



CHAPTER 8

General Discussion

Foot problems are highly prevalent in patients with RA, but receive limited attention in clinical practice and research. The first part of this thesis (Chapters 2-4) covers multidisciplinary foot care for patients with rheumatoid arthritis (RA). Multidisciplinary recommendations for diagnosis and treatment of foot problems in patients with RA were developed based on scientific literature and expert opinion (Chapter 2). Systematic reviews were performed to summarize the evidence on therapeutic shoes (Chapter 3) and different types of foot orthoses (Chapter 4). In the second part of the thesis (Chapters 5-7) the role of plantar pressure measurements in the management with foot orthoses was investigated. In this chapter (Chapter 8), the main results of the studies in this thesis are summarised and discussed. Furthermore, suggestions for future research are given.

Multidisciplinary foot care

In Chapter 2 multidisciplinary recommendations for diagnosis and treatment of foot problems in patients with RA were developed. The recommendations were based on the best available evidence and the opinions of experts with varying specialities and of patients. Forty-one recommendations were developed and approved by the expert group. Two recommendations concerned a framework for diagnosis and treatment with involvement of multiple disciplines. Thirty-nine recommendations addressed foot care: seven on diagnosis (including check-ups of feet and shoes and diagnostic imaging), 27 on treatment (including corticosteroid injections, foot surgery, therapeutic shoes, foot orthoses, exercise therapy, toe-orthoses and toenail-braces, treatment of toenails and skin), four on communication, and one on organisation of RA-related foot care.

In Chapter 3 the evidence on the effectiveness of therapeutic shoes was summarized. For custom-made therapeutic shoes weak evidence for the reduction of foot pain and improvement of physical functioning was found. For ready-made therapeutic shoes a medium to large effect was found for the reduction of foot pain and a small to medium effect for the improvement of physical functioning. All results were based on within-group differences.

In Chapter 4 the comparative effectiveness of foot orthoses in the treatment of various foot problems in RA were summarized. In the literature comparisons between foot orthoses were made concerning different materials used (soft versus semi-rigid), types of foot orthoses (custom-made versus ready-made; total contact versus non-total contact), or modifications applied (metatarsal bars versus domes). Also, different techniques to construct custom-made foot orthoses were compared (standard custom-moulding techniques versus more sophisticated techniques). A medium effect for (immediate) reduction of forefoot plantar pressure was found in favour of treatment with soft foot orthoses compared to semi-rigid foot orthoses. Other comparisons between foot orthoses resulted in non-significant effects or inconclusive evidence for one kind of foot orthoses over the other.

The findings of Chapters 2-4 clearly indicate that there are gaps in scientific literature on the management of foot problems of patients with RA. Most of the developed recommendations were based on expert opinion, as there is a lack of research evidence. The results of both systematic reviews were based on a small number of studies (Chapter 3 eleven and Chapter 4 ten studies, respectively) and with relatively small sample sizes. Moreover, only a few randomized controlled trials with repeated measures design could be included in both reviews. More research is needed to strengthen the evidence on management of RA-related foot problems.

The recommendations in Chapter 2 were developed in collaboration with a multidisciplinary RA Foot Expert Group. In this expert group multiple healthcare providers (rheumatologists, rehabilitation physicians, orthopaedic surgeons, specialized nurses, podiatrists, orthopaedic shoe technicians, pedicurists and researchers) involved in the management of RA-related foot problems were represented. In addition to these professionals, patients with a history of foot problems were also part of the expert group. The expert group reached consensus on the role and specific skills of the different disciplines involved in management of inflammation (e.g. (teno)synovitis, or bursitis), biomechanical, dermatological and neurovascular impairments, and external and personal factors related to RA-foot disease. This has been translated into a framework for diagnosis and treatment. Furthermore, communication and organisation of foot care were addressed, both from the point of view of the patient and the health professional. The collaboration with this multidisciplinary expert group made the development of the recommendations a unique project. Especially since these are the first multidisciplinary recommendations on RA-related foot care worldwide ⁽¹⁾.

The framework for diagnosis of RA-related foot problems in Chapter 2 was based on the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization ⁽²⁾. The ICF-concept is in development, particularly with regard to the personal factors ⁽³⁾. It seems more plausible to include only items related to the personal background under the personal factors ⁽³⁾. In the introduction to this thesis (Chapter 1), we used a more up-to-date approach of the ICF-classification compared to the diagnostic framework in Chapter 2.

Good communication and collaboration between the patient and the healthcare providers involved, and between the healthcare providers from different disciplines, are important in the management of RA-related foot problems ^(4, 4, 5). All disciplines involved can play a role in the detection of inflammation, biomechanical and dermatological foot impairments. Early diagnosis and treatment of these foot problems is important, because (i) long-term synovitis may lead to pain and joint damage and deformities ^(6, 7), (ii) malalignment of the feet may result in biomechanical alterations in foot function (e.g. the loading pattern of the foot resulting in high plantar pressure) and pain ⁽⁸⁻¹¹⁾, and (iii) biomechanical alterations may lead to dermatological problems such as excessive hyperkeratotic lesions, which can cause pain, corns and wounds/ulcers ^(12, 13). Access to multidisciplinary consultation and collaboration is necessary to provide treatment with sufficient content and timing for the individual patient ^(4, 14, 15). The frameworks for diagnosis and treatment in Chapter 2 may offer guidance in providing foot care and collaboration between different disciplines. In addition, patients can play an important role in their own foot-related health, provided that they are sufficiently coached

and trained by the healthcare providers involved ⁽¹⁶⁾. Good communication, shared decision-making and patient education improve knowledge about the disease, involvement in the treatment process and self-management by the patient ^(12, 17-19).

Adequate organization of RA-related foot care in which several disciplines are involved is complex but essential for accessibility of timely foot care with sufficient content ⁽²⁰⁾. Healthcare providers from different disciplines often work in different departments or settings (e.g. hospitals, outpatient clinics and private practices) with different processes, IT infrastructure and financing structures. This may lead to barriers for structural and integral collaboration ^(21, 22). The development of the recommendations in Chapter 2 was a first step in guiding a multidisciplinary approach and a better organization of RA-related foot care. However, the recommendations do not have the status of a practice guideline and were not issued by a professional organization with the involvement of all stakeholders. In order to be able to provide the right foot care in the right place, a national guideline with support of all the stakeholders involved and official ratification is needed ⁽²³⁾. Such a guideline should include a foot care pathway for the guidance of timely referral for diagnosis and treatment by various disciplines. Treatment of inflammation in the foot will primarily be managed by a medical doctor, while biomechanical and dermatological impairments can be managed with the involvement of different medical and non-medical disciplines, based on a stepped-care approach. Furthermore, the development of international multidisciplinary recommendations could be considered to improve the knowledge and uniformity of RA-related foot care ⁽²⁴⁾, for example by using EULAR standardised operational procedures ⁽²⁵⁾.

