DOI: 10.1111/iwj.13202

ORIGINAL ARTICLE

WILEY

Estimating the economic value of emerging technologies in chronic wound therapy

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Abstract

Estimating the economic value of emerging technologies in clinical medicine presents a number of problems. New technologies may have a limited clinical history, few supportive peer-reviewed publications, and only anecdotal evidence as they enter the market and seek clinician approval and reimbursement from payers. Although clinical efficacy/effectiveness research is a minimal starting point for making the case for adoption of a product, establishing a competitive costeffectiveness position against other products and establishing the case for economic value must be made as well when presenting to health plans or other payers. Economic valuation methods have been well developed in the business community. Reviewed here are the components of a well-crafted case for the economic value of a product in general and in the wound industry specifically, in a multidomain approach to demonstrate values using demographic, clinical, financial, operational, and intangible assessments.

KEYWORDS

chronic wounds, cost effectiveness, economic, outcomes, value

1 | INTRODUCTION

Chronic wounds present common aetiologies, high complication rates, high treatment costs, and long-term recidivism with recurrence. Given that wounds can present multiple, synergistic drivers of health cost, it would seem self-evident that any technology that can effectively and definitively treat wounds would be cost effective. However, emerging wound treatment technologies struggle initially to gain a foothold in both their adoption by clinicians and in their reimbursement by health plans and payers. To be successful as product strategies, they need to exceed, even excel, at both. An ability to separate evidence-based support on the efficacy and safety of a product from opinions or non-validated beliefs lies at the heart of the success of these efforts. However, developing the level of evidence necessary to do so can be problematic. Assessing the added economic value in addition to clinical value can be even more difficult. Health plans and government agencies have encountered this issue with respect to other clinical breakthroughs, devices, and even disease management programmes.^{1,2} Reviewed here is how some of those approaches that may be applied to the wound care product environment.

Health economists have faced a number of challenges in evaluating emerging technologies. Economic analyses are best performed with total costs over time and at multiple sites of service. Anecdotal case examples or small case series are clearly insufficient to support clinical decisionmaking or an informed product review. Multicentre, randomised controlled clinical trials require significant effort and cost and typically address only initial treatment and results in a defined homogeneous population and for a

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defined time period. This is difficult with the fragmented data collection system in place, with different shifting payers, changing benefit plans, non-interoperability of information, and so on.

At a macrolevel, current large economic analyses are often limited to the use of claims data or large registries, which present a number of practical problems. Emerging technologies may not have established coding or sufficient market presence to establish minimal exposure for statistical analysis. Longitudinal data are required for a cohort of individuals if long-term outcomes are to be known. This is unavailable for most patients of non-Medicare age but is essential for assessing real outcomes and/or connecting results across several episodes of care or sites of service for chronic disease. Claims data does not always capture important endpoints such as death, which is located elsewhere in tables that cannot be linked to claims, or more nuanced clinical information such as severity. Claims data also are only useful for measuring the cost of individually reimbursed services and do not capture non-reimbursed services, capitated services, or the services of individuals using other payers or systems. "Episode of care" approaches are weak for chronic diseases that persist across many months (such as diabetes), and non-claim information is frequently not standardised, unreported, unable to be integrated, and so on. The list goes on. Informatics tools are only as good as the underlying data, which demonstrate a number of such issues.

Other issues relate to the ability to statistically evaluate health outcomes. Natural variation in both clinical manifestations of disease and costs is a major issue in proving effectiveness. Due to their skewness, cost data often display more



FIGURE 1 Example of the Markov model diagram illustrating the potential "states" one can move to from an initial "state" of diabetic foot ulcer. Rates of movement between the states can be calculated, as can the cost of an episode of care provided for each state. The sum of the overall costs for a period of time under different treatment scenarios can thus provide an estimate of cost savings by noting the differences in total costs under various scenarios

Key Messages

- estimating the economic value of emerging wound treatment technologies is a difficult challenge that can be addressed using existing valuation techniques
- this article develops an analytical structure for composing an economic value statement for an emerging wound care product
- the approach presented uses a multidimensional approach for valuation that would be useful in medical policy review, health plan evaluations, and other purposes to develop an economic analysis in the absence of complete information
- the approach builds on business valuation principles in health care that combine domains in demographics, clinical knowledge, utilisation management, operations assessment, financial analytics, and the effect of intangibles in a value proposition
- the approach can be used by vendors, health plans, and governments to create an optimised valuation review

variability than clinical variables and thus require larger samples for making valid inferences.³ Because of both high disease variation and small effect size, chronic wound trials in particular typically require hundreds of patients to confirm a statistically significant effect by a new product over standard of care.

