Institution: University of Wolverhampton

Unit of Assessment: 24 Sport and Exercise Sciences, Leisure and Tourism

Title of case study: Exercise as Medicine

Period when the underpinning research was undertaken: 2010-2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Professor George Metsios	**Professor in Clinical Exercise Physiology**	**2007 to the Present**
Professor Yiannis Koutedakis	**Professor in Applied Exercise Physiology**	**1991 to the Present**

Period when the claimed impact occurred: 2014-2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

Rheumatic and musculoskeletal diseases (RMDs) affect more than 4 million people in Europe with an estimated societal cost of 0.5 to 2% of the gross domestic product. In the UK, it has been estimated that 30.6 million sick leave days are lost due to RMDs annually. Our research has investigated the effects of physical activity, most notably exercise, on non-communicable diseases, accumulating robust evidence that physical activity works as an adjunct treatment strategy for managing RMDs. The impact arising from our work flows through three areas:

- Working with organisations to improve training for healthcare professionals and clinical guidance – We have worked with the European League Against Rheumatism (EULAR) and the European Society of Cardiology (ESC) to create new guidance, and associated training. The ability to shape better implementation strategies for physical activity through clinical guidance has improved clinical practice allowing for an informed and more specialised management of RMD patients.

- Improved Health Outcomes for Patients: Provision of physical activity for people with musculoskeletal conditions and supporting people to improve their own health; and

- Enhancing public understanding through the National Rheumatoid Arthritis Society (NRAS): this has impacted on the ways RMD conditions are managed, permitting new interventions involving physical activity that have, in some cases, saved lives. The development of intervention resources is integral to this process and is of further benefit to patients.

2. Underpinning research

Our collective research is focussed on generating improved health outcomes and has significantly enhanced quality of life in patients with RMDs. The results of our research have, therefore, been utilised to improve healthcare guidelines and practices, through implementing physical activity in everyday clinical practice. Our findings, evidenced via published clinical trials, systematic reviews with meta-analyses, and as reported in the underpinning research [R1 to R6], consistently reveal the beneficial effects of physical activity and detrimental effects of physical inactivity on different

outcomes for health in RMDs. Our group works with the EULAR, the largest RMD organisation, in order to implement our interventions within clinical practice.

The group's findings [F] are central to the impacts and are described below:

F1. Physical Activity and RMDs

Our findings highlight important beneficial effects of physical activity on physiological, patient- and clinically-relevant outcomes in RMDs. Specifically, low cardiorespiratory fitness (CRF) is a significant predictor of cardiovascular disease (CVD), and interventions aiming at increasing CRF are known to reduce CVD risk. Importantly, our work has developed pioneering theories by which effective interventions can be implemented successfully in clinical practice [R1 and R2]. The most important aspect of these is that a programme of physical activity designed to meet individual needs and physical abilities significantly improves microvascular and macrovascular function in parallel with disease-related characteristics in RA (Rheumatoid Arthritis) patients.

We have also designed and developed robust frameworks which provide a pathway of successfully implementing physical activity in clinical practice [R3], focussed on addressing unmet key patient-identified barriers, such as pain and fatigue [R4]. Our work on addressing these key gaps has been, and continues to be, funded by EULAR and ERASMUS+ where we act as principal investigators working with twelve different EU Universities and patient organisations. The research objective is twofold: to change healthcare professional practices (medical schools, nursing, and physiotherapy) and to implement physical activity in clinical practice for frontline healthcare practitioners.

F2. Sedentary Behaviour and RMDs

We have extended our research from F1 and are investigating the whole of the physical activity spectrum, also focusing on sedentary behaviours (i.e., time spent sitting). We are the first team to identify the detrimental associations between sedentary behaviours and adverse patient and clinical outcomes (i.e., increased risk for cardiovascular disease) in RMD patients [R5, R6]. Changing patient behaviours to reduce sedentary lifestyles has been an important focus of recent public health strategies to improve health of the general population, particularly patients with RMDs, who tend to sit more than the general population due to the symptoms of their condition (pain, fatigue and functional disability).

A crucial factor that makes the research base so robust is the involvement of clinical stakeholders and users throughout the research journey: from design to delivery and evaluation of the research. This co-design and co-evaluation are also essential in enabling the research to be applied readily and speaks to speed of delivery.

3. References to the research

The following references have been through a rigorous peer review process and have been published in peer-reviewed journals. They have been points of reference for further research beyond the original institution. For example, R6 has higher than average citation data, informing further research into rheumatoid arthritis. Evidence of peer-reviewed funding is below.

