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Analysis of a trial assessing the long-term effectiveness of salicylic acid plasters compared with scalpel debridement in facilitating corn resolution in patients with multiple corns

Running title: Corn resolution using salicylic acid plasters

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Abstract

This study assesses the effect of salicylic acid plasters on the time to resolution of 324 corns experienced by 201 participants taking part in a randomised controlled trial. While the rate of corn resolution was substantively higher in the treatment group than in the control group, treatment was found to be not significantly related to time to corn recurrence when analysed over the full 12-month follow-up period. Parametric survival analysis modelling of interval-censored data and incorporating patient-specific frailty terms was utilised, to model correlation of corns within patients (hazard ratio [HR] 1.189; 95% confidence interval 0.780 to 1.813; p=0.422). Median resolution times were 10.0 months for corns in the treatment group and 13.4 months for corns in the control group. Controlling for treatment, corn type was found to be related to resolution time, with dorsal/inter-digital (ID) corns showing better resolution than plantar corns (HR 1.670; 95% confidence interval 1.061 to 2.630; p=0.027). Median resolution times were 5.9 months for dorsal/ID corns and 14.9 months for plantar corns.

Secondary measures relating quality of life (QoL) and foot-related disability, using the EQ-5D questionnaire and the Manchester Foot Pain and Disability Index, were also assessed at the patient level in multivariate models. Treatment was not significantly related to any of these measures over the whole period of analysis. However, a trend analysis revealed a quadratic trend in QoL and MFPDI scores, arising from a substantive initial improvement between baseline and 3 months, followed by a gradual decrease between 3 and 12 months.

Key words

Corns; Debridement; Foot; Pain; Podiatry

Introduction

Corns are a common foot problem affecting a large proportion of the population, particularly the older population. A large-scale (n=784) study of the prevalence of foot and ankle disorders
in community-dwelling adults aged over 65 years [1] found 58.2% to have one or more corns; the third most common foot condition after toenail disorders and lesser toe deformities. A study of 301 independently living older people [2] found that 60% had at least one plantar hyperkeratotic lesion. Corns generally show increased prevalence in older people and in females [3] with up to 4 times the incidence rate in females than males [4], and are thought to form in response to over-prolonged and excess mechanical stresses, including shear and friction [4]. The most common corn types are plantar corns beneath the third and fourth metatarsal heads. Dorsal and inter-digital corns are somewhat less common than all types of plantar corns [4].

Scalpel debridement is often the first professional treatment administered for corns. The effectiveness of scalpel debridement was assessed against sham debridement in a parallel randomised controlled trial (n=80) [5]; while both control and treatment groups in this study reported reductions in pain over a 6-week analysis period, no significant differences in pain reduction between groups was observed.

Salicylic acid is widely used as the active ingredient in non-prescription liquids, gels (up to 17% concentration) and plasters (up to 40% concentration) for the home treatment of calluses and corns. It softens the epidermis, allowing the corn to be removed easily, is inexpensive but must be used with caution. However, experimental studies into its effectiveness are limited. A study of 102 patients with dorsal corns [6] compared two different matrix types of salicylic acid corn plasters, finding that plasters with an adhesive matrix cause less extensive maceration than plasters with a waxy matrix, although this study did not include comparison of plasters against a control. A study by Lang et al. [7] found that 40% salicylic acid plasters used over various periods of time were significantly more effective in the removal of corns than a placebo; however, no significant differences were found between treatment groups applying the treatment for different periods of time.
More recently a multi-centre parallel-group randomised controlled trial to assess the effectiveness of salicylic acid plasters was undertaken [8] finding that 40% salicylic acid corn plasters was associated with a higher proportion of resolved index corns (a corn nominated by each participant as the largest or the one causing the most pain), prolonged time to corn recurrence, less pain and reduced corn size in comparison to usual scalpel debridement \((n=202)\). The current investigation represents further analysis of an expanded version of this data set.

**Methods**

**Participation**

Data was collected from on adult patients with one or more corns, who were recruited to the study from one National Health Service (NHS) podiatry service, a university podiatry clinic, and the local population of two localities in the North of England between September 2009 and October 2011. A number of research podiatrists participated in data collection, all of whom were trained in the application of corn plasters, and all of whom reinforced the advice which was also given in written format on the information sheet.

