

Sex Differences in Human Aortic Smooth Muscle Cell Phenotypes  
(Technical Paper)

Food Access: A Racial and Socioeconomic Problem  
(STS Paper)

A Thesis Prospectus Submitted to the  
Faculty of the School of Engineering and Applied Science  
University of Virginia • Charlottesville, Virginia  
In Partial Fulfillment of the Requirements of the Degree  
Bachelor of Science, School of Engineering

Sarah Meng  
Fall 2020

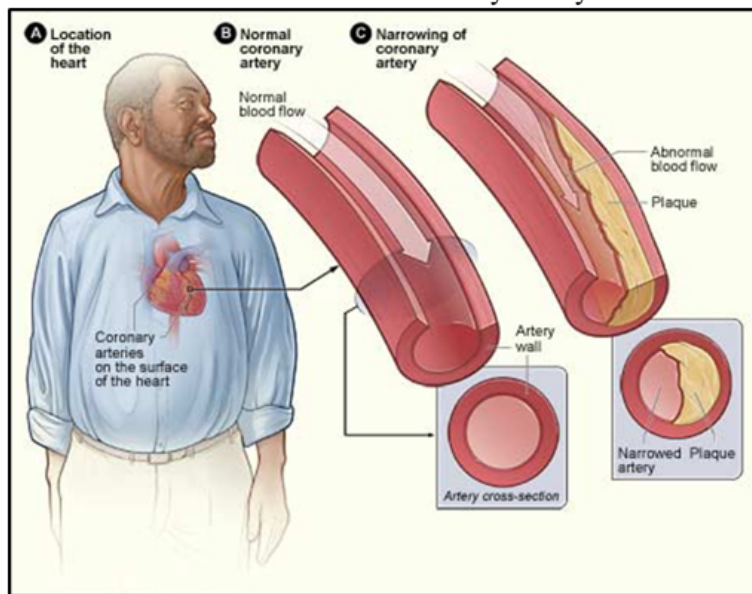
Technical Project Team Members  
Rita Anane-Wae

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

## Introduction

**Figure 1**

### Effect of Atherosclerosis on the Coronary Artery



Coronary artery disease (CAD) is the leading cause of death in the United States, and it remains one of the major diseases strongly affected by diet; each year approximately 500,000-700,000 deaths related to CAD occur, making it the cause of an estimated one-third of all deaths in the population for those older than 35

years (Brandhorst 2019, Zafari 2020). CAD is caused by the buildup of plaque, which is also known as atherosclerosis, inside the lining of larger coronary arteries, as shown in Figure 1. This buildup either partially or totally blocks blood flow in the large arteries of the heart and subsequently causes many health problems, such as heart failure (Hansson, 2005).

Environmental, lifestyle, and genetic factors contribute to the likelihood of developing CAD, such as age, obesity, a family history of CAD, and unhealthy eating habits (Hajar, 2017).

Data from the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIB study has shown that CAD presents differently clinically in males than in females. Typically, females are likely to be diagnosed with CAD 7 to 10 years after males and have a higher expression of cardiovascular risk factors (Maas, 2010). For example, women with diabetes are at greater risk for cardiovascular complications than their male counterparts and a low high-density lipoprotein (HDL) cholesterol implicates a higher risk of developing CAD in

women than in men (Maas, 2010). The Capstone project will investigate the differentially expressed genes in men and women, excluding those on the X and Y chromosomes, that are correlated with the risk of developing CAD. If there are such genes, then gene-based therapies, like gene transfer or genome editing, should potentially focus on targeting these specific genes or demonstrate that men and women need different treatment plans in treating CAD. Furthermore, the exact cause of atherosclerosis is unknown. By finding differentially expressed genes in males and females, the project results will give insight into the cause of atherosclerosis and the difference in risk potential between males and females for developing CAD.

The second project is in relation to unhealthy eating habits, which increases the risk of developing CAD. The Science and Technology Studies (STS) thesis will investigate the socioeconomic and racial inequalities present in food accessibility. There have been studies that have shown that there are socioeconomic barriers to food access and racial and socioeconomic disparities in food accessibility (Azétsop, J., & Joy, T. R., 2013). Furthermore, there has been evidence of food deserts -- an area that has limited access to affordable and nutritious food--and evidence that chain grocery stores are less likely to be found in minority neighborhoods and low-income neighborhoods (Powell, Lisa M. et al. 2007). The STS topic will investigate the relationship between racial and socioeconomic inequalities and food access.