Finally, there are a number of practical considerations in evaluating the efficacy and effectiveness of emerging technology in the "real-world" environment. There is no general consensus on a standard tool or checklist to assess the cost of illness in wounds.⁴ We also know that "real-world" data from claims databases may misrepresent the emerging technology in wounds since products may not be used properly (eg, weekly with good debridement), patients show selection bias, no or improper controls are used, and so on.^{5,6}

Although the assessment of the true economic contribution of an emerging technology or specific procedure is complicated, it *is* possible, and a number of approaches have been advanced. Economic valuation methods are well known in business circles—an integrated approach is needed to address multiple outcome measures.

The word economic is used here in the broader sense, which includes other estimates of "value" besides simple "return on investment" or accounting definitions of worth. This approach to an economic analysis of a health

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technology proceeds across multiple domains, each of which presents the various elements in product value validation.¹ In the wound care space, this is done to portray the rich texture of the value provided by products and involves the following domain categories:

- *Demographic information relevant to the analysis*—A correct population definition and the scope and impact of chronic wounds at the individual level, for example, must be defined to develop definitions, population level scope, and impact estimates.
- *Utilisation-related statistics and impact*—Service usage rates determine both resource use and cost. How often problems occur and how utilisation is currently being managed and tracked temporally provides a second piece of the puzzle.
- *Clinical efficacy: performance of the material*—This is the "medical policy question." Efficacy or proof that something works in ideal circumstances is a minimum requirement needed to approve reimbursement.
- *Clinical effectiveness: Outcome measurement in actual practice*—Measurement variables in clinical trials and in claims data can assess economic impact, but developing good ones can be a complex task.
- Financial statistics/return on investment (ROI) impact— Financial information, often registry or claims based, is needed to estimate overall costs. Ideally, emerging technology should offer an estimated return on investment or at least define a value that warrants adoption.
- Operational savings—Practical operational advantages provide economic value by improving practice efficiencies as well. Value is defined in terms of adding speed to the delivery of health care or improving patient throughput, *without* adding delays or complexity of service delivery.
- *Intangibles*—Benefits to patients and the system may not be readily apparent. In the absence of truly measurable metrics, value is typically obtained from "willingness to pay" (WTP) estimates in these cases. The commercial or marketing definition of this concept refers to the maximum price an individual would pay for a service or item based on its utility. For example, one might pay as much as \$1000 for a wound treatment if it would provide a definitive cure, without being able to accurately calculate what that is financially worth.^{7,8} A more academic assessment of WTP might similarly postulate a price per quality-adjusted life-year (QALY) threshold using an incremental cost-effectiveness ratio (see later).

To further elaborate on each of the above domains, consider the following.