Implementation of the recommendations in Chapter 2 is needed to improve foot care for the individual patient ⁽²⁶⁾. Ideally, the implementation is based on a structured analysis of the current situation and barriers and facilitators for implementation ⁽²⁶⁾. Using the results of such an analysis, an implementation plan must be developed ⁽²⁶⁾. This can consist of improving insight and knowledge among healthcare providers from different disciplines, e.g. by developing an educational programme. Furthermore, the application of the recommendations in clinical practice can be facilitated by the development of an interactive digital platform for patients and healthcare providers, whereby information can be exchanged at various levels; a) general information (open access), b) geographical network of cooperating healthcare providers, and c) individual patient and treating healthcare providers. Moreover, a patient education programme could be developed and provided as e-Health to improve self-management ^(17, 26-28). Besides implementation of knowledge transfer, implementation strategies can be aimed at dissolving financial barriers (e.g. compensation of costs for foot orthoses or therapeutic shoes), or barriers concerning timely referrals (e.g. a referral pathway for foot care by the different involved disciplines).

The role of plantar pressure in treatment with FOs

In Chapter 5 a protocol for optimizing foot orthoses by using the feedback of in-shoe plantar pressure measurements was evaluated. In this proof of concept study 43 patients with foot pain were treated with usual care foot orthoses. Based on the protocol 70% of these usual-care foot

orthoses (in 30 patients) were adapted. In these patients, usual care foot orthoses resulted in a mean 9% plantar pressure reduction (PTI) compared to no foot orthoses. Adaptation of usual care foot orthoses led to an additional mean 3% PTI reduction. The protocol was considered feasible by patients. Podiatrists considered the protocol more useful to achieve individual rather than general treatment goals. A final protocol was proposed. In Chapter 6 the outcomes on pain, physical function and forefoot plantar pressure three months after foot orthoses delivery (follow-up) were presented. A statistically significant within-group improvement on pain (medium effect size), physical functioning (large effect size) and forefoot plantar pressure (small effect size) was found. Furthermore, the relationship between change in forefoot plantar pressure and change in pain or physical functioning was investigated in Chapter 6. Analysis in a subgroup of 23 patients with combined forefoot pain and high forefoot plantar pressure showed non-significant relations between change in plantar pressure and changes in pain or physical functioning. In Chapter 7 we investigated the relationship of forefoot disease activity (inflammation) and forefoot deformity (biomechanical impairment) with plantar pressure in 172 patients from the Amsterdam Foot (AMS-foot) cohort. Statistically significantly higher plantar pressures were found in forefoot regions with deformities, compared to forefoot regions without forefoot pathology. No significant differences in plantar pressures were found when solely forefoot disease activity was present in forefoot regions.

The primary goal of the foot orthoses optimization protocol was to reduce plantar pressure in painful foot areas, since high forefoot plantar pressure is associated with forefoot pain⁽¹¹⁾. However, in a part of the patients included in the proof of concept study in Chapter 5 a relatively low plantar pressure in the painful foot area was detected. This may possibly be due to an offloading strategy caused by inflammation^(7, 29). This implies that the treatment strategy in patients with a biomechanical impairment should be different from that for forefoot problems caused by inflammation. In patients with a biomechanical impairment, foot deformity may lead to high plantar pressure in the painful foot region. Because of the deformity, the patient cannot apply an offloading strategy, therefore the main goal of foot orthoses treatment is reduction of plantar pressure in the painful foot region. Patients with foot problems caused by inflammation, without a deformity, in the painful foot region may use an offloading strategy leading to low plantar pressure and pain avoidance. In these patients, medical treatment of disease activity should have treatment priority. In addition, foot orthoses treatment could be prescribed aimed at normalizing the loading pattern of the foot. A final foot orthoses optimization protocol has been proposed in which individual treatment goals are set aimed at redistribution of plantar pressure in painful foot regions.

The concept of biomechanical impairments versus foot problems caused by inflammation was partly supported by the findings in Chapter 7. With regard to biomechanical foot impairments, a relation was found between forefoot deformity and high forefoot plantar pressure. However, in Chapter 6 no relation between change in plantar pressure and change in pain could be proven. This could possibly be explained by the small sample size or a threshold for plantar pressure. The hypothesis that in patients with foot problems caused by inflammation, pain is related to low plantar pressures could not be confirmed in Chapter 7. In contrast, such an association was found in previous research from Bowen et al.⁽⁷⁾. In

that study, inflammation in the forefoot was detected by ultrasonography, while we only used palpation. The use of ultrasonography to detect inflammation should be considered in clinical practice and future research⁽³⁰⁻³²⁾. Furthermore, the reduction of disease activity should be given priority in the treatment through the use of systemic medication or local steroid injections⁽³³⁾. In addition, foot orthoses can be used to redistribute plantar pressure.

In patients with diabetes mellitus (DM) a comparable protocol with the use of sequential in-shoe plantar pressure measurements for the adaptation of therapeutic shoes resulted in shoes with better plantar pressure-distributing properties, as shown by previous research by Bus et al.^(34, 35). Because both the intervention and the study populations differed between the protocol for DM and ours, different treatment criteria were established in both protocols⁽³⁴⁾. In patients with diabetic neuropathy, offloading of foot regions with high plantar pressures is necessary to prevent ulceration⁽³⁶⁾. The diagnosis and treatment of DM and foot problems is guided by guidelines⁽³⁷⁻³⁹⁾. An annual foot screening is recommended⁽³⁷⁾. In the event of foot problems, the patient is referred for an extensive foot examination, including barefoot plantar pressure measurements for early detection of regions with high plantar pressure⁽³⁹⁾. In-shoe plantar pressure measurements are recommended as diagnostic tool to evaluate the plantar pressure distribution properties of shoes in order to prevent (re)ulceration⁽³⁸⁾. A similar approach might also be useful in the detection and diagnosis of foot problems in RA. A yearly check-up of the feet can lead to early detection of foot problems, especially as the most frequently used instrument to detect disease activity (with a 28-joint count⁽⁴⁰⁾) excludes examination of the feet. When foot problems are identified, barefoot plantar pressure measurements can be considered to support the distinction between foot problems caused by inflammation or a biomechanical impairment. In the case of complex biomechanical foot problems, in-shoe plantar pressure measurements can be used to guide the optimization of foot orthoses or therapeutic shoes.

The final protocol, as proposed in Chapter 5, may also, in addition to daily clinical care for patients with RA-related foot problems, be useful in other contexts. In the first place, the protocol may be applicable for the optimization of foot orthoses in patients with foot problems due to rheumatic disorders other than RA, such as spondylarthritis, (pseudo) gout, tendonitis/fasciitis/enthesitis and osteoarthritis. Secondly, the protocol can be used in podiatry education, as feedback from in-shoe plantar pressure measurements provides insight into the relationship between foot pain and plantar pressure. It can provide guidance in the student's clinical reasoning process to determine and evaluate treatment goals. Thirdly, the protocol can be used in research when investigating the plantar pressure outcomes of different types of foot orthoses or therapeutic shoes.

