

METHODS

Patients

For this study we used data from the patients who were included in our recently completed randomized clinical trial regarding donor site treatment (Rembrandt trial; www.trialregister.nl; NTR1849) on the effectiveness of six commonly used dressings, and had a complete POSAS score, i.e. without any missing data. This trial, involving 14 Dutch university and general hospitals, included adult patients who had a single donor site wound (DSW) with a surface area of at least 10 cm^2 after split-skin grafting for any indication. All patients gave written informed consent. The study was approved by the medical ethics review boards of the contributing hospitals. Inclusion criteria and study protocol have been described in detail previously[16].

Observers

Twelve weeks after complete wound healing a group of specialized wound care nurses, surgical nurses, and researchers judged the DSS in vivo using the observers' part of the POSAS. We defined complete wound healing as re-epithelialization of the total wound surface, i.e. without any remaining scabs.

The POSAS contains seven questions on vascularity, pigmentation, pliability, thickness, relief, surface area, and overall opinion. All items were scored on a 10-point scale, ranging from 1 (best possible outcome) to 10 (worst possible outcome). The caregivers had some, but not extensive, experience in scar assessment, because the POSAS can be used reliably even by inexperienced observers[14]. Nevertheless, all professionals were instructed on the use of the POSAS by an expert. Patients and observers scored the POSAS during the same outpatient visit. Patients were asked to rate their scar using the Patient and Observer Scar Assessment Scale, i.e. the patients' part of the POSAS, containing seven questions about pain, itching, color, pliability, thickness, relief, and overall opinion. Subsequently, the caregivers also assessed the scar. Caregivers and patients were unaware of each other's judgment.

Data analysis

We collected basic demographic data of the patients, comprising age, sex, location of the DSS, and mean time to complete wound healing.

Inter-observer agreement

Inter-observer reliability (IOR) regarding the POSAS scores between caregivers and patients was expressed as intra-class correlation coefficient (ICC), including their 95% confidence intervals (CI), using a one-way ANOVA model for single measure

agreement. This IOR is the measure we used to assess the agreement between patients and caregivers. The ICC takes values from zero (no agreement) to one (perfect agreement)[17]. We considered an ICC above 0.8 as 'very good', between 0.8 and 0.6 as 'good, between 0.6 and 0.4 'moderate' and below 0.4 'poor'[7]. The ICC was calculated for all POSAS-items the caregivers and patients had in common. Furthermore, we used the 95% limits of agreement approach (a.k.a. Bland & Altman plots) to assess the score agreement between the patients' and observers' judgment as expressed by the POSAS-items[18].

Prediction of cosmetic satisfaction

Next to the IOR, we determined which item(s) of the POSAS best predict the overall opinion of patients and caregivers regarding scar cosmetics. We used the same analytic strategy for both patients and caregivers. First, we calculated the Spearman rank correlation for every POSAS item because of non-normal score distributions, with ''overall opinion'' as the dependent variable.

Subsequently, we included the item with the highest Spearman rank correlation using a forward multivariable regression model. The significance criterion for inclusion of an item in a multivariable regression model was set at a p-value below 0.10. Next, other POSAS-items were entered one by one in the order of their strength of the univariable association with the overall opinion score. A new item was considered relevant to the model if its addition resulted in an absolute increase in R^2 of more than 0.05. Data analysis was carried out using SPSS software (PASW statistics, version 18.0, IBM, Armonk, NY, USA). Due to the non-normal distribution, we conducted a log-transformation of the dependent variable.

RESULTS

Patient and observer characteristics

We studied 106 patients, including 75 men and 31 women, with a mean age of 59.6 years (SD 16.6, range 18 to 90). Mean time until complete wound healing was 25.3 days (SD 12.4, median 22, range 9 to 65). Most of the DSSs were located on the thigh (n = 102; 96%), and rarely on the buttock (n = 2; 2%) or upper arm (n = 2; 2%). Eleven caregivers judged the DSS, including five specialized wound care nurses, two surgical nurses, and four researchers with a medical or nursing background. They were employed in five different medical centers.

Inter-observer reliability and score agreement

For each common item the IORs between patients and caregivers are shown in Table 1. Agreement regarding their overall judgment of the DSS was 'moderate' at best (ICC 0.44, 95% CI 0.27 to 0.58). Agreement regarding the other POSAS-items was 'poor', although their 95% CIs were wide. The limits of agreement approach showed that 95% of the overall opinion scores of patients differed up to three points from the caregivers' scores without a systematic difference (Figure 1).

Table 1. Inter-observer reliability between patients and caregivers

	ICC	95% Confidence Interval
Thickness	0.31	0.13 – 0.47
Relief	0.35	0.17 – 0.51
Pliability	0.38	0.19 – 0.52
Overall opinion	0.44	0.27 – 0.58

The intra-class correlation coefficient (ICC) was calculated using a one-way ANOVA model for single measure agreement.

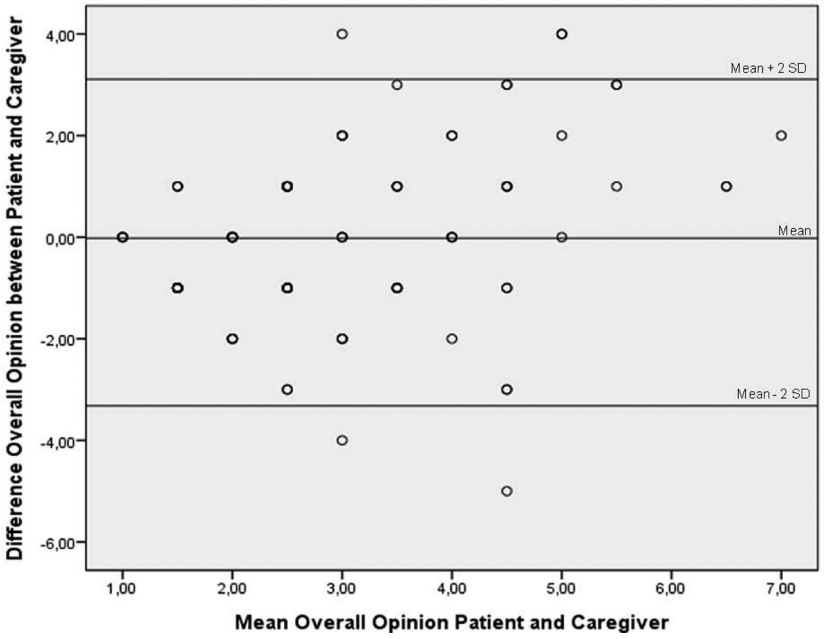

Figure 1. Bland & Altman plot of POSAS-scores between patients and caregivers. Each circle represents a donor site scar judged by patient and caregiver; many circles overlap.

Difference against mean plot for measurements of overall opinion by patients and observers using the POSAS (mean difference -0.02, SD 1.65).

Items predicting overall judgment

Correlation

For both patients and caregivers, each POSAS item score was significantly associated with their overall opinion (P-value < 0.10). Correlation coefficients ranged from 0.17 to 0.33 in patients, and from 0.22 to 0.50 in caregivers (see Table 2).

Table 2. Associations between POSAS-items and overall opinion of the patients and caregivers. Items with the highest association are stated first.

Patients		Caregivers	
POSAS-items	**Spearman's correlation coefficient**	**POSAS-items**	**Spearman's correlation coefficient**
Relief	0.33	Pliability	0.50
Itching	0.30	Pigmentation	0.45
Pliability	0.27	Relief	0.42
Color	0.26	Thickness	0.37
Pain	0.23	Vascularity	0.32
Thickness	0.17	Surface	0.22

Multivariable analyses

For patients, relief and itching showed the highest association with their overall opinion in the multivariable model (Table 3). Although relief was not significant anymore after adding itching, we forced relief into the model, together with itching, because of the highest association univariable. Adding itching to the model explained another 5.1% of the variance in overall opinion score, leading to an R^2 of 17.4%. Subsequently, we added and removed each POSAS item to the model with relief and itching, but the R^2 did not increase with more than 5%. Together with relief in the multivariable model, itching was statistically the most significant predictor. However, relief discriminated best (b = 0.13, 95% CI 0.01 to 0.26, P-value = 0.066) (see Table 4). This means that a one-point higher score for relief resulted in a 14% higher overall score of the DSS.

For the caregivers, pliability and pigmentation of the DSS showed the highest association with their overall opinion in the multivariable model and were statistically significant predictors of their overall judgment (Tables 3 and 4). Pliability was statistically the most significant predictor and discriminated best. A one-point higher score for pliability resulted in a 19% higher overall score of the DSS (95% CI 10 to 29%). Adding pigmentation to the model explained another 7.8% of the variance in overall opinion score, resulting in an R^2 of 31.8%.

Table 3. Overview changes in R^2 adding POSAS-items

Patients			Caregivers		
POSAS-item(s)	**R^2***	**Adding new item increased R^2 with:**	**POSAS-item(s)**	**R^2***	**Adding new item increased R^2 with:**
Relief	0.123		Pliability	0.240	
Relief, itching	0.174	**0.051**	Pliability, pigmentation	0.318	**0.078**
Relief, itching, pliability	0.187	0.013	Pliability, pigmentation, relief	0.356	0.038
Relief, itching, color	0.202	0.028	Pliability, pigmentation, thickness	0.340	0.022
Relief ,itching, pain	0.176	0.002	Pliability, pigmentation, vascularity	0.361	0.043
Relief, itching, thickness	0.185	0.011	Pliability, pigmentation, surface	0.320	0.002

*: The correlation coefficient squared (R^2) is a measure of the amount of variability in the dependent variable "overall opinion" explained by the other POSAS-items.

Table 4. POSAS-items included in the final model

POSAS-item	Unstandardized Coefficient b	Standard Error	95% Confidence Interval for b	P-value
Patients				
Relief	0.13	0.07	-0.01 - 0.26	0.066
Itching	0.11	0.04	0.02 - 0.20	0.013
Caregivers				
Pliability	0.17	0.04	0.09– 0.25	<0.001
Pigmentation	0.08	0.02	0.03 – 0.12	0.001

DISCUSSION

Patients and caregivers appreciate different characteristics when judging the scar of a donor site wound. Itching and relief appear to be the most important characteristic of patients' overall satisfaction, whereas for caregivers pliability and pigmentation have more impact.

The limited agreement we observed between caregivers and patients is consistent with previous studies in other wound types. O'Toole et al. found that surgeons' perceptions of cosmetic outcome differed from those of patients with lower extremity traumas[19]. Kaija et al. found a moderate agreement in cosmetic outcome after

conservative treatment of breast cancer[20]. In our study we found a poor agreement for almost all items of the POSAS (excluding opinion on overall judgment) between caregivers and patients. However, agreement between caregivers in burn- and linear scars has shown to be good[3;14;15]. So, although the POSAS seems to be a reliable tool in the communication among professionals, patients and caregivers appreciate the scars differently.

Caregivers should realize that the patients' own view of their scar affects quality of life[21]. The serious impact of itching on patient satisfaction, as found here, is in accordance with previous studies regarding burn- and linear scars[3;14;22]. Thus, the proper action of caregivers dealing with scar minimization should be to focus on patient-relevant issues, such as itching and a smooth scar surface. They should encourage patients to value pros and cons of treatment options, so that patients can balance both when deciding with the caregiver for the most suitable treatment option[23]. These treatments should match the needs and preferences of the patient (e.g. less relief and itching). For donor site wounds, the results of our recently completed trial will help choose the dressing material that best suits this purpose[16]. These considerations are also true for research on scar prevention, where the outcomes patients value the most are often disregarded[24].

Some limitations of this study should be mentioned. First, we assessed the DSSs after twelve weeks. This is a rather short period, but does allow analysis of the agreement between the patients' and caregivers' judgments, which is not likely to improve in the long term. Nevertheless, patient satisfaction may vary in time, especially when the acceptor site is completely healed, and scar characteristics may change even after complete re-epithelialization. After complete maturation of the scar, patients' overall satisfaction may be more influenced by other items in the POSAS, for example color instead of itching. Therefore, the predictive value of POSAS-items should be assessed and compared on different time-points. Second, different caregivers judged the wounds, which could influence the results. Yet, this mimics the real life situation in which several caregivers may be involved in the care for such patients. Up to now the agreement among various caregivers regarding their judgment of DSSs remains unclear. Third, although the judgments of patients and caregivers were compared, there was no reference standard with regard to the ''truth'' about the scar characteristics. This is of minor importance in our study as the patients' perception seems the ultimate outcome caregivers should deal with, when pursuing the ideal of patient-centered care. Finally, the precision of the agreement we found was limited, as illustrated by the wide confidence intervals. This may imply an insufficient number of patients with DSSs investigated. However, this imprecision does not affect the conclusions of our study, as the upper limit of the ICCs indicated a moderate agreement at best. More patients would likely have narrowed down the confidence intervals to ''poor'' levels.

We conclude that patients and caregivers adhere to different characteristics of donor site scars. Scar perception is dependent upon many variables, which have different predictive values, depending on the perspective of the assessor. Given this discrepancy, patient preferences should be considered in decision-making on wound treatment and scar prevention options.

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Chapter 9

Do stakeholders in wound care prefer evidence-based wound care products? A survey in the Netherlands

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ABSTRACT

Background: For several wound products compelling evidence is available on their effectiveness, for example, from systematic reviews. The process of buying, prescribing and applying wound materials involve many stakeholders, who may not be aware of this evidence, although this is essential for uniform and optimum treatment choice.

Methods: In this survey, we determined the general awareness and use of evidence, based on (Cochrane) systematic reviews, for wound products in open wounds and burns among wound care stakeholders, including doctors, nurses, buyers, pharmacologists and manufacturers.