2 | **DEMOGRAPHICS**

One of the most significant drivers of economic impact of any technology is the underlying demographics of the diseases being treated. The key questions are, "Who is affected and how many are impacted? It is important to define terms carefully-simply pulling claims for "diabetes" from a claim database can identify a significant number of false-positively labelled individuals (as much as 20 to 50% or more), and detailed algorithms are necessary.^{9,10} It is well known that as little as 5% of the population can drive as much as 50 %of health care costs.¹¹ Current technology options for wounds focuses on lower extremity diabetic ulcers and venous leg ulcers, both highly prevalent problems in the population. Diabetes is present in approximately 8.3% of the population, with some subpopulations demonstrating numbers as high as 50 to 70%.^{12,13} Populations with higher levels of illness (eg, Medicaid, Medicare, seniors, blue collar groups) will have magnified effects of illness impacts on costs also due to the increased number of correlated comorbidities in these populations, to change costs by as much as 10-fold.^{14,15} Lower extremity ulceration is a common complication for patients with diabetes, affecting some 15% of individuals with Medicare claims each year and with a lifetime risk as high as 25%. Lower extremity ulcers are found in up to 85% of diabetic amputations.¹⁶ Venous leg ulcers similarly are similarly common and also associated with increased morbidity and mortality through the development of cellulitis and hospitalisation for complications.¹⁷ By even conservative measures, and only in the categories of diabetic and venous leg ulcers alone, the number of affected individuals with lower extremity chronic wounds alone runs in the millions.¹⁸ Proving that any new or emerging technology can impact these statistics will be significant, particularly at the health plan level.

Demographic analysis can also include market share analysis. Rapid uptake in the market with replacement of existing products may be due to an intensive marketing campaign, but may also be related to improved performance of the product. Proving the latter can add a further statement of "value."

3 | UTILISATION

A second driver of health care costs is the utilisation of services within the disease demographics. Economic impact is driven by the number of affected people times the total cost of the care they require across various services. Nussbaum et al performed a comprehensive analysis of Medicare claims data and found the actual amount in the case of wounds that is probably underestimated by current common calculations; the total cost of wounds in the United States is as much as \$96 billion annually.¹⁹ Costs were noted to be higher than historically noted in their study due to a more comprehensive Medicare claims database review, including inpatient and outpatient claims and a broader definition of wounds. Efforts by any technology that can impact this amount for wounds by decreasing utilisation, even by a small percentage, present a significant value.

A related need here is to define the conditions and terms of product adoption, payment, and use. Clearly, there are cost savings associated with negotiating the price and cost of delivered services. Anticipated issues with overuse, underuse, misuse, and abuse of new technologies also need to be addressed to assure proper adoption of the technology, and an accurate measure of economic impact. These issues occupy a significant part of the analysis carried out by payers who must monitor societal uptake of new technology, assure proper use, define payment levels, and assess the outcomes. Health plans rightly focus in on these issues as they refine the guidelines for appropriate product reimbursement.

4 | CLINICAL IMPACT

Positive economic impact necessitates that a product in fact works. Clinical impact is often considered in two parts. First is the *medical policy* question, or proof of concept, that historically was often separated from the issue of product cost and considered first. The primary concern here is whether a new treatment is efficacious. Proof of concept has become an incredibly onerous task, with Medicare, health plans, the FDA and others requiring multiple clinical trials, exhaustive research, and a review process that requires dozens of reviews, elaborate evidence requirements, and multiple committees and opinions to conclude whether something works. In the end, it reduces to the simple question, "Does the technology lead to clinically meaningful improvements in outcomes?", which can be initially answered with basic evidence for market entry.

Clinical impact is often supported with basic science or preclinical studies that confirm that the suspected underlying mechanism of action of the product in question in fact makes. Current science, for example, strongly supports the biochemical activity in amniotic membrane allografts that induce various cell effects at the local level and that demonstrate cell proliferation, cell migration, and stem cell activation by amniotic membrane itself in the wound environment in a way that confirms and underscores the clinical impression.²⁰⁻²⁶

The second part of the clinical impact issue is the *medical quality* question, "How do you measure the outcomes that are produced?" Outcome measurement of emerging technology impact is typically multifactorial, and ranges from hard numbers, such as a lab measurement, to softer impacts such

as patient preference, patient satisfaction, "safety profile," and quality of life impacts. For a technology to be truly useful, it must deliver values in a way that is clinically significant as well as statistically significant and across several domains. A listing of impact measurements contributes to the overall economic value assessment and should be provided and investigated as part of a vendor's analysis.

5 | FINANCIAL EVALUATION

In the case of a new product, financial cost savings in various new wound therapies accrue from a number of validators including the following:

- Lower product cost than competing alternatives such as composite synthetic skin substitutes.
- Improved quality and time to healing to reduce total care costs and the number of clinic visits required.
- Lower wastage through the ability to manufacture various sizes as needed.
- Lower comorbidity complication rates due to reduced open wound time exposure.

