Thesis Project Portfolio

Design of a novel *ex vivo* murine brain slice model for analysis of pericyte morphology in diabetes

(Technical Report)

Life or Death: A Sociotechnical Analysis of the Factors that Influence the Cost of Insulin

(STS Research Paper)

An Undergraduate Thesis

Presented to the Faculty of the School of Engineering and Applied Science

University of Virginia • Charlottesville, Virginia

In Fulfillment of the Requirements for the Degree

Bachelor of Science, School of Engineering

Stephen Charles Muzyka

Spring, 2022

Department of Biomedical Engineering

Table of Contents

Sociotechnical Synthesis

Introduction

Diabetes is one of the world's most prevalent and dangerous diseases that often comes with long-term complications that negatively impact the quality of life of those afflicted and even death if not treated properly. A greater understanding of the physiology at a cellular level in the disease state of diabetes can offer illumination on development of long-term complications. The technical project is focused upon improved understanding of endothelial cell and pericyte interactions and malfunctions in hyperglycemic conditions and the possibility of extracellular vesicles as a therapeutic option to reverse diabetic maladies that arise as complications. Insulin is the current optimal diabetic treatment by maintaining normal physiologic glucose levels in which complications do not arise. However, due to a complex dynamic of countless stakeholders with intertwined interests around profits the price of insulin has risen drastically over the last decade. This intense rise means some individuals can not purchase their insulin or must ration the limited insulin they have as they try to save money for more, facing detrimental health risks as a result. The sociotechnical project seeks to offer a deeper analysis of exorbitant insulin prices within the United States and possible solutions to provide a foundational framework to improving diabetic quality of life. Together, both projects can offer hope for a brighter and better future for diabetic individuals by assessing tangible and harmful problems that affect their everyday lives.

Technical Project

The technical project is centered around the effects of diabetes and hyperglycemic conditions leading to long term complications and possible death. Previous research has found that in a diabetic mouse model that within the retina at a microvascular level there were abnormal interactions of certain cell types. Specifically, the endothelial cells and pericytes that

provide structure and function of capillary systems. The pericytes were found to detach themselves, coalesce into bridges or change their shape as a result of hyperglycemia which was predictive of being a biomarker to the development of retinopathy over longer time spans. The retina has a 1:1 ratio of pericytes to endothelial cells, as does the central nervous system and brain. While diabetic complications around the eyes, nerves and heart are studied in depth, the brain is under researched. Therefore, a project built upon analyzing *ex vivo* mouse brain slices in normoglycemic and hyperglycemic conditions was constructed. Further development led to the application of extracellular vesicles to hyperglycemic conditions to reverse effects on pericyte and endothelial cell interactions. Determining pericyte and endothelial cell behavior and interactions in the brain alongside the efficacy of extracellular vesicles as a therapeutic would provide invaluable information in the fight against diabetes. Diabetic individuals and clinical professionals would be provided greater understanding on a microvascular level of how diabetes effects the brain, which could open the potential to explorations that create tangible solutions that lead to the cure or improvement of treatment for diabetic individuals, leading to a vastly improved quality of life.

Sociotechnical Analysis

The focus of the STS research paper is to apply a sociotechnical analysis to exorbitant insulin prices within the US healthcare system and the impact on the lives of diabetic individuals while determining novel solutions to improve their quality of life. The research question is: In what ways are the current prices of diabetic treatment by pharmaceutical companies within a for-profit healthcare system harming diabetic individuals by decreasing quality of life and what solutions exist to remedy this in an equitable way? The application of Horst Rittel and Melvin Webber's wicked problem framing will lead to a greater understanding of how pricing currently effects diabetic life and generation of ideal solutions to improve diabetic quality of life through the navigation of the actors, policy, economics, societal

perception and myriad of factors affecting insulin prices. Fundamentally, a narrative on compassion for those in need, and a shared responsibility in society to support one another will be at the core of the sociotechnical analysis. The success of the analysis within the field of STS and Biomedical Engineering will have a profound impact on society. A life for diabetics that is already driven by intense responsibility to monitor and maintain glucose levels to prevent long term complications will no longer be plagued by the stress of how insulin will be purchased at high prices. Instead, a large population of America will be able to live their lives fully, with more equitable access to healthcare resources and be better supported to pursue happiness.

Conclusion

The analysis of diabetes through a technical and sociotechnical lens in tandem provided invaluable insight into diabetes. The sociotechnical analysis offers the perspective of diabetic individuals facing exorbitant insulin prices, the effect that has on physical and mental health and the system construction that has led to the situation experienced daily by diabetics. However, it also creates a foundational opportunity to address the exorbitant prices by providing initial solutions that can immediately improve quality of life for diabetics while starting the conversation on vast change that is yet to come to address the wicked problem. The stark reality from the sociotechnical analysis is that a vast majority of diabetic Americans live their lives with limited access to insulin and often experience hyperglycemia. The technical project creates an initial physiological understanding utilizing a mouse model of how diabetes effects the microvascular interaction within the brain during the hyperglycemic conditions many people face daily. The microvascular understanding offers a possible view of how long-term complications often originate and what must be addressed to prevent them. By thoroughly understanding the diabetic experience through a detailed physiological and societal perspective along with compact solutions to initiate change begins the process of improving the diabetic

experience within the United States. The problem and disease are far from being solved or eradicated but the slow march of progress, hard work and desire for change brings forth an incredible sense of hope for the future in which anyone who receives the diagnosis of diabetes feels only safe and secure in a high-quality life and better future that starts here.