DR FARINA HASHMI (Orcid ID : 0000-0002-6257-2165)

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The EVerT2 (Effective Verruca Treatments) Trial: a randomised controlled trial of needling versus nonsurgical debridement for the treatment of plantar verrucae

Running heading: Needling versus nonsurgical debridement for the treatment of verrucae.

Authors: F. Hashmi[1], C. Fairhurst[2], S. Cockayne[2], M. Cullen[1], K. Bell[2], E. Coleman[2], M. Harrison-Blount[1], D. Torgerson[2]

1. University of Salford, School of Health Sciences, Brian Blatchford Building, Salford M6 6PU, United Kingdom

2. University of York, Department of Health Sciences, York Trials Unit, ARRC Building, Ground Floor, York YO10 5DD, United Kingdom.

Corresponding author:

Dr Farina Hashmi

Podiatry Lecturer

University of Salford

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School of Health Sciences

Brian Blatchford Building PO 41

Salford M6 6PU

United Kingdom

Email: F.Hashmi@salford.ac.uk

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Conflicts of interest

The authors declare no financial or personal relationships between themselves and others that might be perceived as biasing their work.

What's already known about this topic?

- Verrucae are notoriously difficult to treat, can last for many years, and cause pain and discomfort.
- There is a lack of high quality evidence evaluating verrucae treatments and considerable uncertainty regarding optimal treatments.
- Current common treatments of choice are salicylic acid and cryotherapy; however, although both treatments are equally effective, the clearance rate for these treatments is low (14%).

What does this study add?

- This trial evaluated the clinical and cost effectiveness of a needling technique, relative to callus debridement.
- There are two published studies on this treatment: a retrospective case series evaluation and a small randomised controlled trial which reports needling to be more effective than cryotherapy.
- This trial found no evidence to suggest that needling increases verrucae clearance rates.
- This trial provides evidence that needling significantly reduces pain compared to callus debridement.

ABSTRACT

Background: Verrucae are a common foot skin pathology which can in some cases persist for many years. Plantar verrucae can be unsightly and painful. There are a range of treatment options including needling.

Objectives: The EVerT2 trial aimed to evaluate the clinical and cost effectiveness of the needling procedure for the treatment of plantar verrucae, relative to callus debridement.

Methods: This single centre randomised controlled trial recruited 60 participants (aged 18 years and over with a plantar verruca). Participants were randomised 1:1 to the intervention group (needling) or the control group (debridement of the overlying callus). The primary outcome was clearance of the index verruca at 12 weeks after randomisation. Secondary outcomes include recurrence of the verruca;

clearance of all verrucae; number of verrucae; size of the index verruca; pain; and participant satisfaction at 12 and 24 weeks. A cost-effectiveness analysis was carried out from the NHS perspective over 12 weeks.

Results: Sixty eligible patients were randomised (needling group n=29, 48.3%; debridement group n=31, 51.7%) and 53 were included in the primary analysis (needling n=28, 96.6%; debridement n=25, 80.7%). Clearance of the index verruca occurred in 8 (15.1%) participants (needling n=4, 14.3%; debridement n=4, 16.0%, p=0.86). The needling intervention costs were on average £14.33 (95% CI 5.32 to 23.35) more per patient than debridement.

Conclusions: There is no evidence that the needling technique is more clinically or cost effective than callus debridement. The results show a significant improvement in pain outcomes after needling compared to the debridement treatment alone.

Trial registration number: Current Controlled Trials ISRCTN16429440

INTRODUCTION

Plantar verrucae (or warts) are common, with prevalence rates estimated between 0.84% (USA)[1] and 12.9% (Russia).[2] A Cochrane systematic review of 21 trials for wart treatments with placebo groups[3] reported clearance rates that averaged 27% (range 0% to 73%) in the placebo groups after an average period of 15 weeks (range 4 to 24). Whilst these data have led some practitioners to recommend that warts should not be treated at all,[4,5] patients often still seek treatment if verrucae are

unsightly or painful. There is uncertainty around the optimal treatment of verrucae and a need for high quality trials to evaluate therapies.