Results: We included 262 stakeholders. Doctors preferred conventional antiseptics (e.g. iodine), while specialized nurses and manufacturers favored popular products (e.g. silver). Most stakeholders considered silver-containing products as evidence-based effective antiseptics. These were mostly used by specialized nurses (47/57; 82%), although only few of them (9/55; 16%) thought using silver is evidence-based. For burns, silver sulfadiazine and hydrofiber were most popular. The majority of professionals considered using silver sulfadiazine to be evidence-based, which contradicts scientific results. Awareness and use of the Cochrane Library was lower among nurses than among doctors ($P < 0.001$). Two thirds of the manufacturers were unaware of, or never used, the Cochrane Library.

Conclusion: Available compelling evidence in wound care is not equally internalized by stakeholders, which is required to ensure evidence-based decision-making.

BACKGROUND

To date, health care professionals are expected to keep abreast of current professional knowledge, and to apply research evidence in their daily practice in order to deliver the highest possible quality of care. Ideally, the evidence-based practice (EBP) paradigm promotes evidence-based decision-making with patients in clinical practice, preferably derived from proper (Cochrane) systematic reviews, if any, or well-performed clinical trials. Reality, however, shows that 30–40% of patients receive care that is not in accordance with available high quality research evidence, while another 20–30% of patients receive care that is even contraindicated[1]. Furthermore, the existence of guidelines does not guarantee its actual application. Guideline recommendations are followed in on average 67% of the treatment decisions made[2]. From these figures, it is obvious that the EBP paradigm has not yet been adopted by all health care professionals in their daily practice[3].

In wound care, an additional phenomenon is apparent. The available therapeutic options to choose from may be influenced by many different health care stakeholders (i.e. doctors, nurses, manufacturers, buyers, pharmacists), as well as by the patients' preferences. Although the experiential knowledge from all these stakeholders is a necessity, it is not a sufficient basis for clinical decision-making[4]. Hence, odds are high that the eventual treatment given is not evidence-based if one or more of these stakeholders do not make an evidence-based decision or are not aware of available high quality evidence. In other words, a joint venture is needed to make evidence-based wound treatment work.

Evidence-based wound care could also be seen as a challenge. Because of the lack of high quality research evidence or evidence-based guidelines to help choose the most appropriate form of local wound care and thus challenging evidence-based decision-making[5]. However, for some indications in wound care high quality evidence is available, which does make evidence-based treatment decisions possible[6-11]. Recently, well-performed systematic reviews with recommendations as to the use of antiseptics for preventing and treating wound infections have been produced and disseminated at various (inter)national conferences and among different audiences[6-10]. These reviews, for example, present high quality evidence about the effectiveness of honey dressings, iodine and silver sulfadiazine for specific wounds. For many years, iodine has been dissuaded because of its purported adverse effects, but was recently shown to be at least as effective as other antiseptics without serious harmful effects, such as a delay in wound healing, particularly in chronic and burn wounds[6]. In contrast, silver sulfadiazine, although still the treatment of choice in burn wounds, was found not to counteract infections more than other antiseptic agents, while decelerating wound healing in patients with partial-thickness burns[9;11].

Because of the growing body of high quality evidence on the (in)effectiveness of certain (antiseptic) wound dressings or agents, it seems unethical to administer ineffective treatments or to withhold patients from the best available evidence-based treatments. Therefore, the aim of this study was to explore the general awareness and use of compelling research evidence, based on available (Cochrane) systematic reviews, among several groups of wound care stakeholders in health care.

METHODS

Study setting

From April to September 2010, we contacted 31 Dutch medical centers, including all university (n = 8) and burn centers (n = 3), 13 home care institutions, 100 primary care facilities and 12 manufacturers of wound care products to take part in this study.

Participants

A representative, broad range of different health care professionals involved in wound care was recruited. These involved surgeons, plastic surgeons, dermatologists, general practitioners (GPs), surgical nurses, home care nurses, specialized wound care nurses, as well as manufacturers of wound care products, totaling eight professional groups. We aimed for about 25 professionals per group to obtain a full scale of possible answers. We included twice as many clinical and wound specialist nurses as they are key performers in daily wound care. Furthermore, interviews were planned with the heads of the hospital's buyer and pharmacy departments.

Questionnaire

To assess awareness and use in daily practice of the available, high quality research evidence on antiseptics and wound care products by wound care stakeholders in the Netherlands, a short questionnaire was designed. It consisted of five questions, each relating to personal preference and awareness of evidence from (Cochrane) systematic reviews:

1. When considering an antiseptic dressing for an open wound, what would be your top three of wound care products?
2. For which antiseptic wound care products has the effectiveness been established, based on high-level evidence, for the treatment of open wounds?
3. What would be your top three wound care products for the local treatment of open partial-thickness burns?

4. For which wound care products has the effectiveness been established, based on high quality research evidence, for the treatment of open partial-thickness burns?
5. How often do you consult the Cochrane Library?

A list of various wound care products was given to choose from (Tables 1 and 2). This list was based on common usage in daily practice and available evidence from (Cochrane) systematic reviews[6;8;9;11]. Participants also had the opportunity to choose 'other'. Furthermore, we noted the stakeholders' age and function.

Collection of responses

We used different methods to collect the responses. Firstly, during a national meeting of specialized wound care nurses and during presentations of Plastic Surgeons and Dermatologists we used electronic voting devices: ResponseCard™ keypads linked to Turning-Point for Microsoft® PowerPoint® (Turning Technologies, Ohio – version: 4.1.0.9020). No discussion was allowed. Secondly, we contacted medical centers and home care institutions by telephone. Thirdly, we distributed 35 CDROMs with the questions to doctors and nurses of 12 Dutch medical centers. Fourthly, some hospitals and home care centers requested we should attach the questionnaire to a cover letter addressed to the local doctors, nurses, and manufacturers, which was distributed via email. Health care professionals could only respond once to the questions.

Data analysis

Data were entered into PASW statistics 18.0 (SPSS Inc., Chicago, IL, USA). Statistical analyses included descriptive statistics of the top three choice of wound care products used, and awareness of evidence. The relation between age and the use of the Cochrane Library among the different groups were compared using the Kruskal–Wallis test, with P-value < 0.05 considered significant. The same test was used to detect differences between the professional groups. The Mann–Whitney U test was used to compare the awareness and use of the Cochrane Library among doctors and nurses. We used the chi-square ($\chi 2$) statistic to whether the different methods of investigation (by email, phone or plenary presentation) influenced the results.

RESULTS

A total of 262 professionals were included in this survey; 96 doctors, 143 nurses and 23 manufacturers of wound care products. The age distribution of the professionals is shown in Table 3. The age distributions are representative of the Dutch health care professional situation.

Table 1. Choices of antiseptic products in the treatment of open wounds and awareness of evidence

Professionals		Total (N)*	Chlorhexidine (%)	Eusol® (%)	Fucidin® (%)
Surgeons	Usage	24	13 (54)	7 (29)	6 (25)
	Evidence**	22	14 (64)	6 (27)	3 (14)
Plastic surgeons	Usage	25	8 (32)	13 (52)	14 (56)
	Evidence**	25	12 (48)	8 (32)	11 (44)
Dermatologists	Usage	37	15 (41)	11 (30)	19 (51)
	Evidence**	37	17 (46)	7 (19)	15 (41)
General practitioners	Usage	8	3 (38)	0 (0)	6 (75)
	Evidence**	7	2 (29)	1 (14)	4 (57)
Specialized nurses	Usage	57	6 (11)	14 (25)	11 (19)
	Evidence**	55	2 (4)	11 (20)	8 (15)
Surgical nurses	Usage	65	27 (42)	25 (38)	13 (20)
	Evidence**	51	26 (51)	14 (27)	14 (27)
Home care nurses	Usage	17	5 (31)	6 (38)	7 (44)
	Evidence**	15	5 (33)	6 (40)	4 (27)
Manufacturers	Usage	23	2 (9)	6 (26)	4 (17)
	Evidence**	21	1 (5)	1 (5)	1 (5)

NA, not applicable. *N is total number of participants who answered the question. **Evidence is number of respondents who have the opinion that the effectiveness of a particular product is evidence-based

Table 2. Choices of wound care products in the treatment of open partial-thickness burns and awareness of evidence.

Professionals	Item	Total (N)*	Chlorhexidine (%)	Film (%)	Hydrofiber (%)
Surgeons	Usage	23	0 (0)	1 (4)	11 (48)
	Evidence**	23	1 (4)	1 (4)	10 (43)
Plastic surgeons	Usage	25	1 (4)	6 (24)	13 (52)
	Evidence**	24	2 (8)	5 (21)	10 (42)
Dermatologists	Usage	34	2 (6)	6 (18)	11 (32)
	Evidence**	33	3 (9)	4 (12)	5 (15)
General practitioners	Usage	6	1 (17)	0 (0)	2 (33)
	Evidence**	7	2 (29)	0 (0)	2 (29)
Specialized nurses	Usage	56	2 (4)	4 (7)	49 (88)
	Evidence**	57	3 (5)	1 (2)	36 (63)
Surgical nurses	Usage	50	6 (12)	12 (24)	23 (46)
	Evidence**	41	9 (22)	12 (29)	19 (46)
Home care nurses	Usage	16	1 (7)	2 (13)	6 (40)
	Evidence**	10	2 (20)	1 (10)	2 (20)
Manufacturers	Usage	21	0 (0)	4 (19)	16 (76)
	Evidence**	19	1 (5)	3 (16)	11 (58)

NA, not applicable. *N is total number of participants who answered the question. **Evidence is number of respondents who have the opinion that the effectiveness of a particular product is evidence-based.

Furacin® (%)	Honey (%)	Iodine (%)	Silver product (%)	Other (%)
1 (4)	6 (25)	9 (38)	9 (38)	8 (33)
4 (18)	10 (45)	9 (41)	12 (55)	NA
8 (32)	6 (24)	8 (32)	6 (24)	1 (4)
10 (40)	9 (36)	14 (56)	9 (36)	NA
1 (3)	2 (5)	24 (65)	21 (57)	2 (5)
1 (3)	7 (19)	14 (38)	19 (51)	NA
0 (0)	1 (13)	8 (100)	3 (38)	2 (25)
1 (14)	1 (14)	4 (57)	4 (57)	NA
2 (4)	31 (54)	24 (42)	47 (82)	24 (40)
3 (5)	13 (24)	35 (64)	9 (16)	NA
7 (11)	15 (23)	23 (35)	37 (57)	33 (51)
7 (14)	17 (33)	25 (49)	26 (51)	NA
0 (0)	7 (44)	9 (56)	11 (69)	2 (13)
1 (7)	8 (53)	5 (33)	8 (53)	NA
0 (0)	13 (57)	7 (30)	20 (87)	15 (65)
0 (0)	6 (29)	14 (67)	13 (62)	NA

Honey (%)	Iodine (%)	Paraffin gauze (%)	Silver sulfadiazine (%)	Silver-containing dressing (%)	Other (%)
0 (0)	2 (9)	11 (48)	20 (87)	2 (9)	4 (17)
3 (13)	2 (9)	2 (9)	7 (30)	4 (17)	NA
1 (4)	0 (0)	15 (60)	20 (80)	4 (16)	0 (0)
2 (8)	4 (17)	6 (25)	18 (75)	6 (25)	NA
2 (6)	2 (6)	21 (62)	15 (44)	14 (41)	11 (32)
3 (9)	4 (12)	8 (24)	8 (24)	7 (21)	NA
0 (0)	2 (33)	4 (67)	5 (83)	0 (0)	0 (0)
2 (29)	2 (29)	3 (43)	3 (43)	1 (14)	NA
3 (5)	1 (2)	31 (55)	40 (71)	16 (29)	0 (16)
2 (4)	6 (11)	3 (5)	41 (72)	4 (7)	NA
5 (10)	3 (6)	37 (74)	27 (54)	12 (24)	5 (10)
10 (24)	12 (29)	17 (41)	21 (51)	19 (46)	NA
3 (20)	1 (7)	12 (80)	9 (60)	4 (27)	3 (20)
2 (20)	1 (10)	7 (70)	7 (70)	3 (30)	NA
2 (10)	0 (0)	5 (24)	8 (38)	10 (48)	13 (62)
2 (11)	1 (5)	1 (5)	3 (16)	8 (42)	NA

Table 3. Age distribution of professionals (in years)

	<31	31-40	41-50	51-60	>61
Surgeons (n=24)	5	8	5	3	3
Plastic surgeons (n=25)	13	7	3	2	0
Dermatologists (n=39)	21	9	4	5	0
General practitioners (n=8)	0	2	3	2	1
Specialized nurses (n=57)	3	15	25	12	2
Nurses (n=69)	38	8	9	13	1
Home care nurses (n=17)	5	4	6	2	0
Manufacturers (n=23)	5	7	4	7	0

Completeness of data

In total, 126 of 262 (48%) questionnaires were filled in completely, without any missing data. The main reason for missing data was a lack of experience with treatment of patients with burn wounds or not supplying three preferences. After comparing the complete questionnaires with the results of the incomplete ones, no substantial differences were found in the top three. Therefore, we present the results of all answers given. No significant differences were found between a shorter (telephone or electronic voting devices) or longer (email or CDROM) answering time.

