

1. Specific Aims.

In the United States, about 62% of Medicare recipients have two or more chronic conditions at age 65 to 74. The frequency of **multimorbidity** increases dramatically to 82% above age 85 (multimorbidity defined as ≥ 2 chronic conditions). Rapid growth of the elderly population is leading to an overwhelming level of morbidity and disability, and thus to increasingly unaffordable healthcare utilization. These healthcare trends may be changed by delaying the onset of morbidity, and particularly multimorbidity, through modification of risk factors or determinants of diseases. However, current preventive efforts have partly failed because they have focused on one disease at a time too late in life (e.g., after age 65). For this reason, there is a critical need to identify – earlier in life – groups of individuals at risk and to develop interventions to prevent multimorbidities and their adverse health outcomes in a more integrated and data-driven way. These priorities were outlined in the Multiple Chronic Conditions Strategic Framework of the US Department of Health and Human Services (**US DHHS**) of 2010. **Therefore, the unifying theme of this application is multimorbidity and its causes and consequences.** The Rochester Epidemiology Project (**REP**) is an ideal environment to study multimorbidity and its causes and consequences because the REP maintains a comprehensive medical records-linkage system for Olmsted County, MN (since 1966) and for an 11-county region of Southeastern MN (since 2009). The REP has information for all age strata from newborns to death, regardless of insurance status or health care setting (both inpatient and outpatient care), and it has accumulated longitudinal data over almost half a century. Therefore, in this renewal application, we propose to identify groups of people with different levels of multimorbidity across 7 age cohorts spanning the entire population, and to identify possible interactions across specific diseases (**Aim 1**). In addition, we will identify causes (**Aim 2**) and long-term adverse health outcomes of multimorbidity (**Aim 3**). This knowledge will guide earlier and more integrated preventive interventions leading to reduced multimorbidity and will improve outcomes in those with multimorbidity. Finally, we will develop and implement an innovative approach to data sharing by making REP data accessible to users worldwide through a Data Exploration Portal accessible on the internet (**Aim 4**). To accomplish these goals, we propose **4 Specific Aims**:

Aim 1. Measure the prevalence and incidence of multimorbidity (≥ 2 chronic conditions) across all ages in an entire population. We will focus on 20 selected chronic conditions recommended by the US DHHS; however, we will also systematically assess all other conditions. In particular, we will:

- a. Measure the prevalence and severity of multimorbidity and discover possible interactions by identifying dyads and triads of conditions (cross-sectional analyses; also used in **Aim 3**);
- b. Measure the incidence and severity of multimorbidity over 20 years of follow-up among subjects free of multimorbidity at baseline (with 0 or 1 conditions; longitudinal analyses; also used in **Aim 2**).

Aim 2. Test the hypothesis that there are identifiable causes or predictors of incident multimorbidity across all ages. We will study the following determinants using a cohort design:

- a. Body mass index (**BMI**), cigarette smoking, and alcohol consumption;
- b. Preceding medical conditions;
- c. Sex/gender, race/ethnic group, education, socioeconomic status, and marital status.

Aim 3. Test the hypothesis that levels of multimorbidity and specific disease combinations at baseline can predict long-term outcomes (from 2000 to 2019; 20 years). We will study the following outcomes:

- a. Death;
- b. Overall health care utilization including hospitalizations, emergency room visits, and drug prescriptions (including polypharmacy);
- c. Patient reported outcomes (**PROs**) including functional status (e.g., activities of daily living).

Aim 4. Use innovative methods to broadly disseminate the REP data. We will develop a Data Exploration Portal accessible on the internet to allow investigators and practitioners to study incidence of diagnoses, procedures, and drug prescriptions (e.g., time trends in colonoscopy or use of statins), and to explore their interrelationships (e.g., association of head trauma with dementia or of statins with myocardial infarction). Data visualization and analysis tools will be developed for both the Olmsted County, MN population (n~140,000) and for the 11-county region of Southeastern MN (n~500,000).

The strengths of the REP will be used to identify distinct groups of people with multimorbidity across the entire life span, and to study causes and consequences of multimorbidity. These findings will inform more effective interventions to reduce multimorbidity and to improve health outcomes for those with multimorbidity, as recommended by the US DHHS. In addition, broad sharing of the comprehensive and longitudinal REP data to the wider scientific community will allow investigators worldwide to efficiently explore patterns of diseases, procedures, and drug prescriptions and their associations rapidly and at no cost. This new data sharing approach will accelerate research and discovery.