

## Comment on “An observational pilot study using a purified reconstituted bilayer matrix to treat non-healing diabetic foot ulcers”

Dear Editors,

As the hunt continues for the “holy grail” material to treat diabetic foot ulcers, we read with interest this pilot study describing what may be a unique advanced wound care matrix when compared to other skin substitutes. In this small series of 10 patients presenting with hard to heal diabetic foot ulcers (DFUs), which failed to heal after a minimum of 4 weeks standard treatment, the authors report a mean time to closure of 2.7 weeks and 90% of patients achieving wound closure at the conclusion of the study. Notably, the mean total cost of the product was \$1203 in patients achieving closure.<sup>1</sup> These performance metrics trend towards clinical and financial benefits for selection of this new product compared to other skin substitutes in general, and in particular other xenograft materials such as porcine-derived small intestine submucosa (SIS) or urinary bladder matrix (UBM).

We agree, as the authors suggest, that differences in material source and preparation may play a role in improving clinical outcomes. However, in a recent meta-analysis by Huang et al, which examined the efficacy and safety of acellular matrix therapy for DFUs, the authors present results from nine pooled randomised controlled trials evaluating several acellular materials, which suggest that regardless of material source, acellular therapies as adjuvant treatment of DFUs can further promote healing without undue adverse events.<sup>2</sup> Likewise, other recent meta-analyses of multiple heterogeneous trials report similar conclusions of the benefit of using acellular material for non-healing DFUs. These meta-analyses were both focused on human-derived products such as reported by Luthringer et al<sup>3</sup> or focused on biologic grafts sourced from human and animal sources as was reported by Guo et al.<sup>4</sup>

During these historically challenging times, now more than ever, our selection of treatment options must consider clinical outcome and economic efficiency.

Assuming reasonably similar safety and efficacy outcomes, we believe clinicians should look more critically at cost of care and quality of life. In a randomised controlled trial of porcine SIS material, Cazzell et al reported improved healing in the SIS group compared to the standard-of-care control arm.<sup>5</sup> When assessing the economic value of the material, Guest et al reported the cost associated with SIS applications in that specific randomised trial at \$3019.84. Even with limitations associated with the trial and subsequent retrospective modelling, there was a measurable economic benefit of use of the porcine graft as an adjunct to standard of care for treating DFUs.<sup>6</sup> In a subsequent comparative study, citing a mean cost of  $\$1901 \pm \$5394$  for SIS, Nherera et al suggest that SIS is a less expensive option compared to other biologic dressings and should therefore be considered a dominant strategy.<sup>7</sup> The \$1203 mean cost of the porcine-derived purified reconstituted bilayer matrix (PRBM) material used in Armstrong's pilot study was substantially lower—60% and 37%, respectively—than either reference for porcine SIS material, and we will continue to monitor whether similar cost-effective outcomes using PRBM will be achieved in a larger cohort.

Although no quality-of-life outcomes are presented by Armstrong et al in the present study, the cost profile of the PRBM material in this small series is notable. We agree with the authors that further clinical evaluation of this PRBM graft is warranted and suggest that these investigations include additional data on cost of care and impact on patient-reported quality of life.

### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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