Is acupuncture an alternative or adjunctive treatment option for diabetes-related neuropathic pain? A feasibility study

Christopher Joyce, David Watterson, Caroline McIntosh

Distal symmetric polyneuropathy is a common problem in people with diabetes. Painful neuropathy is challenging to treat. Despite pharmaceutical management,many patients live with chronic pain. Acupuncture acts by stimulating the nervous system. In Western medicine, its most widespread application is for pain relief in musculoskeletal pain and chronic pain such as neuralgia and cancer. Although acupuncture has been cited as a potential therapy for neuropathic pain, the evidence to support its use is lacking. The authors explore the potential impact acupuncture has on diabetes-related neuropathic pain via a case-series pragmatic study.

Pain has been described as an "unpleasant sensory and emotional experience that can have a significant impact on a person's quality of life, general health, psychological health and social and economic wellbeing" (National Institute for Health and Care Excellence [NICE], 2013). Neuropathic pain arises from disease of the somatosensory nervous system, and can significantly impact health-related quality of life by restricting activities of daily living, negatively impacting on sleep and generally reducing the ability to enjoy life (Ziegler, 2009). Diabetes-related neuropathic pain is common in people with diabetes, and approximately one in every three people with diabetes is affected by distal symmetric polyneuropathy (DSP; Ziegler, 2008).

The treatment of painful diabetes neuropathy is challenging. Neuropathic pain is often difficult to manage because it is resistant to many pharmaceutical agents. This may be due to the fact that the pathogenesis and mechanisms of action of DSP are not fully understood.

The pharmaceutical management of neuropathic pain often involves the use of antidepressants, anti-epileptic drugs and opioids. In reality, treatment for neuropathic pain is often multimodal. The principles of treatment for diabetes-related neuropathic pain can be based on four cornerstones (Ziegler, 2008):

1. Multifactorial treatments aimed at achieving normoglycaemia and reducing cardiovascular risk.
2. Intervention to target pathogenic mechanisms.
3. Management of symptoms.
4. Avoidance of risk factors and complications.

Approximately one in every three patients who suffer from non-cancer-related chronic pain use complementary and alternative therapies, particularly when Western medical interventions such as surgery and medication fall short of patient expectations (Lee and Raja, 2011).

Acupuncture for diabetic neuropathic pain

In Western medicine, acupuncture is the insertion of fine needles that act on the nervous system, through modes such as local antidromic axon reflexes, segmental and extrasegmental neuromodulation, as well as other central nervous system effects (White, 2009). Acupuncture has been incorporated into Western medicine, but despite the known positive impact of acupuncture on pain, its research potential in diabetes-related neuropathic pain is still inadequate (Medical Research Council, 2000). Several reasons have been suggested for the poor uptake of acupuncture in modern Western medicine. Methodological limitations of existing research means there is a lack of high-quality, scientific studies, specifically placebo-controlled randomised clinical trials. Cultural differences also exist between Western

Citation: Joyce C, Watterson D, McIntosh C (2016) Is acupuncture an alternative or adjunctive treatment option for diabetes-related neuropathic pain? A feasibility study. *The Diabetic Foot Journal* **19**: 75–83

Article points

1. Despite the known positive impact of acupuncture on pain, its research potential in diabetes-related neuropathic pain is still inadequate.
2. Participants noted improvements in perceived pain after a short course of acupuncture, with males responding better than females, through unknown mechanisms.
3. Improvements in various domains of participant's quality of life were noted particularly in the areas of sleep disturbance, lower extremity function and depression.
4. The use of acupuncture as an adjunctive therapy for diabetes-related neuropathic pain is plausible, however the creation and implementation of a two-armed randomised control trial would allow for stronger acceptance of acupuncture's impact on the medical management of diabetes-related neuropathic pain.

Key words

- Acupuncture
- Diabetes mellitus
- Diabetic neuropathies
- Neuropathic pain

Authors

Author details can be found on the last page of this article.