Innovations in real-time in-shoe plantar pressure measurements and direct communication of data, to an application that is accessible to both the patient and the healthcare professional involved, may lead to early detection of abnormal plantar pressures to support the management of foot problems. Smart textiles with integrated pressure sensors and antimicrobial properties can possibly be used to develop an innovative cover layer for foot orthoses or inner lining for therapeutic shoes^(41, 42). In addition, integration of temperature sensors could be considered to monitor compliance with foot orthoses or therapeutic



shoes⁽⁴³⁻⁴⁵⁾. Moreover, localized temperature measurements can also be used to detect and monitor inflammation (caused by RA or by infection) and therefore may be supportive in the management of local disease activity and wounds/ulcers⁽⁴⁶⁻⁴⁸⁾.

Methodological aspects

The studies in this thesis have methodological strengths and limitations. To highlight some strengths, the methodology used to develop the recommendations (Chapter 2) is based on published strategies for the development of practice recommendations^(25, 49). Second, these are the first recommendations on the management of RA-related foot problems with the involvement of several disciplines. Third, both systematic reviews (Chapter 3 and 4) were prepared in accordance with the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)⁽⁵⁰⁾. Fourth, the multi-level analyses used in the second part of this thesis (Chapter 6 and 7) enabled us to use different areas of both feet of the same patient, apart from the dependency within a person. Important limitations in the studies that were included in the systematic reviews (Chapter 3 and 4) were the small sample sizes, the methodological quality and the limited between-group results. With regard to the proof of concept study (Chapter 5) as performed by our research group, a limitation is the lack of a control group that did not receive the protocol to adapt foot orthoses based on in-shoe plantar pressure measurements. Therefore, we could only report within-group results and no established effects of benefit of the protocol over usual care regarding the manufacturing of foot orthoses (Chapter 6).

Directions for future research

Based on the study findings in this thesis, the following directions for future research are suggested.

Overall, more research is needed to strengthen the evidence on diagnosis and treatment of RA-related foot problems. Research on the value of (yearly) check-up of the feet for the prevention or delay of progression of RA-related foot problems is indicated. For the treatment of RA-related foot problems definitive, high-quality RCTs are needed to investigate the effectiveness of corticosteroid injections in the foot, different types of (fore-)foot surgery, treatment of nails and hyperkeratotic lesions. Furthermore, definitive high-quality RCTs are needed to investigate the (cost) effectiveness of different types of foot orthoses and therapeutic shoes.

Implementation of the recommendations (Chapter 2) could be the next step in improving multidisciplinary foot care in RA. First, a strategy and plan for implementation should be developed based on a structured analysis of the current situation and barriers and facilitators for implementation. Implementation could be aimed at knowledge transfer among healthcare providers and patients, or dissolving barriers e.g. concerning timely referrals, cooperation

between healthcare providers, or (financial) organization of foot care. Development, evaluation and implementation of a referral- and foot care pathway based on a stepped-care approach with the involvement of multiple disciplines is needed. This could be part of a multidisciplinary practice guideline developed and issued by a professional organization with the involvement of all stakeholders in the management of foot problems in patients with RA. An official ratified guideline is necessary to improve (i) uniformity, (ii) adequate timing and content, (iii) communication and organization of multidisciplinary foot care. Furthermore, development, evaluation and implementation of a foot-specific education program for patients with RA seems mandatory.

Whether treatment with foot orthoses developed according to the final foot orthoses optimization protocol (Chapter 5) is (cost) effective, warrants further investigation. A definitive RCT with stratification in order to control for confounding of pain and function driven by biomechanical impairments and/or foot problems caused by inflammation could be considered. Furthermore, development and evaluation of an educational program for the implementation of the foot orthoses optimization protocol in podiatry practice and education is needed.

Lastly, to better understand how foot orthoses work in the treatment of RA-related foot problems, studies exploring the potential mechanisms underlying the observed effects on pain and physical functioning are warranted. Besides further research into the role of plantar pressure, the relationship between the change in foot position by wearing foot orthoses and the change in clinical outcomes could be quantified. Furthermore, the role of shearing forces and patients' expectations from treatment with FOs could be investigated.

Conclusions

In summary, the following conclusions can be drawn from this thesis:

Multidisciplinary foot care

- We developed multidisciplinary recommendations for diagnosis and treatment of foot problems in patients with RA. These recommendations may contribute to uniformity and adequate timing of diagnosis and treatment of RA-related foot problems. They may also contribute to adequate communication and improved organization of RA-related foot care.
- Therapeutic shoes are likely to be effective in patients with RA, based on within-group results. Treatment with custom-made and ready-made therapeutic shoes leads to a reduction of foot pain and improvement in physical functioning.
- In the treatment of RA-related foot problems different kinds of foot orthoses can be used. Evidence was found that foot orthoses made of soft material may lead to more (immediate) forefoot plantar pressure reduction compared to foot orthoses constructed of semi-rigid materials. For other characteristics (such as type of foot orthoses, construction techniques and applied modifications) inconclusive evidence was found, necessitating more research in this area.

The role of plantar pressure in treatment with FOs

- The immediate feedback of in-shoe plantar pressure measurements leads to small additional pressure reduction, and offers guidance in the clinical reasoning process of the podiatrist. It can be helpful in setting individual treatment goals, and in evaluating and adapting foot orthoses.
- Foot orthoses developed according to a protocol for optimizing the plantar pressure reduction lead to clinically relevant outcomes. Within-group comparisons after three months of foot orthoses treatment resulted in medium to large improvements in pain and physical function and a significant reduction of forefoot plantar pressure. The hypothesis that more plantar pressure reduction would lead to better clinical outcomes could not be proven.
- Deformities of foot joints in the medial, central and lateral forefoot regions were related to higher plantar pressures measured in these regions. The expected association between local disease activity (as detected by palpation) and plantar pressure could not be established. In future research, the use of ultrasonography in the detection of local inflammation should be considered.

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Management of foot problems in patients with rheumatoid arthritis

Summary

Summary

Foot problems are highly prevalent in patients with rheumatoid arthritis (RA). These foot problems often start with pain, swelling and stiffness caused by inflammation of joints and soft tissues. Long-term inflammation can have a destructive impact on the quality and structure of the joints and surrounding soft tissues. This may lead to structural malalignment of the feet due to damage and deformities of foot joints. Malalignment of the feet may result in pain and biomechanical alterations in foot function, i.e. the loading pattern of the foot, resulting in high plantar pressure. In addition to inflammation and biomechanical impairments, dermatological and neurovascular impairments, and external and personal factors can also play a role in RA-related foot problems. These foot problems may lead to restrictions in daily activities and participation, and a reduced quality of life.

