Urinary Extracellular Vesicle Diagnostic Tool Development –
Computational Model for Dilution Determination
(Technical Paper)

The Role of the National Institute of Diabetes and Digestive and Kidney Diseases in Regard to Racial Health Disparities Surrounding Chronic Kidney Disease
(STS Paper)

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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 for Thesis-Related Assignments.

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Introduction

The federal spending budget for the 2022 fiscal year for the National Institutes of Health (NIH) totals approximately $45 billion (Fogarty International Center, 2022). Despite the United States of America's global reputation for continuous biomedical innovation and adamant institutionalized public health measures, one in every three Americans with diabetes are unaware that they have such conditions (NIH & CDC, 2015). Furthermore, according to the Centers for Disease Control and Prevention (CDC), currently one in every seven Americans are predicted to have chronic kidney disease with 90% of those individuals unaware of their conditions (CDC, 2022). Although the statistics surrounding renal health are significant, it unveils a necessity to investigate current kidney health measures as well as the institutionalized systems present in protecting the population from diseases. The proposed technical research will investigate the lack of formal early detection modeling present in the diagnosis of kidney diseases as well as aim to develop a novel tool used in detection of diabetes mellitus. The proposed STS research will investigate the prominent historical effects that the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) have had in regards to racial health disparities surrounding chronic kidney disease (CKD).

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Diabetes Mellitus (DM) is a chronic disease that is estimated to impact over 470 million people Worldwide by 2030 (Tabák et al., 2012). DM disables the proper functioning of the kidneys and includes various severe long-term health complications such as progressive nephropathy, neuropathy, and cardiac damage, and is one of the most prevalent causes of death (Lin et al., 2020). The current methods for diagnosis and management of diabetic kidney disease

include testing serum creatinine and urine albumin secretion which are unspecific late markers of kidney damage.

Urinary extracellular vesicles (EVs) are promising new kidney disease biomarkers. EVs are membranous particles containing cell cargo with inherent biological information that are shed into the extracellular space. EVs are not bound to a specific location and can travel throughout the body via biofluids, including blood and urine (Erdbrügger et al., 2021). Urinary EVs have been already tested with flow cytometry as early markers of kidney damage, however these methods are not specific to the site of damage and biased towards larger vesicles. Despite availability of sensitive instruments for EV analysis, most require processing of EV containing samples. These enrichment methods lead to unclear effects on EV properties, highlighting the need for novel methods using unprocessed samples. Following enrichment, characterization of EVs includes western blot analysis, flow cytometry, particle analysis, and omic approaches. These combined methods require large volumes and long processing times to complete, limiting their use when less volume is available such as existing biobanks, animal studies, and limited patient samples.

Given the lack of non-invasive early detection methods, the research proposed aims to generate a new EV detection tool for DM that requires less than 50 microliters of unprocessed sample and can be completed, without the need for enrichment, within 48 hours of sample collection. The project will test and optimize a new high-throughput microchip technology (ExoviewR100) for application in urine samples. The long-term goal will be to develop a combination of markers specific for glomerular or tubular cells of the nephron which characterize pathophysiological DM phenotypes. It is hypothesized that this microchip

technology using minimal raw urine volume can provide basic EV characterization and be used for detection of glomerular and tubular damage markers in diabetes.

Upon achieving the defined aims of the project, a novel early detection diagnostic tool will be developed. The methodology discovered will be translatable into other diseases as well as incorporated for detection of other biofluids including saliva and blood. Furthermore, the device would be an affordable long-term solution in early detection of chronic, life-threatening diseases, thus improving quality of life and overall health.

Racial Health Disparities, CKD, and the NIDDK

Health disparities definitively marginalize and harm the affected population in both overt and covert manners. The extent of health disparities ranges from the denial of access to specific resources for proper care and wellbeing to the unnecessary forced exposure to specific harmful scenarios. The characterization of health disparities is dependent on the shared quality of the population and is discriminatory based on aspects including race, gender, and sexuality (Braveman, 2014). CKD is a progressive disease with no known notable cure. The current progression of the disease results in complete loss of function of the kidneys requiring a combination of consistent dialysis filtration treatment and potential renal transplantation. Additionally, CKD also has additional long-term complications including cardiovascular disease and nerve damage (Levey et al., 2009). Within a study conducted by Dr. Hoerger et al, a statistical analysis and model concerning the prevalence of CKD projected more than half of US adults above the age of 30 to be diagnosed with CKD by 2030 (Hoerger et al., 2015).