Accounting methods prevail, but precise, "hard dollar" financial estimates of the short- and long-term impact of wound treatments have been difficult to define for various reasons. It is difficult to report with certainty that investment of "xxx" additional dollars of wound treatment results in "yyy" additional dollars of cost savings. "Soft dollar" or broader estimates are easier and typically used for general estimates. Statistical samples of hospitalisation costs, average clinic costs, and so on, are combined to create ballpark estimates of wound treatment costs, which can be substantial. Driver et al have demonstrated that aggressive wound therapy programmes can reduce amputations.²⁷ Given that an amputation can cost as much as \$65 000, Dr Driver makes the case that attention to wound healing is cost effective at an absolute level. This approach is a good starting point in getting to the highest cost wound complication.

Issues of *cost-effectiveness* are addressed when emerging technology is compared with existing strategies to determine whether there is an advantage in adoption. "Costs" of treatment here refer to the recorded amounts paid, which are typically different from the prices charged. "Cost-effectiveness" further adds a connection between the cost for a service and the value delivered, often in comparison with a benchmark or standard of care. Researchers look for emerging technology that, given the same cost, is more effective, or given the same effectiveness is cheaper. These technologies are therefore more "cost effective." For more complex calculations involving *both factors*, "efficient frontier" or "effectiveness plane" concepts have been used, integrating both concepts

into an evaluation that incorporates varying levels of cost and quality. This approach has been employed when comparing more than two treatment options, one or more of which is dominated by others. But more often, cost and outcome estimates are used to calculate the *incremental costeffectiveness ratio* and the ratio is compared with a threshold, usually \$100 000 to \$200 000.²⁸⁻³⁰

6 | SIMULATION MODELS FOR FINANCIAL IMPACT ASSESSMENTS

The absence of total cost data, longitudinal claims/clinical data, and sufficient linkages to complication rates makes it difficult to compute the full impact of emerging technology in the wound industry. One solution frequently used in health care includes the use of simulation models.³¹ These models examine how a patient with a clinical condition (eg, wound) at one point in time can move to different future states within a fixed time period, such as a year. Subsequent "states" for example, might include healed, unhealed, cellulitis, hospitalisation, amputation, and even death. In Markov models, the rates and probabilities of progressing to each of these states can be estimated from available data sources, and the cost of being in each state can also be estimated (See Figure 1). Thus, a simple model may look at progression from having a wound to several future states within a given time period where the wound has healed or progressed. The cost for each of the outcomes as the rate per 1000 individuals could be estimated, and then summed to predict the total cost of the original disease, in this case a diabetic foot ulcer. Graphically, this might be represented as follows:

Comparing the models under various scenarios whether the emerging technology (eg, a new wound treatment) is used, with appropriate model adjustments, then permits a comparison of total costs under both scenarios. The more accurate and complete the model, the more accurate would be the cost estimates. This approach has been used in the wound care industry before and is an accepted method of comparing cost and quality outcomes.³²⁻³⁷

Simulation has been used in wounds to examine the impact of proper clinical care on outcome measures. Ragnarson et al concluded from such a model that "An intensified prevention strategy including patient education, foot care, and footwear is cost-effective if the risk for foot ulcers and lower extremity amputations can be reduced by 25%."³³ These models can become considerably complicated, as the study indicates. Other models have looked at the specific impact of various approaches on cost-effectiveness in the treatment of ulcers. Lawrence expanded on the concept with financial models looking at amputation prevention, finding that relatively low-cost procedures can result in the avoidance of significantly costlier events in

patient care.³³ Barshes et al have also looked at cost savings through the adoption of primary prevention in diabetic foot ulcer patients.³⁷ Using a Monte Carlo simulation and Markov state model, they simulated the 5-year survival, incidence of foot complications, and total health care costs in a hypothetical population from available data, and noted significant values in the adoption of primary prevention measures.

