

**Prospectus**

**Nitric Oxide Supplements Use for Prediabetics and Diabetes Controlled for Menstrual  
Cycle**  
(Technical Topic)

**Gender Bias in Crash Test Dummies**  
(STS Topic)

By Lucas Sarantos

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines of Thesis-Related Assignments.

Signed: Lucas Sarantos

Date: 7/23/21

Lucas C. Sarantos

Approved: \_\_\_\_\_

Date: 7/23/21

Dr. Ben Laugelli, Department of Engineering and Society

Approved: Frederick H. Epstein

Date: 7/23/21

Dr. Frederick Epstein, Department of Biomedical Engineering

## **Introduction**

Diabetes is a glucose metabolic disorder affecting millions of people across the country, with millions more are also considered to be prediabetic. When diabetic there is a wide range of symptoms including: peripheral neuropathy, blurred vision, and an increased risk of vascular disease (CDC, 2020). Prediabetics and diabetics often have issues producing and metabolizing nitric oxide (NO), an important biochemical for vascular health (Woessner et al., 2018). One way NO is produced is from the amino acid L-arginine, which can then be used to help the body regulate vascular dilation (Piattie et al., 2001). Without an active form of this biochemical, seen in prediabetics and diabetes, vascular health can deteriorate causing severe symptoms, such as peripheral vascular disease and ischemic heart disease

It is common for diabetics to take NO/L-arginine supplements to help mitigate some of the health risks associated with the disorder. However, it is not well known how female hormones, such as estrogen and progesterone, play a role in the metabolism of NO. There have been studies done in animal models, but no human studies have been done that consider the female menstrual cycle for NO production and metabolism in prediabetics and diabetes. Due to the varying levels of hormones throughout the menstrual cycle there could be an optimal time to take NO/L-arginine supplements for females. The neglect of the difference in female metabolism is only one example of a long list of gender bias in scientific research. This gender bias has led to a gap in knowledge between the sexes due to the lack of studying of women.

When designing my technical project, I will be considering key stakeholder groups, so it may be useful to consider a similar case in which various social groups and values play a role in the design process. For my STS project I will use Humanetics, a major producer of crash test dummies, as a case study to investigate how they design their products and the role gender bias

plays. Actor-network theory (ANT) will be used to investigate the sociotechnical system and how human and nonhuman actors will have to be altered to create a stable network. The goal of this paper is to propose a research study to design a NO/L-arginine supplement schedule for females while addressing the gender bias within research and design.

### **Technical Topic**

In the United States of America approximately 88 million adults are considered prediabetic, with another 34.2 million that have been diagnosed with diabetes (CDC, 2020). Diabetes affects how someone digests sugar by either not producing insulin or not responding to insulin. It is observed that these patients have reduced nitric oxide (NO) activity, a natural biochemical compound important for vascular health (Woessner et al., 2018). NO works as a hypoxic vasodilator to widen blood vessels to increase blood flow and restore oxygen supply (Van De Walle, 2018). NO also helps maintain glucose-insulin homeostasis through mitochondrial regulation, insulin secretion, and glucose uptake (Woessner et al., 2018). It is known that prediabetics and diabetics have a reduced ability to generate NO from the amino acid L-arginine leading to other severe health problems commonly observed in diabetics, including swelling and peripheral neuropathy (Burke, 2015). There have been studies to show that taking NO supplements can help mitigate these symptoms and even delay the progression of type 2 diabetes (Van De Walle, 2018). Since L-arginine is a precursor to NO it can be used as a dietary supplement to augment vasodilation. Current studies have shown that L-arginine supplements help to increase NO availability and sensitivity to insulin while decreasing vascular resistance (Piattie et al., 2001). NO supplementation also helps to increase glucose uptake by increased glucose transporter 4 (GLUT4), via the AMP-kinase pathway (AMPK) (Woessner et al., 2018).

The cellular mechanism of NO and L-arginine is fairly understood, allowing physicians to intervene in prediabetics cases to prevent further complications. However, current studies fail to consider the role the menstrual cycle plays in NO bioactivity. It has been theorized that female hormones can affect the production and metabolism of NO with progesterone being a key inhibitor of the gene expression of NO synthase, the enzyme responsible for the conversion of L-arginine to NO (McAllister et al., 2008; Miller et al., 1996). However, studies on this have been limited and only done in cell culture and not in human participants. There is currently a knowledge gap between the sexes within health and disease, with the majority of preclinical studies done in male-derived cells or male animal models (Reusch et al., 2017). To properly assess the effectiveness of NO/L-arginine supplementation in prediabetics and diabetics studies should include their effectiveness in female populations considered to be prediabetics and diabetic controlled for their menstrual cycle. This gap of knowledge could lead to the ineffective treatment of females and lead to higher morbidities within these populations. By conducting proper studies the true effectiveness of NO supplements can be assessed for all prediabetics and diabetic patients.