Management of foot problems in an early disease stage seems important to reduce pain and activity limitations, and to prevent deterioration of foot function. Also in a more advanced disease stage, treatment of foot problems is often necessary. However, underuse of foot care seems apparent. Among patients there is limited knowledge of the possibilities of, and access to, foot care. Among healthcare providers, there is often limited attention and expertise in the management of RA-related foot problems. Various disciplines can be involved in the management of RA-related foot problems. However, healthcare providers from these different disciplines often lack insight into the specific skills of professionals from another discipline. In order to improve foot care for patients, an overview of the multidisciplinary diagnosis and treatment of foot problems in RA is first necessary. This is needed to provide guidance to healthcare providers and patients in the organisation of timely, appropriate and evidence-based foot care. The objective of the first part of this thesis was to provide an overview of multidisciplinary foot care for patients with rheumatoid arthritis (RA) (Chapter 2-4).

Foot orthoses are frequently used in the treatment of RA-related foot problems. The general aims of prescribing foot orthoses are reducing foot pain and improving physical functioning by influencing biomechanical factors, such as plantar pressure, to an optimum. However, the reported treatment effect of foot orthoses on foot pain in RA is small to medium (effect size 0.40 – 0.45). Efforts to increase the effectiveness of foot orthoses are needed. Plantar pressure measurements can provide a better insight into the loading of the foot during gait. Improving the effects of foot orthoses by using the immediate feedback from in-shoe plantar pressure measurements seems promising. Since high plantar pressures are related to foot pain in RA it is hypothesized that a reduction of forefoot plantar pressure leads to reduction of pain and subsequent disability. Nevertheless, there is a lack of evidence supporting this hypothesis. The objective of the second part of this thesis was to investigate the role of plantar pressure measurements in the management with foot orthoses (Chapter 5-7).



Chapter 1 provides a general introduction of the research topics of this thesis. Insights in the cause and course of RA-related foot problems were described. The factors of influence on these foot problems were depicted in an overview by using the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization. Furthermore, the current management of RA-related foot problems and the role of plantar pressure in the treatment with foot orthoses were addressed. At the end of this chapter, the aim and outline of this thesis was presented.

In Chapter 2 multidisciplinary recommendations for the management of foot problems in patients with RA were developed. The recommendations were based on research evidence and consensus among experts, following published strategies for the development of practice recommendations. The expert group was composed of 2 patients and 22 experienced professionals (rheumatologists, rehabilitation physicians, orthopaedic surgeons, specialized nurses, podiatrists, orthopaedic shoe technicians, pedicurists, and researchers) in the Netherlands. In total, 41 recommendations were developed. Two recommendations concerned a framework for diagnosis and treatment. Thirty-nine recommendations addressed foot care: seven on diagnosis (including check-ups of feet and shoes and diagnostic imaging), 27 on treatment (including corticosteroid injections, foot surgery, therapeutic shoes, foot orthoses, exercise therapy, toe-orthoses and toenail-braces, treatment of toenails and skin), four on communication, and one on organisation of RA-related foot care. These multidisciplinary recommendations can provide guidance in the organisation of timely, appropriate and evidence-based foot care. Implementation of the recommendations, based on a strategy and plan addressing barriers and facilitators for implementation, is needed to improve foot care for the individual patient.

In Chapter 3 the literature was systematically summarized on the effectiveness of therapeutic shoes in patients with RA on the outcomes foot function, foot pain, physical functioning, health-related quality of life, adherence, adverse events and patient satisfaction. Therapeutic shoes include custom-made and ready-made shoes. Custom-made shoes are developed for the individual patient based on specific measures and specifications, whereby a variety of technical adaptations can be incorporated. Ready-made shoes are serial-produced shoes with extra depth, support, incorporated inlays or technical adaptations. Eleven studies were identified, with a total number of 429 participants, of which three were of high quality. Two studies investigated custom-made therapeutic shoes, eight studies ready-made therapeutic shoes, and one study investigated both. For custom-made shoes, a best evidence syntheses showed weak evidence for the reduction of foot pain and improvement of physical functioning. For ready-made shoes, meta-analysis showed a medium to large effect for the reduction of foot pain and a small to medium effect for the improvement of physical functioning. All results were based on within-group differences, since insufficient studies reporting between-group differences were available. The results of this chapter implicate that treatment with therapeutic shoes is effective in patients with RA. However, definitive high-quality RCTs to investigate whether patients with RA benefit more from therapeutic shoes than from non-

therapeutic shoes (i.e. the patient's own shoes or standardized conventional shoes) are needed.

In Chapter 4 the literature was systematically summarized on the comparative effectiveness of foot orthoses in the treatment of various foot problems in patients with rheumatoid arthritis on the primary outcomes foot function and foot pain, and the secondary outcomes physical functioning, health related quality of life, compliance, adverse events, the costs of foot orthoses and patient satisfaction. Ten studies, with a total number of 235 patients, were identified of which three were of high quality. These studies made a comparison between different materials used (soft versus semi-rigid), types of foot orthoses (custom-made versus ready-made; total contact versus non-total contact), or modifications applied (metatarsal bars versus domes). Also, different techniques to construct custom-made foot orthoses were compared (standard custom-moulding techniques versus more sophisticated techniques). Meta-analysis showed a medium effect for (immediate) reduction of forefoot plantar pressure in favour of treatment with soft foot orthoses compared to semi-rigid foot orthoses. Other comparisons between foot orthoses resulted in non-significant effects or inconclusive evidence for one kind of foot orthoses over the other. Based on the results of this chapter, it can be concluded that there is still limited insight into the effectiveness of one kind of foot orthoses compared to another. Therefore, definitive high quality RCTs are needed to investigate the comparative (cost-) effectiveness of different kinds of foot orthoses for the treatment of specific RA-related foot problems.

In Chapter 5 a protocol for optimizing the plantar pressure reduction achieved with foot orthoses treatment by using the feedback of in-shoe plantar pressure measurements was evaluated. Forty-five RA patients with foot problems were included in this observational proof-of concept study. Custom-made foot orthoses were made by a podiatrist according to usual care. In 43 patients usual care foot orthoses were evaluated using in-shoe plantar pressure measurements and, if necessary, adapted. Adapted foot orthoses were developed in 70% of the patients. In these patients, usual care foot orthoses showed a mean 9% reduction in forefoot plantar pressure compared to no-foot orthoses. Foot orthoses adaptation led to an additional mean 3% plantar pressure reduction. Semi-structured interviews were held with patients and podiatrists to evaluate the feasibility of the protocol. The protocol was considered feasible by patients. Podiatrists considered the protocol more useful to achieve individual rather than general treatment goals. A final foot orthoses optimization protocol has been proposed in which individual treatment goals are set aimed at redistribution of plantar pressure in painful foot regions. The results of this chapter may have several implications for both clinical practice and podiatry education. First, in-shoe plantar pressure measurements can be used as an additional diagnostic tool in RA patients with foot problems; it provides insight in the relation between foot pain and plantar pressure during walking with shoes. Second, the immediate feedback of in-shoe plantar pressure measurements may offer guidance to the process of evaluation and adaptation of foot orthoses.