Simulation approaches permit an estimate of financial impact in the absence of a full claims data set with all claims over a long longitudinal timeframe, but permits reasonable estimates of the economic impact of various scenarios on specified cost outcomes.

7 | OPERATIONAL ADVANTAGES

Operational value to the clinician with emerging technology accrues when the introduced technology is not disruptive to the regular work flow in the delivery system. Although occasionally a disruption is well worth it, as occurred in the development of outpatient surgi-centers in lieu of hospitalisation, simple integration of technology is preferred. In the case of amniotic membrane allografts, for example, historical use was cumbersome, requiring proximity to a labour/delivery unit and an inability to preserve the material. The development of other allografts and/or synthetic tissue grafts offered one solution, but more complex storage and usage requirements were needed. Preservation methods improved the stability of amniotic tissue, shifting us back to that modality in many clinics and practices that have now placed this material into the routine wound clinic environment. Minimal storage requirements have offered an improvement over perishable synthetic biologicals that required refrigeration, where wastage levels were high and application techniques with newer materials do not disrupt clinic work flow. This improved ease of implementing the technology makes it both less expensive from an operational perspective and easier to increase adoption, hence presenting higher economic value.

8 | INTANGIBLE BENEFITS

The best way to think about intangible benefits is to consider the following: If you spent \$10 million dollars on a programme or device and you saved \$10 million in health care costs, would you still do the project? Technically, it is somewhat of a poor investment, with only a 1:1 return. Yet, you still might see a lot of additional values in intangible benefits that while hard to quantify, this needs to be somehow added into the estimation of value. These might include the following: \perp WILEY_ \square

- Improved patient's satisfaction with care, and less work for the patient, faster healing, medical coverage, and so on. This is an economic benefit to wound centre managers who are looking to differentiate value of the centres from routine care, or who are operating under capitated payment schemes.
- Improved overall health and function of the patients, with lower rates of complications, future costs, job loss, caregiver requirements, rehab costs, and so on. Qualityadjusted life-years (QALYs) are often used in this type of evaluation.
- Improved public relations—an employer or health plan can claim that they provide therapies that are "on the frontier of specialty care."
- Employers' desire coverage from one offering if other offerings do, often called "benefit equality."
- Improved healing means return faster to normal activities—quality of life (QOL) issues.
- Clinician satisfaction—Patients may require less clinical work; doctors can use new treatments.
- Improved healing means return faster to normal activities
- Productivity indicators for employers may be impacted if patient employability is affected.

Examples of the above valuation concerns are also presented when someone states that it "is cheaper to cut off a leg than to spend money trying to save it" or "treatment of a wound to avoid amputation only pushes the ultimate need for amputation off a bit into the future, at a high interim treatment cost." Economic arguments from a financial perspective can be cold, even unethical, and most believe a broader approach is needed, thus mentioning that other intangible but important outcomes assist the economic assessment.

As mentioned above, the review of intangible benefits often adds to the overall economic value argument for a product, but typically cannot identify a specific dollar contribution. Estimates made on the "willingness to pay" or WTP concept used in economics can be provided if reasonable numbers are used. An estimate of what it is worth to be able to not stay at home, or get back to work, or have a higher self-esteem is often built into the price of a product by estimating what someone or society might add for those benefits. This concept is well known in business and academic economic analyses.³⁸

9 | CONCLUSION

"Economic impact" in the general sense further extends beyond simple financial cost estimates of potential savings when one considers the other drivers of economic value in the wound market. The clinical acceptance of an emerging technology has followed along the currently adopted path of using evidence-based medicine to establish efficacy and effectiveness. Developing an estimate of "economic value" requires an additional calculus evaluating the material in both clinical research and real-world applications. Estimates of economic impact can be expanded by using claims data to estimate the progression of wounds to various health states at the individual and population level using Markov models, which logically permits an estimate of the total impact of product adoption when compared with standard of care.