Study participants were excluded if they had diabetes or rheumatoid arthritis; poor peripheral circulation or peripheral neuropathy; a history of foot ulceration; were taking oral steroid medication; had a marked dermatological condition (e.g. eczema, psoriasis, etc.); were allergic to zinc oxide plaster, salicylic acid, peanuts or soya; were unable to reach their own feet; had callus rather than corns, or corns that were infected or neurovascular; were pregnant or breastfeeding; were under the age of 18 years; or did not give consent to participate in the study.

The *patient*-level parameters of age and gender; and the *corn*-level parameters of corn diameter (cm) and corn type (categorised as either plantar, or dorsal/inter-digital (ID)) were
recorded at baseline. Data from up to 3 corns per patient was recorded, with one index corn nominated by each participant.

Ethical approval for this study was obtained from Leicestershire, Northamptonshire and Rutland Research Ethics Committee 2(09/H042/07), Medicines and Healthcare Products Regulatory Agency and local research governance approval. The work conforms to the provisions of the Declaration of Helsinki. All participants gave informed consent before participation in the trial.

**Treatment**

Eligible participants who gave written consent to participation were randomised (using simple randomisation) to either a control group or a treatment group.

Patients assigned to the control group received scalpel debridement of corns by a podiatrist, and were instructed to return for treatment at 3-monthly intervals for a maximum of 12 months from initial examination. Standard foot health and footwear education was also given at each appointment.

Patients assigned to the treatment group had a corn plaster (Carnation corn plasters®, Cuxson Gerrard & Co) applied to each corn (up to three corns per person) by a podiatrist, and appropriate dressings applied if necessary to keep the plasters in place. The plasters contained 40% salicylic acid. Each participant was advised to keep the corn plasters dry until the follow-up appointment which was scheduled for one week after application of the corn plasters. Advice was given about removal and neutralisation of the salicylic acid with a warm salt foot bath if any adverse reaction was experienced. At the next appointment new corn plasters were applied if the corns were still present, and this was repeated for up to four weeks, or until the corns could be lifted off via blunt debridement by the podiatrist. The participants were instructed to return for treatment at 3-monthly intervals for a maximum of 12 months from
initial examination, and received ‘usual’ scalpel debridement of any remaining corns. Standard foot health and footwear education was also given at each appointment. Corns after plaster removed and after blunt debridement are illustrated in Figure 1(a) and Figure 1(b).

***INSERT FIGURES 1(a) AND 1(b) HERE***

Outcome measures

The primary outcome was the time to corn resolution; this being defined as absence of the corn, or a corn measurement of less than 1 mm in diameter. Corns which were observed to be absent at a given appointment and then to have recurred at a subsequent appointment were not judged to have resolved at the earlier appointment.
Corn resolution was assessed by an independent podiatrist blind to patient group allocation, who also measured the type and size of the corns at baseline, and at each of the three-monthly follow-up appointments.

Secondary outcomes included quality of life, as measured by the EQ-5D instrument, and the functional limitation (FL), pain intensity (PI) and concern about appearance (CA) sub-scales of the Manchester Foot Pain and Disability Index (MFPDI). All secondary outcomes were measured at baseline and at 3-monthly intervals up to a maximum of 12 months. High EQ-5D scores, which may range from 0 to 100, represent better quality of life. The FL sub-scale of the MFPDI instrument comprises 10 items, the PI subscale comprises 5 items and the CA subscale comprises 2 items. All items were scored on a scale from 1 to 3; and hence possible scores ranged from 10 to 30 for FL; 5 to 15 for PI; and 2 to 6 for CA. Lower scores represent better functionality.

Items were assigned to the appropriate subscale using the factor structure devised by Garrow [9]. The remaining sub-scale of the MFPDI instrument, activity restriction, was not considered in the current analysis, as it would not apply to a large proportion of patients in the study who were above retirement age.

A pain score, obtained using a visual analogue scale, was also elicited from respondents and reported in an earlier analysis of data collected from these patients [8]; however, as this was a single patient-level measure applied to the index corn only, it was not included in the current analysis, as a corresponding individual corn-level measure was not available.

Sample size

The sample size was calculated at the patient level for the purposes of the previous analysis conducted on part of the current data set [8] using data from previous studies [6, 7] suggesting expected resolution rates of 60-90% at 3 months and under the assumption that a 20% absolute difference in recurrence rates would be of clinical importance. The given sample
size for the original study was chosen to give a power of 80%. The power of the current study, which included additional corns, should be in excess of this value.