"Acupuncture may be effective in the treatment of diabetes-related neuropathic pain, particularly in patients who fail to respond to pharmacological intervention."

acupuncture and traditional Chinese medicine acupuncture, which results in inconsistent approaches to treatment.

A number of studies support the use of acupuncture for diabetic peripheral neuropathy with claims that the beneficial effects of acupuncture may last for up to 6 months and may reduce the need for pharmaceutical intervention (Boulton, 2005).

The use of acupuncture is advocated in national guidelines. The Scottish Intercollegiate Guidelines Netwxork (2013) recommends the use of acupuncture as an alternative treatment modality for neuropathic pain when other pharmacological treatments have failed or are contraindicated.

Acupuncture studies

The largest known study to date on the application of acupuncture for diabetes-related neuropathic pain was conducted by Abuaisha et al (1998). They investigated 46 patients (mean age 57) with type 1 or type 2 diabetes (duration of disease 13.2 years) and neuropathic pain, confirmed via the neuropathy disability score (NDS) and vibration perception threshold testing (VPT) with a calibrated neurothesiometer of >25 volts. Participants had six sessions of acupuncture over 10 weeks, using traditional Chinese acupuncture points (Liver 3, Spleen 6 and 9 and Stomach 36). A total of 44 patients completed all six sessions with two withdrawals (one due to discomfort and one due to an unrelated myocardial infarction). After six sessions, 34 participants (77%) reported an improvement in their symptoms (P<0.01). Seven participants were able to stop their medical treatment for neuropathic pain. No significant changes were noted in NDS, VPT or HbA_{1c} levels after the course of acupuncture. The findings suggested that acupuncture may be effective in the treatment of diabetes-related neuropathic

pain, particularly in patients who fail to respond to pharmacological intervention.

Tong et al (2010) examined the use of acupuncture over 15 consecutive days for diabetes-related DSP in two cohorts. All patients had diabetes, were taking no medication for DSP, an ankle brachial pressure index (ABPI) of >0.8 and either an absent Achilles tendon reflex or a VPT reading >25 volts. Participants received acupuncture (n=42) or sham acupuncture (n=21). Acupoints used were Liver 4 and 11 Stomach, Stomach 36 and 40 and Spleen 6, and were inserted for 30 minutes during each session, with rotation of the needles every 5 minutes. In the sham group there was no rotation of the needles. Subjective symptoms of pain, numbness and temperature, along with HbA_{1c} and VPT were collected. Statistically significant improvement in VPT readings was noted between the acupuncture and sham group (P<0.05), with subjective symptoms by the patients also improving, with reductions in pain and numbness in the acupuncture group (P<0.05).

The findings of published studies seem to support the use of acupuncture in diabetes-related DSP, but the results should be interpreted with caution due to methodological limitations. There is a paucity of good quality, scientific studies investigating the effectiveness of acupuncture for painful diabetes-related peripheral neuropathy, and therefore the effectiveness of acupuncture for DSP is unclear.

A systematic review of acupuncture studies in diabetic neuropathy concluded that even though acupuncture has shown its effectiveness in treating the symptoms of neuropathic pain in diabetes, all studies demonstrated a high bias rate and no clear or internationally recognised outcome measures for studies currently exist in this area (Chen et al, 2013). Due to methodological limitations there is a limited understanding on the longitudinal effects of acupuncture – is acupuncture just a short-term solution to a long-term problem?

Aims

This aim of this study was to undertake a feasibility study that would evaluate the effectiveness of acupuncture as an alternative or adjunctive therapy for people suffering from diabetes-related neuropathic pain. The primary outcome was to determine if acupuncture decreased neuropathic pain while secondary outcomes investigated various domains of health-related quality of life (HR-QOL)pre and post treatment using the Quality of Life in Neurological Disorders (Neuro-Qol) questionnaires. Additional secondary outcomes aimed to test the difference in the participants' perceived expectation of acupuncture treatment before and after the course of therapy. The findings of this feasibility study will inform the design of a large, prospective, randomised controlled trial of acupuncture for diabetes-related painful DSP by the research team.