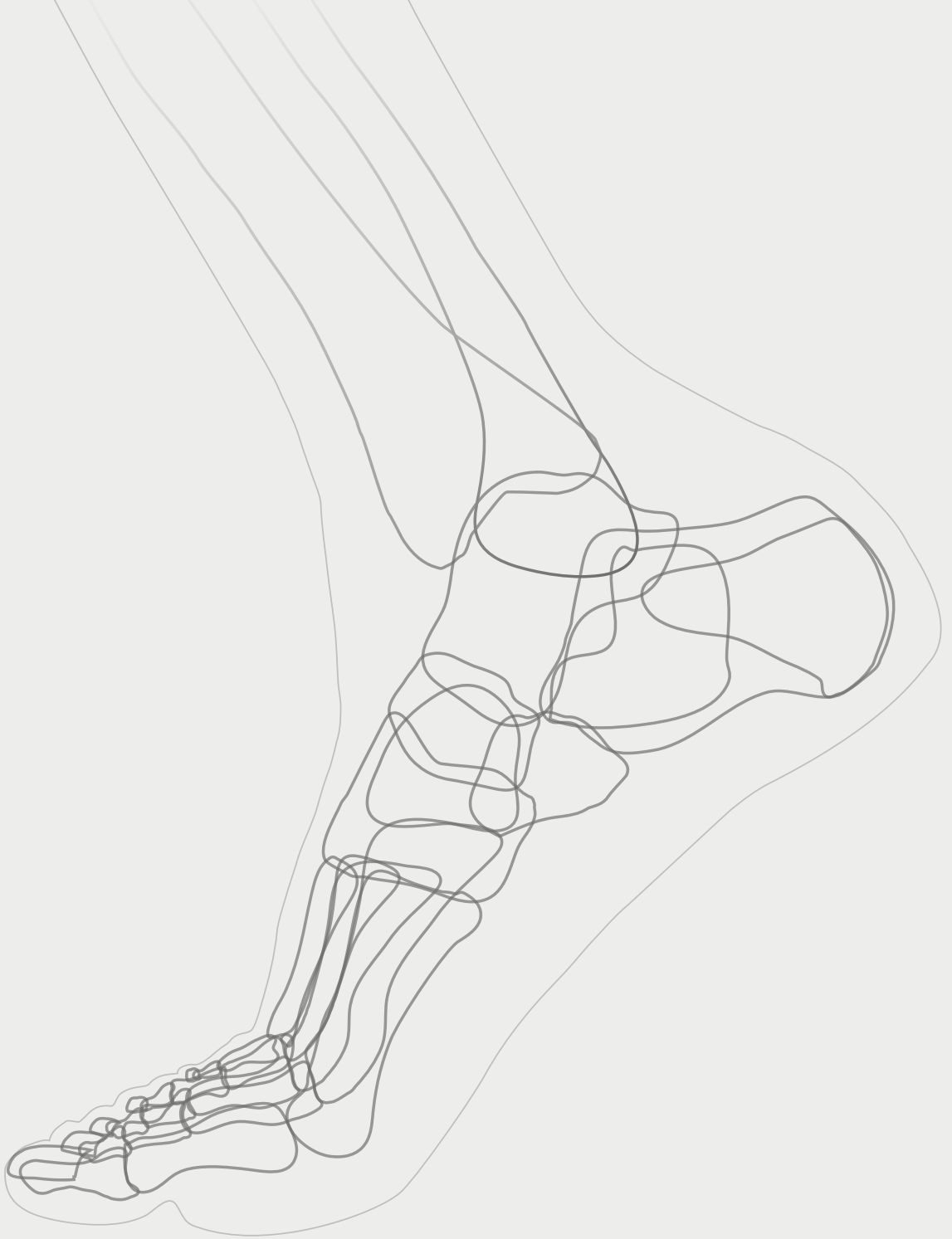


In Chapter 6 the developed foot orthoses according to the ‘foot orthoses optimization protocol’ (as described in Chapter 5) were evaluated on pain, physical functioning and plantar pressure of the forefoot after three months of wearing foot orthoses in 38 patients. The within-group change scores showed a medium effect on pain reduction, a large effect on improvement of physical functioning and a small effect on forefoot plantar pressure reduction. Whether foot orthoses developed according to the ‘foot orthoses optimization protocol’ may lead to better clinical outcomes compared to foot orthoses developed without this protocol is unclear. Further investigation on the clinical relevance of using the protocol is required. Furthermore, the relationship between change in forefoot plantar pressure and change in pain and physical functioning was determined in a subgroup of 23 patients. In these patients no statistically significant relations were found between change in plantar pressure and change in pain or physical functioning. Therefore, the hypothesis that more pressure reduction would lead to better clinical outcomes could not be proven.

In Chapter 7 the association of plantar pressure with disease activity and deformity in the forefoot was investigated in a cross sectional study, using data of 172 RA patients with forefoot problems from the Amsterdam Foot (AMS-foot) cohort. Plantar pressure in the forefoot was measured with a pressure platform. Forefoot deformity was assessed using the Platto score. Forefoot disease activity was defined as swelling and/or pain assessed by palpation of the metatarsophalangeal joints. Higher plantar pressures were found in forefoot regions with deformities compared to forefoot regions without forefoot pathology. This confirms our hypothesis and findings of previous research that forefoot deformities are related to higher plantar pressures. No association between local disease activity and lower plantar pressure could be confirmed. Future research with sensitive imaging measures to detect disease activity is recommended to reveal the effect of forefoot disease activity on plantar pressure.

Finally, in Chapter 8 the main results of this thesis are summarized and discussed and directions for future research are provided.





Management of foot problems in patients with rheumatoid arthritis

Nederlandse samenvatting

Samenvatting

Voetproblemen komen veel voor bij patiënten met reumatoïde artritis (RA). Deze voetproblemen beginnen vaak met pijn, zwelling en stijfheid veroorzaakt door ontsteking van gewrichten en weke delen. Langdurige ontsteking kan leiden tot schade in deze structuren, met deformiteiten van gewrichten en standsafwijkingen van de voeten als gevolg. Hierdoor kunnen biomechanische veranderingen tijdens het belasten van de voet ontstaan, zoals een hoge druk onder de (voor)voet. Naast ontstekingen en biomechanische stoornissen kunnen ook dermatologische en neurovasculaire stoornissen en externe en persoonlijke factoren een rol spelen bij RA-gerelateerde voetproblemen. Deze voetproblemen hebben vaak pijn, beperkingen in dagelijkse activiteiten, restricties in participatie en een verminderde kwaliteit van leven als gevolg.

