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Prevention and adherence in Rheumatic and Musculoskeletal disease

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A B S T R A C T

Rheumatic and Musculoskeletal Diseases (RMDs) are chronic conditions that affect a substantial number of people. RMDs are significantly related to co-morbidity. Therefore, focusing on prevention in RMDs is of importance to promote and maintain health. Prevention includes primary-, secondary-, tertiary-, and clinical prevention. Primary prevention aims to prevent the onset of disease before the disease process begins, secondary prevention includes detecting and reducing disease and risk factors at the earliest possible point, and tertiary prevention aims to limit the influence of a recognized or verified disease and to address or reduce further development or worsening of the disease, including physical and psychosocial disability. Clinical prevention attempts to integrate prevention into the disease management to limit disease progression and prevent complications and relapse. This chapter will focus on the evidence for prevention and highlight how innovations and trends can contribute by using digital technologies as an example.

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Prevention and rheumatic and musculoskeletal diseases

Rheumatic and musculoskeletal diseases (RMD) comprise a diverse group of diseases that commonly affect the joints and includes, for example, rheumatoid arthritis, psoriasis arthritis, and spondyloarthritis. RMDs are in most cases chronic diseases and affect a substantial number of people [1]. RMDs increase health care costs for the individual patient and for society [2]. In addition, RMDs are significantly related to co-morbidity. For instance, a Danish nationwide register study found that patients with seropositive rheumatoid arthritis (RA) had higher odds for several co-morbidities prior to and, particularly, after the diagnosis of RA [3]. Hence, a two-fold higher risk of cardiovascular disease was found in patients with e.g. RA compared with the general population [4]. Consequently, a lower overall survival resulting in high risk of premature death is reported [5]. Therefore, focusing on prevention in RMDs is of importance to promote and maintain health.

Prevention includes, among other things, primary prevention, secondary prevention, tertiary prevention [6,7], and clinical prevention. *Primary prevention* aims to prevent the onset of disease before the disease process begins by eliminating specific risk factors or increasing an individual's resistance to the condition. Vaccines against infections are a good example of primary prevention. Also, good dental hygiene and teaching sexual health in school relate to primary prevention.

Secondary prevention includes detecting and reducing disease and risk factors at the earliest possible point. Thus, secondary preventive intervention includes measures that can lead to early diagnosis and start up treatment of disease. An example of secondary prevention includes early identification of cancers through screening programs such as mammograms and colonoscopies, but also early detection of patients with chronic obstructive pulmonary disease (COPD) in general practice is related to secondary prevention. Secondary prevention typically takes place in the primary health sector, but also in hospitals and in other sectors (e.g. education and social sectors).

The aim of *tertiary prevention* is to limit the influence of a recognized or verified disease and to prevent further development or worsening of the disease, including physical and psychosocial disability. Tertiary prevention is defined within the frame of the disease, while rehabilitation is defined from the patient's overall situation including own needs and desires. Tertiary prevention is often a natural part of rehabilitation. Examples of tertiary prevention include prevention of (new) fractures in patients with osteoporosis, hygiene instruction for patients with oral disease, interviews with the general practitioners or other health professionals for smoking cessation in patients with e.g. chronic obstructive pulmonary disease, or promotion of physical activity in patients with RMDs who are at increased risk of cardiovascular disease.

Clinical prevention is an additional way of thinking about prevention. The intention of clinical prevention is to focus on and integrate this approach into the disease management to limit disease progression and prevent complications and relapse, thus achieving the greatest possible disease management and quality of life. Clinical prevention takes place in the health care system and is based on patient activation and involvement. The efforts and interventions therefore also include elements of health promotion and rehabilitation. In clinical prevention, the actors are health professionals in interaction with the patients who are always the target group. Examples of clinical prevention are initiatives in clinical care such as smoking cessation during pregnancy, pre-surgery alcohol withdrawal, physical activity programs for the mentally ill, and diabetes educational programs.

Prevention and RMDs

It is a relatively new option to discuss prevention in rheumatology. However, with increasing knowledge about the development of RMDs and knowledge of the best treatment and treatment outcomes, prevention has become increasingly relevant for health professionals targeting the healthy population, as well as patients with RMDs.