Products for open wounds

The first choice of antiseptics used for the treatment of open wounds as given by the professional groups is shown in Table 4. The first choice within the groups of specialized nurses and manufactures for the local treatment of open wounds was silver-containing products. Doctors were more inclined to use conventional antiseptic products (e.g. Eusol®, chlorhexidine and iodine) than nurses, who more often chose popular antiseptic agents (e.g. silver products). Usage and awareness among the respondents of available evidence for each antiseptic wound care product is given in Table 1. In the majority of the professional groups (six of the eight groups), over

Table 4. Stakeholders' first choice of antiseptic products in the treatment of open wounds

Surgeons	Chlorhexidine (42%)
Plastic surgeons	Eusol (28%)
Dermatologists	Iodine (65%)
General practitioners	Iodine (38%)
Specialized nurses	Silver-containing products (32%)
Surgical nurses	Chlorhexidine (20%)
Home care nurses	Iodine (59%)
Manufacturers	Silver-containing products (48%)

50% of the respondents held the opinion that the effectiveness of silver-containing products is evidence-based. This opinion was also found in half of the groups for iodine and in 2/8 groups for chlorhexidine. In contrast, neither Eusol® nor Furacin® was considered supported by evidence. Notably, silver-containing products were mostly used by specialized nurses (47/57; 82%), but only few (9/55; 16%) stated to be aware of any evidence about the effectiveness of silver for open wounds. Remarkably, the number of doctors who used honey was lower than the number of doctors who stated to be aware of the evidence of its effectiveness. The opposite was observed in specialized wound care nurses and manufacturers.

Table 5. Stakeholders' first choices of wound care products in the treatment of partial-thickness burns

Surgeons	Silver sulfadiazine (67%)
Plastic surgeons	Silver sulfadiazine (76%)
Dermatologists	Silver sulfadiazine (32%)
General practitioners	Silver sulfadiazine (38%)
Specialized nurses	Hydrofiber (54%)
Surgical nurses	Silver sulfadiazine (29%)
Home care nurses	Paraffin gauze (41%)
Manufacturers	Hydrofiber (39%)

Products for burn wounds

The majority of professionals reported silver-sulfadiazine, as their first choice for the local treatment of open partial-thickness burns (Table 5). In half of the groups (4/8), over 50% of the respondents answered that the effectiveness of silver sulfadiazine is evidence-based. This was also the case in 2/8 groups for hydrofiber and in 1 group for paraffin gauze, but none of the groups considered the effectiveness of chlorhexidine, film, honey, or iodine as evidence-based (Table 2). Strikingly, all groups often used paraffin gauze (with the exception of manufacturers), but only few in each group stated to be aware of any evidence about its effectiveness.

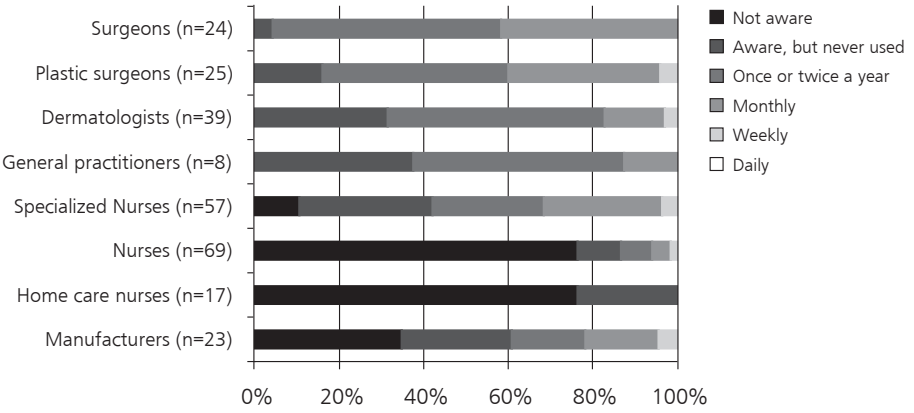
Awareness and use of the Cochrane Library

Figure 1 shows the awareness and use of the Cochrane Library in daily practice.

Doctors

All doctors were aware of the Cochrane Library; almost half of them used it once or twice a year. Surgeons (10/24; 42%) and plastic surgeons (10/25; 40%) tended to use the Cochrane Library more frequently (monthly or more often) than dermatologists (6/39; 15%) and GPs (1/8; 13%). However, this difference was not statistically significant (P-value = 0.724). Surprisingly, more than a quarter of the dermatologists and GPs was aware of the Cochrane Library but never used it.

Figure 1. Cochrane Library knowledge and use



Nurses and manufacturers

Awareness and usage of the Cochrane Library was lower among nurses than among doctors (P-value < 0.001). Nevertheless, this awareness was much higher in specialized nurses than in surgical and home care nurses (P-value = 0.001), of whom more than 75% stated to be unaware. The usage of the Cochrane Library among these nursing groups was poor, although more than a quarter of the specialized wound care nurses used it on a monthly basis. Among the manufacturers, two thirds were not aware of, or never used, the Cochrane Library.

Age and use of the Cochrane Library

No significant relations were found between age and awareness or use of the Cochrane Library among any of the groups.

Buyer and pharmacy departments

From the interviews with representatives of the buyer and pharmacy departments we learned that they had no preference and were not aware of any evidence regarding the effectiveness of the wound care products and could therefore not answer the questions posed. They merely ordered and delivered the products as requested by the doctor or nurse taking care of the wound patients.

DISCUSSION

Choices made in wound care by the various stakeholders are not always evidence-based, despite the availability of compelling research evidence from systematic reviews with recommendations for practice. For example, most health care professionals

hold the opinion that the effectiveness of silver-containing wound care products, in particular silver sulfadiazine, is established, but this is in contrast with the results of three Cochrane systematic reviews[8;9;11], which suggest silver sulfadiazine has more disadvantages compared with other antiseptics. These reviews report on evidence that is sometimes over 10 years old, but this has not reached the minds of present-day wound care professionals yet. The latency between the publication of evidence and its integration in daily practice may take a quarter of a century, and the scientific and clinical realms seem to have reconciled themselves with this notion[12].

There is an ongoing discussion about the usefulness of Cochrane systematic reviews[13;14]. Most of these reviews end by concluding that the volume and quality of the existing research is low, the consistency of study designs is lacking (e.g. regarding study endpoints), few replication studies exist, meta-analysis is usually impossible because of heterogeneity of the studies, and most included studies are at high risk of bias[13]. Therefore, clinicians often receive no recommendations what to do in daily practice[14]. On the other hand, reality shows that many published trials have methodological inadequacies. Therefore, it is important that Cochrane reviews highlight these methodological inadequacies, so that researchers pay more attention to the methodological quality of future research. In the case of the absence of compelling evidence, clinicians should rely on expert-opinion and consensus-based guidelines to assist clinical decision-making[13].

Findings in our study are supported by previous cross-sectional studies. Knops et al. showed that surgeons use only about half of the convincing evidence[3]. Four other studies investigated the awareness and use of the Cochrane Library; they concluded that there is little awareness[15-17], and subsequently little use of the Cochrane Library among health care professionals[16-18]. From a study performed by Sigouin et al. it is known that differences between professional groups exist, as they found a significant difference in favor of oncologists compared with oncology nurses related to awareness of the Cochrane Library[15]. Therefore, our results seem also true for other countries than only the Netherlands.

To turn the tide, Adamsen et al. proposed to develop an education strategy to provide stakeholders with evidence-based knowledge that empowers them to make evidence-based decisions[19]. Nevertheless, a recently published systematic review showed that there is insufficient evidence about which types of interventions are effective to encourage the use of systematic reviews by professionals in clinical decision-making[20]. Although it is accepted that not all professionals should be involved in research, stakeholders should be able to critique and apply research pertinent to their area[21;22]. This is in accordance with the conceptual framework Strauss et al. described, in which they propose that professionals can practice evidence-based medicine in one of three modes – as a doer, a user or a replicator[23]. Journal clubs may

also be used as a feature to keep abreast of the latest research evidence and enable continuing professional education[24].

Not solely educational features will bridge the gap between evidence and practice. Other strategies are also needed. For example, a multidisciplinary local wound care committee, including those able to search and present relevant evidence, should coordinate the wound care policy within an institution or region. In addition, this may reduce the variability between professionals and institutions in the use of wound care materials (e.g. wound care materials used for the treatment of donor site wounds[25]. Furthermore, opinion leaders and managers should be involved as they are important in improving and promoting evidence-based care[26]. Moreover, to improve the change of professional practice and implementation of evidence-based recommendations, barriers should be identified and dealt with[27].

It is not only the task of the professionals to bridge the gap. Scientists should reach out and carry out reliable and relevant research and produce readable information[28]. This is seldom the case; scientists pay relatively little attention to the implementation of the findings of their research in routine clinical care and usually use passive approaches to disseminate information (e.g. publication in professional articles). These approaches are generally ineffective, and at best, result only in small changes in practice[29]. Hence, scientists and professionals should work together to investigate relevant clinical questions derived from daily practice. Finally, the awareness-to adherence model which describes seven stages (awareness, acceptance, applicable, available and able, acted on, agreed to, and adherence) may help to get insight if the transfer between the different stages is insufficient[30;31]. If this is the case, specific interventions could be used to improve this. For example, electronic scanning and alert services may be useful to help stakeholders to become aware of important changes, such as the journal of Evidence-based Medicine and Evidence-based Nursing[31]. Furthermore, stakeholders should act aptly in terms of internalizing convincing evidence in their daily practice. In some cases, simple reminders help to act correctly[31]. Finally, stakeholders should not forget the role of the patient. Patients are to be informed adequately on potential risks and benefits to improve their adherence to the wound protocol after discharge from hospital.

A limitation of this study is the small scope of the (Cochrane) systematic reviews we used for the assessment of awareness and usage of evidence. However, the wounds involved (possibly with the exception of burn wounds) reflect daily practice in wound care and may well be indicative of the situation for other indications. Second, it could be possible that stakeholders rarely turn to the Cochrane Library for answers to clinical dilemmas. Currently, an increasing number of medical schools and residency programs are instituting curricula for teaching evidence-based principles[32]. Therefore, modern stakeholders in wound care should be aware of the available evidence in the Cochrane Library, but its use is not (yet) sufficiently implemented. Third, we used a self-reported questionnaire, which may have led to socially desirable answering and, subsequently,

to an overestimation of Cochrane Library usage[33]. Yet, this does not change the inferences from our study. Fourth, the questionnaire used is not validated. However, at present, there is no validated questionnaire available. We tried to obtain a first insight in this problem and to make the issue clear for future, more focused studies. Fifth, it is unclear whether the respondents answered reliably, that is, were they really aware of the evidence if they stated there is evidence of effect. Hence, we may even have overestimated their awareness. Lastly, the number of GP respondents in this study was limited, despite of our efforts to contact them. Therefore these results should be interpreted with caution. However, our results from GPs seem to be in accordance with two previous studies[18;34]. They found that despite the preferences of GPs for evidence-based information (e.g. systematic reviews and randomized clinical trials)[34], the majority of respondents were unaware of, or did not use, the Cochrane Library[18;34].

Present-day reality is that producing systematic reviews with recommendations and disseminating the results does not naturally result in more awareness and use of the evidence in the Netherlands. Using wound care products while contradicting evidence is available endorses this statement. Although our results may not be surprising, it is important that the basic premise has been confirmed by a quantitative analysis to invoke improvement actions. The present availability of compelling research evidence and the positive attitude towards EBP[3;17;35-37] should make evidence-based decision-making in wound care possible.

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Chapter 10

Competencies of specialized wound care nurses: a European Delphi study

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ABSTRACT

Aims: This paper is a report of an e-Delphi study to reach consensus among six European countries on the competencies for specialized wound care nurses that meet international professional expectations and educational systems.

Background: Healthcare professionals responsible for patients with complex wounds should have a particular level of expertise and education to ensure optimum wound care. However, uniform education for those working as wound care nurses is lacking, while a wide range of nursing titles are being used within and among various countries.

Design: Digital 3-round Delphi technique.

Methods: Wound care experts including doctors, wound care nurses, lecturers, managers, and head nurses completed online questionnaires based on the outcomes–based "CanMEDS" framework. The experts rated the importance of each competence on a 9-point Likert-scale. In round 1, they were allowed to add competencies they felt were missing. Consensus was defined as an agreement of at least 75% for each competence.

Results: Response rates ranged from 62% (round 1) to 86% (rounds 2 and 3). The experts reached consensus on 77 out of 96 competences (80%). Most competencies chosen belonged to the domain "scholar" (n = 19), while few addressed those associated with being a "health advocate"(n = 7). Competencies related to professional knowledge and expertise, ethical integrity, and patient commitment were considered most important.

Conclusion: Consensus was reached amongst experts about a set of core competencies that specialized wound care nurses should have to ensure optimum wound care. This may help achieve a more uniform definition and education of specialized wound care nurses.

BACKGROUND

Many patients with wounds require expert help from healthcare professionals[1]. A mix of skills and experience of these professionals can improve the quality of care[2]. A minimum level of education among professionals caring for (complex) wounds is a prerequisite to provide optimum wound care[3]. This is particularly important for specialized wound care nurses, as they provide most of the direct care for such patients.

In Western Europe a range of educational opportunities are available to become a wound care nurse at the postgraduate level. These include degree level courses (see Table 1). However, confusion still abounds regarding the scope of practice, and expectations of graduates from such courses. Different titles are used to describe such individuals, for example "advanced wound care nurses", "tissue viability nurses", "wound consultants", or "wound experts", that increases the confusion. Substantial curricular decisions are taken and these are often based on informal consensus or local efforts and may depend on the context of the healthcare organization. It is an educational challenge to determine what the content and level of wound care curricula should be[3].

Table 1. Examples of different educational opportunities in Europe

Wound consultant education at the Erasmus Medical Centre, the Netherlands
Akademie für zertifiziertes Wundmanagement (ZWM)®, Germany
Bachelor of Science module in the Principles of Wound Care Management, University of Glamorgan, UK
Master of Science in Wound Healing and Tissue Repair, Cardiff University, UK
Master of Science in Wound and Tissue Viability, Catholic University, Portugal

Despite a lack of uniform education for those working as wound care nurses, the term "specialized" or "advanced" seems unequivocal to describe their role and position[4]. The term "specialized" nurse leads in some instances to disharmony between general and specialist nurses[5]. In general, "advanced" nurses are defined as nurses who are employed in a clinical area with direct patient contact, are able to set the pace for changes in practice, and are innovators. These attributes are underpinned by educational experiences beyond the level required for initial registration[4]. However, it remains unclear if this is commensurate with the ideal profile of specialized wound care nurses.

