Article key points:

1. There is a lack of information about the holistic impact of non-removable offloading devices (NROLD) for people living with diabetes.
2. Levels of physical activity declined over time in this cohort of NROLD users which may have implications for their cardiovascular health and wellbeing.
3. Participants' reported that wearing an NROLD impacted on their financial wellbeing and an self-reported an increase in ~~reported~~ non-compliance.
4. Innovation is required to enable personalised care for people living with diabetic foot ulceration treated with NROLDs.

Key words:

Diabetes, Foot ulcer, quality of life, physical activity, casts, sedentary behaviour, personalised care

Abstract

Recurrent diabetic foot ulcers are associated with poor health-related quality of life and reduced mobility. Current guidelines recommend application of non-removable offloading devices (NROLDs) as they may improve healing of diabetic foot ulcers but there is a lack of information on the wider effects of wearing these devices. Few studies have examined the impact of NROLDs on holistic wellbeing or physical activity. We aimed to investigate the short-term impact of NROLDs on physical activity and diabetic ulcer-related quality of life (DFU-QoL) in a small sample of community-dwelling people with recurrent diabetic foot ulcers.

We measured DFU-QoL and physical activity (GPAQ) in 18 people with diabetic foot ulcers, recruited from a single clinic before NROLD application, and at three and six weeks after device fitting.

Participants were aged from 39 to 81 years (mean 58.4; SD 10.1) with an equal number of males and females. Fourteen participants (78%) completed six-week questionnaires.

Although there was some interim decline observed within individual domains of the DFU-QoL (financial, mean difference (MD) 16.2 (95% CI 2.1, 30.2); p=0.03); non-compliance MD 12.5 (95% CI -0.2, 25.2); p=0.05), no differences were observed over six weeks. Levels of physical activity declined over time, with half (56%) of participants classified as having low levels of physical activity at baseline, rising to two-thirds (67%) at follow-up.

Future studies should explore the longer-term holistic impact of NROLDs and develop more personalised approaches to care at the point of prescription, during, and post-device use.

Background:

Foot ulcers are one of the most common serious complications in diabetes, affecting up to 34% of people living with diabetes during their lifetime.[1] Outcomes from foot ulcers are variable but infected ulcers are associated with high levels of morbidity, including hospitalisation, and increased risk of limb amputation and mortality.[2] Consequently, the management of diabetic foot ulcers (DFUs) costs the National Health Service (NHS) £600m per year and these costs will likely increase as the prevalence of Type 2 diabetes mellitus rises.[3-5]

Current treatment guidelines recommend a multifaceted, multidisciplinary approach to the management of DFUs.[3 6] Once a DFU is established, local ulcer management, infection management, revascularisation, and pressure offloading are considered core elements of effective care.[3 6] Offloading devices can reduce mechanical stress on DFUs and improve ulcer healing, thus are now widely used in the NHS. Studies have shown that non-removable offloading devices (NROLDs) improve ulcer healing rates compared to removable offloading devices.[7-9] The mechanisms of action are due in part to improved pressure redistribution, but also arise from what has been termed as the 'enforced adherence', inherent in the application of a non-removable device.[8 10] Non-removable knee-high offloading devices are now recommended for neuropathic forefoot and midfoot ulcers in people with diabetes without moderate to severe ischaemia or moderate to severe infection. [3 6 10]

Although systematic reviews suggest that NROLDs improve DFU healing rates, there has been little exploration of the wider consequences of wearing these devices.[7 8] Possible adverse effects of NROLDs include physical inactivity with subsequent implications for cardiovascular/general health, muscle weakness, increased osteoporotic risk, risk of falling and/or fracture, risk of incident ulcers because of poor fitting, and musculoskeletal complaints because of device-induced limb-length discrepancy.[9 11] There is some evidence that people prefer removable devices because of their reduced impact on activities of daily living, such as walking, sleeping, bathing, or driving, but this remains poorly

understood.[12-14] Maintaining activity and mobility may be particularly important in a population with higher incidence of psychological morbidity, poor cardiovascular outcomes, and lower levels of physical activity.

