Institution: Teesside University		
Unit of Assessment: 3		
Title of case study: Informing and changing national and international public health guidelines in physical activity and jet lag.		
Period when the underpinning research was undertaken: 2008-2015		
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:**
Greg Atkinson	Professor of Health Sciences and Biostatistics Research	Mar 2012 to present
Alan M Batterham	Professor of Exercise Science	Sep 2005 to present
Kathryn Weston (née Taylor)	Senior Lecturer in Applied Biosciences for Health	Feb 2014 to Oct 2020
Matthew Weston	Reader in Exercise Science	Sep 2009 to present
Period when the claimed impact occurred: 2017-2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

Research at Teesside University on the association between physical activity and colorectal cancer and cardiorespiratory fitness and the effectiveness of jet lag treatments has led to changes to evidence-based public health guidelines for the UK and USA. Our evidence synthesis research on physical activity and cancer risk, and high-intensity interval training and fitness, critically informed the official Government physical activity guidelines for population health in the USA and UK. Our evidence synthesis and randomised controlled trial research on jet lag led directly to the co-production of changes to the guidelines for the management of jet lag in international travellers (Centers for Disease Control and Prevention 'Yellow Book', Civil Aviation Authority, the National Health Service, and the National Institute for Health and Care Excellence).

2. Underpinning research (indicative maximum 500 words)

The impacts in this case study are underpinned by our evidence synthesis and randomised controlled trial research, focusing on the association between physical activity and colorectal cancer and cardiorespiratory fitness, and the effectiveness of jet lag treatments.

Insufficient physical activity is one of the major behavioural risk factors for chronic disease. Our research examined the associations between different levels and types of physical activity and health outcomes in two areas – colorectal cancer and cardiorespiratory fitness. A systematic review and meta-analysis of the association between leisure-time physical activity and colorectal cancer risk was conducted in 2008-2009 and published in 2009 [3.1]. We estimated summary risk ratios for uppermost vs lowermost categories of physical activity. To quantify dose-response, we applied a novel bootstrap resampling method to explore risk ratios as a function of cumulative percentiles of physical activity distribution, as heterogeneity in methods of measurement of physical activity levels meant that there was no common metric across the studies. For colon cancer, the research found that greater leisure-time physical activity was associated with a 20% relative risk reduction in men and 14% in women. The dose–response analysis revealed linear reductions in risk of colon cancer with increasing leisure time physical activity in both genders.

Increased cardiovascular-respiratory fitness is strongly associated with reduced all-cause mortality. Our systematic review and meta-analysis of the effects of low-volume high-intensity interval training (HIT) on fitness in adults was conducted in 2013-2014 and published in 2014 [3.2]. The research showed that low-volume HIT produces substantial improvements (6-10%) in

the maximal oxygen uptake of active non-athletic and sedentary people. Subsequently, the notion that HIT could be a viable physical activity option for public health benefits was advanced at a debate at the International Society for Behavioral Nutrition and Physical Activity Annual Meeting in 2015: High-intensity exercise as a public health strategy? This debate was reported in a full journal article [3.5].

Jet lag is due to the internal body clock(s) of an individual being out of phase with the environmental timing of light/dark and meals after a flight that crosses three or more time zones. In 2017, airlines carried 4,100,000,000 passengers worldwide on scheduled services. The precise incidence of jet lag is unknown, but it negatively affects a substantial proportion of travellers, with symptoms including sleep disorders, daytime tiredness, exhaustion, attention, concentration and memory problems, gastrointestinal problems, and anxiety. We conducted a critical review of jet lag research between 2013 and 2014 [3.3]. As part of this review, we undertook an insightful cumulative meta-analysis that showed the reported effectiveness of melatonin for alleviating jet lag symptoms reduced substantially over time, as higher quality and larger studies were published. This is an example of the 'decline effect' in science, where initially large beneficial effects in small early studies are later shown to have been exaggerated substantially. We also led the very first randomised controlled trial on the effectiveness of artificial bright light for reducing jet lag symptoms after a transmeridian long-haul flight [3.4]. We showed that the proposed benefits of bright light, suggested by animal studies and laboratory simulations, do not necessarily translate to clinical/ practical usefulness following an actual transmeridian flight. Previously, guidelines for the treatment of jet lag symptoms have not been informed by higher-grade evidence. The key novel work that we have undertaken since 2012 is the scrutiny of evidence translation from laboratory studies to real-world jet lag treatment.