Methods

Design

A prospective, case-series, descriptive study design was utilised. The study was conducted as a feasibility study

"The findings of this feasibility study will inform the design of a large, prospective, randomised controlled trial of acupuncture."

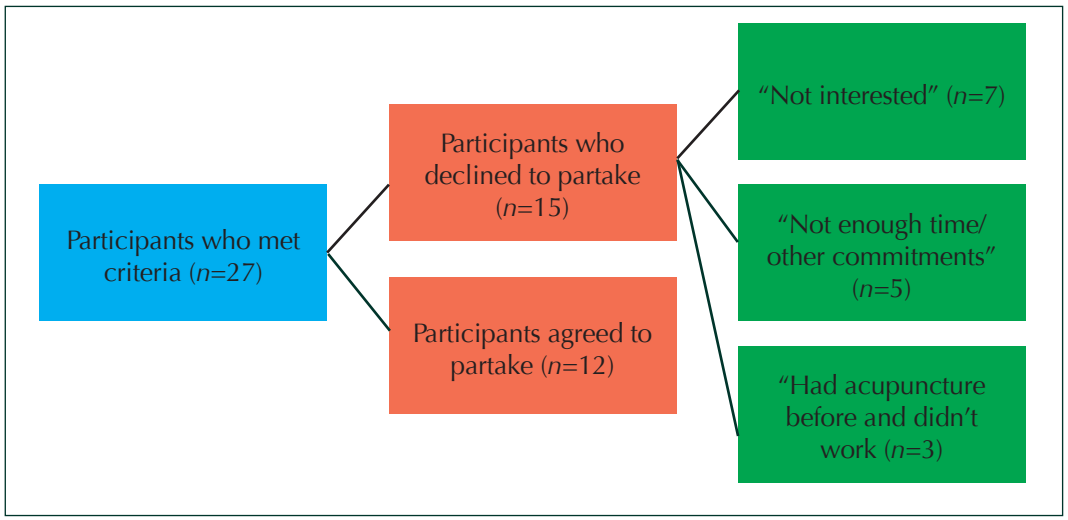

Figure 1. Participants were recruited into the study using convenience sampling.

Figure 2. Five acupuncture sites were used on each foot, chosen based on previous studies.

to help inform the planning of a larger trial by this research team.

Setting

The study took place at Merlin Park Podiatry Clinic (MPPC), the teaching facility for clinical education for students of podiatry at the National University of Ireland Galway. This clinic treats a wide variety of podiatric conditions.

Study criteria

All participants were recruited from MPPC. Inclusion criteria were:

- Over the age of 18 years.
- Clinically diagnosed with diabetes (type 1 or type 2).
- History (> 3 months) of diabetes-related neuropathic pain.
- Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale (LANSS) score >12.
- VPT >25 volts, measured by a calibrated neurothesiometer.
- ABPI >0.8.

Exclusion criteria included:

- Under 18 years of age,.
- No history of diabetes.
- Peripheral arterial disease (ABPI <0.79).
- Current or history of foot ulceration or current sepsis.
- Previous amputation.
- Reduced tissue viability and/or skin infection at site of needling.
- Patients on anti-coagulant therapies.
- Needle phobia.
- Unwilling or unable to give consent.

All participants gave informed consent to participate in the study.

Participants

Twelve participants were recruited into the study by convenience sampling (*Figure 1*). A demographic questionnaire recorded patients' gender, age, type of diabetes, disease duration, diagnosis of diabetes-related neuropathic pain (if known) and duration of diabetes-related neuropathic pain. Each participant completed the LANSS questionnaire (Bennett, 2001). This seven-item tool is a clinically and research validated questionnaire in evaluating whether pain is due to neuropathic mechanism (indicated by a score of >12). or not. This tool has demonstrated good internal consistency, with a Cronbach's alpha of 0.76 (Bennett et al, 2005).