Further information is needed on the impact of wearing NROLDs to enable clinicians and people with DFUs make informed shared decisions about their care, and whether additional support is required during wear and after NROLD removal. We aimed to investigate the short-term impact of NROLDs on physical activity and diabetic foot ulcer-related quality of life (DFU-QoL) in a small sample of community-dwelling people living with DFUs.

Methods:

Study Design: Observational study at single NHS podiatry service

We designed a longitudinal study to examine diabetic foot ulcer related quality of life (DFU-QoL) and physical activity before and after NROLD application in a convenience sample of patients attending a single community-based NHS health care centre. Data were collected pre-application (baseline) and at three and six weeks after fitting of NROLDs.

Ethical approval was granted by the health Research Authority (REC: 17/SC/0579, IRAS: 229586), sponsored by the University of Southampton (ref: 28465) and registered on the National Institute for Health Research Clinical Research Portfolio network. All participants gave written informed consent prior to enrolment into the study and all aspects of this study conformed with the Declaration of Helsinki.

Study population

Participants were eligible if they were aged ≥18 years, had a confirmed diagnosis of diabetes mellitus, a previous history of foot ulceration, and a current plantar forefoot ulcer suitable for NROLD treatment. Ulcers were assessed using the University of Texas Wound Classification System and only those deemed Grade A1 (i.e. non-infected, non-ischaemic, superficial wounds) were eligible for NROLD treatment, in line with local care pathways and clinical guidelines.[3 9 15]

NROLD fitting

Following ulcer care, consented participants were fitted with a non-removable knee-high offloading device; the TCC-EZ® Total Contact Cast System (Integra Life Sciences, Princeton, USA) and outer boot casing, in accordance with the manufacturer's instructions. All participants had an additional 5mm semi-compressed felt placed over their anterior tibia and dorsal surface of the foot, plus the border of the first and fifth metatarsophalangeal joints if required. Initial casts were applied on day one, then replaced in line with the manufacturer's instructions on day three, day eight, and then every week thereafter. Cast use was discontinued during the six week follow up period if: the DFU healed; became infected; increased in size or depth; the boot was not tolerated; or the clinician no longer deemed the cast an appropriate treatment.

Outcomes

The primary outcome was DFU-QoL measured using the self-completed Diabetic Foot Ulcer Scale (DFS).[16 17] This questionnaire captures participants' perspectives of different aspects of DFU-QoL. The full scale consists of 58 items, divided into 11 domains: leisure, physical health, daily activities, emotions, medical noncompliance, family, friends, positive attitude, treatment, satisfaction with medical care, and financial impact. Each item is scored on a five-point Likert scale and scoring ranges from 0 to 100, with higher scores indicating better quality of life.

The secondary outcome was self-reported physical activity as measured by the Global Physical Activity Questionnaire (GPAQ) Version 2.0.[18 19] This comprises of 16 questions to capture physical activity participation in three domains (work, travel, and recreational activities), and sedentary behaviour.

We collected baseline data on age, gender, type and duration of diabetes, duration of current ulcer, number of previous ulcers, history of previous foot infection, and history of amputation. All baseline data were collected by questionnaire in the podiatry clinic after signed consent was obtained. Follow-up data, including cast-associated adverse events, were collected by questionnaire in clinic.

Statistical Analysis

This was a small exploratory, pilot study, and in the absence of an agreed level of clinical significance for the DFS, a formal sample size calculation was not undertaken. Instead we aimed to recruit 18 participants which exceeds the published minimum recommendations for pilot studies.[20]

Data were entered and cleaned within Microsoft Excel and analysed using IBM SPSS Statistics (version 27.0). Prior to analysis, data distribution was checked for inconsistencies, outliers, data missingness and confirmation of distribution normalcy. Demographic data are presented using mean, standard deviation (SD). We followed the recommended statistical guides for analysis of the DFS and GPAQ. We calculated mean difference (SD) and 95% confidence intervals (CI) in each DFS domain over two time periods, from baseline to three and six weeks respectively, using paired t-tests. We undertook repeated analysis of variance (ANOVA) to examine change in DFS score, for the subset of participants reporting data across all time points. Adjustment for baseline variables was not undertaken due to the small sample size. GPAQ data were calculated and categorised as low, moderate, or high in accordance with the GPAQ scoring manual.

