

Thesis Project Portfolio

Standardization and Optimization of Urinary Extracellular Vesicle Isolation by Modifying

Hydration of a Healthy Cohort

(Technical Report)

The Role of Health Insurers in Chronic Kidney Disease-Related Disparities

(STS Research Paper)

An Undergraduate Thesis

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Sociotechnical Synthesis

The research in the technical report, *Standardization and Optimization of Urinary Extracellular Vesicle Isolation by Modifying Hydration of a Healthy Cohort*, strives to develop a method that makes urinary extracellular vesicles (uEv) more accessible to researchers. Specifically, the goal is to standardize urine collection protocol by implementing a water-restriction period to optimize uEv size and yield. These membrane-bound structures contain transmembrane proteins indicative of the various stages of kidney injury. They serve a potentially critical role in chronic kidney disease, or in the inadequate filtration of waste product and excess water from the body for an extended period of time, as diagnostic tools and therapeutic agents. Once the disease state progresses to the end-stage, management by dialysis or transplantation can delay kidney failure, but there is no return to complete kidney function. Thus, early detection of chronic kidney disease is critical. Beyond the physical and lifestyle burdens associated with end-stage kidney disease, the cost of management is enormous. The sociotechnical research paper, *The Role of Health-Insurers in Chronic Kidney Disease-Related Disparities*, strives to understand shortcomings in affordable preventative healthcare for vulnerable groups. Of those most greatly impacted by chronic kidney disease are minority and low socioeconomic groups. The paper investigates how several social determinants of health are inadequately accounted for by health insurers, exacerbating this disparity. Specifically, this research seeks to understand healthcare inequality in the hands of health-insurers due to lack of access to nutritious food, transportation, or facilities within the network. Overall, chronic kidney disease demands early detection and preventative healthcare to reduce the physical, psychological, and financial burden on those impacted, particularly vulnerable populations.

Early detection is critical to delay the progression of chronic kidney disease to end-stage. Urinary extracellular vesicles have diagnostic and clinical potential due to enclosed biomarkers indicative of kidney injury and the non-invasive, highly available nature of urine collection. Prior to uEv applications, researchers need a standardized approach to urine collection that optimizes uEv quality and yield. In this pilot study, we investigated the impact of water-deprivation on a healthy cohort of 10 volunteers. Each volunteer consented to providing two first-morning urine samples: one after an 8-hour water-restriction period and one after no hydration limitations. Urine creatinine content is expected to be elevated in dehydrated urine and serves to validate the effectiveness of the water-restriction period. Upon completion of a T-Test, we rejected the null hypothesis at an alpha level 0.01 and determined that creatinine levels are elevated in water-deprivation conditions. Differential centrifugation was used to separate the uEvs and Nanoparticle Tracking Analysis (NTA) to determine the size and concentration of uEvs. Results indicate that the size and concentration of uEvs is not significantly impacted by water-deprivation, and therefore, there may be no perceived benefit to abstaining from water-intake prior to first-morning urine collection for uEv analysis.

Health insurers play a critical role in exacerbating chronic kidney disease disparities through the lack of preventative healthcare. Specifically, insurers fail to adequately address social determinants of health, such as food insecurity and geographical needs, that demonstrate a strong association with chronic kidney disease development and progression. The paper acknowledges local initiatives to provide nutritious food and public transportation, but the lack of widespread solutions to these health barriers for low-income populations leaves many individuals, particularly in remote regions, without adequate care. Publicly-funded health insurers are only minimally to blame for this shortcoming. Rather, health insurers compete in a

much larger system that includes for-profit competitors who dominate the hemodialysis market. The for-profit stakeholders in the healthcare market establish monopolies that allow them to inflate costs and establish network boundaries that further hinder access to care. Thus, the limitations of publicly-funded health insurers are worsened by the environment in which they exist; one that enables profiteers to establish a competitive price point and geographical dominance.

The technical report and sociotechnical thesis allowed me to understand the need for preventative medicine in chronic kidney disease as both a scientific and financial need. The technical report highlights the irreversible nature of disease progression at the end-stage. The burden of chronic kidney disease and the associated management demand the ability to detect initial kidney injury and non-invasive, innovative therapeutics to delay progression. The shortcomings in early diagnosis and the irreversibility of end-stage kidney disease served as motivation to identify groups most vulnerable to chronic kidney disease. The sociotechnical thesis built upon the scientific shortcoming by calling attention to social determinants of health that are also unmet needs. The lack of insurance coverage for nutritious food, transportation, and out-of-network coverage for low-income and minority populations are measures associated with poorer health outcomes. The aforementioned scientific and financial needs together demand preventative approaches to chronic kidney disease to minimize the exacerbated burden on populations most vulnerable.