Author's response to reviews

Title: The ANKLE TRIAL (ANKLE TReatment after Injuries of the Ankle Ligaments): what is the benefit of external support devices in the functional treatment of acute ankle sprain? : a randomised controlled trial

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Concerns: Revised manuscript of study protocol randomized controlled trial ANKLE TRIAL (MS: 4138964585132804)

Dear Editor,

We are pleased to send you the revised manuscript of our study protocol, after reading and implementing given comments of the reviewers. Below you will find a point-by-point response to the concerns of the three reviewers; also we highlighted all main changes (coloured yellow) in the manuscript itself. Actually we totally updated it, revised it conform to the journal style and made language corrections throughout the whole text.

Referee 1 (Domhnall MacAuley):
- Title: We agree the title was confusing, so we changed it in the manuscript.
- Discussion of literature / systematic review: We revised the literature part. Also, drs. van den Bekerom (3rd author of the manuscript) and me are conducting a systematic review at the moment. In this review we are updating the literature about effectiveness of different functional treatment strategies after acute ankle ligament injuries versus minimal or no-treatment, following the meta-analysis of
Pijnenburg et al [9]. We plan to publish results of this review at the end of 2011.
- Protocol details: concerning the methods items, like participants (with eligibility criteria and description of severity of injury), interventions and blinding are now described in more detail following the CONSORT elements, also named by reviewer 3.
- Writing: again we revised the whole manuscript on language issues, we hope it has improved sufficiently.

Referee 2 (Sally Lee):
- Sample size: our statistician explained that she calculated our sample size with an alpha level of 0.01, power of 80 % and number of dropouts of 10 %.
  # ad alpha level: actually, according to Bonferroni correction for multiple comparisons, the alpha level is more precise (0.05/3) 0.017 in stead of 0.01, which was chosen as a safe completion.
  # ad power 80 %: this is a current percentage to choose, which has also been chosen in sample sizes calculations of comparable studies, for example in the study of Hupperets et al [21] and Bleakley et al [22].
  # ad drop rate: determining the number of dropouts will of course depend of follow-up period and we found 10 % seemed realistic in our study.

Altogether, if we recalculate our sample size more precisely with exact alpha of 0.017 and power of 80 %, then we only have to include (49 x 3 =) 147 patients, without correction of dropouts. So, with our calculated sample size of 183 patients we are actually correcting for > 20 % drop rate, which seems quite safe. Also because the medical ethical committee already approved this calculation this is why we choose to let our sample size unchanged. We described the sample size at page 7 more precisely.

Referee 3 (Carl J Lombard):
- Title: also mentioned by reviewer 1 and changed in manuscript.
- Objectives: also revised, more explaining / less confusing.
- Methods (CONSORT): following the CONSORT checklist 2010 we supplemented the methods description, including called aspects participants (including and excluding criteria), interventions (including a table with exercise schedule), outcome measures, randomization and blinding.
- Page 6: Karlsson score was added and we explained how this scale relates to the described objectives.
- Page 6: For sure, Bauerfeind only provides new, not previously used braces. Patients don’t have to pay for participating the trial. Risks of all three investigated treatments are low, but when one of the treatments will indicate harm to a patient we will stop the treatment in that patient, which will be given treatment following the current protocol of the involved hospital (which is tape bandaging in both Jeroen Bosch hospital and Slotervaart hospital).
- Hypothesis: we putted some minor changes to the description of the hypothesis without changing the scope of our study.

- Inclusion/exclusion criteria, diagnosis and severity of pain: see manuscript page 7. In addition to what I mentioned above I can declare that in both departments of inclusion (which at the moment are only two sites in stead of three because of the recent fusion of two locations of the Jeroen Bosch hospital, which moved to one big new hospital) similar inclusion protocols are used, including only minor local (mostly logistical) differences.

- Dropouts: see above ad reviewer 2.

- CONSORT 23,24: these items are now stated in the text of our revised manuscript as well.

In recent years several studies concerning treatment of acute ankle ligament injuries have been published. For we know the ANKLE TRIAL is the first randomized controlled trial (which follows the CONSORT statement) in which we compare two functional treatment strategies with external support to a control group, without any form of external support. We hope that this revised version of the manuscript will now be suitable for publication in the journal BMC Musculoskeletal Disorders, because the results of this study could lead to a changed view on treatment of acute ankle sprains.

We hope to hear from you soon.

Yours sincerely,

Suzanne Witjes
(on behalf of co-authors Gresnigt, Van den Bekerom, Olsman and Van Dijk)