3. References to the research (indicative maximum of six references)

[3.1] Harriss DJ, Atkinson G, Batterham A, George K, Tim Cable N, Haboubi N, Renehan AG, The Colorectal Cancer, Lifestyle, Exercise and Research Group. 2009. Lifestyle factors and colorectal cancer risk (2): a systematic review and meta-analysis of associations with leisure-time physical activity. Colorectal Disease. 11:7, 689-701. https://doi.org/10.1111/j.1463-1318.2009.01767.x. Cited 124 times (Web of Science). Output selected for REF2014 (95.5% 2* and above).

[3.2] Weston M, Taylor KL, Batterham AM, Hopkins WG. 2014. Effects of low-volume high-intensity interval training (HIT) on fitness in adults: a meta-analysis of controlled and non-controlled trials. Sports Medicine. 44:7, 1005-17. https://doi.org/10.1007/s40279-014-0180-z. Cited 173 times (Web of Science) and classified as a 'Highly Cited' output. The output is in the top 5% for citations worldwide for a review paper of its type, age, and subject area. Output selected for REF2021.

[3.3] Atkinson G, Batterham AM, Dowdall N, Thompson A, van Drongelen A. 2014. From animal cage to aircraft cabin: an overview of evidence translation in jet lag research. European Journal of Applied Physiology. 114:12, 2459-2468. https://doi.org/10.1007/s00421-014-3026-3. Cited 5 times (Web of Science).

[3.4] Thompson A, Batterham AM, Jones H, Gregson W, Scott D, Atkinson G. 2013. The practicality and effectiveness of supplementary bright light for reducing jet-lag in elite female athletes. International Journal of Sports Medicine. 34:7, 582-589. https://doi.org/10.1055/s-0032-1331160. Cited 16 times (Web of Science).

[3.5] Biddle SJH, Batterham AM. 2015. High-intensity interval exercise training for public health: A big hit or shall we hit it on the head? International Journal of Behavioral Nutrition and Physical Activity. 12:95. https://doi.org/10.1186/s12966-015-0254-9. Cited 141 times (Web of Science) and classified as a 'Highly Cited' paper in the top 1% for citations worldwide for a paper of its type, age, and subject area.

4. Details of the impact (indicative maximum 750 words)

The underpinning research has resulted in changes to evidence-based public health guidelines for physical activity and jet lag for the UK and USA. Our research has critically informed the current Government physical activity guidelines for population health in the UK and USA. These

guidelines are the primary, authoritative, evidence-based resource for health professionals, policy makers, and individuals on the recommended levels of physical activity to promote population health and reduce chronic disease risk. The development of the guidelines follows a similar process in each country. First, a panel of experts is assembled to rigorously review and scrutinise the evidence base on the relationship between physical activity and health. These experts place primary emphasis on high-quality systematic reviews. Subsequently, recommendations are drafted, reviewed critically, and finalised. Relevant, high-quality research used to underpin these recommendations is typically cited in the accompanying scientific reports and working group papers. The live debate at the International Society for Behavioral Nutrition and Physical Activity Annual Meeting in 2015, and associated paper [3.5], acted as a catalyst for the subsequent impact. For the Senior Policy Manager at the UK Government Department of Health and Social Care: 'the live debate and subsequent paper created a substantial buzz on social media among physical activity scientists, policy makers, and public health commissioners, and stimulated thinking about the potential for very vigorous intermittent physical activity to be included for the first time in the UK physical activity recommendations for public health' [5.1].