The Falknor needling technique[6], first described in the 1960s, and has recently received renewed interest as a treatment, involves administering a local anaesthetic and repeatedly inserting a needle into the verruca until it enters the underlying dermis and subcutaneous fat layer. The mechanical trauma to the viral tissue is believed to evoke inflammation and hence enhance the immune response in the area.[7] In a retrospective review of 45 patients who received needling, thirty-one (69%) experienced clearance of verrucae, three (7%) demonstrated a reduction in size and pain, and 11 (24%) showed no improvement eight weeks after treatment.[8] To our knowledge, there is only one published randomised controlled trial (RCT) evaluating the effectiveness of the needling procedure.[9] This trial randomised 37 participants to receive either needling or cryotherapy. There was a statistically significant reduction in clearance of the primary verruca 12 weeks after the initial treatment (needling 64.7% (11/17), cryotherapy 6.2% (1/16); p=0.001).

The objective of the EVerT2 (Effective Verruca Treatments 2) trial was to evaluate the clinical and cost effectiveness of the needling procedure compared with callus debridement for the treatment of plantar verrucae.

PATIENTS AND METHODS

Trial design

Full details are published elsewhere[10] and are provided in brief below. This was a single centre, pragmatic, open, two-armed RCT with an economic evaluation. Ethical approval was obtained from the University of Salford, Department of Health Sciences

Ethical Approval Committee (HSCR15/24), and the University of York, Department of Health Sciences Research Governance Committee (HSRGC/2014/98/B).

Study population

Patients were eligible if they were aged 18 years or over and had a plantar verruca on weight bearing skin that, in the opinion of the podiatrist, was suitable for both treatments. Potential participants were excluded if they: were unsuitable for local anaesthesia; had impaired healing; were immunosuppressed (or taking immunosuppressant drugs); had peripheral neuropathy or renal failure requiring dialysis; or were pregnant, unable or unwilling to give informed consent, or taking part in a trial evaluating other treatments for their verruca(e).

Recruitment and randomisation of participants

Participants were recruited between March 2015 and March 2016 from the University of Salford Podiatry Clinic. Eligible participants gave written informed consent and baseline measures were taken. They were then randomised 1:1 to immediately receive needling or callus debridement. A member of the research team telephoned the secure, remote randomisation service at the York Trials Unit (YTU), University of York, to obtain the allocation. Block randomisation with randomly permuted block sizes of 2 and 4 was used. The block size was kept secret from the recruiting clinicians.

INTERVENTIONS

Treatments were conducted by two podiatrists proficient in the needling technique who received training in trial procedures. For participants presenting with mosaic or multiple plantar verrucae, the largest and thickest lesion (the *index* verruca) was identified.

Control group

The skin surrounding the index verruca was disinfected and the callus overlying the lesion was removed using a surgical blade.

Intervention group: needling procedure

Intervention participants were treated as described for the control group with the addition of the administration of a local anaesthetic (Scandonest 3% plain) via tibial nerve block, according to the location of the lesion, prior to callus debridement.

An empty surgical needle (21 gauge) was used to repeatedly puncture through the lesion to the subcutaneous tissue to produce point bleeding until there was no more resistance, or reactive pressure, from the epidermis. This was done for the whole lesion. The total number of punctures varied according to the size of the lesion. In the case of large mosaic verrucae, a section of the verruca was needled. This follows the practice reported by Longhurst et al[8].

All participants were asked not to take anti-inflammatory drugs (such as ibuprofen) for 48 hours but were permitted to take paracetamol for pain relief.

FOLLOW-UP

Participants in the needling group attended a review appointment one week after the treatment where debridement of any uncomfortable eschar was performed.

Participants completed questionnaires at one day, 12 and 24 weeks and were invited for follow-up appointments at 12 and 24 weeks after randomisation. At 12 weeks in both groups overlying callus was debrided if the lesion was causing discomfort. At 24 weeks, if the verruca had not cleared then further, alternative treatments were offered.

All participants received £20 of high street shopping vouchers, divided equally between the 12 and 24 week appointments, to offset any incidental expenses associated with trial participation.

OUTCOME MEASURES

Baseline assessment

Data on the participant and verruca were collected and a digital photograph of the verruca was taken (see Supplementary Materials 1).