Diagnostiek en behandeling van voetproblemen in een vroeg stadium van de ziekte lijkt van belang om pijn en beperkingen in activiteiten te verminderen en om een verslechtering van voetfunctie te voorkomen. In een verder gevorderd ziektestadium is de behandeling van voetproblemen ook vaak noodzakelijk. Er lijkt echter sprake te zijn van ondergebruik van voetzorg. Bij patiënten is de kennis over de mogelijkheden van en de toegang tot voetzorg beperkt. Bij zorgverleners is er vaak beperkte aandacht voor en expertise in het behandelen van RA-gerelateerde voetproblemen. Daarnaast hebben zij vaak onvoldoende inzicht in de specifieke vaardigheden van zorgverleners van andere disciplines die betrokken kunnen zijn. Om de voetzorg voor patiënten te verbeteren is allereerst een overzicht van de multidisciplinaire diagnostiek en behandeling van voetklachten bij RA noodzakelijk. Dit is nodig om zorgverleners en patiënten handvatten te bieden voor het organiseren van tijdige, passende en evidence-based voetzorg. In het eerste deel van dit proefschrift is een overzicht gegeven van de verschillende opties voor multidisciplinaire voetzorg bij patiënten met reumatoïde artritis (RA) (Hoofdstuk 2-4).

Plantaire voetorthesen (zolen) worden vaak voorgeschreven in de behandeling van RA-gerelateerde voetproblemen. Het algemene doel van zooltherapie is het verminderen van voetspijn en het verbeteren van fysiek functioneren door het beïnvloeden van biomechanische factoren, zoals plantaire druk. Het gerapporteerde effect van zooltherapie op voetspijn bij RA is echter klein tot middelgroot (effectgrootte 0,40 - 0,45). Het verbeteren van de effecten van zooltherapie door gebruik te maken van de directe feedback van plantaire drukmetingen in de schoenen lijkt veelbelovend. Plantaire drukmetingen kunnen een beter inzicht geven in de belasting van de voet tijdens het lopen. Aangezien hoge druk onder de voorvoet gerelateerd is aan voetspijn bij RA, wordt verondersteld dat meer verlaging van de plantaire druk leidt tot meer pijnvermindering. Voor deze hypothese is echter nog geen wetenschappelijk bewijs. Het doel van het tweede deel van dit proefschrift was om de rol van plantaire drukmetingen in de behandeling met zolen in kaart te brengen (Hoofdstuk 5-7).



Hoofdstuk 1 geeft een algemene inleiding op de onderzoeksthema's van dit proefschrift. Inzichten in de oorzaak en het beloop van RA-gerelateerde voetproblemen zijn beschreven. De factoren die van invloed zijn op deze voetproblemen zijn weergegeven in een overzicht aan de hand van de International Classification of Functioning, Disability and Health (ICF) van de World Health Organization. Daarnaast is de huidige aanpak van RA-gerelateerde voetproblemen en de rol van plantaire druk in de behandeling met zolen beschreven. Aan het eind van dit hoofdstuk zijn het doel en de hoofdlijnen van dit proefschrift weergegeven.

Hoofdstuk 2 beschrijft een project waarin multidisciplinaire aanbevelingen zijn ontwikkeld voor de diagnostiek en behandeling van voetproblemen bij patiënten met RA. De aanbevelingen zijn ontwikkeld op basis van wetenschappelijk bewijs en de opinie van experts, waarbij gepubliceerde strategieën voor de ontwikkeling van praktijk aanbevelingen zijn gevolgd. De expertgroep bestond uit twee patiënten en 22 ervaren professionals (reumatologen, revalidatieartsen, orthopedisch chirurgen, gespecialiseerde verpleegkundigen, podotherapeuten, orthopedisch schoentechnici, pedicures en onderzoekers) in Nederland. In totaal werden 41 aanbevelingen ontwikkeld. Twee aanbevelingen hadden betrekking op een kader voor diagnostiek en behandeling. Negenendertig aanbevelingen gingen over voetzorg: zeven over diagnose (inclusief controle van voeten en schoenen en diagnostische beeldvormende technieken), 27 over behandeling (inclusief corticosteroïdeninjecties, voetchirurgie, therapeutische schoenen, zolen, oefentherapie, teenortheses en teennagelbeugels, en de behandeling van teennagels en huid), vier over communicatie en één over de organisatie van de RA-gerelateerde voetzorg. Deze multidisciplinaire aanbevelingen kunnen een leidraad zijn voor het organiseren van tijdige, passende en evidence-based voetzorg. Implementatie van de aanbevelingen, gebaseerd op een strategie en plan voor het aanpakken van bevorderende en belemmerende factoren voor implementatie, is nodig om de voetzorg voor de individuele patiënt te verbeteren.

In **Hoofdstuk 3** is de literatuur over de effectiviteit van orthopedische schoenen bij patiënten met RA systematisch samengevat op de uitkomsten voetfunctie, voetpijn, fysiek functioneren, gezondheid-gerelateerde kwaliteit van leven, naleving van de behandeling, bijwerkingen en patiënttevredenheid. Orthopedische schoenen kunnen bestaan uit volledig op-maat-gemaakte schoenen (in Nederland: orthopedische schoenen A) en semi op-maat-gemaakte schoenen (orthopedische schoenen B). Orthopedische schoenen A worden op basis van specifieke maatnames en specificaties voor de individuele patiënt ontwikkeld, waarbij verschillende technische aanpassingen kunnen worden geïntegreerd. Orthopedische schoenen B zijn in serie geproduceerde schoenen met extra diepte, ondersteuning, ingebouwde inlays of technische aanpassingen. Elf studies zijn geïdentificeerd, met een totaal aantal van 429 patiënten, waarvan drie van hoge kwaliteit. Twee studies onderzochten orthopedische schoenen A, acht studies orthopedische schoenen B en één studie onderzocht beide. Voor orthopedische schoenen A toonden best-evidence-syntheses een zwak bewijs voor de vermindering van voetpijn en verbetering van fysiek functioneren. Voor orthopedische schoenen B toonden meta-analyses een middelgroot tot groot effect voor de vermindering

van voetspijn en een klein tot middelgroot effect voor de verbetering van fysiek functioneren. Alle resultaten zijn gebaseerd op verschillen binnen de groep, aangezien er onvoldoende studies beschikbaar waren die verschillen tussen de groepen rapporteerden. De resultaten van dit hoofdstuk impliceren dat behandeling met orthopedische schoenen effectief is bij patiënten met RA. Definitieve RCT's van hoge kwaliteit zijn noodzakelijk om te onderzoeken wat de meerwaarde is van orthopedische schoenen ten opzichte van confectieschoenen.

