

## Research proposal 3: The Seasonal Utilisation of Nitric Oxide and Its Implications for Vascular Health (750 words)

Listing:

<https://www.findaphd.com/phds/project/seasonal-utilisation-of-nitric-oxide-implications-for-vascular-health-the-sun-project/?p139316>

1. A) A brief description of your relevant experience and skills

### *Relevant experience and research skills*

My relevant research experience includes completing an undergraduate and masters degree in Sport and Exercise Science and Sport Nutrition. I have also worked as an Assistant Scientific Officer at the Ministry of Defence, with the British Army. At the MOD I was part of an occupational medicine physiology research team which currently focuses on improving health and performance of British Army Standard Entry Recruits. My role required me to assist with data collection on large MOD-funded research projects. My duties included, dietary intake collection as part of an energy intake study, conducting literature reviews surrounding data collection in the field, proof reading MOD research and ethics documents, and providing operational support by booking rooms and organising travel. I was also fortunate enough to present at the 2018 student BASES conference.

Additionally, I worked as an intern for 12 months alongside my masters degree at Science in Sport supplement company (SiS). I was situated in a team of researchers called "Performance Solutions" who shaped the direction of innovative evidence-based supplement production. As part of this role, I was required to build out frameworks that helped SiS deliver world-class sport nutrition knowledge to elite partnerships. My main project whilst at SiS was the development of a novel cooling product which involved a laboratory trial of the product. For this project I was required to conduct literature reviews, collect data from human participants and gained experience in study design. I was a key contact for the executives at SiS which meant delivering back project updates. This experience combined with my experience at the MOD has led to good communication and written skills, with a key focus on adapting my communication and writing style to suit the relevant audience, may that be a soldier, chef, researcher, medical GP, chief executive, or athlete. Conducting an internship alongside my MSc degree demonstrates my ability to prioritise tasks and work to tight deadlines. I like to use the Pomodoro technique for time management when conducting writing and literature search tasks, and I'm always conscious of Parkinson's law - the adage that "work expands so as to fill the time available for it's completion."

1. B) An indication of what you would uniquely bring to the project

Light exposure can influence nitric oxide (NO) metabolism, blood pressure and vasodilation (Monaghan et al., 2018). Indeed, if NO metabolism influences the regulation of cardiovascular function, seasonal variations in sunlight could influence NO availability and subsequent cardiovascular health. The proposed research project explores this idea and maps out potential mechanistic causes.

A multitude of physiological, behavioural, and individual-environmental interactions occur throughout the seasons (Stewart et al., 2017). To examine seasonal changes in NO bioavailability and its influence on cardiovascular health, we first need to understand how cardiovascular health and disease risk is influenced by a myriad of changing conditions. Typical changes in climate conditions result in increased winter disease incidence, periodic cold snaps, pollution, seasonal temperature variations and alterations to sun-seeking behaviours (Stewart et al., 2017).

Indeed, the change in conditions, for example cold weather, can result in suboptimal health outcomes such as elevated heart rate and increased blood pressure (Castellani and Young, 2016), which may exacerbate an individual's risk for cardiovascular disease (Stewart et al., 2017). As such, the present research proposal should feature an updated review of novel literature examining the influence of seasonal variation on health outcomes. I will draw upon my literature search skills developed at the MOD and SiS to conduct a comprehensive systematic review of the available literature.

At present, limited data on seasonal changes in NO metabolism exists (Widlansky et al., 2007; Honda et al., 2020). Therefore, data is needed to examine the seasonal inter-individual and intra-individual variations in NO bioavailability. Additionally, lifestyle and behavioural parameters associated with NO bioavailability must also be explored. Parameters associated with NO bioavailability could include physical activity, diet, sleep, sun-seeking behaviour, exercise, mouthwash use and sun-holidays (Ohta et al., 2005; Stewart et al., 2017). The present research proposal could feature a cohort study examining the seasonal variation in sunlight exposure on NO bioavailability and cardiovascular health in officer workers. Office workers are at increased risk for cardiovascular disease and officer work is characterised by regimented and predictable behaviour (Thorp et al., 2012), making them a suitable population to examine.