Results:

Study cohort characteristics

A total of 18 participants attending outpatient clinic were invited to participate in the study and all agreed to participate. Mean age was 58.4 (SD 10.1) years, with an equal number of male and female participants recruited (Table 1). Follow-up data were obtained from 15/18 (83%) and 14/18 (78%) at three and six weeks respectively. Mean (SD) time from recruitment to follow-up was 22 (2.5) days and 43 (1.7) days.

At baseline most participants (12/18; 67%) had lived with diabetes for 15 years or more and had history of at least four DFUs (14/18; 78%) before cast fitting. Despite reporting that diabetes impacted across multiple aspects of their QoL, particularly impacting on family relationships, participants reported high levels of satisfaction with medical care when entering the study. The majority (56%) of the recruited participants reported low levels of physical activity at baseline, before NROLD treatment.

After recruitment, four participants had their boot removed due to adverse events: two participants developed ulcer infection, and one participant experienced repeated falls linked to another health condition prior to the three week timepoint, and one developed Bullosis Diabeticorum prior to the six week timepoint.

At three weeks follow-up, there were no marked differences in DFU-QoL scores, other than for non-compliance (MD 12.5; 95% CI -0.2, 25.2; p=0.05), indicating that cast application was associated with increased non-compliance, and that wearing the cast impacted upon participants financially (MD 16.2, 95% CI 2.1, 30.2; p=0.03), (Table 2). However, we found no differences in DFU-QoL scores over six weeks or across multiple time points for those with complete data (Table 3). We found that overall physical activity levels were low at baseline, with only 2/18 (13%) participants reporting they were very active on a regular basis (Table 4). Sedentary behaviour increased over time, with two-thirds of respondents reporting low levels of physical activity at three and six weeks (Table 4).

Discussion:

We measured DFU-QoL and physical activity (GPAQ) over a six-week period in small sample of patients fitted with NROLD for their diabetic foot ulcers at one community-based NHS outpatient clinic. Although there was some interim decline observed within selected domains relating to finance and compliance with diabetes treatment, no other differences were observed in the DFU-QoL over the six-week period. Physical activity levels amongst this patient group were low, and we found some evidence of a decrease in activity over the follow-up period.

Results from this study suggest that NROLDs may have a negative effect on patients' compliance with overall diabetes treatment, and these devices may lead to other wider consequences, affecting financial wellbeing. Despite patients being treated within the UK NHS, a publicly funded health system, these devices may be associated with indirect costs, such as travel to attend regular clinic appointments and reduced income due to restricted ability to work. Novel findings like this require further examination in future research, to reduce potential for Type I error, and because we had some incomplete data within the DFS, as can be common in research involving patient reported outcome measures.

Within the DFS, the non-compliance domain consists of two questions: i) 'have you done things that you knew were not good for you such as eating, drinking, or smoking too much?'; and ii) 'Did you disregard medical advice about how to care for your ulcer?' Therefore, care must be taken not to extrapolate our finding beyond these two specific points but this should be considered in future research. The DFS also presents some specific conceptual challenges, which to our knowledge have not previously been discussed in the literature. To enable scoring of the whole DFS, the instructions require users to transform some subscales so that high scores always mean better DFU-QoL. The noncompliance subscale is one that is reversed, so that higher scores are better, and lower scores

are worse. On face value this appears counter-intuitive in a domain labelled 'non-compliance' where it would be logical for higher scores to indicate an increase in non-compliance. Respondents are faced with a similar challenge when completing these questions as they are asked 'did you disregard medical advice…' but responses range from 'none of the time' to 'all of the time'. These double negatives can only make the scale more challenging for respondents to complete and bring into question how much this PROM should be used in future.

Although, the DFS scores suggest an increase in non-compliance with treatment, increasing adherence and patient empowerment are central to good clinical care. Future studies are needed to examine the wider consequences of wearing these devices and provision of holistic care packages designed to address the needs of patients.