The NIDDK is a federal government research institution classified within the larger functional groupings of the National Institutes of Health. The mission of the NIDDK is to disseminate scientific information surrounding renal, endocrine, and metabolic diseases with the

aims at improving health and quality of life (NIDDK, 2022). Given the overarching hierarchical structure of the NIDDK as a formal federal institution with the responsibility to advance renal health measures, the STS research will aim to examine the current functioning role of the NIDDK with reference to its involvement with racial health disparities promoting CKD.

The frameworks that will be utilized for this project will be the theory of technological politics developed by Langdon Winner as well as the correlated concepts surrounding power and knowledge originally disclosed by Michel Foucault. Langdon Winner, a prominent political theorist, proposes technology to inherently have association with the disposition of power. Regardless of the conceived outcome of usage, Winner's theory emphasizes the concept that the development and design of technology is inherently linked to politics as the process involves generating a tool to aid in a perceived problem in spite of its moral or social status (Winner, 1980). The major critique of Winner's theory of political technology resides in the inherent functioning of artifacts. The association between power and technology is functionally undeniable, however, the question arises in whether politics functions as an artifact or technology or technology is the artifact of politics (Joerges, 1999). The theory of political technology will be useful in analyzing the functioning of the NIDDK. Specifically, the framework will reveal if there are specific artifacts deeply internalized within the organization that attribute to a correlation with racial health disparities.

Michel Foucault, a notable French philosopher, confers the concept of knowledge as a functional unit of power. The concepts proposed by Foucault are useful in challenging preconceived aristocratic assignment of form and function (Foucault & Gordon, 1980). Critiques of Foucault's ideology often challenge the unconventional refinement of terms such as power and government (Keenan, 1987). With the NIDDK being one of the most expansive medical

bodies of knowledge in the world, Foucault's framework will be particularly useful in the recognition of the hierarchical status in relation to those affected by kidney disease. The proposed research will be paramount in discovering the direct features that the NIDDK has attributed towards racial health disparities present amongst CKD as it will showcase the effectiveness or lack therefore in regards current methods and initiatives. In functioning as a national governmental organization, the mission of the NIDDK self-appoints a duty to protect and advance the health, safety, and equity of all afflicted by kidney disease.

Research Question and Methods

The focused STS research question will be as follows: how has the formal institutionalization of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) affected racial health disparities present with regards to chronic kidney disease (CKD)? To conduct this research, documentary research methods in combination with policy analysis will be utilized. The documentary research methods will examine sources focused on the institutional history of the NIDDK as well as numerous national statistical publications relating to CKD and race. The statistical publications will examine reports of those affected by CKD as well as other social health determinants including education and economic status. The primary sources examined will showcase the apparent functional role of the NIDDK as well as its correlated effectiveness in addressing health disparities overtime. Additionally, policy analysis will be used to analyze the current conditions of public awareness campaigns and research initiatives of the NIDDK focused towards addressing racial health inequities. The various policies identified will be beneficial in revealing the broader impact and relevance of the concentrated projects ongoing at the NIDDK. The research will be organized chronologically in order to develop a cohesive timeline concerning the bureaucratic evolution of the NIDDK. The

keywords that will be of interest when collecting sources include CKD, health disparities, social determinants of health, and race.

Conclusion

Despite the federal funding put forth towards research and development, public health issues remain widespread within the United States. Kidney disease, one of the most pressing concerns, requires urgent attention given its associated debilitating health complications and continued rise in those affected. Through the technical research, a novel diabetic early detection model will be developed that will promote primary care and preliminary treatment prior to onset of disease. Furthermore, through the investigation of the inherent role of the NIDDK in relation to racial health disparities and CKD, the functional role of the NIDDK as well as the effectiveness of its presence will become transparent. In combination, the proposed research projects will provide a concrete analysis of the current situational conditions surrounding renal health and medical care that can further advance current public health measures and overall health and wellbeing.

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