What's new in 2017/18:

Chronic Diabetic Foot Ulcers

Mr David Russell

Consultant Vascular Surgeon and Honorary Clinical Associate Professor

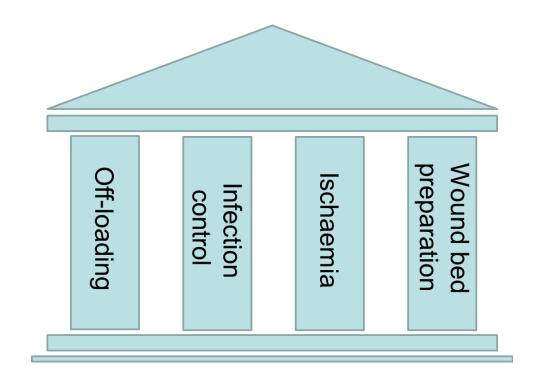Leeds Teaching Hospitals NHS Trust

- Disclosures:
  - Advisory board member
    - URGO medical
    - Integra
  - Chief Investigator MIDFUT NIHR HTA funded trial

Introduction

- Diabetes affects 4.5million adults in UK

- 25% lifetime ulcer risk; 2.5% (112,500) have a DFU at any one time

- Significant financial burden on NHS

    - 2014/15 £1billion spent on DFU healing

    - Additional societal costs

Off-loading

Infection control

Ischaemia

Wound bed preparation

Introduction

- Delayed healing is associated with adverse events:
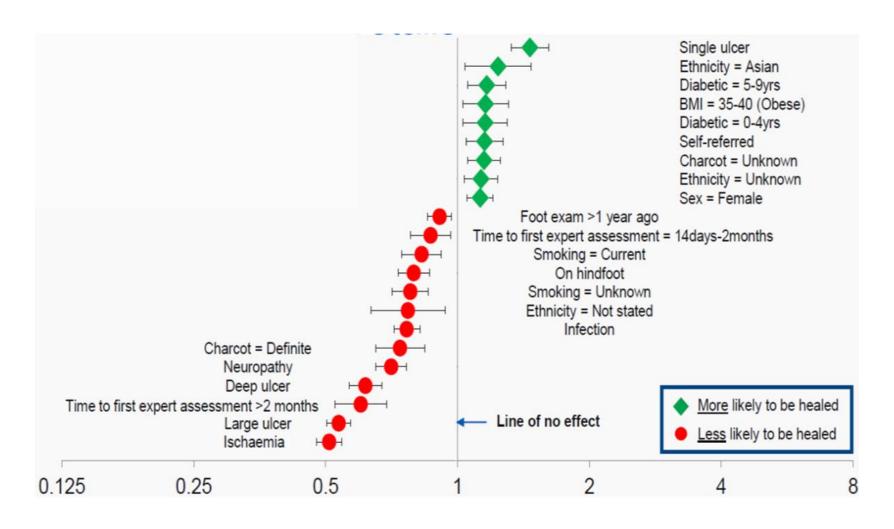
- NDFA 2014-17 data[1]

  - Alive and ulcer free at 12 weeks: 48.2%

  - Alive and ulcer free at 24 weeks: 65.5%

- Healing by 50% at 4 weeks is a predictor of outcome

  - Failure associated with only 9-30% healing at 12 weeks

1. National Diabetes Foot Care Audit Report 2014-2017. https://files.digital.nhs.uk/pdf/e/9/ndfa-3ar-rep.pdf

Factors Associated with Non-Healing

1. National Diabetes Foot Care Audit Report 2014-2017. https://files.digital.nhs.uk/pdf/e/9/ndfa-3ar-rep.pdf

Ischaemia

- Questions:

    - How do we identify ischaemia?

    - Who benefits from revascularisation?

    - What's the best method of revascularisation?

