

as a chemosensor for harmful exogenous compounds and mediates pain and neurogenic inflammation. More recently, TRPA1 has been found to be activated also by endogenous compounds formed in inflammation, such as reactive oxygen and nitrogen species. That prompted us to investigate the role of TRPA1 in inflammatory conditions including osteoarthritis.

Monosodium iodoacetate (MIA)-induced arthritis is a widely used animal model of osteoarthritis. We found that MIA evoked acute inflammation, degenerative cartilage changes and joint pain in wild type mice; but interestingly, those responses were significantly attenuated in TRPA1 deficient animals. Furthermore, TRPA1 was found to be expressed and inducible by inflammatory factors including IL-1 and IL-17 in primary human OA chondrocytes; and the TRPA1 channel was shown to be functional based on calcium influx assays. Pharmacological inhibition and genetic depletion of TRPA1 downregulated the production of inflammatory factors and MMP enzymes in mouse cartilage and primary human OA chondrocytes.

The present results introduce TRPA1 as a plausible factor involved in the pathogenesis of OA and provide a novel target for analgesic and anti-inflammatory drugs with disease modifying potential in OA.

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## Wearable technologies in 21<sup>st</sup> century healthcare —

### SP0023 REVIEW OF WEARABLE TECHNOLOGIES

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Working environments have in recent times become less physical with the increase in sedentary, computer-based occupations. Sedentary time is known to be associated with a number of health-related outcomes, including obesity, heart disease, diabetes, cardiometabolic risk factors, some cancers and early mortality, independent of physical activity. There is limited research that has examined sedentary time and physical activity and associations with musculoskeletal conditions, despite these being responsible for the majority of work-related ill health and days absent from work.

The validity and practicality of objective and subjective techniques to measure physical behaviour have been widely reported; however, there is no gold standard that is valid, accurate, reliable and also practical. Self-reported methods can be practical and low-cost, but are subject to recall and social desirability bias; whereas objective devices, such as accelerometers, can be expensive, but allow for information on intensity, frequency and duration of activity to be measured.

The Health Survey for England 2008 used both subjective and objective measures of physical activity: they found that 39% of men and 29% of women were meeting the recommended levels of physical activity when asked via a questionnaire. In comparison, when physical activity was objectively measured using an accelerometer, it was found that only 6% of men and 4% of women met these targets.

Wearable technologies, including research grade accelerometers (e.g. activPAL™) and consumer wearables (e.g. FitBit), are increasingly being used in research, not only to measure physical behaviours but may also be useful in facilitating and monitoring behaviour change. This work will present an overview of wearable technologies used in research, what they can (and can't) measure, and in particular their application in musculoskeletal research.

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### SP0024 WEARABLE TECHNOLOGIES IN RESEARCH AND CLINICAL TRIALS

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The use of wearable technology in clinical trials has the potential to be one of the most disruptive innovations in drug development. The cost and duration of the current clinical trial design has been under scrutiny for a number of years with the sustainability of the existing model under question. A critical success factor is adequate patient recruitment and retention. Recent initiatives to redesign the clinical trial process have focused on the creation of trials that are more patient focused. A wealth of medical grade physiological data is now readily available from wearable technology, with the potential to create a new future where patients no longer have to visit research sites and where real-time data are available remotely.

However, integrating wearables into a clinical trial is more complex than simply giving the patient a smartwatch and spontaneously generating clinically relevant data. Focusing on technology and sandwiching it into a trial is not a best practice. Wearables need to be viewed as a component of an overall patient-centric strategy rather than solutions in themselves. When creating a remote trial, simply shifting the burden from the sites to the patients, requiring them to carry out a number of tasks in an unsupported, uncontrolled environment is neither welcome nor sustainable. The process for successful selection and integration of wearables needs to take a number of criteria into consideration; clinical hypotheses, the

value that is gained by the inclusion of wearables, the robustness of the data generated by the devices, and ensuring that the data adds clarity not additional complexity to the trial.

The re-engineering of the clinical trial to create a patient focused trial goes beyond mere convenience. Wearables and sensor have the potential to generate digital maps of individual's physical behaviours. Wearable technology is facilitating the remote capture of real life data but also has the potential to create new end points and outcome measures that are meaningful to the patient and could hold the key to a new clinical trials paradigm.

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## Assessment and management of osteoporosis —

### SP0025 THE USE OF BIOMARKERS FOR OSTEOPOROSIS CLINICS

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The balance between bone resorption and bone formation is maintained through a complex regulatory system of systemic and local factors acting on bone cells, such as calcium regulating and sex hormones, growth factors and cytokines. Furthermore, the competence of the bone cells and the number of active cells will determine the production of bone matrix proteins, while other incompletely understood intrinsic mechanisms will determine mineralization and micro-structure. Exposure of the matrix after osteoclastic activation allows for proteolytic enzymes to commence the degradation of the collagenous structure. The signals responsible for termination of bone resorption and initiation of bone formation (coupling) are not yet completely understood. Nevertheless, a tight coupling between resorption and formation is required to maintain bone mass and to preserve the micro-architectural integrity of bone.