Statistical analysis

The sample was summarised descriptively. The primary outcome was analysed using parametric survival (time-to-event) methods. As exact times of resolution could not be recorded, a positive observation (i.e. the resolution of a corn) was recorded as an interval-censored observation. In such cases the lower censoring time was given by the time (in months) from baseline of the latest observation of the non-resolved corn. The upper censoring time was given by the time (in months) from baseline of the earliest observation of the resolved corn; subject to no subsequent observation of the same corn in the unresolved state. A corn which was not recorded as having resolved by the time of the last observation was recorded as a right-censored observation, with a censoring time equal to the time (in months) of the latest observation since the baseline reading.

A number of candidate distributions were assessed for goodness-of-fit to the data, including the exponential, Weibull, Gompertz, log-logistic, log-normal and generalised Gamma distributions. Distributions were assessed using the Akaike Information Criteria (AIC) statistic, defined as follows:

\[
\text{AIC} = -2\ln L + 2(k + c)
\]

where \( L \) is the value of the maximum likelihood, \( k \) is the number of model covariates and \( c \) is the number of model-specific distributional parameters. Distributions were compared using models including the key treatment variable only. Testing of assumptions of proportionality was also undertaken.

Data analysed for the primary outcome formed a multilevel structure, with corns being clustered within patients. Both patient-level and corn-level variables were included in the
analysis of the primary outcome. This was facilitated in a survival analysis framework by formulating random effects arising from the assumption of an underlying hierarchical structure as patient-specific frailty terms, modelling correlation of corns within patients; i.e. random effects that enter multiplicatively on the hazard function, and are independent of censoring. Frailties shared across patients were added to the regression function of the multiple regression models, modelled using the Gamma distribution with zero mean.

All patient-level and corn-level predictor variables were assessed for baseline imbalance post-randomisation, and controlled statistically within the regression models if necessary.

Secondary outcomes were analysed using repeated measures analysis of variance (for EQ-5D scores) and doubly multivariate repeated measures analysis of variance (for the FL, PI and CA sub-scale scores of the MFPDI instrument), following exploratory procedures to assess the correlation between these measures and the suitability of the data for the analysis procedures. The extent and nature of data missingness was investigated. Sphericity was assessed using Mauchly’s test and an appropriate correction factor applied if necessary. Any patient-level variable exhibiting a substantial imbalance across treatment groups was controlled for statistically. Trend analysis was also conducted on the data. Secondary analyses were not conducted at the level of the individual corn.

Analysis was conducted using Stata IC (Version 11) and IBM SPSS (Version 20.0) statistical software.

Results

A total of 317 patients were initially assessed for inclusion in the trial. Following exclusions, (mostly due to refusals) usable data was obtained from 201 patients, of which 100 were randomised to the treatment group and 101 to the control group. All patients supplied at least one corn to the analysis. Additionally 87 patients supplied a second corn to the analysis (35 in the control group and 52 in the treatment group); and 36 patients supplied a third corn to the
analysis (12 in the control group and 24 in the treatment group); hence a total of 324 corns were included in the analysis. Patient and corn characteristics are summarised in Table 1. Categorical variables are summarised in terms of frequencies and valid percentages.

***INSERT TABLE 1 HERE***

Hence while the sample was well matched across treatment groups with respect to age, gender and baseline corn size, it was not well matched on corn type. This variable was included in subsequent analyses of the primary outcome as a controlling variable.

Amongst the foot disability measures, some substantive reductions (representing improved functionality) were observed between baseline and the 3-month time point, particularly in the control group: beyond 3 months, readings were fairly static. There were no obvious trends in quality of life across any time period in either group.

Analysis of primary outcome

Analysis of AIC statistics indicated the 2-parameter Weibull distribution, parameterised in the proportional hazards metric, to be the most appropriate modelling distribution. Log-cumulative hazard plots, constructed using non-interval censored data, (Figures 2(a), 2(b)) indicated that the proportionality of hazards assumption across treatment groups and corn type was broadly tenable, although some deviations from proportionality were observed when comparing across treatment groups towards the end of the follow-up period.

***INSERT FIGURES 2(a) AND 2(b) HERE***
A multiple Weibull survival model incorporating frailty terms and including both the treatment variable, and corn type as a controlling covariate was derived. The interaction between the treatment variable and the corn type variable was initially assessed and found to be non-significant: following standard procedures, the interaction was removed and the model re-cast as a main effects model.