In Hoofdstuk 4 is de literatuur over de effectiviteit van verschillende soorten zolen in de behandeling van voetproblemen bij RA patiënten systematisch samengevat. In deze studie zijn de primaire uitkomsten voetfunctie en voetspijn en de secundaire uitkomsten fysiek functioneren, gezondheid-gerelateerde kwaliteit van leven, naleving van de behandeling, bijwerkingen, kosten van zolen en patiënttevredenheid. Tien studies, met een totaal aantal van 235 patiënten, zijn geïdentificeerd, waarvan drie van hoge kwaliteit. Deze studies maakten een vergelijking tussen verschillende gebruikte materialen (zacht *versus* semi-rigide), typen zolen (op-maat-gemaakt *versus* kant-en-klaar; total contact *versus* niet-total contact) of uitgevoerde aanpassingen (metatarsale balk *versus* pelotte). Ook werden verschillende technieken om op-maat-gemaakte zolen te construeren met elkaar vergeleken (standaard custom-moulding technieken *versus* meer geavanceerde technieken). Meta-analyses toonden een middelgroot effect aan voor (directe) vermindering van de druk onder de voorvoet in het voordeel van een behandeling met zachte zolen (in vergelijking met semi-rigide zolen). Andere vergelijkingen tussen de zolen resulteerden in niet-significante verschillen of niet sluitend bewijs voor het ene soort zolen in vergelijking met het andere. Op basis van de resultaten van dit hoofdstuk kan geconcludeerd worden dat er nog beperkt inzicht is in het verschil in effectiviteit tussen verschillende soorten zolen. Daarom zijn definitieve RCT's van hoge kwaliteit nodig om de (kosten-)effectiviteit van verschillende soorten zolen met elkaar te vergelijken.

In Hoofdstuk 5 is een protocol geëvalueerd voor het optimaliseren van plantaire drukreductie door zooltherapie, waarbij gebruik gemaakt wordt van de directe feedback van drukmetingen in de schoenen. Vijfenvestig RA-patiënten met voetproblemen zijn geïncludeerd in deze observationele proof-of-concept studie. De op-maat-gemaakte zolen zijn door een podotherapeut vervaardigd volgens usual-care. Bij 43 patiënten zijn deze usual-care zolen geëvalueerd met behulp van drukmetingen in de schoenen en, indien nodig, aangepast. Bij 70% van de patiënten is aanpassing van de zolen uitgevoerd. Bij deze patiënten werd een gemiddelde plantaire voorvoet drukreductie van 9% gevonden tijdens het dragen van usual-care zolen ten opzichte van het niet dragen van zolen. De aanpassingen van de zolen leidden tot een extra gemiddelde plantaire drukverlaging van 3%. Semigestructureerde interviews zijn gehouden met patiënten en podotherapeuten om de haalbaarheid van het protocol te evalueren. Het protocol werd haalbaar geacht door patiënten. Podotherapeuten vonden het protocol bruikbaar om individuele behandeldoelen te bereiken dan vooraf vastgestelde, algemene behandeldoelen. Er is een definitief optimalisatieprotocol voor zooltherapie voorgesteld, waarin individuele behandeldoelen worden vastgesteld die gericht zijn op herverdeling van de plantaire druk in pijnlijke voetgebieden. De resultaten van dit hoofdstuk



hebben verschillende implicaties voor zowel de klinische praktijk als voor onderwijs en scholingsprogramma's gericht op (toekomstige) podotherapeuten. Ten eerste kunnen plantaire drukmetingen in de schoenen worden gebruikt als extra diagnostisch middel bij RA-patiënten met voetproblemen; het geeft inzicht in de relatie tussen voetpijn en plantaire druk tijdens het lopen met schoenen. Ten tweede kan de directe feedback van drukmetingen in de schoenen een leidraad bieden voor het proces van evaluatie en aanpassing van zolen.

In Hoofdstuk 6 zijn de ontwikkelde zolen volgens het 'zolen optimalisatieprotocol' (zoals beschreven in Hoofdstuk 5) geëvalueerd op pijn, fysiek functioneren en druk onder de voorvoet na drie maanden dragen van zolen bij 38 patiënten. De scores voor de verandering binnen de groep lieten een middelgroot effect zien op pijnvermindering, een groot effect op verbetering van fysiek functioneren en een klein effect op vermindering van plantaire voorvoet druk. Of zolen ontwikkeld volgens het 'zolen optimalisatieprotocol' kunnen leiden tot betere klinische resultaten in vergelijking met zolen ontwikkeld zonder dit protocol is onduidelijk. Verder onderzoek naar de klinische relevantie van het gebruik van het protocol is nodig. Tevens is de relatie tussen verandering in de plantaire voorvoetdruk en verandering in pijn en fysiek functioneren onderzocht in een subgroep van 23 patiënten. Bij deze patiënten zijn geen statistisch significante relaties gevonden tussen de verandering in plantaire druk en de verandering in pijn of fysiek functioneren. Daarom kon de hypothese dat meer drukverlaging zou leiden tot betere klinische resultaten niet worden bevestigd.

In Hoofdstuk 7 is de associatie van plantaire druk met ziekteactiviteit en deformiteiten in de voorvoet onderzocht in een cross-sectionele studie, waarbij gebruik is gemaakt van gegevens van 172 RA-patiënten met voorvoetproblemen uit het Amsterdam Foot (AMS-voet) cohort. Plantaire druk in de voorvoet is gemeten met een drukplatform. De mate van deformiteit van de voorvoet is beoordeeld aan de hand van de Platto-score. Ziekteactiviteit in de voorvoet is gedefinieerd als zwelling en/of pijn, welke is beoordeeld door palpatie van de metatarsofalangeale gewrichten. Hogere plantaire druk is gevonden in gebieden met deformiteit in de voorvoet ten opzichte van gebieden zonder voorvoetpathologie (ziekteactiviteit of deformiteit). Dit bevestigt onze hypothese en bevindingen uit eerder onderzoek, dat deformiteiten van de voorvoet zijn gerelateerd aan hogere plantaire drukken. Er werd geen associatie tussen lokale ziekteactiviteit en lagere plantaire druk gevonden. Toekomstig onderzoek met sensitieve beeldvormende metingen, om ziekteactiviteit te detecteren, is aanbevolen om het effect van ziekteactiviteit in de voorvoet op de plantaire druk inzichtelijk te maken.

Tot slot zijn in Hoofdstuk 8 de belangrijkste resultaten van dit proefschrift samengevat en bediscussieerd en zijn suggesties gedaan voor toekomstig onderzoek.





