Evidence 'in', ignorance 'out': a dilemma for advanced wound care products

The recent European Wound Management Association (EWMA) position statement on evidence in wound management (Gottrup et al, 2010), and the National Prescribing Centre bulletin (NPC, 2010) on evidence-based prescribing of wound products have heated up some old chestnuts. Evidence is 'in', ignorance is 'out'! The challenge to the tissue viability lobby is either to admit that there is next to no evidence for using 'advanced wound care products,' or to do something to show that they are evidence-based. The NPC bulletin (2010) writes that: 'Systematic reviews of advanced wound dressings have repeatedly highlighted the paucity of high-quality studies using clinically relevant endpoints.'

They are correctly stating the obvious, but this should not imply that such a lack exists only in wound care. A lot of what they write is adjectival: belying a non-scientific use of language. What is a 'poor quality' study? What would 'high quality' mean? What would a clinically relevant endpoint be? For the authors, a clinically relevant endpoint in a patient who shrieks with pain when her dressing is removed would be that the next dressing does not stick and that it contributes in some way to the relief of pain. Clearly, the dressing would complement investigating and treating the aetiology of the pain. Here, a suitable endpoint is pain reduction. Simple chemistry or physics would show, repeatedly and reliably, that an adhesive dressing is more likely to stick to periwound skin than one without adhesive.

Dressings are chosen by experts because they know what properties they want to exploit in particular instances, not because published data has been pooled into a meta-analysis. However, we can no longer assume that what is taken to be a foam is actually a foam (Sussman, 2010). Is there really such a thing as a generic hydrocolloid any more? So, it is likely that, whereas you can confidently state what the generic formula of aspirin is, you cannot say the same about wound care products. Thus, you are never going to compare like with like.

Until it is possible to specify what property of a dressing you are testing (moisture vapour transfer rate, acidity, etc), meaningful distinctions cannot be drawn between products. We need to know what our 'target' is to judge whether it has been affected or not. The endpoint called 'wound healing' sounds as if it is a single physiological target, but it is not. Wound management is about dealing with a sequence of multiple micro-targets. Even the doyenne of 'evidence-based' care had a much more nuanced view of what evidence is (Sackett et al, 1996), so must we.

RW/MM

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We are advised that RCTs, and meta-analyses of them are essential for the evidence base in wound care. However, in the absence of such studies, what level of evidence is realistic for wound care?

MM: I would say that level three evidence is realistic for wound care: namely, evidence from well-designed trials without randomisation. However, practitioners should know the properties of materials and select the appropriated tool for the job. For example, if you do not want a dressing to adhere to the wound, do not choose one such as paraffin tulle but use something with properties that minimise the likelihood of adherence. This is a matter of physical science, physics if you like. The decision is based on knowledge and on the experience of seeing the dressing in action, quite the antithesis of a 'blinded' trial.

CI: We are starting from where we are. In time, randomised controlled trials (RCTs) and meta-analyses may become available, but until then we need research that is well-constructed and reliable. Single patient case studies or small outcome evaluations are of little or no use because they do not give a big enough picture.

Increasing their size and improving their methodologies so that they are more trustworthy could be a legitimate halfway point.

There exists a detailed hierarchy of evidence, but it is inflexible. Where do we in wound care want our evidence to be in the current hierarchy of evidence?

MM: I think the problem arises from the idea that there is a hierarchy of evidence in the first place. At first glance it sounds reasonable to rank information so that it helps clinicians to take a less emotive view on what to do in practice. But, the very word 'hierarchy' means that priestly power is attributed to something. Thus, a group of insiders determine what is allowed or not. This preserves control from within the inner sanctum (scientists not priests). So, scientists are not biased or ignorant. 'Statistics' is the appointed judge of what is correct or incorrect. Given that statistics are thought to be intrinsically neutral (and scientific), they are given primacy at the top of the hierarchy of evidence. So, the radical answer to this question of where we want to be in the current hierarchy is — outside it!

CI: Isn't the real issue the quality of the evidence? A badly designed or conducted RCT is useless, whereas a well-conducted outcomes study provides real world, relevant findings.

Outcomes studies are ranked at level 2 currently, yet many clinicians and health economists value them much higher. Similarly, pragmatic trials are also highly valued in some quarters. What is the value of such studies in guiding practice, and would you like to see more of them?