The approach taken in stating the overall value of a particular technology can enhance the first impression in the minds of reviewers of new products. Product vendors should find this approach fruitful as they approach payers, and clinicians evaluating a new product should consider the multidimensional value of the new technology. The more comprehensive the approach, the more convincing is the overall impression that the emerging technology in fact has value and should be further supported. Using the above domains to present an integrated analysis, the inventor/discoverer or manufacturer of a new therapy can make the best case possible. The overall economic impact of introducing a new technology into the wound care space is supported by consideration of the various other nonfinancial economic impacts it can have and can be enhanced by reviewing all of the potential sources of value possible.

REFERENCES

- DMAA. Outcomes Guidelines Report, Volume IV. Washington DC: The Care Continuum Alliance; 2009.
- Fetterolf D. Notes from the field—the economic value chain in disease management organizations. *Dis Manag.* 2006;9(6): 316-327.
- Fetterolf D, Holt A, Tucker T, Khan N. Estimating clinical and economic impact in case management programs. *Popul Health Manag.* 2010;13(2):73-82.
- Chan B, Cadarette S, Wodchis W, Wong J, Mittmann N, Krahn M. Cost-of-illness studies in chronic ulcers: a systematic review. *J Wound Care*. 2017 Apr 1;26(sup4):S4-S14.
- FDA. https://www.fda.gov/science-research/science-and-researchspecial-topics/real-world-evidence.
- Sherman RE, Anderson SA, Dal Pan GJ, et al. Real-world evidence—what is it and what can it tell us. *N Engl J Med.* 2016; 23(375):2293-2297.
- O'Brien B, Viramontes JL. Willingness to pay: a valid and reliable measure of health state preference? *Med Decis Making*. 1994;14 (3):289-297.
- Gafni A. Willingness to pay in the context of an economic evaluation of healthcare programs: theory and practice. *Am J Manag Care*. 1997;(Suppl 3):S21-S32.
- Khokhar B, Jette N, Metcalfe A, et al. Systematic review of validated case definitions for diabetes in ICD-9-coded and ICD-10-coded data in adult populations. *BMJ Open*. 2016;6:e009952.

- Southern DA, Roberts B, Edwards A, et al. Validity of administrative data claim-based methods for identifying individuals with diabetes at a population level. *Can J Public Health*. 2010;101(1): 61-64.
- Mitchell E. Concentration of Health Expenditures in the U.S. Noninstitutionalized Population, 2014. Statistical Brief #497. November 2016. Rockville, MD: Agency for Healthcare Research and Quality. http://www.meps.ahrq.gov/mepsweb/data_files/ publications/st497/stat497.pdf.
- 12. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011.
- Boulton AJM, Kirsner RS, Vileikyte L. Neuropathic diabetic foot ulcers. N Engl J Med. 2004;351:48-55.
- Ashry HR, Lavery LA, Armstrong DG, Lavery DC, van Houtum WH. Cost of diabetes-related amputations in minorities. *J Foot Ankle Surg.* 1998;37(3):186-190.
- Stevens CD, Schriger DL, Raffetto B, Davis AC, Zingmond D, Roby DH. Geographic clustering of diabetic lower extremity amputations in low income regions of California. *Health Affairs*. 2014;33(8):1383-1390.
- Boulton AJ, Armstrong DG, Albert SF, et al. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the ADA, with endorsement by the AACE. *Diabetes Care*. 2008;8:1679-1685.
- 17. Serena TE, Carter MJ, Le LT, Sabo MJ, DiMarco DT, the EpiFix Study group. A multi-center randomized controlled clinical trial evaluating the use of dehydrated human amnion/chorion membrane allografts and multi-layer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. *Wound Repair Regen*. 2014;22(6):688-693.
- Sen CK, Gordillo GM, Roy S, et al. Human skin wounds: a major and snowballing threat to public health and the economy. *Wound Repair Regen*. 2009;17(6):763-771.
- Nussbaum S, Carter M, Fife C, et al. An economic evaluation of the impact, cost, and medicare policy implications of chronic nonhealing wounds. *Value Health.* 2017;19:27-32.
- Koob T, Lim J, Massee M, Zabek N, Denoziere G. Properties of dehydrated human amnion/chorion composite grafts: implications for wound repair and soft tissue regeneration. *J Biomed Mater Res B*. 2014;102(6):1353-1362.
- Koob T, Lim J, Massee M, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: therapeutic potential for soft tissue repair and regeneration. *Vascular Cell*. 2014;6(10):1-10.
- Koob T, Rennert R, Zabek N, et al. Biological properties of dehydrated human amnion/chorion composite graft: implications for chronic wound healing. *Intern Wound J.* 2013 Oct;10(5): 493-500.
- Koob T, Lim J, Zabek N, Massee M. Cytokines in single layer amnion allografts compared to multilayer amnion/chorion allografts for wound healing. *J Biomed Mater Res Part B*. 2015;5 (103):1133-1140.
- Maan Z, Rennert R, Koob T, Januszyk M, Li W, Gurtner G. Cell recruitment by amnion chorion grafts promotes neovascularization. *J Surg Res.* 2015;193(2):953-962.