A recently published Delphi study among 360 caregivers prioritized inclusion of wound education in all professional undergraduate and postgraduate nursing programs[6]. This supports the need for all caregivers involved in wound care to achieve

a uniform standard of education. However, the specific competencies required for a "specialized wound care nurse" remain unclear.

METHODS

Aim

The aim of the study was to reach a consensus within Western Europe on a core set of desired competencies for specialized wound care nurses compatible with international expectations and educational systems.

Design

The Delphi technique is considered as an effective way to measure and obtain group consensus[7]. We used a modified three-round e-Delphi technique using an internet-based questionnaire to reach consensus among experts from six Western European countries on the desired competencies of specialized wound care nurses. This approach differed to the Delphi technique in that closed as well as open-ended questions were posed and respondents were invited to suggest additional competencies to be judged.

Characteristics of "specialized wound care nurses" and definition "core competencies"

For the purpose of this study a "specialized wound care nurse" was defined as a qualified nurse who had successfully completed additional wound-oriented education. In daily practice, these individuals would take care of patients with complex wounds, undertake consultations, decide on appropriate treatments for wounds, and provide professional support for colleagues. Furthermore, they may also have responsibility for the updating of protocols, and take evidence-based decisions regarding wound dressings and devices. This definition was provided to clarify terminology for the experts taking part in the survey.

A "core competence" was defined as the functional adequacy and capacity to integrate knowledge and skills with attitudes and values into the specific context of practice[8]. This principle should underpin the ideal competencies to be chosen for specialized wound care nurses.

Competency framework: CanMEDS domains

We searched the literature to identify the current use of competency frameworks in clinical practice as well as whether there are particular frameworks used. Furthermore, we gathered information on current curricula and examples of course content from different educational institutions in Europe. Various curricula used the current or an

adapted version of the CanMEDS 2005 Physician Competence framework. Therefore it was decided to use this as a structure for the development of the survey[9]. This comprehensive framework comprises 7 domains, each characterized by several attributes. Originally this framework was designed to set out the core competencies for physicians, but has also been adopted by nurses to evaluate competencies. Currently, several countries in Europe (e.g. United Kingdom, the Netherlands, and Denmark) are gradually adopting the CanMEDS framework in specialist education[10-12]. This acceptance seems to indicate the applicability of such a framework in Europe. However, there is a lack of evidence to support the validity of this approach[13].

For the purpose of this study the CanMEDS domain "medical expert" was converted into "nursing expert". Other CanMEDS domains include; "communicator", "collaborator", "manager", "health advocate", "scholar", and "professional". The descriptions of the different domains can be found in Table 2.

Table 2. CanMEDS domains

Domain	Description
Nursing expert	Competencies that focuses on knowledge, skills, and attitudes
Communicator	Competencies that allow an effective patient relationship and includes dynamic exchanges in care
Collaborator	Competencies related to working effectively within a health care team
Manager	Competencies that focuses on decision-making about allocation of resources and organising practices within health care organisations
Health advocate	Competencies that focuses on using expertise to promote health and well-being of patients, communities and populations
Scholar	Competencies that focuses on lifelong commitment to learning, as well as on the creation, dissemination, application, and translation of knowledge
Professional	Competencies that focuses on involves commitment to ethical practice, professional regulation and high standards of behaviour

Preparation of questionnaire

Before commencement of the first Delphi round we gathered relevant competencies by sending open-ended questions to ten Dutch caregivers (one doctor and nine specialized wound care nurses). This questionnaire was divided into the seven domains of the CanMEDS, based on the definitions given in the CanMEDS Framework 2005. The caregivers indicated which competencies they believed specialized wound care nurses should ideally possess. Additionally we undertook telephone interviews with all respondents to identify and resolve any issues with the questionnaire, e.g. problems with the formulation and clarity of the questions. No particular issues were identified. We collected many additional competencies (n = 157) from this pilot. We categorized,

and restructured these competencies being careful to avoid duplication, which resulted in a list of 80 competencies. This was used as starting point for the first questionnaire.

Participants in the main study

We invited experts in the field of wound care or education from six Western European countries (i.e. Belgium, Denmark, the Netherlands, Portugal, Switzerland, and United Kingdom). The convenience sample of six countries has similar healthcare systems, in particular the reimbursement system of healthcare. We aimed to include four groups of experts to obtain a broad spectrum of relevant professionals: six doctors, twelve specialized wound care nurses, six university teachers and six managers or head nurses of wound centers or departments, totaling 36 experts. The numbers of specialized wound care nurses were double those of the other groups as the opinions of these individuals were fundamental to the aim of the study. This resulted in a group of experts that was homogenous as to the field of investigation, but heterogeneous in terms of professional background. All experts were selected purposefully, to ensure that they could give a valuable contribution to the discussion from their specialist background. Inclusion criteria were: (1) at least three years post-qualification experience; (2) involvement in wound care or wound care education; (3) ability to proficiently communicate and write in English. To increase response rates we used personalized letters, and contacted non-responders by email[14]. If individuals did not respond to our initial invitation prior the start of the study, and if they did not complete the first questionnaire, no further mailings or invitations were send. More experts were invited than planned beforehand to ensure that none of the expert groups would be underrepresented after finishing the study.

Data collection

All wound care experts received the link for the URL of the online questionnaire by email, using a commercially available online survey tool (http://www.surveymonkey.com). The experts were asked to complete each Delphi round within two weeks. The three questionnaires were sent out monthly between January and March 2012. The questionnaires included instructions for completion. Up to two reminders were sent per round if necessary. Furthermore, within two weeks of receipt of all questionnaires the experts received feedback on the previous round and the invitation for the next round.

Likert-scale and consensus

In all rounds, experts indicated their opinion about which competencies they thought the ideal specialized wound care nurse should have on a 9-point Likert-scale, ranging from 1; "highly irrelevant", to 9; "highly relevant". We grouped these scores into five

categories: a score of one represented "strongly irrelevant"; scores of 2-3 "irrelevant"; scores of 4-5 "moderately relevant"; scores of 6-7 "relevant"; and scores of 8-9 "highly relevant". This strikes a compromise between offering enough choice and the interpretability of the overall group response.

No standard threshold for consensus exists[15]. Therefore, through a process of group discussion by the authors, we defined consensus if at least 75% of the experts agreed the competence was "highly relevant", and thus a "core competence" of specialized wound care nurses. If more than 25% of the experts scored the competence in one of the other categories, we defined these competencies as "not a core competence" of specialized wound care nurses.

Round 1

The questionnaire in the first Delphi round consisted of three parts. The first part posed questions about baseline characteristics of the experts. The second part contained 80 competencies, compiled from the pilot and structured according to the CanMEDS categories. The third part contained open-ended questions to identify issues that might have been omitted, such as ideas for additional content and further competencies. When adding a competence, we advised experts that they should consider two points: (1) There is no right or wrong competency; and (2) the profile should not be about the current situation or local practices, but rather what they thought should be included in a European set of competencies.

We used the results of the first round to select competencies to be considered as core competencies. Competencies reaching at least 75% consensus in Round 1 were retained as agreed competencies for the final consensus, and not discussed again in Round 2.

Round 2

The second questionnaire consisted of two parts. The first part contained the remaining competencies from Round 1 on which no consensus had been reached. We provided the experts with the overall group response from the first round. Experts could reconsider their original response or leave it unchanged. In the second part of the questionnaire we presented the experts with the additional competencies as suggested by the experts in Round 1.

If the results showed no consensus, after the experts had rated the same competencies twice, we rejected these competencies as core competencies for specialized wound care nurses. This decision was made after group discussion. No straight-forward statements are available when to stop. The competencies that reached consensus in the second part of this questionnaire were retained. Thus, only

the competencies which were added after Round 1 that had not reached consensus here were presented again in Round 3.

Round 3

The third questionnaire consisted of the competencies based on the suggestions made in Round 1 on which no consensus had been reached after Round 2. Again, we provided the experts with the overall group response of each competence.

If the results showed no consensus, the items were also rejected as core competence.

Ethical considerations

The local medical ethics committee waived the need for approval for this study. Willingness to participate was implied when the experts had given written consent before the start of the study or by response to the first questionnaire.

Data analysis

Data analysis was carried out using SPSS software (PASW statistics version 18.0, IBM, Armonk, NY, USA). Summary descriptive statistics were calculated to determine the number of competencies that reached consensus after each round.

We conducted content analysis of all qualitative data from the pilot questionnaire as well as the first Delphi Round. All similar competencies were grouped into CanMEDS categories by the first author (AE). This process was reviewed by three other authors (HV, DU, SH) who independently examined each category for similar competencies that could be collapsed into one.

Validation

Five external experts (1 doctor from Denmark, 2 specialized wound care nurses from United Kingdom, and 2 lecturers from Ireland) reviewed the final list of core competencies needed for specialized wound care nurses. None of them participated in the study and were recommended by experts in the field based on their reputation. We asked the reviewers to provide a brief narrative commentary on the face validity of the final list. Face validity was assessed by judging the relevance and comprehensiveness of items[16]. This was considered essential to make sure the competencies adequately reflect those of specialized wound care nurses in daily practice.

RESULTS

Initially, 26 experts consented to participate. Of these, 20 responded in the first round (77%). To increase our number of experts we sent out an additional invitation to 32 further experts, of these, 16 (50%) responded. In total, 36 participants (36/58; 62%) completed Round 1. Two experts only completed the baseline characteristics, so we excluded their data from the analysis. Only those experts who participated in the first round or gave permission before the start of the study received the second and third questionnaires. Response rates in these last two rounds were 86% (37/43).

The characteristics of the international expert panel are presented in Table 3. This panel appeared representative of the field of investigation.

Round 1

In the first round, we were able to reach consensus regarding 70 out of the 80 competencies, while 10 remained open for a further consensus discussion in the subsequent rounds. From the open-ended questions in Round 1, we identified 16 additional competencies to be judged. Thus, 26 competencies were to be rated in Round 2 (See figure 1).

Round 2

In Round 2, consensus was reached about seven out of the 26 competencies. Eight competencies that were open for further discussion after Round 1 did not reach consensus in Round 2 and were considered as "not a core competence" of specialized wound care nurses.

Round 3

Eleven competencies remained open for further discussion in Round 3. None of these reached the level of consensus and were also considered as "not a core competence" of specialized wound care nurses.

Final list

A total of 96 competencies were considered by the experts during all three rounds. The experts reached consensus regarding 77 of the 96 (80%) for inclusion in the final list of "core competencies" (Table 4). The distribution of competencies included in each CANMEDS domain is shown in Table 2. In Table 5, we give an overview of the competencies that did not reach consensus.

Overall, experts rated "*The application of a high level of wound care knowledge with regards to factors such as wound etiology, underlying causes of problem wounds, and treatment options in patient care*"(rank 1, mean 8.86 on the 9-point Likert-scale)

Table 3. Baseline characteristics of experts

Baseline characteristics	Round 1		Round 2		Round 3	
	N	(%)	N	(%)	N	(%)
Number of participants per round						
	36		37		37	
Country						
Belgium	5	(14)	4	(11)	5	(14)
Denmark	4	(11)	4	(11)	4	(11)
The Netherlands	8	(22)	10	(27)	9	(24)
Portugal	5	(14)	6	(16)	5	(13)
Switzerland	4	(11)	3	(8)	3	(8)
United Kingdom	10	(28)	10	(27)	11	(30)
Gender distribution						
Male	16	(44)	15	(40)	17	(46)
Profession (participants were asked to indicate all categories that apply)						
Doctor	8	(22)	8	(22)	9	(24)
Wound care nurse	23	(64)	23	(62)	23	(62)
Lecturer	10	(28)	10	(27)	10	(27)
Manager or head nurse	8	(22)	8	(22(	8	(22)
No. of years post-graduate experience in wound care						
3 - 5 years	5	(14)	3	(8)	3	(8)
5 - 10 years	3	(8)	3	(8)	3	(8)
10 – 15 years	9	(25)	9	(24)	9	(24)
>15 years	19	(53)	22	(60)	22	(60)
Highest level of education						
Some college but no degree	2	(5)	2	(5)	1	(3)
Associate degree	0	0	0	0	0	0
Bachelor degree	13	(36)	13	(35)	13	(35)
Master degree	10	(28)	10	(27)	11	(30)
Post master degree	10	(28)	11	(30)	11	(30)
Missing	1	(3)	1	(3)	1	(3)
Practice mix						
Mainly acute wounds	0	0	0	0	0	0
Mainly chronic wounds	13	(36)	13	(35)	12	(32)
A mix of both chronic and acute wounds	20	(56)	20	(54)	22	(60)
Not applicable	3	(8)	4	(11)	3	(8)

as most important followed by "*the ability to protect information provided by or about patients, keeping it in confidence, and divulging it only with the patient's permission except when otherwise required by law*" (rank 2, mean 8.83) and "*honesty and integrity in patient care*" and "*commitment to their patients, profession, and society through ethical practice*" (both rank 3, mean 8.72) as the top 3 most important. These competencies belong to the domains "Nursing expert" and "Professional".