Based on this knowledge markers of bone metabolism have been developed. These markers have been evaluated in terms of their ability to predict fracture, change in bone mass, and response to pharmacological treatments in clinical trials and additionally to monitor treatment in clinic.

The lecture will cover the use of markers in clinical trial, interpretation of change in markers from currently available and potential new drugs and to what extent and how to best apply in clinic.

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### SP0026 NOVEL IMAGING TECHNIQUES FOR ASSESSING OSTEOPOROTIC FRACTURE RISK

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The measurement of areal bone mineral density (aBMD) by dual x-ray absorptiometry (DXA) has been the mainstay for the diagnosis of osteoporosis for at least two decades. The sensitivity and specificity of this test, however, remains suboptimal. For example, more than 50% of postmenopausal women with fragility fracture are not identified with DXA. A great deal of research has been performed recently to develop alternative or complementary imaging techniques to overcome DXA predictive limitations. These techniques are based on the non invasive analysis of bone microarchitecture and estimation of bone strength by finite element analysis (FEA).

Texture analysis uses mathematical models based on fractal analysis to evaluate bone microarchitecture using various types of bone images. The trabecular bone score (TBS) has emerged as an approach that may improve fracture risk prediction. The TBS is based on the texture analysis of the DXA lumbar spine image to quantify bone microarchitecture. Several cohort studies have shown that a subset of individuals could be reclassified with TBS. A meta-analysis results have allowed for incorporation of the TBS in the FRAX score calculation, that is widely available.

The measurement of volumetric BMD with quantitative computerized tomography (QCT) at the hip has been shown to predict fracture risk. These images can also be used to perform FEA that may increase the fracture risk prediction. The additional value of this technique compared with DXA remains to be established in a clinical setting.

Bone microarchitecture can also be assessed at peripheral sites such as the distal radius and tibia using high resolution peripheral quantitative tomography (HRpQCT). Numerous cross-sectional and case-control studies have shown a significant association between prevalent fracture and bone microarchitecture and estimated bone strength assessed with FEA. The bone parameters measured at distal sites are also associated with fractures at distant sites, e.g., the vertebrae and the femoral neck. In a recent prospective study, bone microarchitecture at the distal radius - especially the trabecular vBMD - has been associated with incident osteoporotic fracture. The FEA models were also predictive of fragility fracture. The best models and the most appropriate architectural parameters - whether they are trabecular or cortical - remain to be dissected out and their comparative diagnostic value with aBMD by DXA remains to be established.

The measurement of the TBS may allow for reclassification of a subset of

postmenopausal women at higher risk for fracture whereas they display a moderately reduced aBMD. Hip QCT and HRpQCT may also improve the prediction for fracture, but they are still research techniques.

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#### SP0027 EMERGING THERAPIES FOR OSTEOPOROSIS

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Currently, anti-resorptive drug therapy is the cornerstone of fracture prevention. Anti-resorptive drugs decrease bone remodelling, allowing the remaining bone to increase secondary mineralisation, and, with denosumab, also allowing periosteal bone modelling.

Teriparatide is currently the only available bone-forming drug, which increases bone formation more than bone resorption, and has been shown to reduce the risk of vertebral and non-vertebral fractures.

Recently, two randomized clinical trials have been published on the effect of new bone forming agents on the risk of fracture.

Abaloparatide is a 1–34 fragment of PTHrP, with different pharmacokinetics and potential different signalling mechanisms compared to teriparatide. It increases bone formation more than bone resorption, both to a lesser degree than teriparatide. In the double blind, randomised placebo-controlled 18-month ACTIVE study, abaloparatide significantly reduced the risk of vertebral (-86%), clinical (-43%), non-vertebral (-43%) and major fractures (-70%). In a parallel randomised exploratory open-label comparison with teriparatide, bone density increased significantly more with abaloparatide, but the anti-fracture effect was similar, except for a significantly better result on prevention of major fractures.

Romozosumab is a monoclonal antibody that binds sclerostin, which is an inhibitor of bone formation. In contrast to other bone forming agents, it disconnects the increase in bone formation from a decrease in bone resorption. In the double-blind placebo-controlled FRAME study, romozosumab significantly reduced the risk of vertebral (-63%) and clinical fractures (-36%) during the first year, an effect that was maintained by transitioning to one-year denosumab treatment.

The effect on non-vertebral fractures was not significant, but geographic interaction was found. When excluding patients from South America, in whom fracture risk was low, one-year treatment with romozosumab significantly decreased the risk of non-vertebral fractures by 42%.