The Weibull model found that treatment was not significantly associated with time to corn resolution (hazard ratio 1.189; 95% confidence interval 0.780 to 1.813; p=0.422). Median resolution times were found to be 10.0 months for corns in the treatment group and 13.4 months for corns in the control group.

The controlling variable of corn type was significantly associated with time to corn resolution (hazard ratio 1.670; 95% confidence interval 1.061 to 2.630; p=0.027): hence the hazard of corn resolution in dorsal/intra-digital corns was about 67% higher than the hazard of corn
resolution in plantar corns controlling for treatment. Median resolution times were found to
be 5.9 months for dorsal/ID corns and 14.9 months for plantar corns.

The shape parameter for the above model was found to be 0.530 (95% CI 0.402, 0.699). This
corresponds to a monotonically decreasing hazard function; i.e. the instantaneous rate of corn
resolution is highest immediately after initial treatment.

Figure 3(a) illustrates corn “survival” (i.e. non-resolution) for corns in the treatment and
control groups, averaged over both corn types. The lower location of the curve for corns in the
treatment group indicates better, albeit non-significant, corn resolution rates in this group.

***INSERT FIGURE 3(a) HERE***

Figure 3(b) illustrates corn “survival” for dorsal/ID and plantar corns, averaged over treatment
groups. The lower location of the curve for dorsal/ID corns indicates better corn resolution
rates for this type of corn.

***INSERT FIGURE 3(b) HERE***
Analysis of secondary outcomes

Inspection of missing EQ-5D and MFPDI scores revealed that around 10% of data was missing at 3 months, about 25% of data was missing after 6 months, about 40% of data was missing after 9 months and about 55% of data was missing after 12 months. Little’s test for missingness revealed that all data was missing completely at random: however, the amount of missing data was considered too great to merit imputation procedures. Inspection of groups post-randomisation revealed that the patient-level variables of age and gender were well balanced across groups, and hence statistical control of these variables was not needed.

A repeated measures analysis of variance (ANOVA) was conducted on all EQ-5D data with casewise deletion, using treatment as a grouping variable, following exploratory analysis to confirm the suitability of data for this treatment, in which Box’s test revealed no evidence for violation of homogeneity of the variance-covariance matrix and no multivariate outliers were found at $\alpha=0.01$ from inspection of Mahalanobis distances. Mauchly’s test indicated evidence for violations of sphericity, with an associated epsilon value of 0.873: hence the Huynh-Feldt correction factor was applied to the analyses.

The analysis revealed treatment not to be significantly associated with a linear combination of the EQ-5D scores at all time points ($F_{1,86}=1.085, p=0.300$). The time factor was of borderline significance ($F_{3.493,300.4}=2.425, p=0.056$). A test of parallelism revealed that the treatment and
control groups had different patterns of QoL scores over time, although this difference did not reach statistical significance at the 5% level ($F_{3,493,300.4}=2.360, p=0.062$).

Trend analysis revealed a non-significant F-ratio for a linear trend, but significant evidence for a quadratic trend over time ($F_{1,86}=4.815, p=0.031$). Inspection of marginal mean plots revealed that this was grounded in a rise in quality of life scores between baseline and the 3-month time point; followed by a more gradual decrease in values between 3 months and 9 months. This effect was noted over both groups (Figure 4).

***INSERT FIGURE 4 HERE***

Correlational analysis indicated that the three sub-scales of the MFPDI of interest in the current analysis were all correlated with each other ($r=0.705$ for FL and PI; $r=0.606$ for FL and CA; $r=0.509$ for PI and CA). Hence a multivariate approach was considered to be appropriate for the analysis of these measures.

A doubly multivariate repeated measures analysis of variance (ANOVA) was conducted on all MFPDI data with casewise deletion using treatment as a grouping variable, following exploratory analysis to confirm the suitability of data for this treatment, in which Box’s test revealed no evidence for violation of homogeneity of the variance-covariance matrix and no
multivariate outliers were found at $\alpha=0.01$ from inspection of Mahalanobis distances. Mauchly’s test indicated evidence for violations of sphericity on all three sub-scales, with associated epsilon values of 0.900-0.934: hence the Huynh-Feldt correction factor was applied to the analyses.