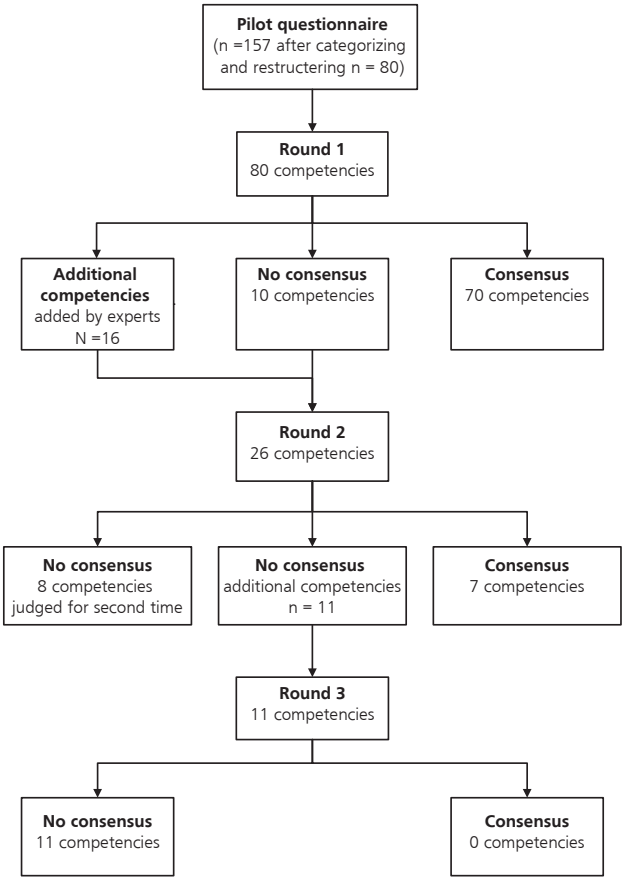

Figure 1. Flowchart of competencies per round

Excluded from final list

Conversely, they rated "*the ability to design a randomized clinical trial in wound care*" (rank 96, mean 4.97), "*the ability to write scientific articles for peer reviewed journals*" (rank 95, mean 5.67), "*to communicate in English (oral as well as written), where English is not the native language*" (rank 94, mean 6.51) as the 3 least important competencies.

Table 4. Competencies for specialised wound care nurses

Domain: Nursing Expert Which competencies should your ideal specialised wound care nurse have in terms of knowledge, skills and attitudes to deliver patient-centred care?	
Competencies	%*
Demonstrate the application of a high level of wound care knowledge with regards to factors such as wound aetiology, underlying causes of problem wounds, and treatment options in patient care	100%
Demonstrate the ability to use preventive and therapeutic interventions effectively	90%
Demonstrate the ability to stimulate patient empowerment and patient self management	86%
Demonstrate the ability to perform a multifocal assessment of the whole patient, to include co-morbidities, environmental hazards, and patient barriers (e.g. lack of knowledge)	87%
Demonstrate the ability to apply evidence-based wound care in clinical practice	84%
Demonstrate the ability to master and initiate treatment of complex wounds	82%
Demonstrate the ability to be ready to respond quickly if the patients conditions changes	82%
Demonstrate the ability to perform specialised skills, such as sharp debridement	79%
Demonstrate the ability to examine current practices and evaluate traditional methods of the management of wounds, based on theoretical knowledge	79%
Demonstrate the ability to use procedural, diagnostic and therapeutic skills proficiently and appropriately	75%
Domain: Communicator Which competencies should your ideal specialised wound care nurse have to effectively facilitate the nurse-patient relationship and the dynamic exchanges that occur before, during, and after the medical encounter?	
Demonstrate the ability to use appropriate terminology taking into account the intended recipient	97%
Demonstrate the ability to accurately communicate relevant information and explanation to patients, colleagues, and other professionals	94%
Demonstrate the ability to provide clear instructions for patients and ensure appropriate follow-up care	94%
Demonstrate the ability to accurately obtain and synthesise relevant information and perspectives of patients and families, colleagues, and other professionals	92%
Demonstrate the ability to communicate effectively and empathetically with patients and their families	92%
Demonstrate the ability to maintain thorough, clear and concise documentation	92%
Demonstrate the ability to be calm, provide clear information, be aware of patient expectations, formulate own expectations, appropriate attitude (polite, correct and interested behaviour)	91%
Demonstrate the ability to develop a common understanding of issues, problems, and plans with patients, families, and other professionals to develop a shared plan of care	89%
Demonstrate the ability to develop trusting, ethical and therapeutic relationships with patients and families	89%
Demonstrate the ability to transform theory into practice that is understandable to the patient	89%

Demonstrate the ability to provide an equal partnership between patient and wound care nurse	89%
Demonstrate the ability to present a patient case in a clear, concise and complete manner	86%
Demonstrate the ability to use a holistic approach to the patient, in which quality of life is essential	86%
Demonstrate the ability to communicate the evidence to support a treatment option to the patient	77%
Domain: Collaborator Which competencies should your ideal specialised wound care nurse have to work effectively within a healthcare team to achieve optimal patient care?	
Demonstrate the ability to establish and maintain effective working relationships with colleagues and other health care professionals	95%
Demonstrate the ability to appreciate the benefit of inter-professional teamwork through learning alongside others from different professions	95%
Demonstrate the ability to be open to other opinions and ideas and to reach a consensus	92%
Demonstrate the ability to share knowledge and information to other colleagues on a specialist level	92%
Demonstrate the ability to communicate (oral as well as written communication) about patients in a clear, concise and complete manner	89%
Demonstrate the ability to work effectively with other health professionals to discuss, prevent, and resolve inter-professional conflicts	86%
Demonstrate the ability to participate effectively and appropriately in an inter-professional healthcare team	83%
Demonstrate the ability to share knowledge of wound management with colleagues who are less informed about wound management	83%
Demonstrate the ability to explain when- why- and how choices are made, and describe the risk of treatments used to patients and other health care professionals	78%
Demonstrate the ability to be reliable, have critical independence and are socially-minded	75%
Domain: Manager Which competencies should your ideal specialised wound care nurse have to act as an integral participant in healthcare organisations, able to organise sustainable practices, make decisions about allocation resources, and contribute to the effectiveness of the health care system?	
Demonstrate the ability to use evidence-based and cost-effective investigations and treatments	92%
Demonstrate the ability to be aware of the financial constraints within organisations	86%
Demonstrate the ability to make timely and well considered decisions	83%
Demonstrate the ability to take control (leadership) and coordinate care for patients with wounds	81%
Demonstrate the ability to lead or implement a change in healthcare regarding wound care	80%
Demonstrate the ability to think analytically and strategically	78%
Demonstrate the ability to participate in activities that contribute to the effectiveness of their healthcare organisation and systems	78%
Demonstrate the ability to think beyond their own institution (e.g. national or international)	78%

Demonstrate the ability to consult with other health care professionals and can justify these choices	75%
Domain: Health advocate Which competencies should your ideal specialised wound care nurse have to use their expertise and influence to advance the health and well-being of individual patients, communities and populations correctly?	
Demonstrate the ability to give, in a specific situation, detailed advice to a patient	92%
Demonstrate the ability to be aware of the underlying psychosocial and socioeconomic problems that may reduce adherence to the treatment	92%
Demonstrate knowledge of risk factors of wound healing	89%
Demonstrate the ability to counsel and educate patients to prevent complications	86%
Demonstrate the ability to be creative and innovative in identifying solutions for individuals	86%
Demonstrate knowledge of coping strategies of patients	81%
Demonstrate the ability to identify opportunities to discuss risk factors with patients	75%
Domain: Scholar Which competencies should your ideal specialised wound care nurse have to demonstrate a lifelong commitment to reflective learning, as well as the creation, dissemination, application and translation of medical knowledge?	
Demonstrate the ability to motivate others to use guidelines	95%
Demonstrate the ability to adapt their working practices based on verified new insights	94%
Demonstrate the ability to be open to feedback and actively seek feedback from patients, colleagues and other health care professionals	89%
Demonstrate the ability to provide bedside-teaching to patients and nurses at each consultation	89%
Demonstrate the ability to provide effective feedback	89%
Demonstrate the ability to keep up with the professional literature	86%
Demonstrate the ability to translate knowledge into professional care	86%
Demonstrate the ability to apply the concepts of evidence-based practice and best-practice guidelines and how they relate to patient care	86%
Demonstrate the ability to support health care institutions to ensure knowledge is kept up to date	86%
Demonstrate the ability to search relevant scientific evidence	86%
Demonstrate the ability to be self-guided in their professional development to include identification of their own learning needs	83%
Demonstrate the ability to critically appraise the literature relevant to wound care	83%
Demonstrate the ability to access a range of available educational resources to enhance patient care	80%
Demonstrate the ability to identify wound care training needs of health professionals	80%
Demonstrate the ability to combine all elements of Evidence-based Practice (including evidence, clinical experience, patient preferences, and costs) in making decisions about care for individual patients	78%
Demonstrate the ability to provide an effective lecture or presentation	78%

Demonstrate the ability to select effective teaching strategies and content to facilitate the learning of others	78%
Demonstrate the ability to interpret scientific research	77%
Demonstrate the ability to develop standards in wound care for other professionals (i.e. assistant nurses) in wound care issues	77%
Domain: Professional Which competencies should your ideal specialised wound care nurse have to show commitment to the health and well-being and society through ethical practice, professional regulation, and high personal standards of behaviour?	
Demonstrate the ability to provide care in a responsible manner	98%
Demonstrate the ability to protect information provided by or about patients, keeping it in confidence, and divulging it only with the patient's permission except when otherwise required by law	97%
Demonstrate a commitment to their patients, profession, and society through ethical practice	97%
Demonstrate honesty and integrity in patient care	95%
Demonstrate a commitment to their patients, profession and society through participation in profession-led regulation	95%
Demonstrate the ability to strive for high-level expertise in light of evidence-based practice in wound care	95%
Demonstrate a commitment to nurse health and sustainable practice	91%
Demonstrate a compassionate and a non-judgmental approach to all patients	89%

* Percentage of experts that rated these items as core competence

External review

The elected list of 77 competencies was presented to an external review panel to judge face validity. The following quotes were received: "I think this list is useful and important and in line with international expectations and educational systems", "In my opinion the list of core competencies for wound care nurses demonstrates good face validity and appears to reflect the essential competencies for an ideal wound care nurse", "I absolutely agree with all the elements of the competencies which are well thought out. I would like to order 5 new nurses like these please!", "Basically all of them are relevant" and the fifth reviewer answered "the listed competencies are good, however, some could be listed as essential and others as desirable". Some additional suggestions concerned adding competencies related to patients' and staff attitudes and basic knowledge about health economics. Finally, an advice was given to think about a numbering system for each within its subsection as this type of document will be useful for appraisals, teaching etc. These points should be considered in future research.

Table 5. Number of core competencies that did not reach consensus

Competencies	**%***
Nursing Expert	
Demonstrate knowledge and application of controversial issues related to wound healing and tissue repair	61%
Communicator	
Demonstrate the ability to use social media/ICT in contacting patients and colleagues	57%
Demonstrate the ability to communicate in English (oral as well as written), where English is not the native language	43%
Manager	
Demonstrate the ability to undertake pioneering work, implement innovations and provide access to optimal quality of patient care	74%
Demonstrate the ability to understand organisational structures	54%
Demonstrate the ability to manage a wound care service and budget	54%
Demonstrate the ability to play a key role in the negotiation between health care institutions and industry	46%
Demonstrate the ability to use contacts out of their network to improve the financial balance of national healthcare (e.g. stimulate out-patient care)	43%
Scholar	
Demonstrate the ability to search for new knowledge using scientific electronic databases with scientific publications (e.g. Pubmed, Cinahl, Ovid Medline, Cochrane Library etc.)	70%
Demonstrate the ability to participate/assist in scientific research	66%
Demonstrate the ability to take an active role in imparting scientific knowledge to colleagues	65%
Demonstrate the ability to have knowledge of word processing and spreadsheet software e.g. Microsoft Office® or similar programs	64%
Demonstrate the ability to interpret randomized clinical trials	62%
Demonstrate the ability to write articles for popular (non-scientific) journals	46%
Demonstrate the ability to perform scientific research	37%
Demonstrate the ability to publish scientific research	35%
Demonstrate the ability to write scientific articles for peer-reviewed journals	28%
Demonstrate the ability to design a randomized clinical trial	8%
Professional	
Demonstrate the ability to seek to understand other cultures and to appreciate other cultures	57%

%* Percentage of experts that rated these items as core competence

DISCUSSION

Wound care experts from six different countries in Western Europe reached consensus regarding 77 core competencies for specialized wound nurses based on the CanMEDS framework. In general, competencies related to professional knowledge and expertise, ethical integrity, and patient commitment were considered to be

essential competencies. These competencies are rather generic statements that do not strongly distinguish between general and specialist practice, but are competencies all health care professionals should have. Other competencies, like teaching ability and research utilization, may discern specialist nurses. Conversely, research activities (e.g. performing and publishing research) were considered less relevant. This is helpful to map the educational outcomes expected of specialized wound care nurses.

This consensus may contribute to a more uniform education and performance of specialized wound care nurses in developed countries. Moreover, it may standardize the definition and position of such specialized nurses in clinical practice. Such harmonization is pivotal in the recognition of wound care as a large, multidisciplinary area within healthcare that deserves attention by highly trained professionals to ensure quality of patient care.

The experts judged the competencies in the domain "scholar", i.e. performing, participating and publishing scientific research, as less relevant. The conceptual framework of Strauss et al.[17], regarding the levels of usage of evidence-based medicine, was designed for doctors but can be extrapolated to specialized wound care nurses. Following this framework, our study indicates that one should practice evidence-based medicine as "user", instead of "replicator" or "doer". The competencies referring to "scholar" are in accordance with the view that not all caregivers should be involved in wound care research. However, stakeholders such as specialized wound care nurses, should be able to critique and apply research pertinent to their area[18;19], and in teaching activities.