- Massee M, Chinn K, Lei J, Lim JJ, Young CS, Koob TJ. Dehydrated human amnion/chorion membrane regulates stem cell activity in vitro. *J Biomed Mater Res B.* 2015 [Epub ahead of print]. 2015. (00B);00:1-9.
- 26. Massee M, Chinn K, Lim J, Godwin L, Young C, Koob T. Type I and II diabetic adipose-derived stem cells respond in vitro to dehydrated human amnion/chorion membrane allograft treatment by increasing proliferation, migration, and altering cytokine secretion. Adv Wound Care. 2016;2(5):43-54.
- Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: the economic case for the limb salvage team. *J Vasc Surg*. 2010;52(2):175-225.
- Cost-Effectiveness Frontier. Cost-Effectiveness Frontier [online] 2016. York; York Health Economics Consortium; 2016. https: //www.yhec.co.uk/glossary/cost-effectiveness-frontier/; 2016.
- Detsky AS, Naglie IG. A clinician's guide to cost-effectiveness analysis. Ann Intern Med. 1990;113(2):147-154.
- Owens DK. Interpretation of cost-effectiveness analyses. J Gen Intern Med. 1998;13(10):716-717.
- Marshall DA, Burgos-Liz L, IJzerman MJ, et al. Selecting a dynamic simulation modeling method for health care delivery research—part 2: report of the ISPOR simulation modeling emerging good practices task force. *Value Health*. 2015;18(2):147-160.
- 32. Schonfeld WH, Villa KF, Fastenau JM, Mazonson PD, V F. An economic assessment of Apligraf[®] for the treatment of hard-toheal venous leg ulcers. *Wound Repair Regen*. 2000;8:251-257.
- Ragnarson Tennvall G, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. *Diabetologia*. 2001;44(11):2077-2087.
- Carter M, Waycaster C, Schaum K, Gilligan A. Cost-effectiveness of three adjunct cellular/tissue-derived products used in the management of chronic venous leg Ulcers. *Value in Health.* 2014;17 (8):801-813.
- Romanelli M, Gilligan AM, Waycaster CR, Dini V. Difficult-toheal wounds of mixed arterial/venous and venous etiology: a costeffectiveness analysis of extracellular matrix. *Clinicoecon Outcomes Res.* 2016 May;8(4):153-161.
- Gilligan AM, Waycaster CR, Motley TA. Cost-effectiveness of becaplermin gel on wound healing of diabetic foot ulcers. *Wound Repair Regen*. 2015;3(23):353-360.
- Barshes NR, Saedi S, Wrobel J, Kougias P, Kundakcioglu OE, DG A. A model to estimate cost-savings in diabetic foot ulcer prevention efforts. *J Diabetes Complications*. 2017;31(4): 700-707.
- Lawrence M. Cost effectiveness of preventing diabetic foot ulcers. *Diabetes in Contol*, 2017. http://www.diabetesincontrol.com/costeffectiveness-of-preventing-diabetic-foot-ulcers/. Accessed August 21, 2019.

How to cite this article: Fetterolf DE. Estimating the economic value of emerging technologies in chronic wound therapy. *Int Wound J.* 2019;16: 1391–1397. https://doi.org/10.1111/iwj.13202