The analysis revealed treatment not to be significantly associated with a linear combination of the MFPDI sub-scale scores at all time points ($F_{1,71}=0.126, p=0.723$ for FL; $F_{1,71}=0.371, p=0.544$ for PI; $F_{1,71}=0.036, p=0.850$ for CA). The time factor was significantly associated with the FL and PI subscale scores, and exhibited some substantive association with the CA subscale scores ($F_{3.601,255.7}=5.749, p<0.001$ for FL; $F_{3.737,255.7}=7.421, p<0.001$ for PI; $F_{3.471,255.7}=2.130, p=0.082$ for CA). Tests of parallelism revealed no evidence that the treatment and control groups had different patterns of QoL scores over time, with no substantive differences observed.

Trend analysis revealed a non-significant F-ratio for a linear trend, but significant evidence for a quadratic trend over time ($F_{1,71}=7.498, p=0.008$). Inspection of marginal mean plots revealed that this was grounded in a decrease in scores (representing an improvement in functionality) between baseline and the 3-month time point; followed by a generally rising pattern from 3 months onwards. This effect was noted over both groups (Figures 5(a), 5(b), 5(c)).

***INSERT FIGURES 4(A), 4(B), 4(C) HERE***
Discussion

The scope of the current study, including both plantar and dorsal corns, extends the scope of previous research into the effectiveness of salicylic acid plasters, which in general is non-experimental and includes only digital corns.

While studies such as Landorf et al. [5] have found that scalpel debridement is ineffective in reducing pain compared with a sham procedure, the use of this treatment as the control in the current analysis reflects widespread current podiatric practice for the treatment of corns; as Landorf et al. also report, scalpel debridement is inexpensive and causes few complications. Landorf et al. also claim that the findings of their study do not preclude the possibility of cumulative benefits over a longer time period or additive effects when combined with other interventions.

The key finding of non-significance of the treatment variable with respect to the primary outcome appears to conflict with a recent report from a sub-set of the current data set reported by Farndon et al. [8] indicating a positive benefit of corn plasters. However, outcome measures are not directly comparable across the two studies: the earlier analysis was concerned with index corns only, and the survival-based outcome was time to recurrence, following debridement, rather than time to corn resolution.

Furthermore, the analysis of Farndon et al. did not use fully parametric survival methods and did not rigorously account for the interval censoring inherent in the data. The current analysis represents a substantial advancement on the Farndon analysis both in terms of both scope (all corns were considered, rather than just index corns) and in methodology, with the inclusion of fully parametric survival methods accounting for the effects of controlling variables, interval censoring and clustering of data. All patients who were not lost to follow-up immediately after the baseline reading provided data for the model. Furthermore, casting survival models in
terms of shared frailties led to appropriate estimation of parameter standard errors through the calculation of robust standard errors. However, extending the analysis beyond the period of the primary analysis of Farndon et al. of 3 months may have led to attrition bias, as patients whose corns had resolved would be less likely to return for a follow-up appointment. As the appointments were at intervals of 3 months, such resolutions might not have been observed by the podiatrist, and would be recorded as censored observations. At all time points after baseline the proportion of appointments kept was higher in the control group than in the treatment group (up to 7.5% higher by 12 months), suggesting that a larger number of events erroneously recorded as censored could have occurred in the treatment group.

While about one third of patients assessed for eligibility refused to take part in the trial, there was no evidence that such patients were untypical of the population, and the proposed intervention did not preclude a large number of patients from participating on health grounds. Hence there is no evidence that ascertainment bias has been introduced to the study.

It could be argued that the specification of the end point of interest in the current analysis of time to resolution represents a more naturally quantifiable measure of the success or otherwise of the intervention being trialled, rather than the outcome of time to recurrence used in the analysis of Farndon et al. One point of consistency is that the direction of association is the same in both analyses; with the treatment group performing better than the control group. The non-significance of the effect in the current analysis may be due in part to the widened standard errors introduced by the use of clustered data; by contrast, the analysis of Farndon et al. considered only one corn per patient; hence unclustered data. It may be inferred from a synthesis of the results of the two studies that the use of corn plasters has some initial benefit (up to 3 months from baseline) when applied to a single corn, but has more limited benefit when applied to multiple corns beyond 3 months. Outcomes of the trend analyses of secondary data in the current study (Figures 4, 5(a), 5(b) and 5(c)) also suggest that
patterns of change in QoL and foot disability in corn patients comprise two distinct time periods: an initial period of improved functionality between baseline and 3 months; followed by a period of static or decreasing functionality between 3 months and 12 months. However, the trends illustrated indicate that QoL and functionality do not return to their baseline minima.

