A retrospective case series from South Africa: Management of diabetic foot ulcers with ActiGraft, an autologous whole-blood clot therapy

Background: Diabetic foot ulcers (DFUs) are a serious complication of diabetes, frequently leading to prolonged hospitalisation, infection, and amputation. In South Africa, this challenge is particularly acute, with DFUs affecting nearly 28% of individuals with diabetes and accounting for more than half of all lower-limb amputations. This underscores a critical need for novel, regenerative therapies that can reliably promote wound closure. ActiGraft (RedDress Medical) is an autologous whole-blood clot (AwBC) therapy designed to address this need. Prepared at the bedside from the patient's own blood, it forms a fibrin matrix that acts as a biologically active scaffold, working to restore the natural wound-healing cascade and rebalance the local wound microenvironment.

Aim: The primary aim of this case series was to assess the effectiveness of ActiGraft in achieving full wound closure and preventing amputation in patients with chronic DFUs. Secondarily, we sought to describe the clinical outcomes, including wound area reduction and therapy safety, and to contribute real-world clinical data on the use of the AwBC therapy in a resource-limited public healthcare setting.

Methods: This retrospective case series evaluates three patients with DFUs that were refractory to standard care for >4 weeks. The patients were selected from referrals to a public podiatry clinic in Johannesburg. Treatment involved weekly adjunctive applications of ActiGraft alongside continued standard wound management (offloading, infection control and debridement). All wound assessments were conducted using a standardised measurement protocol.

Results: All three patients demonstrated rapid granulation and wound area reduction (mean 83% at 5 weeks). Two ulcers achieved full closure with no recurrence during a 3-month follow-up; one ulcer showed substantial improvement, but treatment was paused after a new diagnosis of thrombocytosis. No treatment-related adverse events or amputations occurred.

Conclusion: These findings are consistent with published clinical research, including a recent multicentre randomised controlled trial demonstrating significantly higher healing rates with AwBC therapy. AWBC therapy appears to be a feasible, biologically active adjunct that accelerates DFU healing in resource-limited settings and may contribute to reducing amputation risk.

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Key words
- ActiGraft
- Amputation prevention
- Autologous whole-blood clot therapy
- Chronic wound management
- Diabetic foot ulcer
- Podiatry
- Pressure ulcer

Diabetic foot ulcers (DFUs) are a serious and growing global health concern, driven by the rising prevalence of diabetes (McDermott et al, 2023). These wounds are a leading cause of prolonged hospitalisation, infection, lower-limb amputation, disability, and diminished quality of life, imposing a substantial economic burden on healthcare systems worldwide (Boulton et al, 2005; Akkus and Sert, 2022). The challenge is particularly acute in South Africa, where approximately 28% of individuals with diabetes develop a DFU, often presenting at advanced stages, and more than half of all lower-limb amputations are attributable to this complication (Chastain et al, 2019; Manickum et al, 2019; Turner et al, 2024).

In the cases presented here, a diabetic foot ulcer (DFU) is defined as a full-thickness lesion located distal to the ankle in a person

with diabetes. This definition, aligned with international consensus, recognises neuropathy, peripheral arterial disease and foot deformity. These aetiological symptoms are the triad of the diabetic foot syndrome. Therefore, as a primary aetiological driver that lead to tissue breakdown from repetitive stress or unrecognised trauma (International Working Group on the Diabetic Foot, 2023; Schaper et al, 2023). It is important to distinguish this from a pressure ulcer or injury, which is primarily caused by intense and/or prolonged pressure or shear, typically over a bony prominence, and can occur irrespective of diabetic status (EPUAP/NPIAP, 2019). In clinical practice, particularly in immobile diabetic patients, differentiating a neuropathic heel ulcer from a pressure injury can be complex, as aetiologies may overlap (Reddy, 2018).

The cases presented were clinically assessed as chronic wounds in patients with diabetes. We apply the term 'DFU' where the primary pathology was determined to be diabetic neuropathy (Cases 1 and 3) and specify 'pressure ulcer' where prolonged immobility was the predominant factor (Case 2), ensuring precise and transparent terminology. Standard care for DFUs encompasses debridement, infection control, moisture management, offloading and appropriate dressings.

