Moyer RF, Birmingham TB, Bryant DM, and et al. Valgus Bracing for Knee Osteoarthritis: A Meta-Analysis of Randomized Trials. Arthritis Care & Research 2015; 67: (4) 493–501.

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Design: Systematic Review and meta-analysis of randomized clinical trials

Objective: To evaluate the effects of valgus knee bracing on pain and function, and to describe compliance and complications, in patients with medial knee osteoarthritis (OA).

PICOs:
- **Patients:** Adults with medial compartment knee osteoarthritis (OA)
- **Interventions:** Valgus knee braces
- **Comparison interventions:** No orthosis, a control orthosis (neutral knee brace, neoprene knee sleeve, or shoe insert)
- **Outcomes:** Pain (1^0) and function (2^0)
- **Study types:** Randomized controlled trials (RCTs)

Study selection:

- Databases included The Cochrane Central Registry for Controlled Trials, Medline, Embase, CINAHL, Scopus, ScienceDirect, and Web of Knowledge from inception through January 2014 and only English publications were eligible for inclusion.
- Database searching was supplemented by hand searching the reference lists of potentially eligible articles.
- Studies that used a parallel group or crossover design RCT to compare a custom-fit or off-the-shelf valgus knee brace (experimental) to a control intervention were included. Control interventions used either no orthosis or another type of orthosis (a neutrally aligned knee brace that did not apply a valgus torque to the knee, a neoprene knee sleeve, or a shoe insert).
- Two review authors independently screened articles by title and abstract for trial inclusion utilizing predetermined eligibility criteria and resolved any disagreements by discussion and consensus.
- When available, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subdomain scores for pain and function were used.
- Two reviewers independently scored the methodological quality of each study using the Cochrane Risk of Bias Tool, consisting of 7 items: sequence generation, allocation concealment, blinding of patients and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. Other sources of bias included an imbalance in baseline characteristics, funding provided by a brace company and/or limited reporting of carryover effects in crossover trial designs. Each item was rated as low, unclear, or high risk.
- The overall quality of the evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system (high, moderate, low or very low).

- Pooled estimates and 95% confidence intervals (95% CIs) for standardized mean differences (SMDs) for improvement in pain (and function) were calculated using a random-effects model and were corrected for small sample sizes using Hedge's g. Standardized mean differences (SMD) were used to calculate treatment effect sizes, and to obtain a summary estimate. Positive SMD values were used to indicate that the outcome favored the intervention group. A SMD 0.2-0.5 was considered a small effect, 0.5-0.8 a moderate effect, and $\geq$0.8 a large effect.
- Heterogeneity was assessed using the I^2 statistic and Q statistic. If I^2 was $\geq$ 60%, the planned subgroup analyses were conducted.
- Patient compliance was evaluated descriptively, and complications with brace use were assessed.

Results:
- Overall 6 RCTs with a total of 445 participants with knee OA were included. A total of 274 patients used a valgus knee brace. Age ranged from 34 to 73 years with 245 (55%) males and 200 (45%) females. Three studies were parallel-group designs and 3 studies were crossover designs. Two studies compared a valgus knee brace group to a non-orthosis control group, and 5 studies compared a valgus knee brace group to a control group that used a control orthosis.
- No studies were excluded from the meta-analysis based on quality. The GRADE system determined an overall moderate quality of evidence for the use of valgus braces, with a strong recommendation for improving pain and a weak recommendation for improving function.
- Overall for 6 pooled studies with 412 participants, there was a small, statistically significant difference favoring the valgus brace group for improvement in pain (SMD 0.33 [95% CI 0.13 to 0.52] I^2=0.0%) and function (SMD 0.22 [95% CI 0.02 to 0.41] I^2 =0%).
- For 2 pooled studies with 191 participants that used a control group without an orthosis, there was a moderate, statistically significant difference favoring the valgus brace group for improvement in pain (SMD 0.56 [95% CI 0.03 to 1.09] I^2 = 68.1%), and function (SMD 0.48 [95% CI 0.02 to 0.95] I^2 = 59.7%). Those pooled effect sizes translated into a difference between groups in WOMAC pain change score of 2.53 (95% CI 0.14 to 4.93) on a 20 point scale, and WOMAC function change score of 7.86 (95% CI 0.33 to 15.56) on a 68 point scale. The effect size for WOMAC pain is not quite clinically relevant, but the wide CIs do encompass clinically relevant effect sizes. The effect size for function is clinically relevant.
- For 5 pooled studies with 295 participants that used a control group with an orthosis, there was a small, statistically significant difference favoring the valgus brace group for improvement in pain (SMD 0.33 [95% CI 0.08 to 0.58] I^2 =14.0%), but not function (SMD 0.19 [95% CI to -0.03, 0.42] I^2 = 0%). Those pooled effect sizes translated into a difference between groups in WOMAC pain change score of 1.49 (95% CI 0.36 to 2.62) on a 20 point scale, and WOMAC function change score of 3.11 (95% CI 0.49 to 6.88) on a 68 point scale. These effect sizes for WOMAC pain and function are not clinically relevant, and the CIs also do not encompass clinically relevant effect sizes.
- Risk of bias was scored using the Cochrane Tool for the 6 studies included in the meta-analysis. Two of the studies were unclear or at high risk of bias, and 4 studies

were at low risk of bias. One study had low risk of bias in all categories. All studies, but one, were at high risk of bias for lack of blinding of patients and outcome assessors. Four studies provided sequence generation and allocation concealment, and 2 were unclear on these items.