Our meta-analysis [3.1] has informed the Physical Activity Guidelines for Americans. It is referred to eight times in the Cancer Prevention chapter of the scientific report underpinning these Guidelines by the Physical Activity Guidelines Advisory Committee (PAGAC) [5.2]. The report states: 'one meta-analysis estimated dose-response by percentile of physical activity, and found a linear reduction in risk across the 20th to 95th percentiles and estimated risk reductions between these two percentiles of 0.13 in men and 0.14 in women. This same meta-analysis plotted risk for colon cancer by leisure time physical activity in those studies with MET-hours per week or MET-minutes per week data, and found dose-response risk reductions in both men and women' [5.2, p. F4-17]. Based on our research, the PAGAC concluded that the evidence grade was 'strong' for a dose-response relationship between increasing physical activity levels and decreasing risk of colon cancer in men and women [5.2. p. F4-57]. Consequently, the Committee recommended that all individuals should be encouraged to engage in the recommended levels of physical activity to reduce risk for developing cancer [5.2, p. F4-59].

Additionally, our meta-analysis [3.2] informed the 2019 UK Government physical activity guidelines. It was cited (reference #47) in the Expert Working Group working paper for adults, presenting the evidence underpinning the guidelines [5.3]. Specifically, our findings were used to evidence the benefits of high-intensity interval training (HIIT). Regarding HIIT, the Working Group report states: 'multiple meta-analyses and systematic reviews have demonstrated that HIIT has clinically meaningful effects on fitness (14, 46, 47, 57), adiposity (14, 33, 48), body weight (25), and insulin resistance (25)' [5.3, p.10]. The final recommendation in the adult guidelines relating to high-intensity interval activity is: 'each week, adults should accumulate at least 150 minutes (2 ½ hours) of moderate intensity activity (such as brisk walking or cycling); or 75 minutes of vigorous intensity activity (such as running); or even shorter durations of very vigorous intensity activity (such as sprinting or stair climbing); or a combination of moderate, vigorous and very vigorous intensity activity' [5.4, p. 10].

Importantly, the 2019 update is the first time that HIIT has been included in the UK physical activity guidelines as an option from a menu of choices, based on its demonstrated efficacy in our meta-analysis and other rigorous evidence syntheses. A Senior Policy Manager at the UK Government Department of Health and Social Care stated: "The rigorous research by Professor Batterham and colleagues on high-intensity interval training added significantly to the emerging evidence base for the health benefits of performing very vigorous intensity activity in short bouts interspersed with periods of rest or recovery, which led directly to this form of activity being incorporated as an option into the final recommendation for adults" [5.1].

Our research has also informed changes to publicly available guidelines on the management of jet lag. The underpinning research provided a completely new insight into jet lag management and was critical of laboratory simulation studies (including animal studies) claiming 'cures' for jet lag. Prior to the impact of our research, recommendations for managing jet lag symptoms from multiple authoritative sources contained several non-evidenced claims about treatments and did not focus directly on circadian rhythm disturbances, tending to confuse jet lag and travel fatigue. Following the publication of our critical review and meta-analysis [3.3], we completed an audit of

guidelines on jet lag management in the public domain. Guidelines from the following bodies and authorities were scrutinised: The Civil Aviation Authority (CAA), The National Health Service (NHS) Health A-Z Portal, The Centers for Disease Control and Prevention (CDC), and the National Institute for Health and Care Excellence (NICE). We contacted all these authorities enquiring whether they would like us to help formulate guidelines that have a more robust evidence base. We separated those approaches with a good evidence base, for example, appropriately timed light exposure, from those with a weak evidence base (e.g., dietary manipulation) and sent the research to these authorities to support our enquires.

Previously, jet lag guidelines were not underpinned by robust evidence from studies in humans. Our research led directly to new guidelines from the following authorities, informed by high-grade evidence. The CDC is the leading national public health institute in the USA. Their 'Yellow Book' is published every two years as the definitive reference for health professionals providing care to international travellers and is also a useful resource for any member of the public interested in staying healthy abroad. We co-produced the new 2018 and 2020 guidelines for travel health with a Health Communications Specialist at the CDC. Our research [3.3 and 3.4] was cited and informed changes to the previous guidance [5.5]. For example, it was advised in 2016 to "spend time in the afternoon sun", which was revised to more specific advice on light exposure, including referral to our study on supplemental bright light [3.4]. As of February 2019, views for the jet lag page in 2019 and 2020 (1 Jan-21 Oct) were 11,160 and 10,781 respectively [5.5].