It is well-accepted that there is a pre-clinical period in which the RMD is under development, however asymptomatic [8]. This can be detected in e.g. biomarkers or other processes as, for instance, Periodontal Disease. Furthermore, there is an increasing focus on the challenge of delay of diagnosis, often affecting people with RMDs [9]. Therefore, the European League against Rheumatism (EULAR) among others has, during the past years, and will, in the coming future, continue to create awareness

about RMDs and RMD symptoms among the public, in primary health care, and among general practitioners in order to detect diagnosis early. Since 1996, October 12 is recognized as World Arthritis Day, a global initiative bringing people together to raise awareness of RMDs. This is a strategy to highlight arthritis in general, but also to create awareness of e.g. early symptoms of arthritis. The relevance of such an initiative is emphasized by the fact that a period of 12 weeks between symptom onset and anti-inflammatory medical treatment start is recommended [10]. The longer it takes for the patient to start up medical treatment, the higher the risk of joint destruction and following loss of function [8]. However, meeting the early treatment recommendation is not the case for all patients as demonstrated in a cross-sectional study among 482 patients with RA from a total of eight countries which showed that the median delay for start of medical treatment was 24 weeks [9]. Future directions in the coming decades may improve disease screening and prevention for people with RMDs. It might be that more screening and preventive approaches for some inflammatory rheumatic diseases will be a reality within the next decade.

To illustrate prevention in relation to RMDs, smoking is an excellent example. The number of smokers among people with RMDs worldwide is unknown. However, surveys based on Danish people with rheumatoid arthritis suggest that 25–30% of the people in this patient group smoke [11,12]. Several studies have identified smoking as a factor associated with development of RA in those who are Anti-CCP positive [13,14]. The risk of developing RA is approximately twice as high among smokers as in non-smokers [13]. Many patients with RMDs are not aware of this risk. It is also well known that smoking is harmful and life-threatening, for example in relation to the development of cardiovascular diseases and cancer. Unfortunately, smoking as a factor in the development of RMDs is not widely known among the larger population or people with RMDs. Therefore, the primary prevention for the development of RMDs is that people do not start smoking. This should be included in health campaigns and teaching in, for example, schools and youth education.

If a person has already developed an RMD and is smoking, it is invaluable that the person stops smoking. Supporting this would fall under both the *secondary prevention* and *clinical prevention*. Knowledge of the risk factors for rheumatic diseases is growing (e.g. smoking for RA) [15]. Smoking among people with RA is associated with a quicker disease progression and decreased benefit of the medical treatment [16–18]. It is also suggested that smokers with RA experience worse disease specific outcomes, including increased inflammation and higher disease activity [19,20] compared to non-smokers due to attenuated responses to anti-rheumatic treatments. As previously mentioned, smoking is a major risk factor for the development of cardiovascular disease (CVD), and smoking is an independent risk factor for developing CVD which underlines the need for smoking cessation in this patient population [21]. A recently published study based on data from ten different countries found that smoking cessation in patients with RA was associated with lower disease activity and improved lipid profiles and could predict reduced rates of CVD events. This underlines the need for health professionals in rheumatology departments as well as in the primary care sector, including GPs, to inform patients with RMDs how risky smoking is for their medical arthritis treatment and for the development of CVD. Unfortunately, the evidence of interventions for smoking cessation in people with RMDs is scarce. A Cochrane review from 2019 [22] identified only two intervention studies that had investigated smoking cessation interventions in people with RMDs. Also, the evidence of investigations into the efficacy of smoking cessation interventions specifically in people with RMDs was of poor quality. Given the severity of smoking in patients with RMDs, addressing smoking cessation in clinical practice in this patient group is of great importance. Health professionals and rheumatologists need to be proactive in both informing patients about the impact of smoking and counselling patients in smoking cessation.

Tertiary prevention in RMDs

In relation to *tertiary prevention,* health professionals and rheumatologists focus above all on interventions that prevent disease progression, disability (activity limitations and participation restrictions), or premature death after a patient is diagnosed with an RMD. As stated above, tertiary prevention often includes interventions focusing on *self-management-, physical activity, or pain-management*. The nature of all these interventions is that they are active and involve the patient in order to

be effective and sustainable in terms of effect and costs. That the treatment is active refers to the effort required from the patient, as opposed to a passive treatment where a patient is only a receiver of treatment given by someone else.