- Heterogeneity and publication bias were not statistically significant for any meta-analysis.
- Patient compliance with brace use recorded at the longest follow-up period ranged from 45% to 58% in 2 parallel-group studies, and 71% to 100% in 4 crossover design studies.
- Patient-reported complications varied from 0–25% with brace use in 3 studies that collected this information. Minor complications with valgus brace use included constraining fit, slipping, swelling, blisters, and skin irritation.

Authors' conclusions:

- The pooled results of the meta-analysis of the 6 randomized trials indicates valgus knee bracing improved pain and function in patients with medial knee osteoarthritis. The size of effects on pain and function varied, depending on the type of control intervention that was used.
- Taking into consideration the variability around the estimated effect sizes, the meta-analysis suggests current valgus bracing strategies for medial knee osteoarthritis result in small-to-moderate improvements in pain.
- The trial with the lowest risk of bias provided moderate-to-high effect sizes for pain and function when comparing valgus knee bracing (intervention) and neutral knee bracing (control).
- The personal costs, complications, and poor long-term compliance associated with valgus bracing are noted concerns that may influence patient decisions and clinical practices. Despite previous studies that are generally supportive of valgus bracing and highlight their relatively low cost and low associated risks, the rates of valgus brace prescription are very low. Potential complications should not deter patients and practitioners from attempting valgus bracing, including its long-term use.
- It is clear from the present study that no consensus exists about optimal dose relating to when and how long to wear the brace.
- Limitations in this review include the relatively small number of patients, the low or unclear quality of trials, and the variability in brace designs/manufacturers and their instructions for use.
- Strengths of this review include generally very low heterogeneity and pooled data from randomized trials used to estimate effect sizes for valgus knee bracing.
- Further research is needed that focuses on adequately powered randomized trials designed to control for placebo effects to further elucidate the benefits of valgus braces over simpler knee orthoses.

Comments:

- For the 2 RCTs that compared valgus bracing to standard care without a control orthosis, placebo effects may account for the overall statistically significant, moderate effect sizes (SMD = 0.56 for pain and 0.48 for function). The relatively large 95%

CIs around those point estimates indicate that considerable uncertainty still remains. When translated into the difference between groups for improvements in WOMAC pain and function scores, the effect sizes are borderline clinically important, but the upper ends of the 95% CIs include values that would be considered clinically important (5 on a 20 point scale for pain, and 16 on a 68 point scale for function).

- The 5 RCTs that compared valgus bracing to a control orthosis are more internally valid and therefore might provide a better indication of the treatment's true efficacy. The pooled effect size is somewhat smaller, although still statistically significant for pain (SMD = 0.33), but not for function (SMD = 0.19). When translated into the difference between groups for improvements in WOMAC pain and function scores, the effect sizes are not clinically important, and the upper ends of the 95% CIs include values that would not be considered clinically important, thus calling into question its clinical importance.

- The overall SMDs for pain of 0.33 and for function of 0.22 are considered small. The authors failed to report the translated overall SMDs between groups for improvements in WOMAC pain and function, but it is doubtful they showed clinical relevance.

- There is a very real possibility that an expectation bias plays a role in the perceived improvements observed with brace use. An expected, meaningful outcome that patients attribute to using a brace is likely to influence results, regardless of whether or not substantial biomechanical effects truly exist.

- Studies using valgus knee braces are always challenging to blind appropriately. Since 5 of the 6 RCTs did not blind patients or assessors, performance and detection bias may be present.

- Larger effects were found when the control group used was without orthosis. It is possible, the control orthoses used in these studies (neoprene sleeve or neutral brace) are likely to confer some therapeutic benefit (e.g., proprioceptive benefit, warmth), such that the real effects are likely greater than the SMDs presented for valgus bracing versus the control group with orthosis.

- One strength of this systematic review was that it assessed the methodological quality of each study using the Cochrane Risk of Bias Tool. Applying the GRADE approach to each RCT to determine the quality of evidence also helped to increase the level of confidence in the results.

- Given the modest effects, and despite at times limited adherence, it would be very helpful to identify predictors of therapeutic response and optimize future brace prescription by identifying a phenotype that is most likely to benefit. Clearly identifying those persons who are likely to benefit and actually wear a brace is critical if we are to use limited healthcare resources appropriately.

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Assessment:

- Adequate quality meta-analysis which supports good evidence that valgus knee bracing provides moderate improvement in pain and function compared to those that do not use another type of orthosis, and provides a small improvement in pain compared to those that do use another type of orthosis among patients with medial knee osteoarthritis.