***Project Title:***Are Medication Costs Killing Patients? Cost-Related Non-adherence and All-Cause Mortality in Patients with Chronic Illness.

***Background and Significance***

In the last decade, prescription drug costs in the United States have risen by an average of 6% annually and now account for 40-50% of total hypertension and diabetes expenditures.1 Patients with diabetes and heart disease, a condition strongly associated with hypertension,2 often struggle to afford medication, with 16-20% skipping or delaying medication doses to cut costs in 2004.3 Cost-related non-adherence is associated with higher rates of hospitalization, development of medical comorbidities, and poorly controlled symptoms, all of which may contribute to increased mortality.4–6 The objectives of the current study were to 1) assess the prevalence of cost-related non-adherence in adults with diabetes, heart disease, and hypertension using a nationally representative sample and 2) analyze the relationship between cost-related nonadherence and all-cause mortality risk in adults with diabetes, heart disease, and hypertension in a nationally-representative sample.

***Approach***

Data will be taken from the 2000-2014 waves of the publicly available National Health Interview Survey (NHIS) and National Death Index linkage files provided by the National Center for Health Statistics. Only participants reporting a diagnosis of diabetes, hypertension, or any type of cardiovascular disease (coronary heart disease, myocardial infarction, angina pectoris, stroke, other non-congenital heart condition) will be included in the study. The primary exposure, CRN, will be evaluated based on three binary items asking participants whether they had, in order to save money, 1) skipped medication doses, 2) delayed taking medication, or 3) taken less medication than prescribed in the last year. CRN will be treated as an binary variable, representing any or no cost-saving behavior exhibited by a participant, with sensitivity analyses assessing the association of each individual item with the outcome. The primary outcome, all-cause mortality, will be determined through probabilistic record linkage, with follow-up time defined as time between date of interview and recorded date of death. Potential additional analyses will examine cause-specific sources of mortality (e.g. cardiovascular disease and diabetes).

Multivariate Cox regression models will be used to analyze associations between CRN and all-cause mortality within disease subgroups (i.e. individual models for diabetes, heart disease, and hypertension). Directed Acyclic Graphs will be used to select final covariates based on involvement in unblocked pathways between CRN and mortality, and may include SES, gender, age, insurance status, and number of additional comorbidities. For descriptive analyses (Table 1), all demographic variables and variables included in final models will be assessed for normality and equality of variance across CRN and non-CRN groups, and appropriate bivariate statistical tests chosen to describe unadjusted group differences. Prevalence will be calculated by applying appropriate weighting adjustments to observed percentages of patients with CRN.

***Timeline***

11/8/2019 – 11/22/2019: Write IRB Proposal (Submit by end of period)

11/23/2019 – 11/30/2019: Write in depth introduction for Project Proposal

11/30/2019 - 12/05/2019: Edit Project Proposal for Final Submission + Prepare Oral Pitch

12/06/2019- Oral Pitch

1/13/2020 – 1/20/2020: Recode Variables/ Data Management

1/20/2020 – 1/27/2020: Generate Descriptive Statistics and Draft Table 1

1/28/2020 – 2/12/2020: Run Cox PH Analyses and Draft Table 2

2/13/2020 – 2/27/2020: Literature Review (w/ emphasis for discussion section)

2/13/2020 – 2/20/2020: Write Results Section

2/27/2020 – 3/11/2020: Write Discussion Section

3/11/2020 – 3/25/2020: Edit Manuscript + Reformat Intro/Methods from this proposal

3/25/2020 – 4/1/2020: Finalize draft

***Competencies***

1. *Discuss the means by which structural bias, social inequities and racism undermine health and create challenges to achieving health equity at organizational, community and societal levels.* This project will address how social inequities in economic background and ability to pay for healthcare/medication contribute to disparities in chronic disease mortality by investigating the association of cost-related barriers to medication use and mortality and interpreting these effects in the discussion section of the paper.
2. *Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate.* This project will download, manage, and recode data from the National Health Interview Survey and conduct Cox regression, using R, to determine the association between CRN and mortality.
3. *Communicate audience-appropriate public health content, both in writing and through oral presentation.* Following data analysis, a publication-quality manuscript will be drafted and disseminated through appropriate scientific channels (i.e. submitted to peer review for publication).
4. *Interpret results of data analysis for public health research, policy or practice.* In the results and discussion sections of the manuscript, the results of analyses as well as implications for the U.S. healthcare system will be explained and contextualized for readers.
5. *Apply and interpret common statistical methods for inference (e.g., ANOVA, linear and logistic regression, survival analysis) found in public health studies.* Cox regression will be conducted to determine if CRN is associated with mortality in different subsamples of patients with chronic disease, and results will be explained using plain English within both the results and discussion sections of the manuscript.
6. *Demonstrate an understanding of systematic biases (selection and information biases) that affect observational, quasi-experimental, and experimental studies.* Potential sources of bias and other threats to study validity will be discussed in the limitations section of the manuscript, and efforts to minimize or control for bias will be reported in the methods section.
7. *Demonstrate an understanding of the components of reproducible research.* Code for analysis will be documented with comments and uploaded regularly onto GitHub as changes are made such that others will be able to understand and reproduce analyses. In the methods section of the manuscript, all procedures and analytic decisions will be clearly described such that other researchers could replicate results and build off them in future studies.

References

1. Dieleman JL, Baral R, Birger M, et al. US Spending on Personal Health Care and Public Health, 1996-2013. *JAMA*. 2016;316(24):2627. doi:10.1001/jama.2016.16885

2. Halter JB, Musi N, McFarland Horne F, et al. Diabetes and Cardiovascular Disease in Older Adults: Current Status and Future Directions. *Diabetes*. 2014;63(8):2578-2589. doi:10.2337/db14-0020

3. Piette JD, Heisler M, Wagner TH. Cost-Related Medication Underuse Among Chronically III Adults: the Treatments People Forgo, How Often, and Who Is at Risk. *Am J Public Health*. 2004;94(10):1782-1787. doi:10.2105/AJPH.94.10.1782

4. Herkert D, Vijayakumar P, Luo J, et al. Cost-Related Insulin Underuse Among Patients With Diabetes. *JAMA Intern Med*. 2019;179(1):112-114. doi:10.1001/jamainternmed.2018.5008

5. Heisler M, Langa KM, Eby EL, Fendrick AM, Kabeto MU, Piette JD. The Health Effects of Restricting Prescription Medication Use Because of Cost. *Med Care*. 2004;42(7):626. doi:10.1097/01.mlr.0000129352.36733.cc

6. Ho PM, Magid DJ, Shetterly SM, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. *Am Heart J*. 2008;155(4):772-779. doi:10.1016/j.ahj.2007.12.011