Primary outcome

The primary outcome was clearance of the index verruca at 12 weeks after randomisation as determined by blinded assessment at site. The podiatrist was asked what treatment they believed the participant had received to assess the success of the blinded review.

Secondary outcomes

Clearance or recurrence of the treated verruca was assessed at 24 weeks. Secondary outcomes at 12 and 24 weeks included: time to clearance; clearance of all verrucae; number of verrucae; size of the index verruca; pain; and participant satisfaction with treatment. Pain and the use of painkillers 24 hours after treatment was collected.

Sample size

The EVerT2 trial was powered at 80% to detect a difference in clearance rate of the index verruca from 30% in the debridement group to 70% in the needling group at 12 weeks post-randomisation. Allowing for 10% attrition, we required 58 participants to be randomised (29 to each treatment group).

Statistical analysis

Analysis was conducted in Stata v13[11] using two-sided statistical tests at the 5% significance level for the primary outcome and 1% for secondary outcomes. Available case intention to treat was used including all participants in the groups to which they were randomised irrespective of whether or not they received their

allocated treatment. Baseline and outcome data, including adverse events, are summarised descriptively. The primary outcome was analysed using a chi-squared test. In a sensitivity analysis, logistic regression was used to adjust the primary analysis for duration of the verruca, whether or not the verrucae have been previously treated, and type of verruca (mosaic/non-mosaic). These analyses were repeated replacing any missing blinded outcome data with self-reported clearance where available. Clearance of all verrucae at 12 and 24 weeks, and clearance of the index verruca at 24 weeks, were analysed via chi-squared tests. Cohen's kappa was used to measure the agreement of clearance between the participant and the blinded assessor at 12 and 24 weeks. Poisson regression compared the number of verrucae at 12 and 24 weeks between the treatment groups, adjusting for the number of verrucae at baseline. Self-reported time to clearance of all verrucae in days from randomisation was analysed using Cox proportional hazards regression adjusting for duration of verruca, whether or not the verrucae have been previously treated and type of verruca. Pain and size of the index verruca at week 12 and 24 were analysed via repeated measures covariance pattern models with baseline value, treatment group, time and a treatment group-by-time interaction term as fixed effects and participant as a random effect.

Total costs per participant were calculated (including all resource use and intervention costs) from the perspective of the NHS. A multiple imputation approach was taken to account for missing data.

RESULTS

Seventy six individuals were screened and 61 (80.3%) were randomised (Figure 1). One ineligible participant (allocated to the needling group) was randomised in error as they had a corn and not a verruca. Therefore, 60 eligible patients were randomised; 29 (48.3%) to the needling group and 31 (51.7%) to the debridement group.

The majority of participants were female (n=38, 63.3%), and the average age was 38 years (range 19 to 76) (Table 1). Participants had had their verruca for a median of three years, and most had sought treatment previously (n=47, 78.3%). The most commonly reported reason for seeking treatment was that the verruca was painful (n=24, 70.0%). In general, the two groups were comparable at baseline; however, the proportion of women, patients with a mosaic verruca, and patients who had sought previous treatment for their verrucae was greater in the needling group than in the debridement group, and the average pain experienced was higher.

All participants received their allocated treatment. Two participants allocated to debridement withdrew from the trial: one received debridement but later withdrew as they were not happy with the treatment group they had been allocated to and were not prepared to wait until after the trial to receive needling; and one missed their 12 week review and withdrew when invited for their 24 week appointment.

At 12 weeks, 53 (88.3%) participants had their index verruca assessed for clearance by a blinded assessor (needling n=28, 96.6%; debridement n=25, 80.7%; Supplementary materials 2). Clearance of the index verruca was judged to have occurred in 8 (15.1%) participants (needling n=4, 14.3%; debridement n=4, 16.0%, difference in percentage -1.7, 95% CI -21.1 to 17.6, p=0.86). These eight had complete clearance of all their verrucae (four participants had one verruca at baseline; one each had two, three, four or five). There was no evidence of a difference in the likelihood of clearance between the two groups from the chi-squared test (X^2=0.03, p=0.86) or the adjusted logistic regression (odds ratio (OR) 1.10, 95% CI 0.22 to 5.58, p=0.91). Two participants returned a 12 week participant questionnaire which included a self-assessment of clearance (both not cleared) but didn't return for a clinic assessment. There was only a negligible difference in the parameter estimates and p-values when the analyses were repeated replacing the missing blinded outcome with self-reported clearance (results not presented). Of the eight participants with blinded assessed clearance of all verrucae at 12 weeks, seven self-reported that they believed their verrucae had cleared, while one did not. Two further participants thought their verrucae had gone when they hadn't. The level of agreement between self-reported and blinded assessed clearance was high (kappa 0.79, p<0.001).

