Clinical Drivers For Integrated Solutions To Synthetic Dermal Reconstruction
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Introduction
Skin loss remains a major clinical challenge. In situations where the surgical options for reconstruction are constrained due to extent or chronicity and underlying pathology, artificial skin would provide a significant benefit. However, in spite of three decades of research developing alternative synthetic and tissue engineered skin approaches, only modest success have been achieved, falling short of initial expectations. Annual English/Welsh hospital mortality rates for serious burns have remained level at approx 300, from an incidence of around 14,000. For chronic wounds, there are 200,000 cases annually, and rising with an estimated £2-3bn healthcare cost. The mortality rate is currently around 350. We aim to understand the reasons for the relatively low uptake of synthetic skin in clinical practice. This will enable appropriate focus of future research strategies for next-generation products.

Materials and Methods
We sought clinician opinion on skin reconstruction through circulating a questionnaire to major centers, but received no responses. We have attempted to form a consensus understanding of relevant issues from recent literature1 and informal interviews with several plastic surgeons in the UK and EU.

Results
Cadaveric allografts are the mainstay of artificial skin in clinical use to support autograft procedures. Alternative approaches, including synthetic biomaterials and tissue engineering approaches, are limited through efficacy and ultimately, perceived risk/benefit and cost/benefit considerations. The main issue is efficacy, expressed both by reliability and by long-term result. In challenging clinical situations, the results using alternatives are equivocal. Reasons for failure are due to complicating factors in difficult wounds (infection, seroma, haematoma, chronicity).

Cadaveric allografts currently offer a relatively economic strategy, while possible advantage of alternatives often fail to offset potentially higher costs. The alternatives currently have established therapeutic niches (donor site reconstructions, scar revision, oncological reconstructions, post VAC granulation cover).

Discussion and Conclusions
Gains made by synthetic alternatives in scar revision and to an extent in chronic leg ulceration are important to recognise. Also identifying reasons for the limited performance and failure of current approaches and products is important. These factors together allow for proposing clear strategies for experimental evidence and next-generation design. A problem with commercial products is that gaining negative evidence is difficult, e.g. deaths associated with skin loss usually precipitated by overwhelming sepsis are rarely attributed directly to failure of a skin reconstruction procedure or artificial skin product.

There are compelling arguments that the limited results of synthetic skin products is due to overlooking the complexities of clinical needs in specific patho-physiological contexts. Inherent assumptions associated with experimental models used to develop materials are inadequate to address the complexities of difficult clinical situations. Integrative approaches to designing products for tissue regeneration in specific clinical conditions will improve the robustness and reliability required for wide clinical uptake.

References

Acknowledgments.
Supported by a UK DoH LINK grant and by RAFT charitable funds.

Disclosures. The authors have no financial conflicts of interest to disclose.