Despite this multifaceted approach, a significant proportion of ulcers become chronic and hard-to-heal, underscoring the urgent need for novel, effective adjuvant therapies (Lim et al, 2017). ActiGraft (RedDress Medical) is an autologous whole-blood clot (AWBC) therapy designed to address this need. Prepared at the bedside from the patient's own blood, it forms a fibrin matrix that acts as a biologically active scaffold. This scaffold is designed to restore the dysregulated wound-healing cascade and rebalance the chronic wound microenvironment, providing a protective barrier and a source of native signalling molecules (Snyder et al, 2018; Williams et al, 2022).

A growing body of evidence supports the safety and efficacy of ActiGraft in managing chronic wounds. An international observational pilot study reported rapid wound size reduction and complete healing in chronic wounds that had previously failed advanced therapies (Naude et al, 2022). This is supported by evidence from a multicentre randomised controlled trial, which demonstrated a significantly higher complete closure rate for DFUs treated with ActiGraft plus standard care compared to standard care alone (41% versus 15%), with no device-related adverse events (Snyder et al, 2024). Further real-world data from registry studies in South Africa, Israel and Turkey indicate that ActiGraft can shift chronic wounds from a stalled, inflammatory state into an active proliferative phase of healing (Williams et al, 2022; Gurevich et al, 2023).

Building on this evidence, the present case series evaluates the impact of ActiGraft in a public-sector, resource-limited setting in South Africa. It describes the clinical experience and outcomes including wound area reduction, time to closure, and safety in three adults with hard-to-heal DFUs (>4 weeks duration) treated at a podiatry clinic in Johannesburg. The findings are contextualised within the broader literature on AWBC technology, contributing local, real-world data to the evidence base for this regenerative therapy.

Methods

Study design

This was a retrospective case series of three consecutively treated adult patients with chronic DFUs who received AWBC therapy in addition to standard of care at a South African regional public-sector hospital. A case-series design was chosen to describe real-world clinical outcomes where no control group was available.

Setting

The study was conducted in the Podiatry Department at Leratong Hospital, Johannesburg, South Africa. Leratong is a high-volume public-sector regional hospital serving predominantly low-income communities with a high burden of diabetes and diabetic foot complications. The podiatry service receives referrals of complex DFUs from surrounding clinics and hospitals.

Inclusion and exclusion criteria

Inclusion criteria were:

- Age ≥18 years.
- Diagnosis of type 1 or type 2 diabetes.
- Presence of a DFU or pressure ulcer with delayed healing or high-risk characteristics, typically of >4 weeks duration.
- Wagner grade 1–3 ulcer.
- Documented failure to progress under standard of care (debridement, infection control, offloading, moisture balance).
- Referral for adjunct AWBC therapy.
- Adequate perfusion based on clinical assessment and/or Doppler evaluation.

Table 1. Baseline characteristics of the three cases

Case	Age (years)	Sex	Diabetes type/ duration	Comorbidities	Ulcer location	Wagner grade	Duration before AWBC	Previous treatment
1	60	M	T2D >10 years	Hypertension, glaucoma	Plantar metatarsal	2	>4 weeks	SOC, enzymatic debridement
2	82	M	T2D >20 years	Hypertension, immobility	Plantar heel (pressure injury)	5	SOC	
3	72	F	T2D >15 years	Hypertension	Achilles region	2	>4 weeks	SOC

F = female; M = male; SOC = standard of care; T2D = type 2 diabetes.

Exclusion criteria were:
- Critical limb ischaemia.
- Radiological or clinical evidence of active osteomyelitis.
- Systemic sepsis requiring intravenous antibiotics.
- Untreated severe anaemia or coagulopathy.
- Inability to attend weekly follow-up visits.

A new diagnosis of thrombocytosis in case 3 was made after initiation of treatment and therefore did not constitute an exclusion criterion at baseline.

Wound assessment and measurement

Wounds were assessed at baseline and weekly. Wound area was measured using a standardised method. Maximum length and width were measured in centimetres with a sterile disposable ruler and multiplied to calculate area (cm^2). Depth was assessed using a sterile probe where applicable. Standardised photographs were taken at each visit using a consistent distance and angle, and a calibrated measurement grid was used to confirm measurements where possible.

Clinical status (tissue type, exudate level, odour, peri-wound maceration and signs of infection) was documented at each visit. Infection was assessed using recognised DFU infection criteria consistent with Infectious Diseases Society of America guidelines.

Data recording and analysis

Data collected included demographic details, comorbidities, ulcer duration and location, Wagner grade, baseline wound area, number of ActiGraft applications, weekly wound areas, time to closure and any adverse events. Given the descriptive case-series design and small sample size, data were summarised using descriptive statistics only.