At week 12, there was no evidence that the age of the verruca is associated with clearance (adjusted OR 1.0, 95% CI 0.98 to 1.02, p = 0.74). Also, verrucae that had been treated previously were marginally less likely to clear than verrucae that had not been treated before, but this difference was not statistically significant (adjusted OR 0.8, 95% CI 0.12 to 5.28, p = 0.81). All 8 mosaic verrucae were still present at the end of the 12 week period.

At week 12, the blinded podiatrists reported that they were unable to tell what treatment the participant had received for 48 (90.6%) of the 53 participants assessed (needling 24/28 (85.7%); debridement 24/25 (96.0%)). They believed two needling participants had received debridement, but correctly identified the treatment for two needling participants and one debridement participant.

At 24 weeks, 49 (81.7%) participants had their index verruca assessed for clearance by a blinded assessor, and 11 (22.5%) were judged to have cleared (needling 5/25 (20.0%); debridement 6/24 (25.0%); X^2=0.18, p=0.68). All but one of these had complete clearance of all verrucae (needling 5/25 (20.0%); debridement 5/24 (20.8%); X^2=0.01, p=0.94). Where both self-reported and blinded outcome assessments of clearance were available, there was total agreement (kappa 1.00, p<0.001). One participant judged by the blinded assessors to have complete clearance did not respond to whether they thought their verrucae had all cleared but annotated the questionnaire with “Think it may have gone as for the last 12 weeks I have had no pain. I found it difficult to see the verruca position as it is in an awkward position”. There were no reported instances of reoccurrence between weeks 12 and 24.

The median number of verrucae at 12 weeks in the needling group was 1.5 (range 0 to 8) (24 weeks, median 1, range 0 to 8) and in the debridement group was 2 (range 0 to 19) (24 weeks, median 1, range 0 to 11). There was no evidence of a difference in the number of verrucae at 12 weeks (incidence rate ratio (IRR) 0.89, 95% CI 0.67 to 1.18; p=0.42) or 24 weeks (IRR 0.81, 95% CI 0.50 to 1.31, p=0.39) or in time to clearance of all verrucae (hazard ratio (HR) 2.17, 95% CI 0.72 to 6.54; p=0.17) between the two groups.

Participants in the needling group reported higher levels of pain at baseline and one day after treatment than the debridement group, but lower levels at 12 weeks, and at 24 weeks when the difference was statistically significant (Table 2). There was a small to moderate correlation between pain and verruca size at 12 weeks (r=0.37) and 24 weeks (r=0.15). Fifteen (26.3%) of the 57 participants who returned a Day 1 questionnaire reported using a painkiller after their treatment (all in the needling group). There was no evidence of a difference in the size of the index verruca between the two groups at week 12 or 24 weeks (Table 2).

More participants in the needling group than in the debridement group said that they would be willing to have the same treatment again (82.1% compared with 60.0%) (Table 3). Most of the needling group at both 12 and 24 weeks were either happy or very happy with their treatment; whereas in the debridement group, a greater number were indifferent, unhappy or very unhappy than were happy or very happy.

There were two non-serious adverse events reported, both unrelated to the trial and mild in intensity. One event was expected (pain, needling participant) and one unexpected (GI tract yeast infection, needling participant).

Economic Evaluation

All patients received at least one treatment visit at the podiatry clinic. The mean number of treatment visits was similar between groups (2.14 (SD 0.74) for the needling group [n=29] vs 1.96 (SD 0.54) for the debridement group [n=31]). Only one participant in each group reported visiting a GP/nurse about their verrucae at the 12 week assessment. Accounting for the total number of treatment visits to the podiatry

clinics as well as additional GP/nurse visits, the needling intervention costs on average £14.33 (95% CI 5.32 to 23.35) more per patient compared to debridement.