ABPI values for both limbs were measured at the point of enrolment using a hand-held Doppler and a manual sphygmomanometer. VPT was measured on enrolment using a neurothesiometer at the apex of the right hallux. VPT was used as it has high sensitivity (77%–100%) and specificity (71%–83%) and has been shown to predict loss of sensation before loss of protective sensation is clinically evident (Garrow and Boulton, 2006). The neurothesiometer was calibrated after each participant according to manufacturer's guidelines.

Neuro-Qol is a set of 11 self-reported measures to assess HR-QOL in adults and children with neurological disorders (Cella et al, 2007). There are 11 Neuro-Qol measures for adults, and six were chosen for use in this study:

- Ability to participate in social roles and activities.
- Satisfaction with social roles and activities.
- Depression.
- Fatigue.
- Sleep disturbance.
- Lower extremity function/mobility.

There are a series of questions related to each measure (some measures have up to 45 questions) with a scale of 1–5. Patients were given instructions by CJ on how to complete the measures. Neuro-Qol was used to assess any difference in HR-QOL before and after the course of acupuncture therapy.

"The results of this study suggest that acupuncture may be used as a safe, adjunctive therapy in diabetes-related neuropathic pain"

Ethical approval

Ethical approval was granted by the Galway Hospitals Clinical Research Ethics Committee, in June 2014. No adverse reactions were reported due to the acupuncture therapy.

Data collection

Acupuncture points chosen were based on previous studies in this field. Practitioner experience and expert opinion was sought. Five points per foot were used, and Bafeng and Taichong (also known as Liver 3) were the insertion points (*Figure 2*). Bafeng points are located in the intermetatarsal spaces of digits 1–5, while Taichong is located distally to the Bafeng point of intermetatarsal space of 1–2.

All participants were laid supine to minimise any possible adverse effects such as nausea or dizziness. A "cun-chart" was created for each patient with the "cuns" required for maximum effectiveness of each acupuncture point. According to traditional Chinese medicine, a cun is a measurement equal to the width of the recipient's thumb. These were created by measuring each individual's thumb width and marking it on a piece of paper, which was then laminated. This would allow for the same point of entry for the acupuncture needle at each session. The cun-chart was kept with each patient's file to ensure the correct chart was used at each session.

The single-use acupuncture needles (0.20 mm × 0.30 mm) were inserted perpendicular into the skin until half of the needle had entered the foot to ensure *de qi* was achieved. *De qi* is the descriptive nature of the sensations felt by the recipient, and is often described as a dull ache or tingling feeling. Needles were left *in situ* for 20 minutes with no manipulation. The needles were then removed and the participant was asked to remain supine for 5 minutes to minimise any possible adverse effects. The second session was conducted exactly 4 days after the first, with the remaining sessions taking place on a weekly basis. Five sessions were conducted over a 4-week period.

Demographics, ABPI, neurothesiometer readings, visual analogue scale (VAS,) belief in acupuncture and selected Neuro-Qol questionnaire data were collected at baseline. Pain levels were recorded at all visits, while VAS for pain and belief and selected Neuro-Qol questionnaire data was collected after the final treatment to allow for pre- and post-treatment comparisons.

Table 1. Demographic and disease characteristics

Demographic and disease characteristics (*n*=12)	Mean (SD) or %
Age (years)	64.9 (+/- 10.6)
Gender M:F	8:4
Type of diabetes	Type 1: 25%
Diabetes duration (years)	12.8 (+/- 2.5)
Clinically diagnosed diabetes-related neuropathic pain	Yes: 50% No: 50%
Diabetes-related neuropathic pain duration (years)	3.35 (+/- 2.5)
Ankle Brachial Pressure Index *Right* *Left:*	 1.02 (+/- 0.12) 1.05 (+/- 0.14)
Vibration Perception Threshold	33 (+/-6.25)
Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale score (max=24)	15.33 (+/- 2.57)

Data analysis

Data collected were inputted through a series of codes required for statistical analyses using SPSS version 20 (IBM). A Shapiro-Wilk test of normality was conducted to see if data presented as parametric or non-parametric. Data was found to be parametric, and thus significant P-value was set at 0.05 ($P<0.05$). All assumptions were statistically analysed using a paired samples T-test.