To measure NO bioavailability, I will obtain blood samples from the antecubital vein via phlebotomy and analyse the samples using the gas-phase chemiluminescence technique, as previously described (Pinder et al., 2008). Alongside measuring NO bioavailability, I propose to measure indicators of cardiovascular health including blood pressure, heart rate, arterial stiffness, endothelial function, and lifestyle behaviours (physical activity, diet, etc.). To measure blood pressure, I will use a digital sphygmomanometer, to measure heart rate I will use a heart rate monitor. Additionally, arterial stiffness may be gauged via ultrasound pulse wave velocity, and endothelial function gauged by flow mediated dilation (Wentland et al., 2014, Ghiadoni et al., 2015).

I will record physiological and lifestyle data periodically throughout the seasons across the course of one year. I will eliminate confounding variables by ensuring participants are in full health, do not take nitrate-containing supplementation, refrain from sunbed use, limit alcohol use around data collection and capture whether participants are intending to travel to a sunny country throughout the duration of the study. Indeed, dietary intake of nitrate rich foods is one obvious variable which could confound results. As such, it is imperative that we accurately capture any seasonal changes in dietary intake patterns, to deduce if dietary change is potentially influencing NO bioavailability. To succeed in this project, here, I would draw upon my unique experience of measuring and recording dietary intake in the British

Army, where I utilised a multitude of methods such as researcher-led food weighing, food frequency questionnaires and food diaries.

If NO bioavailability is affected by seasonal variation in sunlight exposure, an intervention to attenuate seasonal declines in NO bioavailability is required during the winter when sunlight exposure reduced. We know that short-term consumption of dietary nitrate in the form of nitrate-rich vegetables is an effective strategy to increase plasma nitrate and nitrite concentrations (van der Avoort et al., 2020). Novel use of Amaranth extract has been demonstrated to increase nitrate levels in the body (Subramanian et al., 2016). However, little data exists on the long-term changes in plasma NO<sub>3</sub> and NO<sub>2</sub> after Amaranth supplementation (Liubertas et al., 2020). Indeed, beetroot juice is the most widely utilised nitrate-containing supplement and it consistently increases NO bioavailability in a range of populations (Milton-Laskibar et al., 2021).

The present research proposal could feature a double-blinded placebo-controlled randomised trial examining beetroot juice supplementation's influence on NO bioavailability and key cardiovascular health markers such as blood pressure, heart rate, arterial stiffness, and endothelial function on an at-risk population such as office workers. To measure NO bioavailability and cardiovascular health markers I would use the same techniques as the cohort study. Additionally, I would include a cardiorespiratory fitness test, suitable for the at-risk population, such as the Six Minute Waling Test, to provide an estimation of VO<sub>2</sub>max (Dourado et al., 2021). Indeed, a typical placebo for beetroot juice is a nitrate-depleted beetroot juice. I would use my skills developed assisting on a menthol intervention study at Science in Sport to help me succeed in the organisation and running of a study of this nature. Due to the long follow up periods required to accurately assess seasonal changes in sun-light exposure, participant attrition is likely and must be considered when recruiting participants. Participant safety is also a concern due to the invasive procedures to obtain blood samples and exposure to high amounts of nitrates can potentially cause gastrointestinal symptoms such as abdominal discomfort and diarrhoea (Wickham et al., 2019).

#### 1. C) Statement of how this research project fits with your future direction

This research project fits with my career goal of working as a research scientist who investigates dietary interventions that improve health outcomes. My experience at the MOD developed my passion for researching interventions which improve health and longevity. Although my masters degree was focused in Sport Nutrition, this could easily have been public health nutrition. My career goal is to conduct research and win funding from supplement brands and manufacturers to test the efficacy of their products on human health and performance. Conducting this research project will give me a wealth of invaluable experience in pursuit of this goal.

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