**Title of proposed program:** Management of Chronic Diseases in Clinical Trials

**Submitting Source:** NIH

**What is the major obstacle/challenge/opportunity that the Common Fund should address? What would the goals of the program be?** Clinical trials require carefully selected populations to evaluate efficacy of specific interventions. Patients typically present with more than one chronic disease. A disease in one trial setting is an eligibility criterion and in another is considered to be a co-morbidity. Co-morbidities can contribute to diagnostic delays, decreases in treatment, and inferior survival, all of which impart a disproportionate impact on minority and underserved populations. Common to clinical research across many diseases is the fact that agents used in clinical trials and subsequently approved by the Food and Drug Administration are implemented in populations different from the clinical trial participants. This initiative is to focus on common ways to identify chronic diseases and conditions among clinical trial participants to enable researchers and practitioners to better understand biologic and clinical consequences of clinical interventions on chronic diseases. Comorbidities that are treatment-induced in all age groups, those that increase with age alone, and those that may be long-term sequelae of both the disease and treatment are important issues faced by practicing physicians world-wide. There is a paucity of research done to address co-morbidities in the context of treatment including a lack of assessment for measurement tools, uniform data collection, and clinical trial designs with embedded research questions germane to the diverse presentations of health conditions, cultures, lifestyles, and medications. Although the development and use of molecularly targeted and genomic therapies are touted to substantially reduce toxicities on noncancerous tissues, to date, freedom from toxicities to the host and from influencing existing chronic diseases has not been realized. The goals of a program focusing on co-morbidities in clinical research are as follows:

- Collaborate with other ICs to enhance the understanding of co-morbidities in the context chronic diseases in the design of clinical trials.
- Determine the critical data elements to collect and sources of data collection for the management of comorbidities.
- Develop methodologies to aggregate data utilizing interoperable standards.
- Develop measurements to assess existing co-morbidities and their influence on participation in clinical research.
- Utilize existing data within the NIH Clinical Trials Network to evaluate key questions related to co-morbidities.

**Why is a trans-NIH strategy needed to achieve these goals? What initiatives might form the strategic plan for this topic?** Factors contributing to the need for a trans-NIH approach include: scientific evidence that exists for associations of chronic diseases such as diabetes mellitus and obesity with increased risk, higher recurrence rates, and poorer survival outcomes for multiple cancers; the rates of recruiting and enrolling patients with multiple co-morbidities into clinical research varies among ICs; and researchers in the field of geriatrics are currently at the helm of evaluating comorbidities and clinical trials but there is ample room for further implementation. There is a critical need for the NIH Institutes studying chronic diseases to design prospective trials that share experiences in the clinical management of comorbidities as the target disease or coexisting disease. There is also a tremendous value of a shared trans–NIH team to define common secondary endpoints, to determine eligibility criteria, to establish management guidelines for known comorbidities in clinical trials (i.e., hypertension, HIV, and bone loss in cancer trials) and to identify a set of harmonized data elements. A trans-NIH research team could convene disease experts and other stakeholders from populations least represented in clinical trials due to comorbidities to recommend the most appropriate ways to prevent and manage comorbidities in screening, prevention, and treatment clinical trials. Such approaches could employ current technologies for improved stratification for risk and response to interventions. An initial working group would be formed to develop the research team, set the goals, and establish common terminology. Within the NCI Division of Cancer Prevention, a 2011 workshop with extramural cardiovascular, geriatric, and endocrine expertise, entitled, “Co-morbidities in Cancer Clinical Trials” focused on comorbidities as a barrier to the enrollment of underserved populations into clinical trials. A second initiative, an NCI Collaborative Partnership with the American Cancer Society, Association for the Advance of Cancer Research, and the American Society for Clinical Oncology, is developing a white paper on cancer disparities in clinical research. This group has identified comorbidities as a barrier to the conduct of clinical research and a priority in cancer disparities research.

**If a Common Fund program on this topic achieved its objectives, what would be the impact?**

- Co-morbidities will be better understood in the context of existing chronic diseases and their treatment.
- The development of management guidelines and the collection of agreed-upon critical data elements will facilitate the enrollment of patients from diverse populations in clinical trials.
- Those patients with a favorable benefit/risk profile after appropriate assessment of co-morbidities could be better managed to attain the scientific outcome of clinical trials and implementation of the advancements from clinical research.