Assessment of Ischaemia

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
Either pedal pulse	0.55 (0.33–0.77)	0.60 (0.45–0.75)	0.41 (0.22–0.59)	0.73 (0.58–0.88)	1.38 (0.79–2.38)	0.75 (0.43–1.30)
Hair loss	0.8 (0.62–0.98)	0.44 (0.28–0.59)	0.42 (0.26–0.58)	0.81 (0.64–0.98)	1.42 (1.00–2.02)	0.46 (0.18–1.18)
Atrophy	0.5 (0.28–0.72)	0.87 (0.77–0.98)	0.67 (0.43–0.91)	0.77 (0.65–0.90)	3.9 (1.54–9.87)	0.57 (0.36–0.90)
Dependent rubor	0	1	Not discriminatory*	0.66 (0.54–0.78)	Not discriminatory*	1
Cool skin	0.3 (0.10–0.50)	0.90 (0.80–0.99)	0.6 (0.30–0.90)	0.71 (0.59–0.84)	2.93 (0.93–9.19)	0.78 (0.57–1.06)
Blue/purple skin	0	0.92 (0.84–1.01)	0	0.64 (0.51–0.76)	0	1.09 (0.99–1.19)
Capillary refill	0.42 (0.20–0.64)	0.63 (0.48–0.78)	0.36 (0.16–0.56)	0.69 (0.53–0.84)	1.14 (0.58–2.24)	0.92 (0.58–1.44)
Venous filling	0	1	Not discriminatory†	0.65 (0.51–0.79)	Not discriminatory†	1
Ankle pressure	0.47 (0.25–0.70)	0.79 (0.66–0.92)	0.53 (0.29–0.77)	0.75 (0.62–0.88)	2.25 (1.03–4.90)	0.67 (0.42–1.05)
Toe pressure	0.45 (0.23–0.67)	0.97 (0.92–1.00)	0.90 (0.71–1.00)	0.78 (0.66–0.89)	17.55 (2.39–128.96)	0.56 (0.38–0.84)
Toe brachial pressure index	0.89 (0.76–1.00)	0.45 (0.29–0.61)	0.45 (0.29–061)	0.89 (0.76–1.00)	1.62 (1.17–2.2)	0.24 (0.06–0.91)
Ankle brachial pressure index	0.68 (0.48–0.89)	0.59 (0.44–0.75)	0.46 (0.28–0.65)	0.79 (0.63–0.94)	1.69 (1.03–2.77)	0.53 (0.26–1.08)
Pole test at ankle	0.28 (0.07–0.48)	0.97 (0.92–1.00)	0.83 (0.54–1.00)	0.73 (0.61–0.86)	10.29 (1.29–81.60)	0.74 (0.55–0.99)
TcPo₂	0.28 (0.07–0.48)	0.66 (0.51–0.81)	0.28 (0.07–0.48)	0.66 (0.51–0.81)	0.81 (0.34–1.93)	1.10 (0.76–1.58)
Waveform analysis	0.85 (0.69–1.00)	1‡	1‡	0.93 (0.85–1.00)	Diagnoses PAD‡	0.15 (0.05–0.43)

Values in parentheses are 95% CI.

*Not discriminatory because dependent rubor was not elicited in any patient.

†Not discriminatory because impairment of venous filling was not elicited in any patient.

‡The gold standard definition of peripheral arterial disease (PAD) used included monophasic (damped) waveforms in any vessel, therefore the specificity and positive predictive value ratios are 1 and, positive likelihood is effectively infinite and diagnoses PAD.

Vriens B et al. Diabet. Med. 2018; 35: 895–902

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TcPo$_2$	0.28 (0.07–0.48)	0.66 (0.51–0.81)	0.28 (0.07–0.48)	0.66 (0.51–0.81)	0.81 (0.34–1.93)	1.10 (0.76–1.58)
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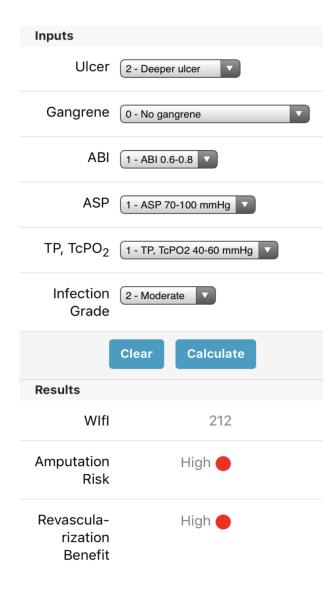
Vriens B et al. Diabet. Med. 2018; 35: 895–902

Selecting Benefit from Revascularisation

- ## WIfI score

  - Wound size/depth; gangrene

  - Ischaemia (ABI, ASP, TP/TcPO$_2$)

  - foot Infection

- ## Internal and external validation

  - Only 4 papers with >75% population DFUs

  - Not validated in UK cohort

Inputs

Ulcer	2 - Deeper ulcer
Gangrene	0 - No gangrene
ABI	1 - ABI 0.6-0.8
ASP	1 - ASP 70-100 mmHg
TP, TcPO$_2$	1 - TP, TcPO2 40-60 mmHg
Infection Grade	2 - Moderate

Clear   Calculate

Results

WIfI	212
Amputation Risk	High ●
Revascula-rization Benefit	High ●

Ischaemia

- Questions:

  - How do we identify ischaemia?

    - Toes pressure/vascular imaging

  - Who benefits from revascularisation?

    - ?WIfI

  - What's the best method of revascularisation?

