"Finally healed": that was the easy bit!

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Dear all, I hope you are all keeping well in these trying circumstances! Here are a few of the recent key diabetic foot publications. The main paper I want to bring your attention to is a review of a very important facet of diabetic foot management (Mueller, 2020). In my opinion, this topic is sub-optimally addressed clinically and certainly within the literature. It is a brief review of post-ulcer mobilisation and was published as part of the proceedings of the diabetic foot symposium held in the Hague last year. I recommend that you read all of the contributions in the *Diabetes and Metabolic Syndrome* journal (2020: 14(4)).

There are lots of publications about treating diabetic foot ulcers from wound care dressing studies, surgery, etc, but very few on a structured approach to relapse prevention. This paper suggests a 5-point approach to safe and effective foot ulcer rehabilitation. It is based on available evidence, which sadly is sparse and not without bias. It is in keeping with the International Working Group on the Diabetic Foot guidelines, here, to develop post-ulcer service provision. I can hear you saying "wait a minute, we all do this ..." but consider that 40% and 60% ulcers relapse in years 1 and 3, respectively. We are getting it universally wrong.

What does Mueller suggest? Firstly, that gradually reducing offloading should continue for 1–3 months after healing with special attention within month one. It recommends offloading for 1–2 hours a day with inspection, slowly increasing until the foot can tolerate full-time shoe wearing by 30 days. There is no guide on how to increase the time of shoe weight-bearing. The second recommendation is to wear properly fitting therapeutic shoes that reduce excessive stresses and protect the foot. Several papers show the effectiveness of therapeutic footwear but we must bear in mind that compliance, 'correct fitting' and availability are all crucial.

Although the author doesn't specify, I would recommend this includes tailored insoles too. The next recommendation is to slowly increase activity level (steps/day); again, this appears logical, and perhaps an overlooked concept. However, there is no evidence on how to do this or, in fact, that this prevents re-ulceration. Reportedly, a fortnightly 10% increase in step count is an effective way to increase activity in those with neuropathy (Mueller et al, 2013). However, during this randomised study, 4 out of 13 subjects developed a foot ulcer. The fourth recommendation is to avoid large variations in steps per day. We know from a few studies that newly healed ulcer sites appear to have considerably reduced stress tolerance and so are easily damaged (Lott et al, 2005; Lazzarini et al, 2019). Hence, this concept would appear to be sensible, although not evidence-based. The last recommendation is for patient education on self-care, particularly regarding daily visual foot inspection either by patients or caregivers during and post remobilisation. This is common sense but also evidence suggests unperceived pre-ulcerative lesions can be halted when a patient becomes aware and protects them.

Ulcer relapse is a huge global problem. While these recommendations give a framework to structure relapse prevention services, more research is needed. Additionally, and this is only my perspective, unless we identify the component ulcer aetiologies, we will fail. Although neuropathy is a large player, it is only part of the problem. In relapse and new ulcer prevention, my question is "why do 66–81% NOT ulcerate?" I think this is a useful team discussion paper for foot ulcer service review and development. ■

Lazzarini PA, Crews RT, van Netten JJ et al (2019) Measuring plantar tissue stress in people with diabetic peripheral neuropathy: a critical concept in diabetic foot management. *J Diabetes Sci Technol* 13(5): 869–80

Lott DJ, Maluf KS, Sinacore DR, Mueller MJ (2005) Relationship between changes in activity and plantar ulcer recurrence in a patient with diabetes mellitus. *Phys Ther* 85(6): 579–88

Mueller MJ, Tuttle LJ, Lemaster JW et al (2013) Weight-bearing versus non-weight-bearing exercise for persons with diabetes and peripheral neuropathy: a randomized controlled trial. *Arch Phys Med Rehabil* 94(5): 829–38

Mueller MJ (2020) Mobility advice to help prevent re-ulceration in diabetes. *Diabetes Metab Res Rev* 36(Suppl 1): e3259

Diabetes Metab Syndr

Statins-related peripheral neuropathy among diabetic patients

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 The authors set out to examine the association between peripheral neuropathy and statins therapy among people with type 2 diabetes. Statins have been identified as being potentially one of the reasons behind peripheral neuropathy.

2 A total of 757 cases seen at Penang General Hospital in Malaysia were placed into two groups (564 in the statins therapy group and 193 without statins) and the diagnosis of peripheral neuropathy was examined retrospectively for 10 years (2006–2016).

3 Of the 564 individuals who underwent statins therapy, 22.9% (*n*=129) had PN, while 15.5% (*n*=30) of the non-statins group had peripheral neuropathy. A significant variance was found between the groups; Spearman's investigation presented a positive correlation (r: 0.078, *P*-value: 0.031) among statins use and peripheral neuropathy prevalence.