### **Technical Topic**

Sex difference has been investigated as a significant determinant in the incidence, prevalence, morbidity, and mortality associated with many diseases. These sex differences are either classified as those that are sex-specific, such as erectile dysfunction in men and hypertensive pregnancy disorders in women, or conditions that are common to both sexes but

manifest differently in terms of presentation and outcomes depending on sex, such as atherosclerosis and stroke (Regitz-Zagrosek V., 2012).

Many studies have shown that CAD presents differently in males than in females. However, the exact cause of this difference in men and women has not yet been determined. The proposed project will investigate the differentially expressed genes in males and females that are correlated with CAD risk using a sample of aortic smooth muscle cell (SMC) RNA sequencing (RNA-SEQ) datasets.

SMCs play a vital role in the development of atherosclerosis. During the advanced stage of CAD, SMCs proliferate and migrate to form the fibrous cap that stabilizes the plaque (Liu, 2018). However, recent studies showed that SMCs play either beneficial or detrimental roles in lesion pathogenesis depending on the nature of their phenotypic changes (Shankman, 2015). Because of their important function in the pathogenesis of CAD, aortic SMC samples will be used for the technical analysis.

The team currently has access to a unique dataset consisting of 118 males and 33 female human aortic SMC samples obtained from heart transplant donors and victims of motor vehicle accidents. In the first part of the analysis, the team will use available statistical and differential gene expression analysis tools to identify differentially expressed genes in aortic SMCs between males and females using the RNA-SEQ data. The second part of the analysis will focus on the SMC phenotypes of migration, proliferation, and calcification, which all play a vital role in the development of atherosclerosis. Migration and proliferation of SMCs to the fibrous cap of a lesion contribute to the beneficial stabilization of the plaque. Calcification, or the hardening of the atherosclerotic plaque, further exacerbates the pathogenic condition of the atherosclerotic lesion, contributing detrimentally to CAD. Using the available phenotypic expression data from

the SMC samples, the team will investigate the differential expression of these phenotypes between the male and female groups.

To validate the findings, the team aims to utilize publicly available data to investigate whether the identified differentially expressed genes in our human aortic SMCs are also identified in different cohorts of SMCs and human atherosclerotic lesions. The findings in the second part of the analysis will determine whether the identified genes are either specific to our unique dataset or are differentially expressed among all human aortic SMCs and human atherosclerotic lesions between sexes. After finding and validating the differentially expressed genes, we will conduct a literature review investigating the known functions of the gene and the potential of associated risk for developing CAD.

Finally, as a design portion, the team will use the R “shiny” package to create a portfolio of the findings. By using this package, it will create an interactive platform for readers to learn about the project. This will present the data and findings in a more user-friendly interface.

### **STS Topic**

The phenomenon of “nutritional inequality” is present in the U.S.; the wealthy eat more healthfully than the poor (Allcott, 2019). The relationship between food insecurity and society in the United States is characterized by two viewpoints: (1) how food access is shaped by society and (2) how food access is shaped around society. First, how society-- in this case socioeconomic status and racial inequality--shapes food access will be investigated. According to a study by Azétsop and Joy, healthy diets are more expensive than unhealthy ones (Azétsop & Joy 2013). Furthermore, a recent US study showed that changing the recommended standard food basket--which is the measurement methodology used by the U.S. to establish the minimum daily food consumption to satisfy nutritional requirements in less-privileged individuals--to a healthier

alternative resulted in an additional 17-19% in cost, equivalent to 35-40% of a low-income consumer's food budget, which is a huge percentage of a low-income consumer's budget, and understandably, they would choose the less healthy option to save money (Azétsop & Joy 2013; Muhutdinova, 2006). It's evident that socioeconomic status plays an important role in healthy food alternatives and food access in general.

This problem is represented by another viewpoint: how society shapes food access around socioeconomic and racial inequalities. The way that society shapes itself around socioeconomic and racial disparities is seen in the phenomenon of food deserts, which are areas with low availability or high prices of healthy foods. Not only do supply and demand dynamics play a role in the placement of grocery stores, but also zoning restrictions, crime rate, and other social factors that discourage entry by grocers that would sell healthy foods in low-income areas (Allcott, 2019). This phenomenon highlights how society shapes technology, which in this case is food access, around socioeconomic inequalities.