Similar changes, informed by our research findings [3.3 and 3.4], have also been made to the jet lag guidelines produced by the following UK authorities. Working with the UK Civil Aviation Authority (CAA), we co-produced new guidelines with the Head of Aviation Health Unit at the CAA and a Specialist at KLM Airways Health Services. These guidelines were made available on the CAA website [5.6]. The Head of Aviation Health Unit at the CAA has confirmed 'that the information on the link on the CAA website is based on the publication Atkinson G, et al., From animal cage to aircraft cabin: an overview of evidence translation in jet lag research. European Journal of Applied Physiology, 2014. 114(12): p. 2459-2468' [5.7].

The NHS Health A-Z Portal (previously NHS Choices Health A-Z) and the National Institute for Health and Care Excellence (NICE) have also revised their guidelines on managing jet lag [5.8, 5.10]. We reviewed the NHS Choices Health A-Z guidelines as part of a topic review, with reference 3.3 informing the revisions to the NHS Health A-Z Portal [5.8]. This work was acknowledged with a formal letter from the Reviews Editor for Health A-Z which clearly stated that [3.3] 'was used as a source for the review' [5.9]. In 2019 we co-produced the Clinical Knowledge Summary (CKS) for jet lag management. Our research [3.3 and 3.4] is cited in the references for the summary and forms part of the evidence base underpinning the specific recommendations. In his testimonial the Medical Director and Editor for Clinical Knowledge Summaries wrote that "We at Clarity Informatics are very happy to confirm that Professor Atkinson and his colleagues, Prof. Batterham and Dr. Thompson, were instrumental in providing this content and feedback for the jet lag topic" [5.11].

Overall, our research has informed and changed national and international evidence-based public health guidelines on both physical activity and jet lag.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] Signed Letter (pdf). Testimonial from a Senior Policy Manager, UK Government Department of Health and Social Care. Received 09 December 2020.

[5.2] Guideline (pdf and link). 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: U.S. Department of Health and Human Services, 2018. https://health.gov/paguidelines/second-edition/report.aspx. Chapter 4: Cancer Prevention (F4-1-F4-67).

[5.3] Working Paper (pdf and link). Expert Working Group Working Paper (Adults Working Group). UK physical activity guidelines: Draft review and recommendations for adults (aged 19-64 years). October 2018. http://www.bristol.ac.uk/media-library/sites/sps/documents/cmo/adults-technical-report.pdf

[5.4] Guideline (pdf and link). UK Chief Medical Officers' Physical Activity Guidelines. September 2019
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/832868/uk-chief-medical-officers-physical-activity-guidelines.pdf

[5.5] Guideline (pdf and link). The Centres for Disease Control and Prevention (CDC) “Yellow Book” 2018 and 2020 guidelines for travel health. https://wwwnc.cdc.gov/travel/yellowbook/2018/the-pre-travel-consultation/jet-lag. And supporting emails from CDC Inquiry Team detailing web views.

[5.6]. Webpage (pdf and link). 24 June 2019. The Civil Aviation Authority (CAA) Travel Health website: https://www.caa.co.uk/Passengers/Before-you-fly/Am-I-fit-to-fly/Health-information-for-passengers/Jet-lag/

[5.7] Signed Letter (pdf). Testimonial from the Head of Aviation Health Unit at the Civil Aviation Authority. Received 17 December 2020.

[5.8] Webpage (pdf and link). 3 August 2020. The NHS Health A-Z Portal: http://www.nhs.uk/Conditions/Jet-lag/Pages/Introduction.aspx.

[5.9]. Signed Letter (pdf) from the Reviews Editor for NHS Health A-Z. Received 28 November 2014.

[5.10] Guideline. 2019. The NICE Clinical Knowledge Summary for shiftwork and jet lag related sleep disorders: https://cks.nice.org.uk/sleep-disorders-shift-work-and-jet-lag

[5.11] Signed Letter (pdf). Testimonial from Medical Director for Clarity Informatics and Editor for NICE Clinical Knowledge Summaries. Received 08 December 2020.