MM: I agree that one should have at least a major outcome in mind when embarking on a course of wound treatment. However, if you do not reach that outcome (or stages along the way) you decide whether the treatment was appropriate or not. The only way you recognise the value of a product is to continually review your objectives as the wound changes. Thus, there are a series of outcomes, not just one. The endpoint could be epithelialisation if the patient is physiologically capable of healing. Outcome studies would be of higher value if they described what happened to the wound/patient on the way towards the major outcome.

CI: As long as they are done well. The challenge is to design them to make sure all the variables other than the treatment are considered. In that way we know whether it was the trial product or a parallel intervention (e.g. dressing or compression) that worked or failed.

I do not agree that there are too many variables in complex patients to make results comparable. What we have to do is anticipate them and make sure that they are represented in the study population, so that we know whether something has a different effect for patients with different comorbidities.

If we must do RCTs, who should pay for them? Industry or the NHS/private healthcare/charities? (This could mean that the cost, if borne by industry, would entail a resultant price increase. A study on the scale of VULCAN [Michaels et al, 2009] would take three years to conduct and cost £500,000)?

MM: I do not think we must do RCTs. I do not base my practice on statistical formulae. Rather, I judge what is happening to the individual I am treating. If dressing A adheres, I change one or more of the parameters. For instance, if it is sticking because it is allowed to dry onto the wound, then more occlusion is needed until the next dressing change. Nevertheless, if someone is trying to 'sell me' a product, I would want them to have tested it, to define the features of their product, to explain what it adds to the armamentarium, and to have sufficient '*in vivo*' examples to assure me that 'it does what it says on the tin'. Perhaps the only way to ensure quality is for companies to do what they did in the past, which was to pay for evaluations to be done by established groups such as the Wound Healing Research Unit in Cardiff. A national centre for the development of clinical evaluations in wound care would be a good investment.

CI: The cynic in me says the manufacturers should pay — after all, they are the ones who are going to recoup the investment financially. The problem is that they may not be prepared to make the investment and smaller companies may simply be unable to afford it.

Of course, we also benefit if improved outcomes result in lower total treatment costs, so why not use the universities to establish research collaborations involving industry and care providers. There is currently provision for NHS organisations to apply for research funding as long as the proposed study has been submitted to and accepted in the National Institute of Health Research (NIHR) portfolio. However, this is not an infinite resource and collaboration would be a way to share costs.

MM: *The decision is based on knowledge and on the experience of seeing the dressing in action, quite the antithesis of a 'blinded' trial.*

CI: *I would like to see original research with industry, clinicians and universities all represented and sharing the workload.*

If RCTs are considered essential, which trials are required? Will every new treatment need a trial on all indications?

MM: I do not think they are. We have to start to examine the classification of wound materials in more detail, then to judge where a product should be placed in terms of performance. For example, if a product is more acidic than alkaline, this should be specified. Again, if a semi-permeable film is high in vapour permeability, just how high is it. These attributes should be tabulated so that a practitioner can decide to opt for one or other on the basis of expected performance.

CI: New approaches or substances that have not been used before should be as rigorously tested as possible to ensure that they are effective and safe. Once that has been done, there should be no need to repeat it with a 'me too' product as long as they are close enough in composition.

As users, we need to be able to consider and assimilate evidence in a more constructive way. For instance, if we know how an antimicrobial agent works on one organism, we can extrapolate the likely effects of that action to estimate what effect it would have on bacteria of the same or similar types which should be equally susceptible to it.

Who will conduct the trials, given that tissue viability nurses are so busy? Will it be contract research organisations, if so, the cost will increase even further.

MM: As I mentioned above, let us work towards nationally recognised centres for evaluation. These will be able to provide systematic information.

CI: Once again, a collaborative approach could deliver significant benefits. I would like to see original research with industry, clinicians and universities all represented and sharing the workload. Research is, after all, often included in specialists' job descriptions, but do we really live up to that obligation?

Studies could then be constructed to allow for the practical factors that are important to users in addition to therapeutic outcome. Including academics and statisticians should also reduce the problems with flawed methodologies that invalidate so much of what has been done previously. To some extent this already happens, but there is always the risk of bias being alleged as a result of working closely with industry, and, until this approach becomes normal, that is likely to continue. WUK

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