This question will be looked at with two STS theories: political technologies and actor network theory (ANT). American political theorist Langdon Winner says that technological artifacts become political when they become "a way of settling an issue in a particular community" (Winner, 1980). Political technologies are looked at as technological development or inherently political technologies. This paper will look at the former. Technological development shows how artifacts are used to increase the power, authority, or privilege of some over others (Winner, 1980). In this case, the framework will show how food access is used to increase the privilege of white people and those with a higher socioeconomic status.

However, the critiques of the theory will be taken into consideration while researching this topic. In his article, Hans Radder says that many authors struggle to "combine an adequate

theoretical STS perspective with a critical engagement of the political issues brought about by current science and technology” (Radder, 1998). The author must go beyond the traditional actor-network and sociology of scientific knowledge approaches in order to make a successful political technology argument. I will take this critique into account while I research and will formulate both strong theoretical and critical engagements of the political issue.

ANT treats every stakeholder in the social and natural worlds as a continuously generated effect of the webs of relations within which they are located, which is defined as the network in this case. The framework treats this relationship network as a black box; it assumes that nothing exists outside this web. The actors in this network include objects, subjects, human beings, machines, animals, “nature,” ideas, organizations, inequalities, scale and sizes, and geographical arrangements (Cressman, 2009). In this particular case, the thesis will look at the network of food access and the relevant stakeholders in society, like grocery stores, transportation, and low-income families. The primary criticism of ANT is that it does not have the ability to provide accurate descriptions of the social processes that take place within a network (Cressman 2009). This critique will be taken into consideration, and the thesis will demonstrate how social processes are an important part of ANT, which results from the relationship between the relevant stakeholders in society.

## **Methodologies**

Research Question: How does socioeconomic and racial inequality play a role in food access and how does society shape food access around these inequalities? The methods to answer the question will be in multiple stages by reading research articles, watching documentaries, and reading case studies. The first stage will be to provide relevant background information for the topic, like the definition of a food desert. The second stage will look into the socioeconomic and

racial patterns that are seen with the locations of food deserts and grocery stores. The third stage will look into socioeconomic and racial patterns that are seen with the differences in pricing of higher quality and healthier foods. The fourth and final stage will look into socioeconomic and racial patterns that are seen with differences in barriers to food access, like transportation, budget, and zoning. The relationships and patterns that are found will be discussed using the frameworks of ANT and political technologies.

## **Conclusion**

The technical portion of this thesis will investigate the sex-linked differences in CAD. The team will run different analyses on sex-linked genes and different phenotypes that are associated with CAD risk. We expect to see a difference between the sexes and find a sex-linked cause of CAD. The results of the technical portion will be delivered in a report and interactive dashboard format. If there are differentially expressed genes between males and females that are found in the results, then gene-based therapies, like gene transfer or genome editing, should potentially focus on targeting these specific genes or demonstrate that men and women need different treatment plans in treating CAD. The STS portion of this thesis will investigate the socioeconomic and racial disparities in food access by looking at past studies. The expected outcome from this portion is that there should be a significant difference between the socioeconomic and racial groups in food access. The report from this STS thesis will increase awareness and understanding of these social injustices, and hopefully initiate more discussions and catalyze change to improve these disparities in food access.



## References

- Allcott, H., Diamond, R., Dubé, J.-P., Handbury, J., Rahkovsky, I., & Schnell, M. (2019). Food Deserts and the Causes of Nutritional Inequality. *The Quarterly Journal of Economics*, 134(4), 1793–1844. <https://doi.org/10.1093/qje/qjz015>
- Azétsop, J., & Joy, T. R. (2013). Access to nutritious food, socioeconomic individualism and public health ethics in the USA: a common good approach. *Philosophy, ethics, and humanities in medicine : PEHM*, 8, 16. <https://doi.org/10.1186/1747-5341-8-16>
- Brandhorst, Sebastian, and Valter D. Longo. 2019. “Dietary Restrictions and Nutrition in the Prevention and Treatment of Cardiovascular Disease.” *Circulation Research* 124(6): 952–65.
- Cressman, D. (2009). A Brief Overview of Actor-Network Theory: Punctualization, Heterogeneous Engineering & Translation. Retrieved from <https://summit.sfu.ca/item/13593>
- Freeborn, D., & Haldeman-Englert, C. (Eds.). (n.d.). X-linked Recessive: Red-Green Color Blindness, Hemophilia A. Retrieved from <https://www.urmc.rochester.edu/encyclopedia/content.aspx?ContentID=P02164&ContentTypeID=90>
- Hajar R. 2017. Risk Factors for Coronary Artery Disease: Historical Perspectives. *Heart views : the official journal of the Gulf Heart Association*, 18(3), 109–114. [https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS\\_106\\_17](https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_106_17)
- Hansson, Göran K. 2005. “Inflammation, Atherosclerosis, and Coronary Artery Disease.” *New England Journal of Medicine* 352(16): 1685–95.