Results

Demographics

Twelve participants with diabetes and a history of painful DSP were recruited into the study. Neuropathic pain was confirmed via the LANSS questionnaire. Demographics are shown in *Table 1*.

Reduction in pain levels

There was a reduction in the mean pain scores was observed of 2.1 (±1.2) points, but this was not statistically significant ($P>0.082$). There was a statistically significant reduction ($P<0.04$) in pain scores for the eight male participants, but not for the four females ($P>0.74$) (*Figure 3*). No difference was found between pain levels in people with type 1 diabetes versus people with type 2 diabetes ($P>0.82$), or in those participants who had clinically diagnosed

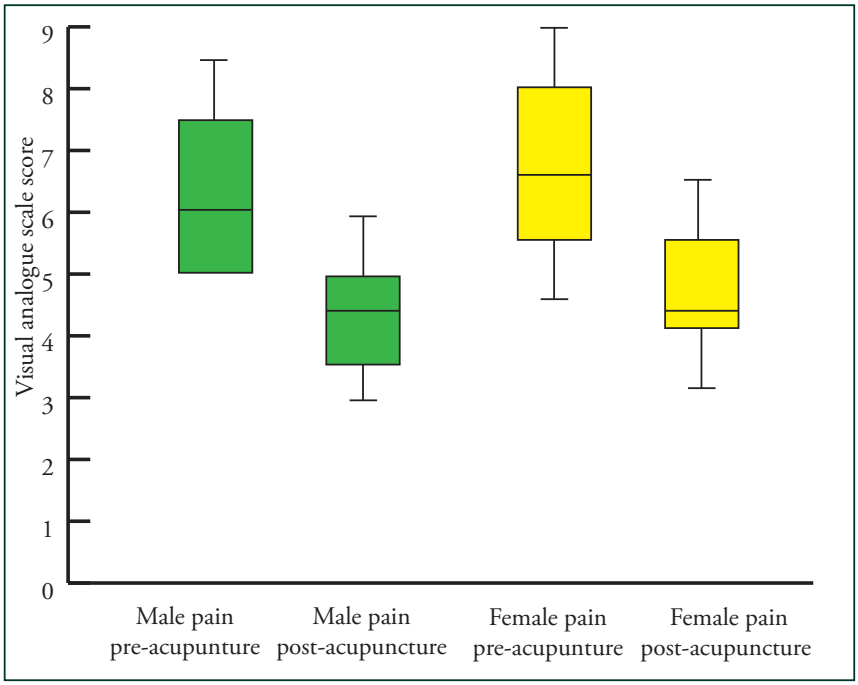

Figure 4. Reduction in pain scores for males and females post-acupuncture.

diabetes-related neuropathic pain versus those whose DSP was not clinically diagnosed ($P>0.32$).

Belief of the effectiveness of acupuncture

Results from the self-reported belief in acupuncture VAS scale showed a statistical difference in belief of the effects of acupuncture before and after a course of the intervention ($P<0.011$), with male participants showing significance ($P<0.033$) compared to the female cohort ($P>0.57$).

Quality of life

Six domains were assessed using the Neuro-Qol tool. All domains showed improvement, but only the measured areas of depression, fatigue and sleep disturbance were statistically significant ($P<0.014$, $P<0.03$ and $P<0.041$, respectively). Further analysis showed no difference in Neuro-Qol measurements between gender and type of diabetes.

Discussion

Acupuncture has the potential to reduce pain and improve quality of life for people with painful DSP. Although the main hypothesis that acupuncture would significantly reduce pain was rejected, the marginal decrease in pain may be of clinical significance. A mean decrease in participant pain levels of 2.1 points (±1.2) was observed across the cohort. This reduction in pain post treatment was not significant enough to reject the authors' null hypothesis, which concurs with the findings of other published studies where a reduction in pain was reported that was not statistically significant (Abuaisha et al, 1998: Abbott et al, 2011).