The findings of significant associations between treatment and the outcomes of MFPDI scores and QoL scores reported by Farndon et al. are reflected in the findings of the current analysis of the expanded data set. Although the Farndon analysis reported significant associations between treatment and QoL scores based on specific time points, these findings were not borne out in the current analysis, which focussed on overall effects of treatment over time.

In the current analysis, patients in the treatment group were requested to keep plasters in place for one week. While the findings of Lang et al. [7] suggest that the effectiveness of the plasters is not related to the length of application, optimum results in this study were obtained with a 7-day regimen, suggesting that lengthening the application period of the current analysis beyond the current 4 weeks would be unlikely to change any inferences.

The median time to resolution of dorsal/interdigital corns of 5.9 months, compared with 14.9 months for plantar corns, may be ascribed to the generally reduced mechanical stresses associated with dorsal/interdigital corns, whether or not corn plasters are applied. This finding, combined with the finding of a non-significant effect of treatment, suggests that the treatment variable may have only limited impact on reducing mechanical stresses.

Although the interaction between treatment and corn type was not significant and hence excluded from the final model, findings from the interim model including an interaction term suggest that the corn plaster treatment may be more effective on dorsal/ID corns than plantar corns. In this model, corn resolution rates were similar for plantar and dorsal/interdigital corns.
in the control group, and substantially better for dorsal/ID corns in the treatment group. Mean corn diameters of plantar and dorsal/ID corns were similar (3.87 cm (SD 1.80 cm) for plantar corns; 3.69 cm (SD 1.67 cm) for dorsal/ID corns); suggesting that corn type was not a proxy for corn diameter. The inclusion of both kinds of corn in the analysis results in an analysis with greater power than corresponding individual analyses on plantar and dorsal/ID corns; and avoids problems of raised familywise error rates arising from testing of multiple subgroups.

In summary, this analysis finds that there is insufficient evidence to conclude that time to corn resolution is reduced with the application of salicylic acid plasters over a 4-week period. Despite this, the 25.4% reduced time to resolution of treated corns (10.0 months compared to 13.4 months) must be considered to be an effect of clinical importance, and it may be concluded that under podiatric supervision, corn plasters are an effective treatment for some patients, and are a less painful treatment than scalpel reduction for some patients.

Likewise quality of life and foot disability parameters are also not significantly affected by the treatment when measured over the full 12-month period, although for all outcomes, noticeable benefits occurred between baseline assessment and the 3-month period.

The lack of additional benefits after 3 months leads to overall inferences of non-significance; however, further more focussed analyses on changes between baseline and 3 months (as in the analysis of Farndon et al.), but including all corns, may lead to alternative conclusions. Dorsal/ID corns resolved more quickly than plantar corns, suggesting that reduction in mechanical stresses should remain the primary objective in corn treatment.

Acknowledgements

None
Conflict of Interest

The authors declare no conflict of interests.