Beside the educational challenge in wound care, the shift of tasks from doctors to nurses is another emerging feature. The range of duties of nurses is changing (e.g. nurses prescribing drugs). This is not only the case in Europe, but also in Canada and the United States. This change of responsibilities has burgeoned not only because of the increased demands and reforms in healthcare, but also through the increasing specialization and advanced educational opportunities in nursing[6;20;21]. Concurrently, many developed countries are seeking to shift provision from doctors to nurses, while trying to cope with an increasing pressure to constrain costs[21]. The consensus reached in this Delphi study may help clarify which competencies are required and also reduce uncertainty and confusion among specialized wound care nurses regarding their responsibilities in the medical and nursing fields. In various settings appropriately trained nurses may produce health outcomes and quality of patient care that are equal to those achieved by doctors[21;22]. Therefore, the results of our study may help doctors defer tasks and relinquish some control (e.g. coordination of care, provision of patient education) to specialized wound care nurses.

Strengths and limitations

The main strength of this study was the use of a digital Delphi technique to achieve consensus in an area where empirical evidence is scarce[23]. This method gives equal weight to the opinion of each expert, allows anonymous inclusion of experts across various countries and levels of expertise, and avoids the domination by one expert of the consensus process[15].

Attrition rates in questionnaire research are a recognized problem[15]. Withdrawal can occur in each stage, but high drop-out rates in the final round may substantially influence the results[24]. In our study the reason for withdrawal was not recorded. However, we achieved high response rates in every round. Therefore, we consider our results to be robust. A possible reason for the high response rate may be that the experts recognized the importance of the topic and considered themselves as partners in the study. Feeling involved is important to bridge the well-described gap between research and practice[25]. Because of the range of specialties and countries involved in this Delphi study, this ultimate set of core competencies is likely to be generalizable to other specialized wound care nurses in other developed countries.

There are also some limitations of our study. First, we included only six out of the 27 European countries (22%) and five external reviewers. However, we chose our contributors purposefully, based on their expertise in wound care. Furthermore, we included only English speaking experts. This was done deliberately to make sure the experts completely understood the described competencies. Second, the present consensus comprises numerous competencies. Stakeholders should organize these competencies thematically to make this framework easier to use in daily practice. However, these themes should include all competencies to reflect the full spectrum of tasks specialized wound care nurses should fulfill. Third, the level of consensus was chosen arbitrarily, because no standard threshold for consensus is available[15]. If we had chosen a higher consensus level (e.g. 80%), more competencies were considered as "not a core competence". This may have provided a more compact, easier-to-use, but less comprehensive list of competencies. Conversely, we could have defined consensus at a lower level of agreement. In that case, competencies regarding implementing innovations and searching scientific evidence would also have been considered as core competencies. Finally, many studies in healthcare support the use of the CanMEDS framework to structure competencies[26-28]. However, an officially adapted version of the CanMEDS for nurses is lacking, although we found that various curricula of nursing schools are based on the CanMEDS framework.

By means of the Delphi technique we were able to reach an international consensus about core competencies for specialized wound care nurses. This consensus may be helpful to achieve a more uniform and better definition of specialized wound care nurses and, ultimately, a more uniform and better quality of wound care. The next

step should be the acceptance and implementation of this set of competencies in education and clinical practice. Furthermore, support from European wound care organizations, such as the European Wound Management Association (EWMA) may helpful to make these steps easier to take.

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Chapter 11

General discussion

GENERAL DISCUSSION

The care for patients with wounds excels in variation. It is often argued that this is due to the large variation in wound types, but this does not mince the matter. A huge variation appears to exist in available dressing products, opinions among doctors and nurses, and levels of wound education. More specifically, many treatment options are known for donor site wounds after split-skin grafting. Therefore, in this thesis we investigated (1) the extent of treatment variation; (2) the niches in available evidence; and (3) strategies to decrease this variation in the care for donor site wounds. In this chapter our findings are discussed and recommendations for the future are suggested.

Extent of treatment variation

Standard wounds, such as donor site wounds, are likely to be treated in a rather standard fashion. However, in the Netherlands we encountered a large variation in the dressing materials currently in use to cover donor site wounds (**Chapter 2**). This variation is unwanted and needs to be explored and addressed. The large variability suggests a potential for research and quality improvement. It emphasizes the need to generate new scientific knowledge and identify new sources to improve the quality of wound care, especially for the donor site wound. Besides, treatment variation was not solely found regarding donor site wounds as we also detected this variation for other indications, e.g. open partial-thickness burns and infected open wounds (**Chapter 9**).

Best available evidence

A possible explanation for the treatment variation found is the lack of evidence and guidelines. We investigated the available evidence on the effectiveness of six commercially available dressings to treat patients with donor site wounds after split-skin grafting. After scrutinizing the available RCTs, hydrocolloid and films appeared to be promising dressing materials for the treatment of patients with donor site wounds. However, the trials found had several methodological flaws (**Chapter 4**).

Therefore, we decided to generate more solid evidence and conducted a well-designed RCT to investigate which dressing would be best to support a quick and uneventful healing of donor site wounds (**Chapter 5-7**). This trial focused on six dressing materials, including five commonly used dressings (i.e., alginates, films, gauzes, hydrofibers and silicones, as discussed in **Chapter 2,** as well as hydrocolloids (**Chapter 4**). The results of this RCT showed that hydrocolloid dressings lead to a 7-day, i.e. a 30%, shorter healing time than the other materials, whereas the use of gauze dressings was found to increase the risk of infection. The effectiveness of hydrocolloids has been corroborated by previous, mostly non-clinical studies showing that hydrocolloids improve re-epithelialization, increase collagen synthesis and

ultimately lead to better healing rates[1-5]. Notably, hydrocolloids were less popular in daily practice (**Chapter 2**); possibly due to the more frequent dressing changes required because of its low fluid absorption capacity and subsequent wound leakage[1]. Another reason for the seemingly reluctant attitude towards hydrocolloids by caregivers may be the fact that new, promising wound care techniques such as negative pressure wound therapy, receive more attention in promotion campaigns. Hydrocolloids were introduced over 40 years ago and may nowadays be considered as a less appealing dressing material[6]. This also suggests that manufacturers have other interests besides the available evidence when defining the indications for their products.

The results of this trial, with regard to wound healing as well as other patient-relevant outcomes (e.g. infection rates, pain, and scarring) should facilitate an evidence-based treatment choice not only *for, but also with,* future patients. Patient preferences should be particularly taken into account, keeping in mind that the patients and their caregivers weigh the various characteristics of a scar differently (**Chapter 8**). For patients, itching and relief appeared to be the most important characteristics, whereas skin pliability and pigmentation had the largest impact on their judgment for caregivers.

Strategies to decrease variation

Guidelines

A first step to decrease variation should involve the results of our study about the effectiveness of dressings for donor site wounds being incorporated into a national guideline on 'acute wounds'[7]. Currently, an interdisciplinary working group is developing a national guideline that endorses a standardized and evidence-based approach to wound care for acute wounds. Grants of the Association of Surgeons of the Netherlands and the Netherlands Organization for Health Research and Development made this possible. The best available evidence will be translated into specific recommendations for clinical practice. This initiative acts upon our finding that the availability of systematic reviews on local care for acute wounds did not result in more awareness and use of the evidence by caregivers and stakeholders in the Netherlands (**Chapter 9**).

Validated tools to classify donor site wounds

Wound classification tools are designed to assist clinical judgment and to get insight into the progression of wound healing in a uniform way. The widely used Red-Yellow-Black (RYB) scheme is validated for chronic and acute wounds[8-11] and, therefore, suggested to be useful in classifying donor site wounds. However, we demonstrated that this scheme does not lead to more uniformity in the assessment of these wounds, perhaps because the variation in the appearance of donor site wounds is too small to

make a proper distinction based on the RYB-scheme (**Chapter 3**). In the absence of a suitable classification scheme, best practice to reduce any variation in care would be direct inter-professional communication based on in vivo judgments.

Uniform set of competencies for specialized wound care nurses

The last initiative we undertook in this thesis to decrease variation in care was to create a uniform set of core competencies for specialized wound care nurses (**Chapter 10**). This was because uniform education for those working as wound care nurses is lacking, while a wide range of nursing titles (e.g., "advanced wound care nurses", "tissue viability nurses", "wound consultants", or "wound experts") are being used within and among various countries. Our results showed that the more general competencies, i.e. related to professional knowledge and expertise, ethical integrity, and patient commitment, were considered to be essential. More specific competencies, like teaching ability and research utilization, may discern specialized wound care nurses. Conversely, research activities (e.g. performing and publishing research) were considered less relevant. This contrasts with the recently developed job profile for registered nurses in the Netherlands[12], which states that nurses should assist in research activities, and even more in contrast with the profile of nurse specialists[13]. They are expected to perform and publish scientific research as well.

Overall, the compiled set of core competencies is helpful to map the educational outcomes that are expected from specialized wound care nurses. Moreover, it may standardize the definition and position of such specialized nurses in clinical practice, which is pivotal in the recognition of wound care as a large, multidisciplinary area within healthcare.

Considerations

In this thesis, we addressed possible solutions to reduce the variation in care of donor site wounds. The implementation process is beyond the scope of this thesis, but we hope that the dissemination of our results will invoke quality improvement actions by specialized wound care nurses, educators and managers. It is unethical to administer ineffective treatments or to withhold from patients the best available evidence-based treatments (e.g. the use of gauze rather than hydrocolloid to treat donor site wounds). Furthermore, to keep patient care up-to-date, unremitting research in the wound care field is necessary to report the advantages and disadvantages of emerging technologies.

Methodological strengths and limitations

The methodological strengths and limitations of each of the individual studies included in this thesis have been discussed in previous chapters. In general, this thesis has

two main strengths. First, we were able to demonstrate that it is possible to conduct rigorous scientific research that offers strong evidence for the effectiveness of wound care interventions. This was in spite of the common reluctance to perform large trials because of heterogeneity in wound etiologies, treatment regimens, and relevant outcomes[14;15]. Second, we were able to show that there is sufficient evidence that helps reduce treatment variation in patients with donor site wounds. In addition, we not focused only on treatment options, but also on other important aspects of wound care (e.g. communication tools, agreement among patients and caregivers, classification tools, and professional competence).

On the other hand, some limitations should be taken into account when interpreting our results. First, we carried out two national surveys, two inter-observer studies, and an international Delphi study in which we used convenience and purposive samples. We strived to include representative samples of the professionals involved in wound care, who all contributed voluntarily to these studies. It is possible that these participants were more positive towards wound care research and research utilization.

Furthermore, in the "Rembrandt trial" we included the required number of patients, based on *a priori* sample size calculation given a presumed clinically relevant difference. Consequently, this trial offers evidence for the effectiveness of a specific dressing type within a group of six materials. Other occlusive or semi-occlusive dressings, such as foam dressings, might have similar healing effects, but these dressings were not included in this trial based on existing evidence (**Chapter 4**) and a national inventory (**Chapter 2**) showing a lower eligibility. Unfortunately, no accurate data were available on costs, which play a substantial part in the economic considerations when deciding on wound treatment. Furthermore, patient preferences were not assessed, but should be considered if one wants to make evidence-based decisions. A more qualitative approach is useful to get insight into patient preferences. Finally, in the "Rembrandt trial, a wide range of both university and nonacademic hospitals across the Netherlands participated, which improves the generalizability and implementation of our results[16].

Further perspectives

Given the expected future developments (e.g. an ageing population, care reimbursement issues, and intense marketing by dressing manufactures) costs of wound care can only increase. Therefore, innovative ways should be thought out to make wound care more affordable while improving the quality of care. To realize this, further progress should be made to reduce variation and to close the gap between research and practice. Given the limited availability of high-quality evidence, more research on the effectiveness of wound treatments is obviously needed. Besides, additional studies are needed to investigate the influence of patients' lifestyle on

wound healing, the influence of wounds on quality of life, patients' preferences regarding wound dressings characteristics, and return-to-work issues.

Moreover, we should not solely focus on research, but also on the implementation of already available evidence in clinical practice (e.g. in hospitals and outpatient clinics). Therefore, caregivers and policy makers should become more familiar with the most effective way to support evidence-based care at an organizational level[17], and to combine an evidence-based approach with quality improvement (QI) projects[18-20]. These two different approaches have similar overall goals, but focus on different parts of the problem[20]. Whereas evidence-based practice focuses more on 'doing the right things' based on the best available evidence, QI focuses more on 'doing the things right'; i.e. making it possible to perform the proposed action in an efficient way[20]. Furthermore, factors that trigger health care professionals to make a mind-change towards evidence-based practice, and to stimulate them to implement scientific evidence in daily practice, should be investigated. Although the ability to assist in scientific research is not a core competence of wound care nurses, we experienced that many of them are enthusiastic to be involved. This may be facilitated by a rather new and promising development in wound care, namely (nurse-led) wound expertise centers (WECs). WECs may play an important role to focus on, and improve, quality of wound care. The ongoing national interdisciplinary initiative to develop a new guideline for treating wounds with an acute etiology can support this[7].

In conclusion, we see many opportunities and challenges for evidence-based wound care. Quite a feat, but well worth the challenge!

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Chapter 12

Summary in English

SUMMARY

Caregivers carry the responsibility of making high-quality decisions, because these decisions directly influence their patient's health. However, in daily practice it is unclear exactly what constitutes good quality, and this is especially true in the realm of wound care. Here, quality of care is confounded by a large variation in wound types, physicians' and nurses' preferences, and the competencies of the caregivers involved. This situation is likely to result in suboptimal care for the many patients suffering from wounds and is a challenge for evidence-based decision-making. This thesis is a compilation of interdisciplinary efforts to contribute to the body of knowledge on wound care, and aims to promote evidence-based decision-making in order to reduce unnecessary variation in the care of wounds.