Abaloparatide and romozosumab are new bone forming agents, with different effects on bone remodelling and remodelling and early effects on clinical fractures. This opens new perspectives in individualised treatment of patients with high fracture risk and for fracture prevention in patients with low bone turnover, multiple vertebral fractures, very low BMD and fractures or bone loss during anti-resorptive treatment.

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## Systematic literature review: the link from science to clinical practice

#### SP0028 SYSTEMATIC LITERATURE REVIEW: WHERE TO START

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Starting a systematic literature review (SLR), particularly for the first time, may be an overwhelming task. As its designation indicates, it requires a systematic approach, in order to ensure that all the relevant literature addressing the research question at hand is covered and appropriately summarized.

SLRs are particularly helpful for clinicians, who have a question based on their clinical practice and want to obtain the best evidence based answer. The large and increasing amount of existing literature makes the life of a clinician difficult when trying to search by him/herself for the answer based on the original studies. An SLR may thus be an efficient way to get the answer, by condensing hundreds of studies into a good summary. They are also of the basis, together with expert opinion, of diagnostic and/or management/treatment recommendations.

The first step of an SLR is always to properly formulate the research question, in a way that the literature covering the topic can be searched. The classic approach is the PICO framework, in which the formulated question includes the different elements guiding the literature search, namely the Population of interest, the intervention to which patients are exposed, the Comparator against which the effect of the intervention is to be compared and the Outcomes on which the assessment of the intervention will rely and in which the SLR will focus (e.g. efficacy, safety outcomes, etc).

A crucial aspect when reviewing the literature is the risk of bias assessment. Studies should be judged for their methodological quality so that one can interpret their findings accordingly. If a study is methodologically not sound, then we know that it will not be very helpful in answering the research question and, most important, this cannot be ignored when performing an SLR. This risk of

bias assessment also requires some knowledge of important epidemiology and biostatistics concepts, which are needed to correctly understand how a study is conducted.

These and other steps contribute to shaping an SLR. Challenges involved when performing an SLR will be discussed in detail in this presentation, as well as the different steps of an SLR and the most critical aspects that should be considered. Tips from experiences with SLRs will be shared. This should ultimately encourage (young) clinicians and researchers on where to start when embarking on an SLR challenge, but hopefully also on how proceed with and bring to an end a successful and informative SLR.

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#### SP0029 LINKING SCIENCE TO CLINICAL PRACTICE: FROM THE SYSTEMATIC LITERATURE REVIEW TO THE FORMULATION OF RECOMMENDATIONS

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Systematic literature review (SLR) is a scientific method to collect the available data in the literature regarding a specific research question, and to compare the quality of different studies, in order to arrive at the best possible answer. SLR is not the same as data-pooling. In contrast to what many clinicians think, SLR is clinical science and not “easy going”, it takes a lot of time and effort, you can make mistakes, and you need to practice and obtain experience. A proper SLR is all but “low hanging fruit”.

Nevertheless, SLRs from the evidence base of guidelines, and as such are integral parts of them.

This lecture will describe how SLRs should be translated into guidelines, and what pitfalls may prevent that the appropriate evidence will be enclosed in recommendations, or that too weak evidence gets a too prominent place.

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#### SP0030 BEYOND THE RECOMMENDATIONS: EXAMPLES OF SYSTEMATIC LITERATURE REVIEW IN DAILY CLINICAL PRACTICE

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Recommendations and guidelines for management and treatment of rheumatic diseases exist to help rheumatologists deliver optimal care for their patients in an evidence-based way. However, not all practical questions and medical difficulties encountered by rheumatologists in daily clinical practice can be addressed using these existing guidelines. Moreover, time in practice is limited and usually does not allow for extensive systematic literature research to find evidence regarding a specific medical question that needs answering in due time. Therefore, an essential skill for doctors and those in training, besides medical knowledge and examination skills, is to be able to search for, withdraw and appraise published evidence applicable to a confined topic. A so called CAT – critically appraised topic – is a compact systematic literature research following a strictly formulated PICO to answer a clinical question encountered in daily practice. Results can be presented in department meetings and stored in a database for education purposes and use in daily practice. This presentation will address the structure, the carrying out, as well as important pros and cons of the CAT. Examples will be given drawn from the experience of young rheumatologists in training in the Netherlands.

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## EULAR Campaign: Don't Delay, Connect Today

#### SP0031 HOW COULD GPS ENHANCE THE EARLY DIAGNOSIS OF RHEUMATIC DISEASES

*C.D. Mallen. Arthritis Research UK Primary Care Centre, Primary Care and Health Science, Keele, United Kingdom*

Primary care and general practice has a key role to play in the early and accurate detection of patients with rheumatoid arthritis.

This talk will explore some of the current barriers to best practice, highlighting the workload associated with musculoskeletal problems in primary care and the challenges in making a prompt diagnosis. Possible solutions will be explored, highlighting the importance of strong patient and professional partnerships

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