R1. Stavropoulos-Kalinoglou A, Metsios GS, Veldhuijzen van Zanten JJ, Nightingale P, Kitas GD, and Koutedakis Y. (2013). 'Individualised aerobic and resistance exercise training improves cardiorespiratory fitness and reduces cardiovascular risk in patients with rheumatoid arthritis', *Annals of the Rheumatic Diseases*, 72(11): 1819-25. doi: 10.1136/annrheumdis-2012-202075

R2. Metsios GS, Stavropoulos-Kalinoglou A, Veldhuijzen van Zanten JJ, Nightingale P, Sandoo A, Dimitroulas T, Kitas GD, and Koutedakis Y. (2013). 'Individualised exercise improves endothelial function in patients with rheumatoid arthritis', *Annals of the Rheumatic Diseases,* 73(4): 748-51. doi: 10.1136/annrheumdis-2013-203291

R3. Metsios GS, and Kitas GD. (2018). 'Physical activity, exercise and rheumatoid arthritis: Effectiveness, mechanisms and implementation', *Best Practice & Research: Clinical Rheumatology*, 32(5): 669-682. doi: 10.1016/j.berh.2019.03.013

R4. Veldhuijzen van Zanten J, Rouse RC, Hale ED, Ntoumanis N, Metsios GS, Duda JL, and Kitas GD. (2015). 'Perceived barriers, benefits and facilitators for regular physical activity in patients with rheumatoid arthritis', *Sports Medicine*, 45(10): 1401-12. doi: 10.1007/s40279-015-0363-2

R5. Fenton SAM, Veldhuijzen van Zanten JJCS, Duda JL, Metsios GS, and Kitas GD. (2018). Sedentary behaviour in rheumatoid arthritis: definition, measurement and implications for health. *Rheumatology*, 57(2): 213-226. doi: 10.1093/rheumatology/kex053

R6. Fenton SAM, Veldhuijzen van Zanten JJCS, Kitas GD, Duda JL, Rouse PC, Yu CA, and Metsios GS. (2017). 'Sedentary behaviour is associated with increased long-term cardiovascular risk in patients with rheumatoid arthritis independently of moderate-to-vigorous physical activity', *BMC Musculoskeletal Disorders*, 18(1): 131. doi: 10.1186/s12891-017-1473-9 (REF 2 Output)

Grants

VANGUARD is the ERASMUS+ Collaborative partnership consortium for Virtual Advice, Nurturing, Guidance on Universal Action, Research and Development for physical activity and sport engagement at the local, national and international level, running from 01 January 2020 to 31 July 2024, (£342,530). It is for collaboration between EU countries' Health Ministries and the World Health Organization to integrate physical activity guidelines within the curricula of five EU medical schools and for UK healthcare professionals.

4. Details of the impact

Our research has led to evidenced change across three impact areas: improvements to clinical training and guidance; better health outcomes for patients; and enhanced public understanding.

I1. Working with organisations to improve training for healthcare professionals and clinical guidance

Our international leadership in this field enables continuous shaping of EULAR recommendations [C1]. We have developed resources to train frontline healthcare professionals so that they can implement physical activity in their clinical practice guidance (the IMPACT RMD project) [C1]. Training also takes place through the VANGUARD project, which implements physical activity in the undergraduate curricula of medical schools and healthcare professional institutions, so that future frontline health practitioners can advise and support increased physical activity in the clinical setting to all patients with non-communicable diseases (NCDs), as well as in pregnancy and perioperatively [C2].

On the basis of F1 and F2, the EULAR has utilised our results to increase RMD healthcare professional awareness through new guidance [C3, C4, C6, and C7] for the use of physical activity in clinical practice. RMD professionals are now utilising physical activity to reduce cardiovascular disease risk and improve disease-related and patient-important symptoms in those with autoimmune diseases.

Moreover, this work has also enabled us to contribute to the development of EULAR recommendations, such as the influential *EULAR Recommendations for the implementation of self-management strategies in patients with Inflammatory Arthritis*. These have been endorsed by the *British Medical Journal* [C1 and C4] and have found their way into practice, thereby proving to be avenues for clear benefit to patients.

The 2019 Position Statement of the ESC, the leading European cardiovascular disease organisation [C5], uses Findings F1 and F2 to inform guidelines for advanced disease prevention strategies and improved healthcare practices for mitigating the detrimental effects of cardiovascular disease in people with RMDs.