    - Basil-2

What's New in Wound Management

- Traditionally trials of DFU wound care poor quality

  - Industry led

  - Heterogeneous or very selected populations

  - Limited to 12 weeks
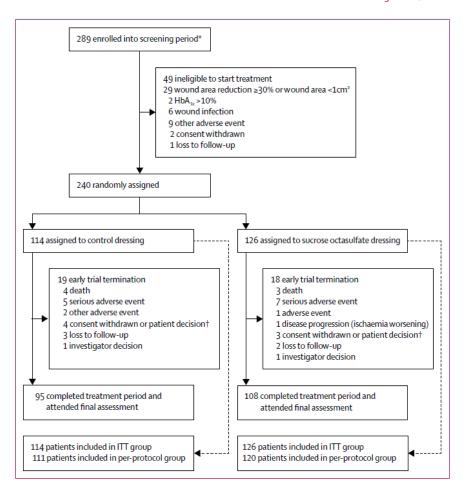
  - Limited relevance of endpoints (Wound area reduction)

Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality

William J Jeffcoate, Sicco A Bus, Frances L Game, Robert J Hinchliffe, Patricia E Price, Nicolaas C Schaper, on behalf of the International Working Group on the Diabetic Foot and the European Wound Management Association

Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (Explorer): an international, multicentre, double-blind, randomised, controlled trial

Michael Edmonds, José Luis Lázaro-Martínez, Jesus Manuel Alfayate-García, Jacques Martini, Jean-Michel Petit, Gerry Rayman, Ralf Lobmann, Luigi Uccioli, Anne Sauvadet, Serge Bohbot, Jean-Charles Kerihuel, Alberto Piaggesi

- Inclusion:
  - ABPI <0.9 or TBI <0.7
  - Toe pressure >50mmHg
  - HbA_{1C} <10%

- Exclusion:
  - Heel ulcers
  - Ulcers <1.0cm^2
  - Infected ulcers
  - Healing >30% in 2 week run-in (using control dressing)

43 centres in 5 countries

Median number - 3/centre

	Control dressing group	Sucrose octasulfate dressing group
Offloading devices prescribed	n=114	n=126
Total contact cast which can be opened	4 (4%)	2 (2%)
Removable devices which could be rendered non-removable†	33 (29%)	40 (32%)
Removable devices that immobilised the ankle joint	14 (12%)	17 (13%)
Removable devices that did not immobilise the ankle joint	45 (39%)	50 (40%)
Customised shoes with adapted sole or adapted insole	12 (11%)	12 (10%)
Wheelchair or confined to bed	6 (5%)	5 (4%)

Healing at 20 weeks:
Control 30%
UrgoStart 48%

- No difference in:
  - Infection
  - Adverse events

- Consider in neuro-ischaemic patients healing <50% at 4 weeks

LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial

Frances Game, William Jeffcoate, Lise Tarnow, Judith L Jacobsen, Diane J Whitham, Eleanor F Harrison, Sharon J Ellender, Deborah Fitzsimmons, Magnus Löndahl, for the LeucoPatch II trial team
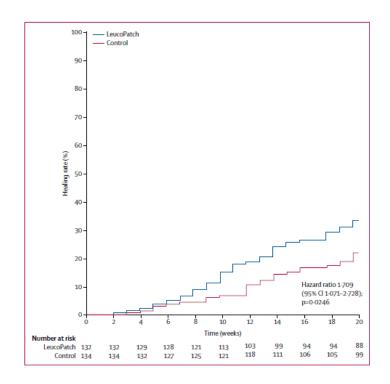

- Inclusion:
  - ABPI 0.5-1.40
  - Wound 50-1000mm^2
  - HbA$_{1c}$ <12%

- Exclusion:
  - Infected ulcers
  - Revascularisation within 4 weeks
  - Growth factors within 8 weeks
  - Healing >50% in 4 week run-in

32 centres in 3 countries

Median number 18 reg, 8 randomised/centre

Healing at 20 weeks:
Control 22%
Leucopatch 34%

- No difference in:
  - Infection rate
  - Antibiotics use
  - Minor/major amputation
  - Any AE/SAE

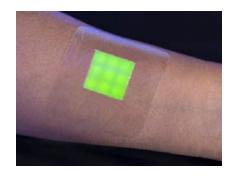- Only 30 patients with ABPI <0.8
  - 9 revascularised

What's on the Horizon?

- NIHR HTA funded trial

- MAMS trial design

- Combinations of Versajet, NPWT and cadaveric dermis vs standard care

- 660 patients across 32 centres over 3 years

- Contact midfut@leeds.ac.uk

Conclusions

- Priority is to ensure systems are in place to provide timely care

- Ensure ischaemia is actively excluded in chronic ulcers

- Re-evaluate and consider adjuvant wound therapies if ulcer failing to heal at 4 weeks

- Consider MIDFUT!