Self-management strategies are of utmost importance for patients to acquire in managing a chronic disease [23,24]. Essential elements of self-management are self-regulation strategies such as goal setting, action-planning, self-monitoring, feed-back and relapse prevention; generic competencies which can be used in the management of any condition or behavior. Tam et al. describes the concept as "a process where patients are actively participating in a variety of activities that contribute to lessening of the physical and emotional impact of their illness. Such activities include adhering to their treatment plan, being physically active, and seeking medical help when the treatment target is not met" [25]. The Chronic Disease Self-Management Program (CDSMP) is perhaps the most well-studied self-management program [26,27] and has proven effective in patients with arthritis on fatigue, self-efficacy, pain, and activity limitations among others [28]. The CDSMP program stretches over 6 weeks and is available for small groups face-to-face, or online [29].

The body of evidence supporting the effects of physical activity is large [30], and EULAR have recently published guidelines for physical activity in RMDs [31]. Besides the effects on cardiorespiratory fitness and muscle strength [30], physical activity reduces the risk of all-cause mortality [32], CVD [33,34], Type 2-diabetes [35–37], obesity [38–40], different forms of cancer [41–45], osteoporosis [46,47], dementia [32,48,49], and depression [32,50]. In medically well-controlled RA, it seems that the functional mechanisms of exercise are the same as in the general population with exercise leading to reduced levels of pro-inflammatory cytokines, such as tumor necrosis factor [51]. Exercise can also have a positive effect on cachexia by increasing the proportion of fat-free body mass in patients with RA [51].

Regarding pain management, the EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis [52] summarizes key aspects for the health professional to focus on in the management of pain. Emphasis is put on adoption of a patient-centered framework within a biopsychosocial perspective, sufficient knowledge of both disease and pain pathogenesis, and ability to differentiate localized and generalized pain. Treatment shall be guided by scientific evidence and the assessment of the individual patient's needs, preferences, and priorities; pain characteristics; previous and ongoing pain treatments; inflammation and joint damage; and psychological and other pain-related factors. The described options of pain treatment suggested were education complemented by physical activity and exercise, orthotics, psychological and social interventions, sleep hygiene education, weight management, pharmacological and joint-specific treatment options, or interdisciplinary pain management. In terms of effects, physical activity/exercise and psychological interventions were the types that mostly had positive effects. Educational interventions, orthotics, weight management, and multidisciplinary treatment can also be effective, but need to be tailored and targeted towards specific disease groups [52].

Digital technologies to support in tertiary prevention

Digitalization of the health care sector ranges from electronic health records in some healthcare systems to the numerous amounts of mobile apps and webpages with health-related focus that exist today. As a consequence, and with the increasing digital presence in society, there is increasing pressure on the health care sector to work smarter and more cost effectively. This in turn has led to an increase in the use of digital solutions within health care [53], an increase that is also evident in the volume of related published scientific literature. A bibliographic-bibliometric analysis on articles published in Journal of Medical Internet Research revealed 1,797 articles with "digital health" as keyword [54], most of them published between 2016 and 2019. Digital technologies include apps, devices, and wearable technology and have a central role in the support of maintenance in lifestyle interventions in RMDs. The combining of digital technology with behavioral science offers a new dimension for how behaviors are measured and influenced [55].

For the clinician, the evidence for the use of digitally delivered interventions is of interest, along with what specific apps or webpages have been evaluated in trials, as well as if there are some solutions that are tailored for specific groups. A systematic review of meta-analyses published in 2017 found 71

meta-analyses including 1,733 studies containing 268 RCTs designed to test digital interventions [56]. The authors concluded that there is a wide range of effective internet-based programs (on substance abuse, mental health, diet, physical activity, insomnia, chronic pain, cardiovascular risk, and childhood health problems), but only few have websites available for public use. A systematic review and meta-analysis investigating what effect computer-, mobile-, or wearable technology has on reduction of sedentary behavior reveal that using these tools can reduce mean sitting time by a little over 40 min per day, but the effects are short-term, and thus not sustained over time [57]. The use of behavioral change techniques (BCTs) was also investigated in the same study using the BCT taxonomy [58], and the most frequently used BCTs were "prompts and cues", "self-monitoring of behavior", "social support", and "goal setting" [57]. In order to promote adherence or maintenance of behaviors, other BCTs needs to be added to the interventions.