Case presentations

The three cases were randomly selected from referrals to the podiatry department, Leratong Hospital, Johannesburg, for wounds of >4 weeks' duration that had not achieved satisfactory healing under standard of care (offloading, infection control and debridement). Patient characteristics are shown in [Table 1]. Cases satisfied the following criteria:
- DFU present for >4 weeks.
- Wound with exposed deep tissue (tendon or bone exposed or probing to bone) or significant peri-wound callus / infection history.
- Referral to our department with the intention of adjunct therapy with the donated autologous blood clot product.

These cases were considered "complex" due to chronicity, depth/exposure and prior treatment failure. The cases were evaluated for their wound properties and condition, including infection assessment, moisture control, presence of necrotic tissue, and wound size.

Case 1

A 60-year-old man with long-standing type 2 diabetes (T2D), hypertension and glaucoma presented with a Wagner grade 2 diabetic foot ulcer on the left plantar metatarsal area, of >4 weeks' duration. The wound exhibited heavy exudate, a malodorous smell and a bed covered with thick slough, with surrounding inflammation and severe peri-wound maceration. Baseline assessment recorded an area of 22.26 cm^2 and a depth of 0.3 cm, with clinically adequate perfusion.

Following enzymatic debridement and

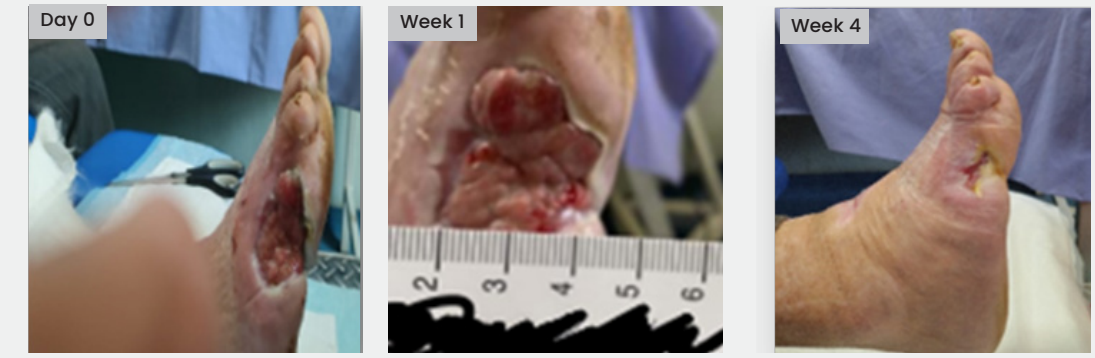

Figure 1

Figure 2

Figure 1. In case 1, a Wagner grade 2 DFU was treated with ActiGraft applications for consecutive 4 weeks, achieving complete wound closure.

Figure 2. In case 2, Actigraft was applied on a right heel pressure ulcer for 5 weeks, achieving complete wound closure.

a period of standard care that yielded insufficient improvement, weekly ActiGraft therapy was initiated. After the first application, the wound area reduced to 18 cm² (depth 0.1 cm), with resolution of infection signs and appearance of granulation tissue. After four weekly applications, the ulcer was superficial, measuring 0.48 cm² with no measurable depth. The patient subsequently transitioned to standard care alone until achieving complete epithelial closure, with no recurrence observed during a 12-week follow-up period [Figure 1].

Figure 1: In case 1, a Wagner grade 2 DFU was treated with ActiGraft applications for consecutive 4 weeks, achieving complete wound closure.

Case 2

An 82-year-old wheelchair-bound man with poorly controlled T2D and hypertension developed a pressure injury on the right plantar heel during hospitalisation for an unrelated condition. The wounds which had been present for approximately 5 weeks and developed during hospitalization, exhibited extensive exudate, slough, malodour, and peri-wound maceration. It was superficial with adequate perfusion upon assessment.

At baseline, prior to debridement of non-viable tissue, the wound measured 13.6 cm². Weekly ActiGraft applications were initiated as an adjunct to standard care. After two applications (week 3), the area had reduced to 8.96 cm² with evident granulation. Following a total of four applications over five weeks, the ulcer achieved complete epithelial closure [Figure 2]. No complications or recurrence were observed during a 3-month follow-up period.