It is notable that the physical activity level in this population was very low at baseline and there was some evidence of a further decline over the observation period. However, these findings should be interpreted with caution, given the challenges of self-reported physical activity and the small sample size in our pilot study. It is not clear whether the baseline level of inactivity reflects a recent decrease or long standing level of activity, but it is well documented that people with DFUs have low levels of physical activity[21] and are often advised to reduce their weightbearing activity levels in order to improve ulcer healing.[22] If this translates into a further reduction in physical activity, this advice may have broader detrimental effects beyond the diabetic ulcer. Physical activity is recognised as a modifiable risk factor for cardiovascular disease in the general population but is perhaps even more important in people with diabetes.[22 23] Physical activity has many benefits for people with diabetes including improved glycaemic control and lipid profiles, and it can reduce the micro- and macrovascular complications associated with the condition.[23-26]

In contrast, the direct impact of physical activity and exercise on DFU healing is less certain. One recent systematic review explored the role of non-weightbearing exercise and concluded that although it is unclear whether non-weight bearing exercise improves ulcer healing, it does appear safe in patients with DFUs.[22] A further systematic review suggested that there may be a role for regular weightbearing activity in people with DFUs and optimal offloading but that more research was needed.[11]

Few studies have reported on the wider effects of prolonged immobilisation with NROLDs.[11] Although this study was not powered to accurately assess their effect on falls, three previous studies have reported rates of falls in participants wearing NROLDs and reported no or few falls in these participants.[27-29] However, prolonged immobilization of the ankle joint with knee-high devices results in muscle atrophy, reduced range of motion and loss of calcaneal bone mass.[30-32] Whilst the importance of ulcer healing should not be underestimated, there is some evidence that use of NROLDs over weeks or months could cause unintended side effects. Future research into NROLDs should adequately capture these broader effects and explore ways of reversing some of these unintended inactivity-related side effects.

This study aimed to explore the short-term impact of NROLDs on physical activity and diabetic foot ulcer-related quality of life in a small sample of people living with DFUs. In this respect it is novel and adds new knowledge. However, our findings should be interpreted with caution in light of the small sample size and limited follow up period. Furthermore, we acknowledge the risk of attrition bias, with some data missingness at follow-up.

Conclusion

This exploratory study investigated the short-term impact of NROLDs in people with recurrent diabetic foot ulcers. Although there was some interim decline within the financial and non-compliance domains of the DFU-QoL, no differences in quality of life were observed over six weeks amongst people wearing these casts. The increased risk of cardiovascular events is well recognised in people with diabetic foot ulcers we found that physical activity levels were low in this patient population and there was some evidence of an increase in sedentary behaviour. These findings should be explored in future, well-designed research studies to investigate how best to support personalised approaches to care for people treated with non-removable devices for chronic diabetic foot ulcers and how best to promote physical activity and rehabilitation.

Figures and tables:

Table 1: Participant characteristics on recruitment

	N = 18
Age, mean (SD)	58.4 (10.1)
Gender, n (%)	
Males	9 (50)
Females	9 (50)
Duration of Diabetes, years, n (%)	
< 5	1 (5.6)
5-15	4 (22.2)
>15	12 (66.7)
Missing	1 (5.6)
DM Type 1	7 (38.9)
DM Type 2	11 (61.1)
Previous amputation, n (%)	8 (44.4)
Previous DFU, n (%)	
1 ulcer	1 (5.6)
2 ulcers	3 (16.7)
3 ulcers	0
4+ ulcers	14 (77.8)
Duration of DFU, months, n (%)	
<6	7 (38.9)
7-12	8 (44.4)
12+	3 (16.7)
N (%) previously treated with offloading boot	8 (44.4)