There are some systematic reviews of digital interventions in this field of people with RMDs. The review by Srikesavan et al. [59] focuses on web-based rehabilitation interventions in patients with RA and concludes that the effects on pain, function, quality of life, self-efficacy, RA knowledge, physical activity, and adverse effects in people with RA are uncertain because of the very low quality of evidence. Only two outcomes showed significant improvements with web-based rehabilitation interventions, self-efficacy, and RA patient knowledge, but the quality of this evidence was very low. They also conclude that adverse effects of web-based interventions have not been evaluated [59]. The review by Griffiths et al. [60] focuses specifically on digital interventions for physical activity in patients with inflammatory arthritis (IA) and their findings suggest that the evidence for the effect of digital interventions on PA behavior is very limited. In this study, the authors also note the low adherence to PA interventions among the patient group and that future studies should focus on longer follow ups. In osteoarthritis, there is some evidence for the value of digital interventions in disease management. A review describing the results from 7 RCTs concluded that digital technology-supported interventions resulted in less pain, improved physical function, and improved health-related quality of life compared to no intervention. The improvements, however, were small and future research highlighting patients' adherence to digital interventions is promoted again [61]. The review by Berry et al. concluded that digital interventions have short-term positive effect on levels of physical activity but agreed that the long-term adherence is unknown and needs attention in future studies [62].

Digital technology to support adherence

Improving outcomes for people with RMDs in the longer term is a key focus for clinicians, with the incorporation of digital technologies monitoring in healthcare offering benefits for optimizing adherence and maintenance. Improving physical activity and other lifestyle changes such as reducing body weight involve significant behavior change with maintenance of the new behaviors in the long term.

Clinicians may wish to know about patient adherence to the intervention as prescribed/delivered as well as knowing if a patient has maintained some gains/benefits obtained from the intervention. Digital technologies offer opportunities for determining if a patient is adhering to a particular regime and also to determine if changes in outcomes are adhered to in the long term. So, how can digital technologies support adherence beyond the intervention period? Key questions for clinicians are how to support adherence to interventions as prescribed and how to monitor longer-term adherence post an intervention.

Incorporation of digital technology into a behavior change intervention (DBCI) offers solutions to the many reported barriers of face to face interventions including reduced cost, individualized treatments, and easily accessed format of information [63–65]. The recent systematic review of DBCIs to facilitate physical activity in osteoarthritis [62] reported that while existing DBCIs have short term benefits, their longer-term effect are not known. Their review included nine studies that aimed to increase PA in adults with OA using interventions delivered by digital platforms (apps and web-based programs). The DBCIs were found to have a positive effect on PA for up to 12 months post-intervention showing the benefit such interventions can have. Interventions like these are a valuable adjunct to clinical care particularly in primary care settings where long waiting lists often prevent people with OA from having regular care.

In considering how to design a web-based intervention or what intervention to choose in clinical practice, a number of recent studies provide some answers. Kelders et al. [66] developed a regression model to predict the factors linked to variance in adherence and found that an RCT study as opposed to an observational study, increased interaction with a counsellor, more frequent intended usage, more frequent updates, and more extensive employment of dialogue support significantly predicted better adherence to a web-intervention. Thus, these characteristics may be important factors to look for when choosing a web-intervention to improve adherence.

Considering the nature of the material and how it is presented is also important and the addition of gamification to the delivery of the content is valuable. Gamification is the application of game design elements in a nongame context [67] and shares common elements (flow, meaningful rewards, and social interaction) with behavior change approaches [68]. In examining social support and gamification features on behavioral and health outcomes in arthritis, a Swiss study (n = 157 patients with RA) allocated to participants four experimental conditions with different types of access to online social support and gamification features with a control group that had no access to the website [69]. The study demonstrated the benefit of a web-based intervention with social support sections on the website leading to decreased health care utilization and medication overuse and increased empowerment. Gamification alone or with social support increased physical activity and empowerment and decreased health care utilization.