These studies also reported a decrease in pain severity, duration or both, yet none of these variables reached statistical significance (Abuaisha et al, 1998; Abbott et al, 2011). However, Abuaisha et al (1998) found that 77% ($n=34$) of participants noted improvement in their pain at 12, 24 and 36 weeks post-acupuncture, with 21% reporting complete relief from neuropathic pain.

It is possible that the small sample size in the current study may have led to a type II statistical error, particularly as P values were approaching significance ($P>0.082$). A further study with a larger sample size is required to confirm these observations. The design of this feasibility study did not allow for follow up with the patients to determine if their pain had reduced several weeks or months after the intervention. Longitudinal studies are required to show the possible long-term benefits of acupuncture in diabetes-related neuropathic pain.

Male participants ($n=8$) reported lower pain levels before and after a course of acupuncture, which was statistically significant ($P<0.04$), while female participants ($n=4$) did not. It is acknowledged that a gender imbalance is present in this study, however this may be reflective of the population under investigation because peripheral neuropathy is more common in men, even though painful symptoms of peripheral neuropathy are noted more frequently by women (Abbott et al, 2011).

Neuropathic pain has shown to have a negative effect on quality of life by restricting activities of daily living and negatively impacting on daily activities including sleep and an ability to enjoy life (Jensen et al, 2007; Ziegler, 2009).

The authors investigated quality of life using the Neuro-Qol tool. An improvement in HR-QOL was reported in all measured areas, although only fatigue, sleep disturbance and depression showed statistically significant improvements. These findings concur with the results of a similar study using Neuro-Qol (Davis et al, 2006). Neuropathic pain has an inherently negative impact on HR-QOL and can dramatically reduce a person's ability to function normally.

Therefore, it is of importance that HR-QOL is assessed in all patients before treatment is commenced to ascertain the effectiveness of the therapy.

Patients' belief in the effectiveness of acupuncture may be low because acupuncture is considered to be an alternative or complementary therapy and as such is not perceived to be a mainstream medical treatment or therapy. This study found that the perceived belief in the effectiveness of acupuncture increased in the cohort following the course of acupuncture therapy (P<0.011). However, it is acknowledged that this data was collected by CJ who also provided the acupuncture therapy, thus there is a possible bias.

These findings concur with those of So (2002) who concluded from a study on acupuncture outcomes and expectations that there is a perceived change in belief of acupuncture post-intervention. White et al (2011) carried out face-to-face interviews with 27 participants and reported that participants within an acupuncture study express "uncertainty regarding the veracity of the treatment" with the treatments' veracity linked directly to the patient's own outcome beliefs.

This finding could be applicable to the current research. Despite this study having a high accuracy of potential effect due to no sham acupuncture being conducted, the participant's belief may be reciprocal to the outcome of pain reduction. Further research could be conducted into of participants' thoughts and beliefs about acupuncture via a qualitative approach.

It is also worth highlighting that many of these participants thought that current medical management of their neuropathic pain had failed them. Consequently they may feel that the acupuncture reduced their level of pain and thus hold a stronger belief in the effectiveness of the intervention when compared to their original mainstream medical management.

Overall, the results of this study suggest that acupuncture may be used as a safe, adjunctive therapy in diabetes-related neuropathic pain, in conjunction with current evidence-based medicines and therapies. Acupuncture was found to marginally reduce pain which may be of clinical significance. Males responded better to the course of acupuncture with a statistically significant reduction in pain. Acupuncture has the potential to significantly improve HR-QOL in people with diabetes-related painful neuropathy, particularly in regards to fatigue, sleep disturbances and depression.