I intend to conduct a study to determine the optimal time to take NO/L-arginine supplements for prediabetics and diabetics, with the consideration of the female menstrual cycle. This will serve to provide a better apply supplement regimens to females considered to be prediabetic and diabetic. The study will use an euglycemic-hyperinsulinemic clamp with glucose infusion before, midway, and after the study; this is used to test how well an individual metabolizes glucose and how sensitive they are to insulin (Piattie et al., 2001). This study would be double blind to eliminate bias and take place over the course of three months, to properly evaluate the effectiveness of the supplement. Separate cohorts would be created, one with a

placebo, one taking the supplement on days 1-14 of the menstrual cycle, and a third taking the supplement on days 14-28. These days are used as they are the average time periods for the follicular phase and luteal phase (Ray, 2018). All participants would be female and considered to be prediabetic or diabetic.

### **STS Project**

Women have been overlooked and discriminated against within the STEM field for generations and still face gender bias within these fields, with less than 30% of the occupying jobs in STEM (Christnacht & Martinez, 2021). However, the gender bias goes beyond employment and can be seen in the products being designed and tested. When it comes to the female population there is a gap in scientific knowledge compared to males which can be attributed to the lack of testing of women in the STEM field, who makeup around one-third of the studied cohorts (Westervelt, 2015). Females have been thought of as “just smaller men”, while in truth females have completely different physiologies than males (Barry, 2019; Westervelt, 2015). The marginalization of females in scientific studies has led to increased risk in many health related fields. In the case of frontal car crashes, women are 73% more likely to be severely injured when controlled for age, height, BMI, and vehicle year and 17% more likely to die; all due to the fact that researchers have yet to recognize women as necessary research subjects (Barry, 2019; Putka, 2021). One researcher from the Insurance Institute for Highway Safety in Virginia says this could be due to the vehicle choice of females, as they tend to be smaller (Putka, 2021). However, this overlooks the fact that companies like Humanetics do not develop crash test dummies that are representative of females and the dummies that are produced are not properly tested.

The Hybrid III is a widely used crash test dummy developed by Humanetics. It is representative of the 50th percentile male at a seated height of 34.8 inches and 171.3 pounds (Pedestrian ATDs, 2020). However, the Hybrid III 5F (the female alternative to the Hybrid III) is only representative of the 5th percentile female; it has a height of 59 inches and weighs 107 pounds (Pedestrian ATDs, 2020). Today's average female is 64 inches and 170 pounds. Humanetics stated that they do not have a 50th percentile female dummy because it can cost up to 1 million dollars to develop a replacement (Putka, 2021). They further stated that using a 5th percentile dummy allows for a wide range of body types to be tested, however, the Hybrid III 5F is a closer resemblance to a 12-13 year old girl and not representative of most female drivers. In addition to not having a representative female crash dummy frontal crash tests performed by the National Highway Traffic Safety Administration (NHTSA) and Insurance Institute for Highway Safety (IIHS) do not place a female dummy in the driver's seat, but in the passenger seat, while the male dummy is placed in both (Barry, 2019). Despite making up half of drivers in the United States there is still a clear bias against women that is bleeding into the designs of crash test dummies and ultimately motor vehicles. Crash statistics clearly show there is an inequality in crash safety, yet there has been no change in safety regulation or how we conduct crash safety tests.

Using the Hybrid III and Hybrid III 5F developed by Humanetics as a case study, I will use actor-network theory (ANT) to investigate how the human and nonhuman actors create an unstable network leading to the flawed design of crash test dummies. ANT is appropriate to use as it considers both the human and nonhuman actors within an already existing network as equals (Cressman, 2009). It uses micro-level studies at the place of creation of the technology, following all the actors and network builders (Cressman, 2009). I will analyze how Humanetics

construct their network to uncover what actors are responsible for the design and creation of human crash test dummies. The primary actors in this network are the current crash test dummies (specifically the Hybrid III and Hybrid III 5F), the NHTSA and IIHS, Humanetics and its employees, and anyone who operates or rides in a motor vehicle. The roles and effects of these actors on the network will be investigated by looking at the gender bias within the technology of the crash test dummies. This will be done by analyzing the specs of multiple crash test dummies produced by Humanetics, investigating the crash test procedure, and analysing data on injury differences between males and females in motor vehicle accidents.

### **Conclusion**

My thesis sets out to better understand how female hormones play a role in NO production and metabolism within prediabetics and diabetics. This is in an attempt to produce an optimal NO/L-arginine supplement schedule to help mitigate health risks in these populations. Using Humanetics as a case study, I will attempt to reveal how the primary actors associate to create technology as a result of gender bias. These projects attempt to address the broader socio-technical problem of gender bias in scientific research. I will draw attention to the lack of women in research studies and attempt to close the scientific knowledge gap between the sexes.

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