Less sophisticated digital supports to improve adherence have also been examined in the literature. A systematic review [70] of 107 articles evaluating the effectiveness of mHealth in supporting the adherence of patients to chronic diseases management found that SMS was the most frequent mobile adherence tool used in 40.2% of studies. Of the studies (n = 27) that employed a randomized controlled trial (RCT) design, the majority (n = 15) demonstrated significant improvements in impact on adherence behaviors. Of the other RCTs that measured effects on disease-specific clinical outcomes (n = 41), only 16 reported significant improvements between groups. A Cochrane review to assess the effects of mobile phone messaging applications in facilitating self-management of long-term illnesses concluded that there were some limited indications that mobile phone messaging is helpful in supporting self-management in long term illnesses [71]. While no participants with arthritis were included in the Cochrane review, the conclusions drawn from participants with asthma, diabetes, and hypertension may offer some value for other chronic illness populations. The use of tailored text messages after three motivational counselling sessions aimed to reduce sedentary time by increasing time in light to moderate intensity was found to be sustained 18 months after the initial intervention in people with RA [72]. In summary, the addition of any digital elements to an intervention designed to improve participation or to monitor adherence to an intervention may be beneficial.

Patients' experiences of digital technology

In order to administer the right technology with the right timing to the right population, both health care providers' and patients' satisfaction with the digital interventions need to be understood [73]. Several studies have investigated patients' experiences and perspectives of different digital health tools and programs [74–82]. Themes that arose from the different studies and from which we can learn were; moderators are appreciated in online discussions to steer conversations [74], web-pages need to feel reliable which was felt if e.g. they are hosted by a university [74], interaction with competent health professionals promotes use of digital technologies [75,76], the easy access and possibility to use at your own convenience and pace is very positive [75,76], it saves time [77], and young people often prefer digital solutions to improve access to resources [82]. However, it also becomes evident that there is still a strong wish to meet a health professional face-to-face during some point of the intervention, most often before it starts [75,77].

Patients frequently ask what the best app is for managing their arthritis. Answering that question can be very difficult due to the wide range of apps available, the clinician's knowledge of such apps, and how to know what makes a good app. In trying to understand what self-management apps patients with arthritis most value, Geuens et al. [83] interviewed 31 adult patients using a mixed-methods approach and asked them to rate app features. In general, participants favored the use of features pertaining to supporting active and direct disease management, which help them to keep a close watch on their disease status, inform their health care professional, and receive personalized information.

Surprisingly perhaps, they strongly disliked features that provided a means of social interaction or provided incentivization for disease-related actions (e.g., being able to compare yourself with other patients, cooperating toward a common goal, and receiving encouragement from friends and/or family). These dislikes reflect the individual experiences of patients with arthritis and different patient and social environment manifestations of the condition.

Summary

Primary prevention of RMDs and clinical prevention when people are diagnosed with RMDs are important in the management of these conditions. Disease prevention and not smoking is of high importance. In terms of clinical prevention, it is essential that patients with RMDs are involved in their own disease management and well-informed about the risks of continued smoking- both in terms of risk of developing CVDs and the risk of not gaining the best possible benefit from the medical treatment. Self-management is very important in managing any chronic disease and should be a focus in the tertiary prevention. Tertiary prevention focuses on limiting the influence of a recognized or verified disease and preventing further development or worsening of the disease, including physical and psychosocial disability. Other core aspects in tertiary prevention are physical activity and pain management. For all three aspects, there is a large body of evidence supporting the effects of such interventions. To make these interventions available to a larger audience, digital technologies can be used. Based on research in the general population, digital solutions for tertiary prevention are effective. The available evidence for digital tertiary prevention for people with RMDs is currently weak. However, the large amount of registered study protocols on this topic suggest an increase in publications in the coming years. It is well established that the digital Chronic Disease Self-Management Program and digital interventions in osteoarthritis are effective to improve physical activity level, pain, function, and quality of life. In designing digital interventions, patients' experiences and perceptions should be taken into account in order to enhance usability.

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Practice points

- Early diagnosis and smoking cessation (or not starting to smoke at all) can improve development of disease and prognosis and should therefore be prioritized.
- In order to limit the influence of a recognized or verified disease, and to prevent further development or worsening of the disease, self-management, physical activity, and pain management should be promoted by health care providers.
- To increase patient activation and involvement, which is key for sustainability, behavior change, and self-management, clinical care needs to be individualized and patient centered.

Research agenda

- In order to increase the knowledge base regarding the use of digital technologies in tertiary prevention interventions in RMDs, high quality research needs to investigate theory-based and patient centered interventions.
- More research is needed on aspects of adherence and maintenance after tertiary prevention interventions.

Declaration of Competing Interest

None.

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