Case 3

A 72-year-old woman with T2D and hypertension presented with a Wagner grade 2 diabetic foot ulcer on the right Achilles area of >4 weeks' duration. The wound was characterised by low to moderate exudate, slimy slough, malodour, peri-wound maceration, and signs of early infection along the wound edges, with intact perfusion. At baseline (week 0), the wound measured 35 cm² with a depth of 0.4 cm. Weekly ActiGraft applications were initiated. After two applications, the area reduced to 21 cm². Treatment continued with consistent weekly improvement, culminating in a total of seven applications. By week 7, the wound area had decreased to 12.6 cm² with no remaining measurable depth.

Subsequently, the patient was diagnosed with thrombocytosis, a systemic haematological condition known to impede wound healing. Considering this diagnosis and the stalled progress, ActiGraft therapy was paused. The patient was transitioned to ongoing medical management for both the wound and the underlying thrombocytosis.

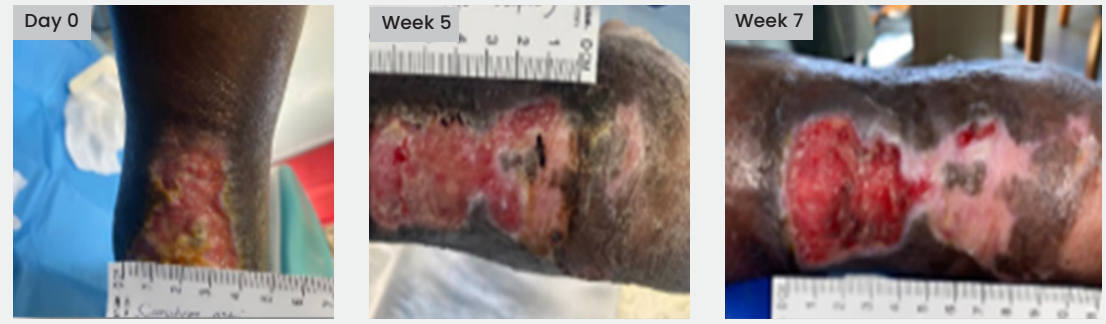

Figure 3

Figure 3. Actigraft was applied to a Wagner grade 2 diabetic foot ulcer for seven applications, resulting in a significant wound size reduction. Treatment was discontinued following the patient's new diagnosis of thrombocytosis.

Results

All three patients showed measurable improvement following adjunct AWBC therapy. Baseline wound areas ranged from 13.6 cm² to 35 cm². All ulcers had been present >4 weeks and had failed to progress under SOC alone.

- Case 1: Area reduced from 22.26 cm² to 0.48 cm² after four weekly applications, with complete epithelial closure thereafter and no recurrence at 12 weeks.
- Case 2: Area reduced from 13.6 cm² to 0 cm² after four applications over 5 weeks, with sustained closure at three-month follow-up.
- Case 3: Area reduced from 35 cm² to 12.6 cm² after seven applications, with complete resolution of depth, but incomplete surface closure at the time of AwBC therapy was discontinued following the patient's new diagnosis of thrombocytosis.

Across the three cases, the mean wound area reduction at 5 weeks was approximately 83%. No ActiGraft-related adverse events were observed. There were no allergic reactions, graft-site infections attributable to the product, wound-related amputations or systemic complications during the treatment period.

These findings align with multicentre evidence confirming ActiGraft's safety and efficacy in managing chronic wounds (Naudé et al, 2022; Williams et al, 2022; Gurevich et al, 2023; Landau et al, 2023; Snyder et al, 2024).

Discussion

This brief case series highlights the clinical use of AWBC therapy (ActiGraft) in managing three chronic diabetic foot and pressure ulcers within a South African public-sector clinic. The cases demonstrated a significant acceleration in wound healing after treatment. Specifically, case 1 showed a decrease in wound area from 22.26 cm² to 0.48 cm², with complete epithelialisation by 4 weeks. Case 2 improved from 13.6 cm² to full closure by week 5, and case 3, despite a partial response, reduced from 35.0 cm² to 12.6 cm² over 7 weeks before therapy discontinued.

These clinical results support the potential of ActiGraft to restart stalled healing, even in patients with substantial comorbidities (McDermott et al, 2023). The diminished response in case 3 coincided with a newly diagnosed thrombocytosis, which indicates that underlying systemic haematological conditions may affect therapy outcomes, emphasising the importance of thorough patient evaluation.