Table 2: DFS scores over time

DFS Domain	Baseline n=18	3 weeks n=18	6 weeks n=18	Baseline to 3 weeks†		Baseline to 6 weeks†	
	Mean (SD) [missing]	Mean (SD) [missing]	Mean (SD) [missing]	MD (95% CI*)	P value	MD (95% CI*)	P value
Leisure	76.9 (18.8) [0]	78.9 (21.1) [3]	81.4 (21.8) [4]	2.4 (-11.3, 16.1)	0.71	-0.6 (-15.0, 13.8)	0.93
Physical health	62.5 (20.9) [1]	56.9 (18.9) [4]	55.0 (22.7) [8]	4.6 (-7.8, 17.0)	0.43	3.3 (-7.0, 13.7)	0.49
Daily activities	68.1 (20.0) [0]	77.4 (16.5) [4]	76.9 (11.3) [4]	-5.2 (-14.8, 4.3)	0.27	-4.8 (-13.0, 3.5)	0.24
Emotions	71.7 (16.0) [4]	65.3 (20.2) [3]	63.9 (20.0) [5]	3.3 (-6.3, 13.0)	0.46	6.5 (-5.5, 18.4)	0.25
Non-compliance	43.5 (17.7) [1]	34.6 (9.7) [5]	36.9 (11.1) [5]	12.5 (-0.2, 25.2)	**0.05**	10.8 (-5.1, 26.7)	0.16
Family	42.2 (19.9) [0]	58.4 (20.6) [3]	40.9 (23.3) [4]	6.7 (-3.4, 16.7)	0.18	4.0 (-6.6, 14.6)	0.43
Friends	60.4 (26.3) [0]	36.5 (18.0) [3]	56.6 (22.2) [4]	3.5 (-8.9, 15.8)	0.56	8.3 (-5.1, 21.7)	0.20
Treatment	63.1 (20.7) [0]	54.2 (23.7) [5]	56.4 (19.8) [4]	7.7 (-14.5, 29.9)	0.47	8.9 (-4.1, 22.0)	0.16
Satisfaction	93.8 (12.0) [2]	100.0 (0) [8]	98.3 (5.8) [6]	-6.0 (-12.90.9)	0.08	-3.6 (-9.1, 1.8)	0.17

Positive attitude	65.2 (20.0) [1]	62.9 (14.7) [4]	67.7 (15.2) [5]	4.0 (-5.4, 13.4)	0.37	-1.9 (-15.9, 12.2)	0.78
Financial burden	56.1 (21.7) [0]	37.7 (23.1) [5]	46.9 (23.9) [5]	16.2 (2.1, 30.2)	**0.03**	6.2 (-9.2, 21.5)	0.40

MD=mean difference; *95% CI of MD. Paired samples t-test. Higher scores indicate better quality of life.

† Calculation of the mean difference was conducted using paired t-test so is provided for respondents with data at both timepoints.

Table 3: DFS scores over time

DFS domain	N	Baseline mean (SD)	3 weeks mean (SD)	6 weeks mean (SD)	P value*
Leisure	14	80.9 (16.2)	79.7 (21.1)	81.43 (21.8)	0.92
Physical health	10	58.3 (23.5)	52.7 (20.5)	55.0 (22.7)	0.72
Daily activities	14	72.1 (19.9)	77.4 (16.5)	76.9 (11.3)	0.43
Emotions	10	66.4 (15.4)	64.7 (24.3)	59.9 (21.3)	0.53
Non-compliance	12	47.5 (19.6)	35.0 (10.0)	36.7 (11.6)	0.33
Family	14	44.9 (21.4)	36.9 (18.6)	40.9 (23.3)	0.31
Friends	14	64.9 (26.8)	58.9 (21.3)	56.6 (22.2)	0.46
Treatment	12	63.3 (22.7)	54.6 (24.7)	55.0 (20.2)	0.52
Satisfaction	9	93.3 (10.0)	100.0 (0)	97.8 (6.7)	0.24
Positive attitude	12	68.3 (21.5)	63.3 (13.4)	68.7 (15.4)	0.42
Financial burden	12	51.7 (22.5)	39.2 (23.5)	45.8 (24.7)	0.11

*Repeated measures ANOVA amongst respondents providing data at all time points

Table 4: Physical Activity Levels over time

Activity Level	Baseline N (%)	3 Weeks N (%)	6 Weeks N (%)
Low	9 (56)	8 (67)	8 (67)
Moderate	5 (31)	2 (17)	2 (17)
High	2 (13)	2 (17)	2 (17)
Missing	2	6	6

References:

1. Armstrong DG, Boulton AJ, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med* 2017;376(24):2367-75.
2. Ndosi M, Wright-Hughes A, Brown S, et al. Prognosis of the infected diabetic foot ulcer: a 12-month prospective observational study. *Diabet Med* 2018;35(1):78-88. doi: 10.1111/dme.13537 [published Online First: 2017/10/31]
3. Excellence NIfHaC. NICE Guideline (NG19): Diabetic foot Problems: prevention and management, 2015 (Updated 2016).
4. Kerr M. Foot care for Peaople with Diabetes: The Economic Case for Change: Insight Health Economics, 2017.
5. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, et al. The global burden of diabetic foot disease. *Lancet* 2005;366(9498):1719-24. doi: 10.1016/S0140-6736(05)67698-2 [published Online First: 2005/11/18]
6. Bus SA, Lavery LA, Monteiro-Soares M, et al. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev* 2020;36 Suppl 1:e3269. doi: 10.1002/dmrr.3269 [published Online First: 2020/03/17]
7. Elraiyah T, Prutsky G, Domecq JP, et al. A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. *J Vasc Surg* 2016;63(2 Suppl):59S-68S e1-2. doi: 10.1016/j.jvs.2015.10.006 [published Online First: 2016/01/26]
8. de Oliveira AL, Moore Z. Treatment of the diabetic foot by offloading: a systematic review. *J Wound Care* 2015;24(12):560, 62-70. doi: 10.12968/jowc.2015.24.12.560 [published Online First: 2015/12/15]
9. Bus SA, Armstrong DG, Gooday C, et al. Guidelines on offloading foot ulcers in persons with diabetes (IWGDF 2019 Update). *Diabetes Metab Res Rev* 2019;36 Suppl 1:e3274.
10. Bus SA, van Deursen RW, Armstrong DG, et al. Footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in patients with diabetes: a systematic review. *Diabetes Metab Res Rev* 2016;32 Suppl 1:99-118. doi: 10.1002/dmrr.2702 [published Online First: 2015/09/06]
11. Jarl G, van Netten JJ, Lazzarini PA, et al. Should weight-bearing activity be reduced during healing of plantar diabetic foot ulcers, even when using appropriate offloading devices? *Diabetes Res Clin Pract* 2021;175:108733. doi: 10.1016/j.diabres.2021.108733 [published Online First: 2021/03/14]
12. Armstrong DG, Lavery LA, Wrobel JS, et al. Quality of life in healing diabetic wounds: does the end justify the means? *J Foot Ankle Surg* 2008;47(4):278-82. doi: 10.1053/j.jfas.2008.02.015 [published Online First: 2008/07/02]
13. Health Quality O. Fibreglass Total Contact Casting, Removable Cast Walkers, and Irremovable Cast Walkers to Treat Diabetic Neuropathic Foot Ulcers: A Health Technology Assessment. *Ont Health Technol Assess Ser* 2017;17(12):1-124. [published Online First: 2017/10/11]
14. Piaggesi A, Goretti C, Iacopi E, et al. Comparison of Removable and Irremovable Walking Boot to Total Contact Casting in Offloading the Neuropathic Diabetic Foot Ulceration. *Foot Ankle Int* 2016;37(8):855-61. doi: 10.1177/1071100716643429 [published Online First: 2016/04/17]
15. Lavery LA, Armstrong DG, Harkless LB. Classification of diabetic foot wounds. *J Foot Ankle Surg* 1996;35(6):528-31. doi: 10.1016/s1067-2516(96)80125-6 [published Online First: 1996/11/01]
16. Ward J, McNulty P, Abetz L. Measuring the impact of diabetic foot ulcers on quality of life from th epatient's perpective. *Value Health* 1999;2(1):18.
17. Abetz L, Sutton M, Brady L, et al. The Diabetic Foot Ulcer Scale (DFS): a quality of life instrument for use in clinical trials. *Practical Diabetes International* 2002;19(6):167-75.
18. Armstong T, Bull FC. Development of the World Health Organization Gobal Physical Activity Questionnaire (GPAQ). *Public Health* 2006;14:66-70. doi: doi:10.1007/s10389-006-0024-x