- Liu, B., Pjanic, M., Wang, T., Nguyen, T., Gloudemans, M., Rao, A., Castano, V. G., Nurnberg, S., Rader, D. J., Elwyn, S., Ingelsson, E., Montgomery, S. B., Miller, C. L., & Quertermous, T. (2018). Genetic Regulatory Mechanisms of Smooth Muscle Cells Map to Coronary Artery Disease Risk Loci. *American journal of human genetics*, *103*(3), 377–388. <https://doi.org/10.1016/j.ajhg.2018.08.001>
- Maas, A H E M, and Y E A Appelman. 2010. “Gender differences in coronary heart disease.” *Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation* vol. 18,12: 598-602. doi:10.1007/s12471-010-0841-y
- Muhutdinova, R. (2006). Standard food basket. In M. Odekon (Ed.), *Encyclopedia of world poverty* (pp. 1023-1023). Thousand Oaks, CA: Sage Publications, Inc. doi: 10.4135/9781412939607.n660
- Powell, Lisa M. et al. 2007. “Food Store Availability and Neighborhood Characteristics in the United States.” *Preventive Medicine* 44(3): 189–95.
- Radder, H. (1998). The Politics of STS. *Social Studies of Science*, 28(2), 325–331. Retrieved from [https://www.jstor.org/stable/pdf/285605.pdf?casa\\_token=L3jifpVp9E4AAAAA:ZquJq8hU2jJwjT4bD24tJQhlilxY3pw9Aq5zWQjEQIghMZUm5Y9AdUBsalHRW6O05LRdNWyKu46MwVVIDhVC6EnDwi3NRzYbDESFC6Xv1rhZMzFCjg](https://www.jstor.org/stable/pdf/285605.pdf?casa_token=L3jifpVp9E4AAAAA:ZquJq8hU2jJwjT4bD24tJQhlilxY3pw9Aq5zWQjEQIghMZUm5Y9AdUBsalHRW6O05LRdNWyKu46MwVVIDhVC6EnDwi3NRzYbDESFC6Xv1rhZMzFCjg)
- Regitz-Zagrosek V. (2012). Sex and gender differences in health. *Science & Society Series on Sex and Science. EMBO reports*, 13(7), 596–603. <https://doi.org/10.1038/embor.2012.87>
- Shankman, L. S., Gomez, D., Cherepanova, O. A., Salmon, M., Alencar, G. F., Haskins, R. M., Swiatlowska, P., Newman, A. A., Greene, E. S., Straub, A. C., Isakson, B., Randolph, G. J., & Owens, G. K. (2015). KLF4-dependent phenotypic modulation of smooth muscle

cells has a key role in atherosclerotic plaque pathogenesis. *Nature Medicine*, 21(6), 628-37. <https://doi.org/10.1038/nm.3866>

Winham, S. J., de Andrade, M., & Miller, V. M. (2015). Genetics of cardiovascular disease: Importance of sex and ethnicity. *Atherosclerosis*, 241(1), 219–228. <https://doi.org/10.1016/j.atherosclerosis.2015.03.021>

Winner, L. (1980). Do Artifacts Have Politics? *Daedalus*, 109(1), 121–136.

Zafari, A. 2020, March 22. What is the mortality rate associated with coronary artery disease (CAD) in the US? Retrieved October 27, 2020, from [https://www.medscape.com/answers/155919-15092/what-is-the-mortality-rate-associated-with-coronary-artery-disease-cad-in-the-us#:~:text=Coronary artery disease \(CAD\) is those older than 35 years.](https://www.medscape.com/answers/155919-15092/what-is-the-mortality-rate-associated-with-coronary-artery-disease-cad-in-the-us#:~:text=Coronary artery disease (CAD) is those older than 35 years.)