The positive trend observed in this series aligns with a growing body of evidence supporting autologous blood clot therapy as a powerful intervention for complex wounds. A South African observational study reported significant reduction in wound size and complete closure in 29 chronic wounds that previously resisted advanced treatments, with 75% of wounds achieving complete closure by 12 weeks and several patients avoiding planned amputations after applying ActiGraft (Naude et al, 2022). This is further strengthened by Level 1 evidence from a multicentre randomised controlled trial involving 119 diabetic foot ulcers, which showed a significantly higher complete closure rate of 41% with ActiGraft combined with standard care, compared to 15% with standard care alone, and no device-related adverse events recorded (Snyder et al, 2024). The consistent results, replicated across real-world registry studies in South Africa, Israel, and Turkey, reinforce the idea that ActiGraft promotes a rapid biological shift from a chronic, inflammatory phase to one characterised by active granulation and progress towards closure (Gurevich et al, 2023; Landau et al, 2023).

Furthermore, a South African cost-effectiveness study comparing autologous whole-blood clot therapy to negative-pressure wound therapy demonstrated that AwBC treatment resulted in 43–46% cost savings over 12 weeks, with superior healing rates (75% versus 43% at 12 weeks) (Naude et al, 2022). This further supports the feasibility and economic viability of AwBC therapy in

resource-limited public healthcare settings, such as the one described in this case series.

The therapeutic mechanism is fundamentally based on the graft's biomimetic properties. By forming an autologous fibrin-based matrix directly on the wound bed, ActiGraft acts as a protective, native scaffold that reduces bacterial colonisation and re-establishes a vital transport network for nutrients and signalling molecules (Snyder et al, 2023). Chronic wounds are characterised by a proteolytic environment with heightened matrix metalloprotease activity and a predominance of pro-inflammatory M1 macrophages, which sustain inflammation and hinder healing (Falanga, 2004; Nerem, 2007). ActiGraft addresses this imbalance by providing a concentrated mixture of platelets, cytokines, and growth factors that encourage macrophage polarisation towards the reparative M2 phenotype (Snyder et al, 2016). This phenotypic shift is crucial, enabling the release of anti-inflammatory interleukin-10 and key angiogenic factors such as PDGF, VEGF, and EGF, thus stimulating extracellular matrix deposition and neovascularisation to drive the wound into the proliferative phase (Snyder et al, 2023).

The applicability of this therapy extends beyond diabetic foot ulcers, showing proven effectiveness in pressure injuries and complex surgical wounds (Gurevich et al, 2023; Landau et al, 2023). From a practical standpoint, this therapy offers distinct advantages in resource-limited settings. Its preparation is a simple bedside procedure using the patient's own blood, it typically requires a limited number of applications, and it can be integrated into existing multidisciplinary care pathways. The positive outcomes observed here, including the avoidance of amputation, suggest that incorporating ActiGraft could potentially reduce the need for more invasive surgical interventions. Successful use requires careful wound bed preparation, appropriate use of secondary dressings for exudate management, and continued standard of care principles such as offloading.

Notwithstanding these encouraging results, our findings must be interpreted within the context of this study's limitations: a small sample size, the absence of a control group, and a relatively brief follow-up period. Future research should prioritise larger, controlled trials that include mechanistic and health-economic analyses to refine patient selection and treatment protocols. Nevertheless, the consistency between our clinical outcomes and the broader literature supports autologous whole-blood clot therapy as a valuable adjunctive treatment for complex, chronic wounds.

Limitations

This case series has several limitations. The small sample size (n=3) and descriptive design limit generalisability and preclude causal inference. There was no control group, and follow-up was limited to approximately three months. Although standardised wound measurement methods were used, measurement bias cannot be fully excluded. Furthermore, systemic factors such as thrombocytosis in Case 3 underline the complexity of interpreting wound responses in the presence of comorbidities.

Despite these limitations, the consistency of the observed improvements and the alignment with findings from larger observational studies and randomised controlled trials support the potential value of AWBC therapy as an adjunctive treatment for chronic DFUs in similar clinical contexts.

Conclusion

This case series demonstrates that ActiGraft, an AwBC therapy, is a safe and effective adjunct for chronic diabetic foot and pressure ulcers, promoting rapid wound size reduction and complete closure in two of three complex cases. These real-world outcomes support the improved healing rates and favourable safety profile documented in a multicentre randomised controlled trial (41% complete closure at 12 weeks with AwBC versus 15% with standard care alone; Snyder et al, 2024) and clinical registries, including South African observational and cost-effectiveness data (Naude et al, 2022; Gurevich et al, 2023).