In **Chapter 2** the variation in current dressing policies for donor site wounds in the Netherlands was studied. Only 32% of the responding centers had a wound dressing protocol. The five most commonly used dressings were: films (56%), alginates (46%), hydrofibers (32%), silicones (26%), and paraffin gauzes (19%). Alginates were mostly used for primary dressings (46%). Additionally, we formulated evidence-based recommendations for the local treatment of donor site wounds based on four available systematic reviews. Based on these results, dressings that create a moist wound environment seemed preferable to non-moist dressings. The lack of evidence-based guidelines on the treatment of donor site wounds calls for an evidence-based guideline on acute wound care, including donor site wounds. This guideline may decrease the variation in wound care and increase the quality of care for such wounds in the future.

The absence of a useful and reliable classification tool may also be one of the reasons why current dressing policies are not standardized. Therefore, in **Chapter 3** we investigated whether the well-accepted Red-Yellow-Black (RYB) scheme was useful for the uniform classification of donor site wounds. Although the RYB-scheme has been validated for classifying chronic and acute wounds, this is not yet the case for donor site wounds. We invited internationally recognized wound scientists, surgical doctors, specialized wound nurses and surgical nurses to judge digital photographs of donor site wounds in various stages of wound healing. Inter-observer agreements among specialized wound care nurses were only moderate. However, agreement tended to be better than that measured amongst scientists, doctors and nurses. Apparently, clinicians and scientists have difficulties classifying donor site wounds by means of the RYB-scheme. Therefore, this scheme does not appear to be useful for the uniform classification of donor site wounds.

Another reason for variation in wound care practice could be a lack of convincing evidence for the effectiveness of different dressing materials. **Chapter 4** addressed the available evidence on the effectiveness of six commercially available dressings to treat patients with donor site wounds after split-skin grafting for any indication. These

dressings included alginates, gauzes, films, hydrocolloids, hydrofibers, and silicones. Evidence from 18 presently available randomized clinical trials (RCTs) showed that gauze dressings have been best studied, but should be avoided as they lead to longer healing times and higher pain scores. Hydrocolloids and films have been relatively well studied and tended to appear effective in terms of wound healing and pain relief. However, a large well–designed trial is warranted to corroborate this recommendation. The design and conduct of RCTs in wound care are considered challenging given the variety of wound types, dressings and patients, therefore, we set out to formulate the minimum requirements for proper RCTs in wound care and designed a framework to deal with methodological problems (**Chapter 5**).

Due to the large practice variation in treatment policies (**Chapter 2**) and the paucity of evidence as found in the systematic review (**Chapter 4**), we designed and conducted a new RCT using the framework developed in **Chapter 5**. The trial protocol and the results of our 14-center 6-armed RCT, entitled the "Rembrandt trial", are described in **Chapter 6** and **Chapter 7**. The acronym stands for "Recognizing Effective Materials by Randomizing and Assessing New Donor Site Treatments". We compared the five most commonly used dressings in the Netherlands (alginates, films, gauzes, hydrofibers, and silicones) combined with the most promising dressing from the literature, namely hydrocolloids. In this trial we recruited 289 patients. Time to complete re-epithelialization using hydrocolloid dressings was one week shorter than the time required by the remaining five dressing types. Overall pain scores were low and slightly lower than those reported with film dressings. Patients treated with gauze had a two-fold higher infection rate of the donor site wound than patients treated with other dressings. Patients receiving film dressings were less satisfied about their overall scar quality. We are therefore able to recommend the use of hydrocolloid based on the shorter wound healing time and low infection risk, whereas gauzes should be avoided due to an increased risk of infection.

In the "Rembrandt trial" we found that although patients treated with films were less satisfied about their scar quality, caregivers did not show any differences in satisfaction among the different dressing groups. Therefore, in **Chapter 8** we measured to what extent caregivers and patients agree on the cosmetic outcomes of the scar caused by the donor site wound. For this purpose we used the Patient Observer Scar Assessment Scale (POSAS) and investigated which POSAS-items are most associated with the overall cosmetic satisfaction of patients as well as caregivers. Health care professionals and patients classified the donor site scar in vivo using the POSAS, which comprises seven items. Inter-observer agreement for the POSAS-items was 'moderate' at best regarding the item 'overall opinion'. Agreement regarding other POSAS-items was 'poor'. Itching and relief best predicted patient's overall satisfaction. For caregivers, however, pigmentation and pliability were most predictive. Apparently, patients and caregivers appreciated different aspects of scar characteristics as indicated by their

POSAS responses. Therefore, patient preferences should be considered in decision-making on wound treatment and scar prevention.

In this thesis we generated new knowledge, which should be employed by all stakeholders in wound care. Therefore, in **Chapter 9** we carried out a national survey to investigate the awareness and use of available evidence on antiseptics and wound dressings amongst 262 stakeholders. Doctors preferred conventional antiseptics (e.g. iodine), while specialized nurses and manufactures favored popular products (e.g. silver). Most stakeholders considered silver-containing products to be evidence-based antiseptics, which contradicts scientific results. In particular, surgical nurses and manufacturers were unaware of, or had never used, the Cochrane Library. These results show that available high-quality evidence in wound care is not equally internalized by the various stakeholders, despite this being a requirement of evidence-based decision-making. Although the awareness and use of evidence was higher among specialized nurses than surgical nurses and manufactures, the competencies and educational levels of these nurses differ widely. In **Chapter 10**, we undertook a three-round e-Delphi study among healthcare professionals in six European countries, to reach a consensus on the desired core competencies for specialized wound care nurses. Results indicated that competencies related to professional knowledge and expertise, ethical integrity, and patient commitment were considered the most important. These competencies may be helpful in the future, when the boundaries of the responsibilities of nurses will change and task substitution with doctors is likely to occur.

Overall, based on the findings in this thesis we advocate a more systematic production and use of scientific research in the daily practice of healthcare professionals, which will likely improve the quality of patient care. There are many opportunities and challenges for evidence-based wound care. Although quite a feat, this is well worth the challenge!

Chapter 13

Summary in Dutch

SAMENVATTING

Zorgverleners dragen de verantwoordelijkheid om beslissingen van de best mogelijke kwaliteit te maken. Deze beslissingen zijn direct van invloed op de gezondheid van de patiënt. Echter in de dagelijkse praktijk is het onduidelijk wat goede kwaliteit exact inhoudt. Dit is voornamelijk het geval op het gebied van wondzorg. De kwaliteit van zorg wordt beïnvloed door de grote variatie in wondtypes, persoonlijke voorkeuren van artsen en verpleegkundigen en de competenties waarover de zorgverleners beschikken. In deze situatie is het aannemelijk dat deze variatie kan leiden tot suboptimale zorg voor patiënten met wonden en is het een ware uitdaging om evidence-based beslissingen te nemen. Dit proefschrift draagt bij aan de kennis en promotie van evidence-based besluitvorming om verschillende vormen van variatie te verminderen in wondzorg.

In **Hoofdstuk 2** wordt een grote variatie tussen en binnen Nederlandse ziekenhuizen in de lokale behandeling van donorplaatsen na split-skin grafting beschreven. Slechts 32% van de deelnemende centra bleken een protocol voor de behandeling van de donorplaatsen te hebben. De vijf meest gebruikte materialen waren folies (58%), alginaten (46%), hydrofibers (32%), siliconen (26%) en gazen (19%). Als primair verband werden alginaten het meest gebruikt (46%) en als secundair verband folies (27%). Vervolgens hebben we op basis van vier gevonden systematische literatuuroverzichten een evidence-based aanbeveling kunnen doen: verbandmaterialen die een vochtig milieu creëren zijn aan te bevelen voor de behandeling van donorplaatsen. Er ontbreken echter richtlijnen voor de behandeling van donorplaatsen en daarom pleiten wij voor een evidence-based richtlijn gericht op acute wonden, inclusief donorplaatsen. Deze richtlijn zou de variatie in wondzorg kunnen verminderen en de kwaliteit van zorg voor dit type wonden in de toekomst verbeteren.

De afwezigheid van bruikbare en betrouwbare classificatieschema's is mogelijk ook één van de redenen waarom de huidige behandeling nog niet gestandaardiseerd is. Vandaar dat wij in **Hoofdstuk 3** onderzochten of het Rood-Geel-Zwart schema bruikbaar is om donorplaatsen op een uniforme manier te beoordelen. Het Rood-Geel-Zwart schema is een bekend en gevalideerd schema om chronische en acute wonden te classificeren, maar nog niet voor donorplaatsen. Daarom nodigden wij internationale bekende onderzoekers, chirurgen, gespecialiseerde wondverpleegkundigen en chirurgische verpleegkundigen uit om digitale foto's te beoordelen van donorplaatsen in verschillende fasen van het wondgenezingsproces. De beoordeling van de gespecialiseerd wondverpleegkundigen kwam redelijk overeen, maar chirurgen, verpleegkundigen en onderzoekers hadden er meer moeite mee. Hieruit blijkt dat het Rood-Geel-Zwart schema niet bruikbaar is om donorplaatsen op een uniforme manier te beoordelen.

Een andere reden voor praktijkvariatie is het ontbreken van overtuigend wetenschappelijk bewijs voor de effectiviteit van verbandmaterialen. In **Hoofdstuk 4** wordt het beschikbare wetenschappelijke bewijs over de effectiviteit van zes commercieel beschikbare verbandmaterialen (alginaten, gazen, folies, hydrocolloïden, hydrofibers en siliconen) beoordeeld voor de behandeling van donorplaatsen na een split-skin graft. Op basis van 18 gerandomiseerde klinische trials (RCT's) bleken gaasverbanden het meest onderzocht te zijn. Gaasverbanden zorgen echter voor een langere wondgenezingstijd en hoge pijnscores. Vandaar dat gaasverbanden voor de behandeling van donorplaatsen afgeraden moeten worden. Ook hydrocolloïden en folies zijn redelijk onderzocht. Deze verbanden lijken effectief te zijn in het versnellen van wondgenezing en het verminderen van pijn. Vanwege het gebrek aan sterk bewijs is er behoefte aan een goed uitgevoerde RCT om deze bevindingen te onderbouwen. Het ontwerpen en uitvoeren van RCT's in wondzorg is een uitdaging omdat er een grote variatie is in wondtypes, verbandmaterialen en patiënten. Daardoor hebben we getracht de minimale vereisten voor goed uitgevoerde RCT's in wondzorg te beschrijven en een schema gemaakt hoe om te gaan met de belangrijkste methodologische problemen (**Hoofdstuk 5**).

Vanwege de grote variatie in behandelopties (**Hoofdstuk 2**), de gebrekkige hoeveelheid bewijs gevonden in het systematische literatuuroverzicht (**Hoofdstuk 4**) en gebruikmakend van het opgestelde schema (**Hoofdstuk 5**), hebben we een nieuwe RCT opgezet en uitgevoerd. Het protocol en de resultaten van de 6-armige RCT, uitgevoerd in 14 centra, genaamd "de Rembrandt trial", staan beschreven in **Hoofdstuk 6** en **Hoofdstuk 7**. Het acroniem staat voor "Recognizing Effective Materials by Randomizing and Assessing New Donorsite Treatments". In deze studie vergeleken we de vijf meest gebruikte verbandmaterialen in Nederland (alginaten, folies, gazen, hydrofibers en siliconen) plus het meeste veelbelovende verband op basis van de literatuur, namelijk hydrocolloïden. In deze trial kregen 289 patiënten een behandeling toegewezen. Tijd tot complete wondgenezing was één week korter bij het gebruik van hydrocolloïden in vergelijking met alle andere producten. Over het algemeen genomen waren pijnscores laag en enigszins lager in de foliegroep. Patiënten die behandeld werden met gaasverbanden hadden een twee maal hogere kans op een infectie van de donorplaats in vergelijking met de andere behandelingen. Patiënten die behandeld werden met folie waren minder tevreden over de kwaliteit van het litteken. Op basis van deze resultaten bevelen we het gebruik van hydrocolloïden aan vanwege een snellere wondgenezing en een laag infectierisico. We raden gazen af in verband met het verhoogde infectierisico.

In de Rembrandt trial hebben we gevonden dat patiënten minder tevreden waren over het litteken bij het gebruik van folie. Deze verschillen werden echter niet bevestigd door de beoordeling van zorgverleners. Zij vonden namelijk geen verschillen tussen de verbandmaterialen in de kwaliteit van het litteken. Daarom

onderzochten wij in **Hoofdstuk 8** of de beoordeling van de cosmetische uitkomst van het litteken veroorzaakt door de donorplaats overeenkomt tussen zorgverleners en patiënten. Hiervoor maakten wij gebruik van een bestaande littekenschaal, namelijk de Patient Observer Scar Assessment Scale (POSAS), bestaande uit zeven items. Daarnaast onderzochten we ook welke onderdelen van deze schaal de algemene tevredenheid het meest beïnvloeden. Zorgverleners en patiënten classificeerden de littekens van de donorplaats in vivo. De beste interobserver-overeenstemming werd gevonden voor het onderdeel "algemene tevredenheid", maar de overeenstemming was slechts redelijk. De overeenstemming voor de overige onderdelen was zelfs slecht. Jeuk en reliëf voorspelden de algemene tevredenheid van patiënten het beste. Voor zorgverleners waren pigmentatie en plooibaarheid van het litteken de sterkste voorspellende onderdelen voor hun "algemene tevredenheid". Op basis van de POSAS blijkt dat patiënten en zorgverleners dus verschillende littekenkarakteristieken van belang vinden. Daarom moeten patiëntenvoorkeuren meegenomen worden in de besluitvorming omtrent behandelkeuzes en de toepassing van littekenpreventie.