The ESC's members and decision-makers are healthcare professionals and world-renowned experts; their opinions are routinely sought and their papers regularly published and referenced. The ESC disseminates evidence-based scientific knowledge to cardiovascular professionals so they can better care for their patients. This is therefore an important change resulting from our research, demonstrating how embedded our research findings are in policy and practice. The ESC is a source of high quality, evidence-based science that pushes the boundaries of cardiovascular medicine and inclusion in their position statement ensures that the impact is widespread and of benefit to patients internationally.

I2. Improved Health Outcomes for Patients: Provision of physical activity for people with musculoskeletal conditions

The Department of Health, NHS England, Public Health England and Arthritis Research UK have published a collaborative report [C8] that has utilised our research findings [F1] to improve health training guidelines in order to manage better the symptoms in patients with chronic inflammatory conditions.

This has had a positive effect on the health of the public through the process of having informed government recommendations. As Professor Dame Sally Davies, then Chief Medical Officer, put it: "It is about supporting people to improve their own health, particularly through physical activity and have a better quality of life" [C8]. That ability and empowerment at the individual level is also both impactful and beneficial societally, as health outcomes improve more widely.

I3. Enhancing public understanding through the NRAS

NRAS is the largest patient organisation in the UK and has used our work to improve healthcare management [C9]. NRAS has developed free online self-management resources for patients in the UK, using our findings [F1 and F2], so that patients are empowered to select from a range of physical activity resources and reduce their cardiovascular disease risk.

Our findings [F1 and F2] have also been used to deliver a webinar (2018) on how to become more physically active. This has been the best attended webinar delivered by NRAS, with more than 300 patients attending online and engaging in Q&A. Patient feedback published in the NRAS member magazine included ''Can you ask Prof. Metsios if he wants a new patient?! His attitude to exercise and the 'you know your body best' approach is inspiring" and "I just saw the exercise webinar recording with Professor Metsios, it was very good and boy did it prompt me to get up. I was there on my wobble board as well as walking machine! Can't wait for the next one!" [C9]. Based on the feedback received from NRAS, many patients who attended the webinar have requested further information on how to become more physically active and are actively considering ways of implementing the advice provided from the webinar.

As the NRAS Chief Executive has put it: "Professor Metsios has helped them [patients] understand much better the benefits of physical activity on their condition but also to seek ways of becoming more physically active, following the advice provided in the broadcast" [C10]. The results of our research and the co-development of new resources in conjunction with key stakeholders is therefore leading to beneficial health outcomes.

5. Sources to corroborate the impact

C1. Testimonial from Chair of the European League Against Rheumatism Healthcare Professionals Groups.

C2. Ann Gates – 'Launch of the Erasmus+ #MovementForMovement resources for physical activity, noncommunicable diseases, surgery, and pregnancy', Council of Deans, 30 November 2020, https://councilofdeans.org.uk/2020/11/launch-of-the-erasmus-movementformovement-resources/.

C3. The Rheumatologist, 2015. RH Moe. EULAR 2015: Benefits of Individualizing Exercise Therapy. https://www.the-rheumatologist.org/article/eular-2015-benefits-of-individualizing-exercise-therapy/?singlepage=1&theme=print-friendly

C4. Agca et al. (2017). 'EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update'. *Annals of the Rheumatic Diseases*, 76(1):17-28. doi: 10.1136/annrheumdis-2016-209775.

C5. Hollan et al., (2019). *Lipid management in rheumatoid arthritis: a position paper of the Working Group on Cardiovascular Pharmacotherapy of the European Society of Cardiology*. pvz033, doi: 10.1093/ehjcvp/pvz033.

C6. Rausch Osthoff et al., (2018). '2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis'. *Annals of the Rheumatic Diseases*, 77(9):1251-1260. doi: 10.1136/annrheumdis-2018-213585, https://pubmed.ncbi.nlm.nih.gov/29997112/

C7. Baillet et al., (2016). Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. *Annals of the Rheumatic Diseases*, 75(6):965-73. doi: 10.1136/annrheumdis-2016-209233.

C8. Collaborative report from the Department of Health, the NHS England, the Public Health England and the Arthritis Research UK (2016). *Providing physical activity interventions for people with musculoskeletal conditions*.

C9. *National Rheumatoid Arthritis Society Members Magazine*, Winter 2018, pages 28 and 29.

C10. Testimonial from Chief Executive of the National Rheumatoid Arthritis Association, UK.