Discussion

This is the largest trial evaluating the clinical and cost effectiveness of the needling technique to date. We found no evidence of a difference in effectiveness between needling and callus debridement in terms of clearance rates and verruca size, and an increase in cost. However, although the pain 24 hours after treatment was greater in the needling group, the pain experienced at 12 and 24 weeks was reduced for this group compared to the callus debridement group. At 24 weeks this difference was statistically significant. The needling technique was found to be safe and acceptable to participants, and 82% of the needling participants stated that they would be willing to have the same treatment again. The needling treatment was associated with higher costs per cured patient. Given that there was no difference in the likelihood of clearance between the two groups, the needling intervention is dominated hence has higher costs for no additional benefit compared to debridement. Needling is thus not cost-effective compared to debridement.

Our results for clearance conflict with the findings of the only other RCT of the needling procedure by Cunningham et al[9]. This was a smaller study of 37 participants and showed a statistically significant difference in clearance rates favouring the needling group after 12 weeks, relative to cryotherapy. The clearance rate for the needling group was 64.7% (11/17), which is 4.5 times greater than our

corresponding rate of 14.3% (4/28). Similarly, Longhurst and Bristow[8] reported a 69% (31/45) resolution of verrucae in a retrospective, case series analysis. However, our results are similar to the EVerT trial that reported a 14% cure rate for both salicylic acid treatment and cryotherapy[12].

Our study followed the same treatment protocols as Longhurst and Cunningham, with the exception that participants in our needling group were given one treatment. Longhurst and Bristow[8] reported a high resolution rate (38/45) after one needling treatment. Cunningham et al[9] reported a median of 2 treatments, 5 weeks apart and a mean (± SD) of 1.61 (0.05) treatments, 5.08 (2.08) weeks apart. Cunningham et al[9] did not report how many verrucae resolved after one or two treatments. The theory that verrucae resolve in response to localised tissue damage (which is yet to be confirmed) would suggest that this could be achieved after one needling procedure. Data on resolution rates is unclear; therefore if two treatments are conducted within a few weeks of each other and the verruca resolves it could be possible that the response from the first treatment is still occurring when the second treatment is administered. We therefore decided that from a trial design perspective, one treatment in each group would provide clarity in this regard. We also based our decision from an ethical perspective in that if it is likely that the verrucae may resolve after one treatment, then it would not be ethical to conduct a second treatment. As this is the first large RCT to test the effects of the needling on verrucae, we felt it necessary to standardise the interventions between both groups. It is possible that multiple treatments are required to stimulate the required immune response and promote clearance, and this may help explain the difference in results. The next step in the evaluation of needling treatment would be to test the number of

treatments required to achieve verruca resolution. Also, the use of combination treatments could be explored, for example the use of home treatments between needling treatments.

There are also differences between the populations in our and Cunningham's trials. The mean and median ages of the participants in our study (Table 1) are greater than those reported by Cunningham et al[9] (mean (± SD) = 26.11 (9.99) years and median (range) = 22.5 (18 – 53) years). Cunningham et al[9] recruited from the university based podiatry clinic only. However, in addition to recruiting from the university clinic, we advertised in community areas accessed by the general public, such as supermarkets, health centres, day centres, leisure centres and athletics clubs. We also placed advertisements in local newspapers and via social media accounts. We can therefore accept that we recruited from a wider population than the Cunningham study. However, there is a general opinion within the podiatry profession (based on peer discussions and not evidence) that people with tenacious verrucae opt for needling after all other treatment options have been exhausted. Our data does show that the majority of the participants (78%) had tried other treatments before participating in the trial. Cunningham et al[9] did not report data on previous treatments in their study.

Though overall the average verruca size at baseline was similar in both trials (56.9mm^2 versus 52.7mm^2), there is an imbalance in verruca size in the Cunningham trial and needling participants tended to have much smaller verrucae (mean 29.1mm^2) compared with cryotherapy patients (75.0mm^2), which wasn't accounted for in the analysis. In addition, our participants tended to have had their verruca for

longer than the Cunningham cohort (58 vs 34 months), with an even bigger difference seen in the two needling groups (60 vs 29 months). Our data showed now association between the age of the verruca and the clearance rate.

