Summary

Osteoarthritis (OA) is the most common rheumatic disease of the musculoskeletal system, with the knee being the most commonly affected joint. The number of people affected with OA is likely to increase due to the ageing society and the obesity epidemic. For this reason, an effective treatment is necessary. Although knee joint replacement has good clinical benefit, this treatment strategy should be postponed as long as possible to prevent costly revision surgery at a later phase with less good outcome than initial joint replacement. Thus, the first step in the management of persons with knee OA should be conservative treatment. Conservative management consist of education, weight loss, exercise, braces and physical therapy. Knee bracing in knee OA includes valgus knee bracing and soft knee braces. Valgus knee braces are designed to decrease loads on the knee medial compartment, given the increased load typically borne by that compartment during walking and higher prevalence of OA in that compartment compared to the lateral compartment. However, clinical effectiveness and adherence to valgus knee braces have been shown low. Soft knee braces - elastic, non-adhesive orthoses - are often self-prescribed by persons with knee OA because of ease of use and access, lack of complications and low cost. However, because of limited evidence, The Osteoarthritis Research Society International does not specifically mention soft knee bracing as a treatment option in the conservative management of knee OA. In addition, although soft knee braces are suggested to induce their effects via sensorimotor mechanisms, to our knowledge, there is no study that has determined working mechanisms of soft knee braces in knee OA. Finally, there is some evidence showing that tightness of a soft knee brace might influence it’s efficacy. There is a reason to replicate that evidence to determine whether tightness of a soft knee brace is of influence on clinical outcomes. This thesis evaluated the effects of soft knee braces in persons with knee OA, compared the effectiveness of a non-tight and a tight soft knee brace, and identified mechanisms underlying these effects. In this chapter, the main results are summarized.

Chapter 1 provides a general introduction to the research themes of this thesis. The main concepts - knee osteoarthritis and soft knee bracing- are introduced and aims and an outline of the thesis are given.

In Chapter 2, we conducted a systematic review with meta-analyses on the effects of soft knee braces on pain and physical function in persons with knee OA. Wearing a soft brace resulted in moderate effects on pain and small to moderate effects on self-reported physical function in the long term in comparison to persons receiving standard care without a soft brace. Because of lack of studies, we were not able to synthesize data on performance-based physical function. This is the first systematic review with met-analysis indicating that soft knee brace are effective treatment option to reduce pain and improve physical function in persons with knee OA. Each meta-analysis included two to three studies with low methodological quality. We concluded that further, high quality studies investigating the efficacy of soft braces in knee OA were warranted to improve confidence in the findings.

In Chapter 3, a mediation analysis of the data from the AMS-OA cohort was conducted, to determine whether proprioception is a mechanism underlying the association between systemic inflammation and muscle weakness in persons with knee OA. It was reported that higher levels of ESR were associated with poor proprioception (p=0.022) and that poor proprioception (p<0.001) and higher levels of ESR (p=0.001) were associated with muscle weakness. Finally, poor proprioception mediated the association between systemic inflammation and muscle weakness (p=0.035). This study indicated that poor proprioception might be one of the pathways via which systemic inflammation is associated with muscle weakness in persons with knee OA. We suggested that, theoretically, improving proprioception, for instance by means of a soft brace, might contribute to better outcome in rehabilitation, adding to the improvements in muscle strength and thus decrease in activity limitations. Nevertheless, longitudinal data are needed in order to determine the clinical significance of the observed effect.

In Chapter 4, we reported the results of our laboratory trial in 44 persons with knee OA and self-reported knee instability. A within-subject cross-over design was used comparing wearing a soft knee brace with not wearing a soft knee brace, and comparing wearing a non-tight with wearing a tight soft knee brace. We showed that wearing a soft brace reduced pain and activity limitations. We observed a 0.6 (95% CI-0.97 -0.23) and 0.8 (95% CI-1.11 -0.43) points decrease of pain on the NRS for level and perturbed walking, respectively. Wearing a soft brace significantly reduced time to complete both the 10-meter walk and GUG tests by 0.23 s (95% CI -0.31 -0.13 and -0.38 -0.07, respectively), compared to not wearing the brace. It was also shown that wearing a soft knee brace significantly reduced self-reported knee instability during level walking (OR 0.41, P=0.002) and perturbed walking (OR 0.36, P<0.001), and reduced lack of knee confidence during level walking (OR 0.45 , P<0.001) and perturbed walking (OR 0.56, P <0.001), compared with not wearing a soft brace. There was no difference in effects between a non-tight and tight brace, except for the 10-meter walk test. These findings strengthen the evidence for the use of soft knee braces to reduce pain and activity limitations in persons with knee OA. In addition, this study indicated that
wearing a soft knee brace is efficacious in improving several knee function-related parameters that might generalize to daily life of persons with knee OA.

In Chapter 5, we evaluated the effect of wearing the soft knee brace on objectively assessed dynamic knee instability; expressed by the Perturbation Response i.e. a biomechanics based measure reflecting a deviation in knee varus-valgus angle after a controlled mechanical perturbation on a treadmill, in respect to level walking. 3D movement of the lower legs, pelvis and trunk were captured via markers on anatomical landmarks using a motion-capture system. It was reported that wearing a brace significantly reduced the PR, compared to not wearing a brace (B -0.16, P=0.01). There was no difference between a non-tight and a tight brace (B -0.03, P=0.60). This study is the first to report that wearing a soft brace results in an objective improvement of knee instability, beyond previously reported subjective improvement.

In Chapter 6, we conducted a mediation analysis to identify the mechanisms underlying the beneficial effect of wearing the brace on activity limitations (Chapter 4). A decrease of pain (NRS) and a decrease of dynamic knee instability (PR) mediated the effect of wearing a soft brace on reduction of activity limitations ($p < 0.05$), while changes of proprioception and PPT did not mediate this effect ($p > 0.05$). Reduction of pain accounted for 43% and 44% decrease of time to complete the 10-meter walk test and the GUG test, respectively. Reduction of dynamic knee instability accounted for 13% and 26% decrease of time to complete the 10-meter walk test and the GUG test respectively, while wearing a brace. This study showed that decrease of pain and reduction of dynamic knee instability are pathways via which wearing a soft knee brace decreases activity limitations in persons with knee OA. We suggested that refinements to the design of the soft knee brace tested in this study may be required in order to maximize effects on knee pain and knee instability.

Finally, in chapter 7 the main results of this thesis are summarized and discussed and implications for future research and clinical practice are given.