Conclusion

Although this study's main hypothesis that acupuncture would significantly reduce pain was rejected, the marginal decrease in pain may be clinically significant. This study demonstrated that the possibility of the creation of a larger two-arm RCT is possible to test the effectiveness of acupuncture for diabetes-related neuropathic pain. This therapy has the potential to be incorporated into clinical practice with patients who present with diabetes-related neuropathic pain but large, prospective randomised controlled trials are warranted to confirm these findings and ascertain the effectiveness of acupuncture for painful DSP. ■

Abbott CA, Malik RA, van Ross E et al (2011) Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the UK. *Diabetes Care* **34**: 2220–4

Abuaisha BB, Costanzi JB, Boulton AJ (1998) Acupuncture for the treatment of chronic painful peripheral diabetic neuropathy: a long term study. *Diabetes Res Clin Pract* **39**: 115–21

Bennett M (2001) The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. *Pain* **92**: 147–57

Bennett M, Smith B, Torrance N, Potter J (2005) The S-LANSS score for identifying pain of predominately neuropathic origin: validation for use in clinical and postal research. *J Pain* **6**: 149–58

Boulton AJ (2005) Management of diabetic peripheral neuropathy. *Clin Diabetes* **23**: 9–15

Cella D, Yount S, Rothrock N et al (2007) The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH roadmap cooperative group during its first two years. *Med Care* **45**: S3–11

Chen W, Yang GY, Liu B et al(2013) Manual acupuncture for treatment of diabetic peripheral neuropathy: a systematic review of randomized controlled trials. *PLoS One* **8**: e73764

Davies M, Brophy S, Williams R, Taylor A (2006) The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. *Diabetes Care* **29**: 1518–22

Garrow AP, Boulton AJ (2006) Vibration perception threshold - a valuable assessment of neural dysfunction in people with diabetes. *Diabetes Metab Res Rev* **22**: 411–9

Jensen MP, Chodroff MJ, Dworkin RH (2007) The impact of neuropathic pain on health-related quality of life: review and implications. *Neurology* **68**: 1178–82

Lee FH, Raja SN (2011) Complementary and alternative medicine in chronic pain. *Pain* **152**: 28–30

Medical Research Council (2000) *A framework for the development and evaluation of RCTs for complex interventions to improve health*. Available at: http://bit.ly/1VBDFa4 (accessed: 25.04.2016)

NICE (2013) *Neuropathic pain in adults: pharmacological management in non-specialist settings*. Available at: www.nice.org.uk/cg173 (accessed: 25.04.2016)

Scottish Intercollegiate Guidelines Network (2013) *SIGN 136. Management of Chronic Pain*. Edinburgh, SIGN. Available at: http://www.sign.ac.uk/pdf/SIGN136.pdf (accessed: 25.04.2016)

So DW (2002) Acupuncture outcomes, expectations, patient-provider relationship, and the placebo effect: implications for health promotion. *Am J Public Health* **92**: 1662–7

Tong Y, Guo H, Han B (2010) Fifteen-day acupuncture treatment relieves diabetic peripheral neuropathy. *J Acupunct Meridian Stud* **3**: 95–103

White A (2009) Western medical acupuncture: a definition. *Acupunct Med* **27**: 33–5

White P, Bishop F, Prescott P et al (2011) Practice, practitioner, or placebo? A multifactorial, mixed-methods randomized controlled trial of acupuncture. *Pain* **153**: 455–62

Ziegler D (2008) Painful diabetic neuropathy: treatment and future aspects. *Diabetes Metab Res Rev* **24**: S52–7

Ziegler D (2009) Painful diabetic neuropathy: advantage of novel drugs over old drugs? *Diabetes Care* **32**: S414–9

"The results of this study suggest that acupuncture may be used as a safe, adjunctive therapy in diabetes-related neuropathic pain."

Christopher Joyce is graduate podiatrist, School of Health Sciences, National University of Ireland Galway; David Watterson is podiatry manager, Merlin Park Podiatry Clinic, Merlin Park University Hospital, Galway and Honorary Clinical Fellow, Discipline of Podiatry, School of Health Sciences, National University of Ireland Galway; Caroline McIntosh is established professor of podiatry, Discipline of Podiatry, School of Health Sciences, National University of Ireland Galway, Ireland.