Dankwoord

Dankwoord

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Over de auteur

Over de auteur

Marloes Tenten-Diepenmaat werd geboren op 4 september 1981 te Enschede. In 1998 haalde ze haar HAVO diploma aan Scholencentrum Het Assink in Haaksbergen. In 2002 studeerde ze af als podotherapeut aan Fontys Hogescholen in Eindhoven. Tussen 2002 en 2005 was ze werkzaam als podotherapeut bij verschillende praktijken in Oost-, Zuid- en West-Nederland. Van 2005 tot 2020 werkte ze binnen haar eigen podotherapie-onderneming met vestigingen in verschillende gezondheidszorgsettingen, in de regio Rotterdam en Gouda. Tussen 2012 en 2017 werkte ze als onderzoeker bij Reade, centrum voor revalidatiegeneeskunde en reumatologie, in Amsterdam. Hier heeft zij gewerkt aan de onderzoeksprojecten die beschreven zijn in dit proefschrift. In 2013 haalde ze het masterdiploma Epidemiologie aan de Vrije Universiteit van Amsterdam. Sinds 2019 werkt Marloes als hoofddocent/ onderzoeker binnen de opleiding Podotherapie van hogeschool Saxion in Enschede. Haar doel is om haar kennis en kunde in te zetten op het snijvlak van onderzoek, onderwijs en praktijk.



List of publications

International journals

Tenten-Diepenmaat M, Dekker J, Steenbergen M, Huybrechts E, Roorda LD, van Schaardenburg D, et al. In-shoe plantar pressure measurements for the evaluation and adaptation of foot orthoses in patients with rheumatoid arthritis: A proof of concept study. *Gait & posture*. 2016;45:45-50.

Tenten-Diepenmaat M, van der Leeden M, Vliet Vlieland TPM, Roorda LD, Dekker J. The effectiveness of therapeutic shoes in patients with rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology international* 2018;38(5):749-762. doi: 10.1007/s00296-018-4014-4.

Tenten-Diepenmaat M, van der Leeden M, Vliet Vlieland TPM, Dekker J. Multidisciplinary recommendations for diagnosis and treatment of foot problems in people with rheumatoid arthritis. *Journal of foot and ankle research* 2018;11:37. doi: 10.1186/s13047-018-0276-z.

Konings-Pijnappels APM, Tenten-Diepenmaat M, Dahmen R, et al. Forefoot pathology in relation to plantar pressure distribution in patients with rheumatoid arthritis: A cross-sectional study in the Amsterdam Foot cohort. *Gait & posture* 2019;68:317-322. doi: 10.1016/j.gaitpost.2018.12.015.

Tenten-Diepenmaat M, Dekker J, Heymans MW, Roorda LD, Vliet Vlieland TPM, van der Leeden M. Systematic review on the comparative effectiveness of foot orthoses in patients with rheumatoid arthritis. *Journal of foot and ankle research* 2019;12:32. doi: 10.1186/s13047-019-0338-x.

Tenten-Diepenmaat M, Dekker J, Twisk JWR, Huijbrechts E, Roorda LD, van der Leeden M. Outcomes and potential mechanism of a protocol to optimize foot orthoses in patients with rheumatoid arthritis. *Submitted for publication*.

National journals

Tenten-Diepenmaat M, Protocollarie in-shoe drukmeting effectief bij reumatoïde artritis. *Podosophia* > uitgave 2 /2017; 11 mei 2017. Bohn Stafleu van Loghum - Uitgeverij voor de gezondheidszorg.

Tenten-Diepenmaat M, Aanbevelingen voor de diagnostiek en behandeling van voetklachten bij patiënten met reumatoïde artritis. *Orthopedisch schoentechniek* > uitgave november 2017. NVOS-Orthobanda.

Contribution to books

E.J. Huijbrechts, M. van der Leeden en M. Tenten-Diepenmaat. Chapter 10: Voetbehandeling en educatie voor mensen met een reumatische aandoening. Third edition. Voeten en Reuma. Bohn Stafleu van Loghum. October 2019.

Online publications

Tenten-Diepenmaat M, van der Leeden M, Vliet Vlieland TPM, Dekker J. Aanbevelingen voor de diagnostiek en behandeling van voetklachten bij patiënten met reumatoïde artritis; hoofddocument, toelichting en samenvatting. Website: Nederlandse Health Professionals in de Reumatologie (NHPR). [Available from: <https://www.nhpr.nl/richtlijnen-en-literatuur/>]



PhD portfolio

PhD training	Year	Workload
Education		
Scientific meetings – in company, Reade, Amsterdam	2012-2016	7 ECTS
Systematic reviews and meta-analysis – EpidM, VUmc, Amsterdam	2012	1
Multilevel analysis – EpidM, VUmc, Amsterdam	2012	1
Scientific writing – in company course, Reade, Amsterdam	2012	1
Master Epidemiology – EpidM, VUmc, Amsterdam	2009-2013	60
Total European credit transfer system		70 ECTS
Congresses and presentations		
<i>International</i>		
EULAR ¹ , Madrid (Spain) – poster presentation	2017	1 ECTS
FIP ² Podiatry World Congress, Rome (Italy) – oral presentation	2013	1
EULAR ¹ visiting Fellowship, Glasgow (Scotland) – oral presentation	2012	0.6
Novel Expert Scientific Meeting, Aalborg (Denmark) – oral presentation	2012	0.6
<i>National</i>		
NVR ³ , Arnhem – oral presentation	2019	10 hours
ASWS ⁴ Pedicurecongres, Nieuwegein – oral presentation	2018	10
NVR ³ , Arnhem – oral presentation	2017	10
NVvP ⁵ Autumn congress, Nieuwegein – oral presentation	2017	10
NERASS ⁶ Autumn Congress, Woerden – oral presentation	2014	10
NVvP ⁵ Autumn congress, Nieuwegein – oral presentation	2014	10
Total European credit transfer system		6 ECTS

Teaching activities and other oral presentations

Saxion, Enschede – oral presentation and clinical lesson	2019	8 hours
Tutor for pedicurists, Rotterdam	2017	16
Fontys, Eindhoven – oral presentation and clinical lesson	2017	8
Tutor for pedicurists, Rotterdam	2016	16
PHD-students meeting, VUmc, Amsterdam – oral presentation	2016	4
Fontys, Eindhoven – oral presentation and clinical lesson	2014	8
Reade, multidisciplinary RA-team meeting, Amsterdam – oral presentation	2014	4
Reade, scientific meeting – oral presentation	2012	4
Total European credit transfer system		6 ECTS

Other

Contribution to KNGF ⁶ -Guideline Rheumatoid Arthritis	2018	16 hours
Member of the foot care-section of the NHPR ⁷	2017-2019	24
Member of the Committee on Science and Innovation of the NVvP ⁵	2012-2019	80
Total European credit transfer system		5 ECTS

Total 87 ECTS

¹ Annual congress European League Against Rheumatism, ² International Federation of Podiatrists, ³ Jaarcongres Nederlandse Vereniging voor Reumatologie, ⁴ ASWS Uitgeverij & Beursorganisatie, ⁵ Nederlandse Vereniging van Podotherapeuten, ⁶ Netherlands Rheumatoid Arthritis Surgical Society, ⁷ Dutch Health Professionals in Rheumatology