19. Bull FC, Maslin TS, Armstrong T. Global physical activity questionnaire (GPAQ): nine country reliability and validity study. *J Phys Act Health* 2009;6(6):790-804. doi: 10.1123/jpah.6.6.790 [published Online First: 2010/01/28]
20. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. *Pharm Stat* 2005;4(4):287-91.
21. Lee M, van Netten JJ, Sheahan H, et al. Moderate-to-Vigorous-Intensity Physical Activity Observed in People With Diabetes-Related Foot Ulcers Over a One-Week Period. *J Diabetes Sci Technol* 2019;13(5):827-35. doi: 10.1177/1932296819848735 [published Online First: 2019/05/30]
22. Tran MM, Haley MN. Does exercise improve healing of diabetic foot ulcers? A systematic review. *J Foot Ankle Res* 2021;14(1):19. doi: 10.1186/s13047-021-00456-w [published Online First: 2021/03/22]
23. Papatheodorou K, Banach M, Bekiari E, et al. Complications of Diabetes 2017. *J Diabetes Res* 2018;2018:3086167. doi: 10.1155/2018/3086167 [published Online First: 2018/05/02]
24. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. *Diabetes Care* 2010;33(12):2692-6. doi: 10.2337/dc10-1548 [published Online First: 2010/12/01]
25. Colberg SR, Sigal RJ, Yardley JE, et al. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care* 2016;39(11):2065-79. doi: 10.2337/dc16-1728 [published Online First: 2016/12/08]
26. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2006(3):CD002968. doi: 10.1002/14651858.CD002968.pub2 [published Online First: 2006/07/21]
27. Armstrong DG, Nguyen HC, Lavery LA, et al. Off-loading the diabetic foot wound: a randomized clinical trial. *Diabetes Care* 2001;24(6):1019-22. doi: 10.2337/diacare.24.6.1019 [published Online First: 2001/05/26]
28. Bus SA, van Netten JJ, Kottink AI, et al. The efficacy of removable devices to offload and heal neuropathic plantar forefoot ulcers in people with diabetes: a single-blinded multicentre randomised controlled trial. *Int Wound J* 2018;15(1):65-74. doi: 10.1111/iwj.12835 [published Online First: 2017/10/24]
29. van Netten JJ, van Baal JG, Bril A, et al. An exploratory study on differences in cumulative plantar tissue stress between healing and non-healing plantar neuropathic diabetic foot ulcers. *Clin Biomech* 2018;53:86-92. doi: 10.1016/j.clinbiomech.2018.02.012 [published Online First: 2018/02/25]
30. Appell HJ. Muscular atrophy following immobilisation. A review. *Sports Med* 1990;10(1):42-58. doi: 10.2165/00007256-199010010-00005 [published Online First: 1990/07/01]
31. Sinacore DR, Hastings MK, Bohnert KL, et al. Immobilization-induced osteolysis and recovery in neuropathic foot impairments. *Bone* 2017;105:237-44. doi: 10.1016/j.bone.2017.09.009 [published Online First: 2017/09/25]
32. Diamond JE, Mueller MJ, Delitto A. Effect of total contact cast immobilization on subtalar and talocrural joint motion in patients with diabetes mellitus. *Phys Ther* 1993;73(5):310-5. doi: 10.1093/ptj/73.5.310 [published Online First: 1993/05/01]

Acknowledgements:

We would like to thank all the participants to this study for their time and commitment. We also thank the Podiatry service within Solent NHS Trust for their support in conducting research within a

clinical service, and the research and development team, particularly Helen Romer, for their support during study set-up and data collection.

Funding:

This report is independent research arising from TD being supported to undertake a Masters in Clinical Research (MRes) Fellowship from The National Institute for Health Research.

MB and JB are supported from NIHR Research Capability Funding via University Hospitals Coventry and Warwickshire.

The views and opinions expressed herein are those of the authors and do not necessarily reflect those of National Institute for Health Research, NHS or the Department of Health.

Authors contributions:

TD and LC conceived of and designed the study. TD and LC contributed to and supported the conduct of the study. TD completed data entry and cleaning. TD, and LC contributed to data analysis. JB also reanalysed data & revised the manuscript. MB contributed to the interpretation of the data; drafted and edited the manuscript.

All authors contributed to the drafting and approval of the final manuscript.