In dit proefschrift hebben we nieuw wetenschappelijk bewijs gegenereerd dat ook bekend zou moeten zijn bij alle belanghebbenden in wondzorg. Om deze reden hebben wij in **Hoofdstuk 9** een nationale inventarisatie uitgevoerd bij 262 belanghebbenden bij wie werd nagegaan welke soort antiseptische verbanden in de praktijk als eerste keus gebruikt werden bij de behandeling van wonden. Verder werd onderzocht in hoeverre men op de hoogte is van het beschikbare bewijs voor het gebruik van deze verbanden. Artsen hadden een voorkeur voor conventionele antiseptische verbanden (bijv. jodium), terwijl gespecialiseerde wondverpleegkundigen en productexperts van wondfabrikanten een voorkeur hadden voor de modernere verbanden (bijv. zilver). De meeste betrokkenen beschouwden de zilverbevattende verbanden als evidence-based, wat niet in overeenstemming is met de wetenschappelijke literatuur. Vooral chirurgische verpleegkundigen en productexperts van wondfabrikanten waren niet op de hoogte van, of gebruikten nooit, de Cochrane Library. Deze resultaten geven aan dat beschikbaar wetenschappelijk bewijs in wondzorg niet bij alle betrokkenen voldoende bekend is, terwijl dit een vereiste is voor evidence-based besluitvorming. Gespecialiseerde wondverpleegkundigen waren beter op de hoogte zijn van beschikbaar wetenschappelijk bewijs. Echter bestaan er grote verschillen in competenties en opleidingsniveaus tussen deze gespecialiseerde verpleegkundigen. In **Hoofdstuk 10** hebben we een e-Delphi studie uitgevoerd om consensus te bereiken tussen zorgprofessionals over de ideale competenties die wondverpleegkundigen nodig hebben. Competenties gericht op professionele kennis en expertise, ethische integriteit en patiëntentoewijding werden het meest belangrijk geacht. De complete set aan competenties zijn mogelijk bruikbaar in de toekomst, omdat wondverpleegkundigen in toenemende mate te maken krijgen met nieuwe verantwoordelijkheden en taakverschuiving.

Gebaseerd op onze bevindingen in dit proefschrift pleiten wij voor een meer systematische productie en gebruik van wetenschappelijk onderzoek in de dagelijkse praktijk door zorgverleners. Dit kan de patiëntenzorg verbeteren. Er zijn veel mogelijkheden en uitdagingen in evidence-based wondzorg. Ondanks dat het een hele klus kan zijn, is het de uitdaging meer dan waard!

Appendices

Curriculum vitae

CURRICULUM VITAE

Anne Eskes was born in Zevenaar on the 28th of February 1986 and grew up in Didam, the Netherlands. After finishing secondary school at Liemers College in Zevenaar in 2003, she started studying nursing at the Saxion University of Applied Sciences in Deventer. During this study, Evidence-Based Practice aroused her interest.

Therefore, directly after obtaining her bachelor degree, she started her Master of Science education in Evidence-Based Practice at the University of Amsterdam. She combined this scholarship with working as a nurse on surgical and non-surgical nursing departments in different hospitals. She received her MSc-degree after finishing her final master thesis under supervision of Dr. Hester Vermeulen and Dr. Dirk Ubbink.

Then she started as a research assistant for the research group of the department of Quality Assurance and Process Innovation at the Academic Medical Center in Amsterdam. During that period, Dr. Hester Vermeulen and Dr. Dirk Ubbink supported and stimulated her to pursue her own topics for research. This resulted in several first-author publications and the start of her official PhD-training.

Throughout this PhD-period she was further educated in more advanced quantitative research methods and gained her BROK-certification (Good Clinical Practice (GCP), and the organization of research). Besides her research activities, she was also appointed as lecturer Evidence-based Practice and Implementation at the Amsterdam School of Health Professions.

Although the topic of her PhD-thesis mainly focused on wound care, she also has a broad interest in other health-related topics. Hence, after obtaining her PhD-degree, she intends to stimulate and inspire her colleagues and future nurses to apply Evidence-Based Practice in the daily care for their patients to enhance and ensure quality of care. For this purpose she looks for new opportunities to combine health care and research in the Netherlands and abroad.

Appendices

PhD Portfolio

PhD PORTFOLIO

Summary of PhD training, teaching and parameters of esteem

Name PhD student: Anne M Eskes

PhD period: July 2009 – December 2012

Name PhD supervisors: Prof. dr. PJM Bakker, Prof. dr. DA Legemate

Name PhD co-supervisors: Dr. DT Ubbink, Dr. H Vermeulen

1. PhD training

	Year	Hours	Workload (ETCS)
Master Evidence Based Practice	2007-2009		
Basis epidemiology and EBP – concepts and design		560	20
Elementary biostatistics		252	9
Advanced EBP systematic reviews and clinical guidelines		168	6
Advanced biostatistics and epidemiology		252	9
Clinimetrics		196	7
Health economics		168	6
Health care policy evaluation		196	7
Capita Selecta		168	6
Additional Courses Research Skills			
Advanced Topics in Biostatistics	2012	60	2.1
Advanced Topics in Clinical Epidemiology	2011	32	1.1
Basic course Law and Organization for clinical researchers (BROK), including ICH-Good Clinical Practice (GCP), WMO and the organization of research	2011	21	0.9
Developing a Cochrane Systematic Review	2008	8	0.3
EBRO course – guideline development	2011	8	0.3
Qualitative Health Research	2011	54	1.9
Research and Finance	2012	5	0.2
General Academic Skills			
Allround English	2011	45	1.6
Oral presentation in English	2012	22	0.8
Scientific Writing in English for Publication	2009	42	1.5
Handling the Media	2012	5	0.2
Seminars, workshops and master classes			
Master classes by Gordon Guyatt (n= 2)	2010 and 2011	8	0.3
Workshop Mindbugs	2012	2	0.1

International presentations			
EWMA conference			
Hyperbaric oxygen therapy for acute wounds; Geneva, Switzerland (oral)	2010	14	0.5
Current treatment donor site wounds – national survey; Geneva, Switzerland (poster)	2010	14	0.5
Use of evidence-based products in wound care; Brussels, Belgium (oral)	2011	14	0.5
Scar assessment donor site wounds; Vienna, Austria (oral)	2012	14	0.5
Ideal donor site dressings; Vienna, Austria (oral)	2012	14	0.5
SAWC conference			
Hyperbaric oxygen therapy for acute wounds; Dallas, USA (oral)	2011	14	0.5
Judgment donor site wounds – inter-observer analysis; Dallas, USA (oral)	2011	14	0.5
Sigma Theta Tau			
Scar assessment donor site wounds; Brisbane, Australia (oral)	2012	14	0.5
Use of evidence-based products in wound care; Brisbane, Australia (poster)	2012	14	0.5
Veith conference			
Delphi studies in wound care; New York, USA (oral)	2012	14	0.5
Other			
Journal club (1 per month; 18 in total)	2011-2012	42	1.5
Research meeting (1 per 2 months; 8 in total)	2011-2012	12	0.4

2. Teaching

	Year	Hours	Workload (ETCS)
Lecturing			
Continuing-education course Evidence Based Practice for nurses (beginner's course and advanced course) – Academic Medical Center, Amsterdam	2009-2012	80	2.9
Evidence based practice (all levels). Amsterdam School of Health Professions, Amsterdam	2010-2011	215	7.7
Implementation. Amsterdam School of Health Professions, Amsterdam	2010-2012	48	1.7
Lecturing courses			
Use of active learning strategies in the classroom	2010	4	0.2
Design of good exam questions	2010	2	0.1
Handling different ability levels in the classroom; how to deal with?	2010	2	0.1

3. Parameters of esteem

Prizes and awards:	The inter-observer analysis to classify donor sites according to the red-yellow-black scheme was rewarded with the prize for best oral abstract. 2010

NB. 1 ECTS = 28 hours, based on the European Credit Transfer System

Appendices

List of publications

INTERNATIONAL PUBLICATIONS

2012

Eskes AM, Brölmann FE, van de Kar A, Niessen FB, Lindeboom R, Ubbink DT, Vermeulen H. What do patients and caregivers value most about donor site scars? An inter-observer analysis between patients and caregivers and prediction of cosmetic satisfaction. Burns; 38(6):796-801

Eskes AM, Brölmann FE, Sumpio BE, Mayer D, Moore Z, Ågren MS, Hermans M, Cutting K, Legemate DA, Ubbink DT, Vermeulen H. Fundamentals of randomized clinical trials in wound care: design and conduct. Wound Repair and Regeneration. 2012;20(4):449-55

Eskes AM, Storm-Versloot MN, Vermeulen H, Ubbink DT. Do stakeholders in wound care prefer evidence-based wound care products? A survey in the Netherlands. International Wound Journal. 2012. [Epub ahead of print]

2011

Eskes AM, Gerbens LA, van der Horst CM, Vermeulen H, Ubbink DT. Is the red-yellow-black scheme suitable to classify donor site wounds? An inter-observer analysis. Burns. 2011:37(5):823-7

Eskes AM, Brölmann FE, Gerbens LA, Ubbink DT, Vermeulen H. Which dressing do donor site wounds need?: study protocol for a randomized controlled trial. Trials. 2011:12(1):229

Eskes AM, Ubbink DT, Lubbers MJ, Lucas C, Vermeulen H. Hyperbaric oxygen therapy: solution for difficult to heal acute wounds? Systematic review. World Journal of Surgery. 2011:35(3):535-42

2010

Eskes A, Ubbink DT, Lubbers M, Lucas C, Vermeulen H. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. Cochrane Database Systematic Reviews. 2010:6(10):CD008059

NATIONAL PUBLICATIONS

2012

Eskes A, Brölmann F, Ubbink D, Vermeulen H. Evidence-based behandeling van donorplaatsen na split-skin grafting. Nurse Academy. 2012;4(3)32-35

Vermeulen H, Maaskant J, Eskes A, Ubbink D. Implementeren van EBP op een verpleegafdeling. Nurse Academy. 2012;4(2)10-15

Eskes A, van Oostveen C, Vermeulen H. Is bij een blaaskatheter tweemaal daags een 'onderwassing' nodig? Nursing. 2012; March.

Eskes A, Tump E, Vermeulen H. Are Journal Clubs effective in supporting evidence-based decision making? A systematic review. Nederlands Tijdschrift voor Evidence Based Practice. 2012:10(1):13-14

2011

Tump E, Eskes A, Vermeulen H. Strengthening organizations to implement evidence-based clinical practices: a mixed methods study. Nederlands Tijdschrift voor Evidence Based Practice. 2011:10(1):14-15

Eskes A, Tump E, Vermeulen H. Interventions aimed at increasing research use in nursing: a systematic review. Nederlands Tijdschrift voor Evidence Based Practice. 2011:09(5):12-13

2010

Eskes AM, Gerbens LAA, Ubbink DT, Vermeulen H. [What is the most commonly used treatment for donor site wounds after split skin grafting: a national survey]. Nederlands Tijdschrift voor Heelkunde. 2010:20(2):66-9 Dutch

Eskes A, Nissink S, Vermeulen H. Vitamin C and vitamin E in pregnant women at risk for pre-eclampisia (VIP trial): randomised placebo-controlled trial. Nederlands Tijdschrift voor Evidence Based Practice. 2010:09(1)13-14

Eskes A, Vermeulen H. Home based versus centre based cardiac rehabilitation: Cochrane systematic review and meta-analysis. Nederlands Tijdschrift voor Evidence Based Practice. 2010:08(5):11-11

Appendices

Dankwoord (Acknowledgments)

DANKWOORD (Acknowledgments)

Dit is het laatste hoofdstuk van mijn proefschrift. Ook al is het 'mijn' proefschrift, zonder input van velen was dit niet mogelijk geweest. Vandaar mijn dank aan iedereen die mij heeft geholpen, op welke manier dan ook.

Dr. Hester Vermeulen en Dr. Dirk Ubbink

In april 2008 heb ik voor het eerst contact met jullie gezocht waarbij ik jullie het volgende voorgelegd heb: "*Ik ben op zoek naar een onderzoeksonderwerp en mijn vraag is of er mogelijkheden zijn binnen het AMC in Amsterdam. Mijn voorkeur gaat uit naar verpleegkundig wetenschappelijk onderzoek en indien mogelijk lijkt mij het opzetten en uitvoeren van een RCT een echte uitdaging.*" Een dag later al ontving ik van jullie een enthousiast antwoord. Dit was het begin van een intensieve en prettige samenwerking die uitmondde in een vaste aanstelling in 2009 als researchverpleegkundige. Vanaf toen kwam alles in een stroomversnelling. Ik kreeg van jullie veel kansen om mijzelf te ontwikkelen, onderzoek te bedenken en uit te voeren. Die RCT, waar ik in 2008 op hoopte, is uitgevoerd en was inderdaad een ware uitdaging!

Hester, ik bewonder je om je idealisme en doorzettingsvermogen om de verpleegkundige beroepsgroep op de wetenschappelijke kaart te krijgen. Als ik naar onze evidence-based club kijk waarin toch veel verpleegkundigen werkzaam zijn, denk ik dat er al een mooie stap gemaakt is.

Dirk, jouw geduld is echt enorm. Ook jou bewonder ik om je visie op het belang van evidence-based handelen in zowel de medische als verpleegkundige zorg. Ik mocht je altijd storen met vragen over onderzoeksmethodologie en statistiek. De plezierige discussies hierover waren voor mij erg leerzaam.

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Prof. dr. Dink Legemate en Prof. dr. Piet Bakker

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Fleur Brölmann & Louise Gerbens

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Catharina, Evelien, Jolanda, Lotte, Marja, Marjon

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Commissieleden, mede-auteurs, patiënten, zorgverleners, leveranciers

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Tom

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2013 wordt voor ons beiden een spannend nieuw jaar. Ik ben benieuwd welke plannen we allemaal gaan uitvoeren, want ja, we hebben er genoeg. Ik kijk uit naar de toekomst!