Strengths and limitations

The major strength of this study is that it is of high quality. The risk of bias has been minimised due to the use of adequate randomisation, allocation concealment, blinded outcome assessment and intention to treat analysis. Our study does have potential limitations. It was a single centre study and therefore results may not be applicable to patients presenting in GP practices or NHS or private podiatry clinics.

This trial did not have a true placebo or 'no treatment' arm. It was envisaged that people would volunteer for this study to access the novel treatment needling procedure, which is not widely available in the National Health Service (NHS) or private podiatry clinics. The risk of losing participants to follow-up would have been high if these participants were randomised into a 'no treatment' group. Therefore, we decided to offer callus debridement (which is currently the treatment provided in some NHS podiatry clinics) to maximise participant retention throughout the trial. All participants in the control group were offered a free needling treatment at the end of the trial if their verruca was still present. The use of a 'sham' needling treatment for the control group was considered; however, the trial team concluded that it would be unethical to administer a local anaesthetic if no treatment was to be given. Therefore, it is likely that the clearance we saw was probably due to natural history rather than any treatment effects.

Summary

The results of this trial reveal that the verruca needling treatment is no more efficacious than callus removal and is more costly. The only significant result was in the pain outcomes, which were reduced in the needling group compared to the debridement group. The intervention was dominated by usual care in the economic evaluation, hence is not cost-effective, compared to usual care.

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Figure legend

Figure 1. CONSORT flow diagram of participants in the EVerT2 trial

Table 1. Baseline characteristics of randomised participants

Characteristic	**Needling (N=29)**	**Debridement (N=31)**	**Total (N=60)**
Age, years	N=29	N=31	N=60
Mean (SD)	42.5 (14.2)	37.1 (12.9)	39.7 (13.7)
Median (minimum, maximum)	40.4 (23.4, 76.0)	36.5 (19.5, 68.7)	38.1 (19.5, 76.0)
Gender, n (%)			
Male	9 (31.0)	13 (41.9)	22 (36.7)
Female	20 (69.0)	18 (58.1)	38 (63.3)
No. of verrucae at baseline	N=29	N=31	N=60
Mean (SD)	4.0 (3.2)	4.2 (3.8)	4.1 (3.5)
Median (minimum, maximum)	3 (1, 11)	3 (1, 16)	3 (1, 16)
Duration of verrucae, months	N=29	N=31	N=60
Mean (SD)	60.3 (53.5)	56.2 (62.9)	58.2 (58.1)
Median (minimum, maximum)	48 (3, 240)	36 (6, 312)	36 (3, 312)
Type of verrucae, n (%)			
Mosaic	5 (17.2)	3 (9.7)	8 (13.3)
Non-mosaic	24 (82.8)	28 (90.3)	52 (86.7)
Size of index verruca, mm^2	N=29	N=31	N=60
Mean (SD)	51.9 (78.2)	61.7 (123.6)	56.9 (103.4)
Median (minimum, maximum)	22 (2, 356)	18 (4, 607)	20.5 (2, 607)
Previous treatment, n (%)			
Yes	25 (86.2)	22 (71.0)	47 (78.3)
No	4 (13.8)	9 (29.0)	13 (21.7)
Type of previous treatments, n (%)[a]			
Over-counter	22 (75.9)	21 (67.7)	43 (71.7)
Podiatrist treatment	18 (62.1)	14 (45.2)	32 (53.3)
GP treatment	9 (31.0)	7 (22.6)	16 (26.7)
Other trial	0 (0.0)	1 (3.2)	1 (1.7)
Other[b]	6 (20.7)	1 (3.2)	7 (11.7)
Reason for seeking treatment, n (%)[a]			