The therapy's mechanism involves deploying a bioactive, autologous scaffold that modifies the chronic wound microenvironment, promoting a shift in macrophage phenotype toward a pro-reparative state to accelerate healing and potentially reduce the need for surgical intervention. Integrating this technology into multidisciplinary wound care holds significant potential for lowering amputation rates and improving quality of life, particularly in resource-limited settings. Further studies are warranted to confirm these findings, optimise treatment protocols, and evaluate long-term cost-effectiveness.

Declaration of interest

The authors have no conflicts of interest to disclose. ActiGraft products used in this report were supplied through a humanitarian donation programme. The manufacturer had no role in the study design, data collection, data analysis, interpretation or manuscript preparation.

References

Akkus G, Sert M (2022) Diabetic foot ulcers: a devastating complication of diabetes mellitus continues non-stop in spite of new medical treatment modalities. *World J Diabetes* 13(12): 1106–21

Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J (2005) The global burden of diabetic foot disease. *Lancet* 366(9498): 1719–24

Chastain CA, Klopfenstein N, Serezani CH, Aronoff DM (2019) A clinical review of diabetic foot infections. *Clin Podiatr Med Surg* 36(3): 381–395

European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel (2019) Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline. EPUAP/NPIAP

Falanga V (2004) The chronic wound: impaired healing and solutions in the context of wound bed preparation. *Blood Cells Mol Dis* 32(1): 88–94

Gurevich M, Heinz SM, Fridman R et al (2023) Use of autologous whole blood clot in the treatment of complex surgical wounds: a case series. *J Wound Care* 32(Suppl 2): S4–9

Hobizal KB, Wukich DK (2012) Diabetic foot infections: current concept review. *Diabet Foot Ankle* 3(1): 18409

IWGDF (2023) International Working Group on the Diabetic Foot Guidelines.

Landau Z, Whitacre KL, Leewood C et al (2023) Utilisation of a topical autologous blood clot for treatment of pressure ulcers. *Int Wound J* 20(3): 806–12

Lim JZM, Ng NSL, Thomas C (2017) Prevention and treatment of diabetic foot ulcers. *J R Soc Med* 110(3): 104–9

Manickum P, Ramklass S, Madiba T (2019) A five-year audit of lower limb amputations below the knee and rehabilitation outcomes: the Durban experience. *J Endocrinol Metab Diabetes* S Afr 24(2): 41–5

McDermott K, Fang M, Boulton AJM et al (2023) Etiology, epidemiology, and disparities in the burden of diabetic foot ulcers. *Diabetes Care* 46(1): 209–21

Naude L, Balenda G, Lombaard A (2022) Autologous whole blood clot and negative-pressure wound therapy in South Africa: A comparison of the cost and social considerations. *S Afr Med J* 112(10): 800-805

Nerem RM (2007) Cell-based therapies: from basic biology to replacement, repair, and regeneration. *Biomaterials* 28(34): 5074–7

Reddy M (2018) Identifying and treating foot ulcers in patients with diabetes: saving feet, legs and lives. *J Wound Care* 27(Suppl 6): S1–52

Schaper NC, van Netten JJ, Apedlqvist J et al. (2023) Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2023 update). *Diabetes Metab Res Rev* 39(S1): e3657

Snyder RJ, Lantis J, Kirsner RS et al (2016) Macrophages: a review of their role in wound healing and their therapeutic use. *Wound Repair Regen* 24(4): 613–29

Snyder RJ, Kasper MA, Patel K et al (2018) Safety and efficacy of an autologous blood clot product in the management of Texas 1A or 2A neuropathic diabetic foot ulcers: a prospective, multicentre, open-label pilot study. *Wounds* 30(7): 84–9

Snyder RJ, Schultz G, Wachuku C et al (2023) Proposed mechanism of action of topically applied autologous blood clot tissue. *J Am Podiatr Med Assoc* 113(3): 20-140

Snyder R, Nouvong A, Ulloa J et al. (2024) Efficacy and safety of autologous whole blood clot in diabetic foot ulcers: a randomised controlled trial. *J Wound Care* 33(9): 688–700

Turner MJ, van Vuuren S, Leigh-de Rapper S (2024) Analysing patient factors and treatment impact on diabetic foot ulcers in South Africa. *S Afr J Sci* 120(3/4): 16301

Williams M, Davidson D, Wahab N et al (2022) Innovative treatment utilising an autologous blood clot for diabetic foot ulcers. *Wounds* 34(7): 195–200