References


### Table 1: descriptive summary of sample

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Treatment group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>42 (41.6%)</td>
<td>42 (42.0%)</td>
<td>84 (41.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>59 (58.4%)</td>
<td>58 (58.0%)</td>
<td>117 (58.2%)</td>
</tr>
<tr>
<td><strong>Age in years (mean (SD))</strong></td>
<td>59.7 (17.5)</td>
<td>58.8 (15.5)</td>
<td>59.3 (16.5)</td>
</tr>
<tr>
<td><strong>Corn type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plantar</td>
<td>121 (82.9%)</td>
<td>129 (73.7%)</td>
<td>250 (77.6%)</td>
</tr>
<tr>
<td>Dorsal/inter-digital</td>
<td>25 (17.1%)</td>
<td>46 (26.3%)</td>
<td>72 (22.4%)</td>
</tr>
<tr>
<td><strong>Corn size at baseline (mm)</strong></td>
<td>3.68 (1.95)</td>
<td>3.70 (1.75)</td>
<td>3.69 (1.84)</td>
</tr>
<tr>
<td><strong>Corn status at last observation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not resolved</td>
<td>60 (40.8%)</td>
<td>73 (42.9%)</td>
<td>133 (41.8%)</td>
</tr>
<tr>
<td>Resolved</td>
<td>87 (59.2%)</td>
<td>97 (57.1%)</td>
<td>185 (58.2%)</td>
</tr>
<tr>
<td><strong>EQ-5D score (mean (SD))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>73.5 (20.3)</td>
<td>74.3 (19.6)</td>
<td>73.9 (19.9)</td>
</tr>
<tr>
<td>3 months</td>
<td>75.4 (19.9)</td>
<td>73.6 (19.2)</td>
<td>74.5 (19.5)</td>
</tr>
<tr>
<td>6 months</td>
<td>73.7 (21.5)</td>
<td>74.9 (20.1)</td>
<td>74.3 (20.8)</td>
</tr>
<tr>
<td>9 months</td>
<td>72.7 (19.5)</td>
<td>75.0 (20.8)</td>
<td>73.8 (20.1)</td>
</tr>
<tr>
<td>12 months</td>
<td>73.0 (19.4)</td>
<td>73.9 (20.7)</td>
<td>73.4 (19.9)</td>
</tr>
<tr>
<td><strong>MFPD-FL score (mean (SD))</strong></td>
<td></td>
<td></td>
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<tr>
<td>Baseline</td>
<td>18.4 (5.33)</td>
<td>17.5 (5.37)</td>
<td>18.0 (5.35)</td>
</tr>
<tr>
<td>3 months</td>
<td>15.0 (4.54)</td>
<td>17.5 (5.84)</td>
<td>16.2 (5.35)</td>
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<tr>
<td>6 months</td>
<td>15.9 (5.18)</td>
<td>17.6 (6.17)</td>
<td>16.8 (5.72)</td>
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<tr>
<td>9 months</td>
<td>15.3 (5.25)</td>
<td>17.3 (5.28)</td>
<td>16.3 (5.34)</td>
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<tr>
<td>12 months</td>
<td>16.2 (5.56)</td>
<td>17.3 (5.86)</td>
<td>16.7 (5.68)</td>
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<td>Baseline</td>
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<td>8.90 (2.81)</td>
<td>9.03 (2.03)</td>
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<tr>
<td>3 months</td>
<td>7.28 (2.48)</td>
<td>8.22 (2.97)</td>
<td>7.51 (2.93)</td>
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<td>8.57 (3.02)</td>
<td>7.75 (2.91)</td>
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<tr>
<td>9 months</td>
<td>7.36 (2.49)</td>
<td>8.74 (2.89)</td>
<td>7.49 (3.25)</td>
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<tr>
<td>12 months</td>
<td>7.76 (2.77)</td>
<td>8.05 (2.77)</td>
<td>7.71 (2.85)</td>
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<tr>
<td><strong>MFPD-CA score (mean (SD))</strong></td>
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<td></td>
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<tr>
<td>Baseline</td>
<td>3.42 (1.43)</td>
<td>3.39 (1.40)</td>
<td>3.41 (1.41)</td>
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<tr>
<td>3 months</td>
<td>2.94 (1.26)</td>
<td>3.22 (1.41)</td>
<td>3.08 (1.34)</td>
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<td>6 months</td>
<td>3.21 (1.44)</td>
<td>3.24 (1.46)</td>
<td>3.22 (1.44)</td>
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<tr>
<td>9 months</td>
<td>2.98 (1.22)</td>
<td>3.39 (1.40)</td>
<td>3.19 (1.31)</td>
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<tr>
<td>12 months</td>
<td>3.20 (1.49)</td>
<td>3.05 (1.36)</td>
<td>3.13 (1.42)</td>
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Figure legends

Figure 1(a): corns following removal of corn plasters
Figure 1(b): corns following blunt debridement
Figure 2(a): log-cumulative hazard plot: treatment and control groups
Figure 2(b): log-cumulative hazard plot: plantar and dorsal/ID corns
Figure 3(a): corn survival in treatment and control groups
Figure 3(b): corn survival by corn type
Figure 4: Estimated marginal means of EQ-5D quality of life scores in control and treatment groups
Figure 5(a): Estimated marginal means of MFPDI (FL sub-scale) scores in control and treatment groups
Figure 5(b): Estimated marginal means of MFPDI (PI sub-scale) scores in control and treatment groups
Figure 5(c): Estimated marginal means of MFPDI (CA sub-scale) scores in control and treatment groups