Pain	25 (86.2)	17 (54.8)	42 (70.0)
Unable to go swimming	10 (34.5)	9 (29.0)	19 (31.7)
Unable to participate in other sports	7 (24.1)	7 (22.6)	14 (23.3)
Other[c]	10 (34.5)	14 (45.2)	24 (40.0)
Pain, VAS 0-100	N=29	N=31	N=60
Mean (SD)	44.5 (32.3)	24 (25.5)	33.9 (30.5)
Median (minimum, maximum)	50 (0, 96)	13 (0, 83)	28.5 (0, 96)
Previous verrucae, n (%)			
Yes	16 (64.0)	21 (67.7)	37 (66.1)
No	9 (36.0)	10 (32.3)	19 (33.9)
No. of previous verrucae	N=16	N=21	N=37
Mean (SD)	4.4 (5.0)	4.7 (6.5)	4.5 (5.8)
Median (minimum, maximum)	2 (1, 20)	3 (1, 30)	2 (1, 30)
Age at which previous verrucae occurred (years)	N=15	N=22	N=37
Mean (SD)	27.9 (21.0)	18.5 (9.2)	22.3 (15.6)
Median (minimum, maximum)	23 (6, 76)	16.5 (8, 38)	18 (6, 76)

[a] More than one category could be checked for each patient

[b] self-filing/debridement (needling n=3, debridement n=1); duct tape (needling n=2); hospital freeze treatment (needling n=1)

[c] aesthetics (needling n=5, debridement n=4); concern about passing verruca to others (needling n=1, debridement n=5); had it so long/want rid (needling n=1, debridement n=1); prevents from walking long distances (needling n=2); invited to take part in EVerT2 trial (debridement n=2); verruca getting worse/larger (needling n=1, debridement n=1); wellbeing (debridement n=1)

Table 2. Verruca pain measured on a visual analogue scale, and verruca size (mm^2) by randomised group and time point

How painful is your verruca today? 0 (no pain)-100 (worst possible pain)	**Needling (N=29)**	**Debridement (N=31)**	**Adjusted mean difference (95% CI) p-value**
Baseline	N=29 44.5 (32.3) 50 (0, 96)	N=31 24.0 (25.5) 13 (0, 83)	-
Day 1	N=29 30.3 (25.6) 21 (0, 89)	N=28 8.8 (10.9) 4 (0, 36)	-
Week 12	N=29 17.0 (19.6) 4 (0, 67)	N=26 20.4 (24.3) 6 (0, 78)	-9.64 (-20.12, 0.85) p=0.07
Week 24	N=24 10.9 (17.0) 4 (0, 70)	N=26 15.5 (21.9) 5 (0, 89)	-12.54 (-23.61, -1.46) p=0.03
Size of index verruca, mm^2			
Baseline	N=29 51.9 (78.2) 22 (2, 356)	N=31 61.7 (123.6) 18 (4, 607)	-
Week 12	N=28 38.3 (69.0) 11 (0, 337)	N=24 50.8 (99.6) 12.5 (0, 423)	0.10 (-20.61, 20.81) p=0.99
Week 24	N=24 46.3 (91.6) 12.5 (0, 411)	N=22 19.0 (33.7) 8.5 (0, 145)	-2.79 (-34.02, 28.43) p=0.86

Data summarised as raw Mean (SD) Median (minimum, maximum)

Table 3. Participant satisfaction with treatment by randomised group

	Needling (N=29)	Debridement (N=31)	Total (N=60)
Would you be willing to have the same treatment again?			
Week 12, n (%)			
Yes	23 (82.1)	15 (60.0)	38 (71.7)
No	2 (7.1)	9 (36.0)	11 (20.8)
Don't know	3 (10.7)	1 (4.0)	4 (7.6)
How happy are you with your treatment?			
Week 12, n (%)			
Very happy	11 (37.9)	7 (26.9)	18 (32.7)
Happy	11 (37.9)	5 (19.2)	16 (29.1)
Neither happy nor unhappy	5 (17.2)	7 (26.9)	12 (21.7)
Unhappy	0 (0.0)	7 (26.9)	7 (12.7)
Very unhappy	2 (6.9)	0 (0.0)	2 (3.6)
Week 24, n (%)			
Very happy	9 (37.5)	7 (26.9)	16 (32.0)
Happy	7 (29.2)	4 (15.4)	11 (22.0)
Neither happy nor unhappy	6 (25.0)	10 (38.5)	16 (32.0)
Unhappy	0 (0.0)	5 (19.2)	5 (10.0)
Very unhappy	2 (8.3)	0 (0.0)	2 (4.0)

Figure 1. CONSORT flow diagram of participants in the EVerT2 trial