4 In conclusion, there was a positive association between peripheral neuropathy and the use of statins. Peripheral neuropathy was higher among the statins users than the non-statins group.

Hammad MA, Sulaiman SAS, Alghamdi S et al (2020) Statins-related peripheral neuropathy among diabetic patients. *Diabetes Metab Syndr* 14(4): 341–6

Int Wound J

An observational pilot study using a purified reconstituted bilayer matrix to treat non-healing diabetic foot ulcers

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 Patients with diabetic foot ulcers (DFUs) that are hard to heal with standard wound care for whatever reason, have an increased risk of experiencing major complications, such as infection and amputation. The authors set out to evaluate the safety and preliminary efficacy of a novel decellularised purified reconstituted bilayer matrix (PRBM) used to treat DFUs.

2 An Institutional Review Board approved trial was set up to study 10 people with diabetes who had refractory wounds that had not healed after at least 4 weeks of standard wound care. The wounds of the 10 patients were treated with PRBM weekly for a period of up to 12 weeks. With the wounds evaluated, photographed and cleaned at each weekly visit, the primary outcome measure was deemed to be wound closure.

3 Complete wound closure was achieved in nine of 10 patients after 4 weeks; only one did not heal fully in a 12-week period. Mean healing time was 2.7 weeks and the authors reported no adverse events or wound complications.

4 PRBM may be a useful element of the clinician's toolkit when treating DFUs, according to the authors.

Armstrong DG, Orgill DP, Galiano RD et al (2020) An observational pilot study using a purified reconstituted bilayer matrix to treat non-healing diabetic foot ulcers. *Int Wound J* doi: 10.1111/iwj.13353 [Online ahead of print]

BMJ Open

Negative pressure wound therapy compared with standard moist wound care on diabetic foot ulcers in real-life clinical practice: results of the German DiaFu-RCT

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The authors assessed the efficacy and safety of negative pressure wound therapy (NPWT) in people with diabetic foot ulcers (DFUs) using the DiaFu study. The DiaFu study was a controlled clinical superiority trial with blinded outcome assessment; patients were randomised in a 1:1 ratio.

2 The study involved 368 randomised patients and 345 participants were included in the modified intention-to-treat (ITT) population. Patients having a DFU for at least 4 weeks and without contraindication for NPWT were included. The primary outcome was wound closure in a 16-week period. Secondary outcomes included quality of life, pain, wound size and wound tissue composition among others.

3 Neither the wound closure rate (P=0.53) nor the time to wound closure (P=0.244) in the ITT population was significantly different between the treatment arms.

4 NPWT was not found to be superior to standard moist wound care. Wound closure rate was low and documentation deficits, as well as deviations from treatment guidelines, adversely affected wound closure.

Seidel D, Storck M, Lawall H et al (2020) Negative pressure wound therapy compared with standard moist wound care on diabetic foot ulcers in real-life clinical practice: results of the German DiaFu-RCT. *BMJ Open* 10(3): e026345

Mater Sci Eng C Mater Biol Appl

A multifunctional nanocomposite spray dressing of Kappa-carrageenan-polydopamine modified ZnO/L-glutamic acid for diabetic wounds

Readability	✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

1 Sprayable bioadhesives with effective healing properties have been developed in recent times. The authors set out to examine a visible light-crosslinkable nanocomposite bioadhesive hydrogel with multifunctional properties.

2 Different concentrations of polydopamine modified ZnO (ZnO/PD) nanoparticles were loaded into the bioadhesive hydrogel (0, 0.5, 1 and 2 wt%), while methacrylated Kappa-carrageenan (KaMA), which mimicked the natural glycosaminoglycan, was applied. In addition, L-glutamic acid was incorporated to expedite wound healing.

3 The nanocomposite hydrogels showed efficacious blood-clotting qualities and biocompatibility — >95% cell viability after 3 days of incubation. *In vivo* studies implied that L-glutamic acid-loaded nanocomposite hydrogel expedited wound healing with superior granulation tissue thickness compared to a full-thickness skin defect model.

4 The authors concluded that visible-light crosslinking nanocomposite hydrogel in spray form is useful in combatting wound infection and accelerating wound healing.

Tavakoli S, Mokhtari H, Kharaziha M et al (2020) A multifunctional nanocomposite spray dressing of Kappa-carrageenan-polydopamine modified ZnO/L-glutamic acid for diabetic wounds. *Mater Sci Eng C Mater Biol Appl* 111: 110837

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