



2010

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Via Electronic Submission to: william.elwood@nih.hhs.gov

February 19, 2010.

Re: Response to RFI (NOT-OD-10-055) on the Priorities for the NIH Basic Behavioral and Social Sciences Research (bBSSR) Opportunities Network (OppNet).

Dear Dr. Elwood:

The American Society of Hematology (ASH) appreciates this opportunity to respond to the National Institutes of Health's January 28, 2010 Request for Information on the Priorities for the NIH Basic Behavioral and Social Sciences Research (bBSSR) Opportunities Network (OppNet).

ASH represents over 16,000 clinicians and scientists committed to the study and treatment of blood and blood-related diseases. These areas include anemia (including sickle cell and thalassemia), thrombosis (including venous thrombosis, heart attack and stroke), bleeding disorders, transfusion medicine, and gene therapy, as well as the malignant hematologic leukemia, lymphoma, and myeloma. In addition, hematologists have been pioneers in the fields of bone marrow transplantation and stem cell research.

We have submitted these comments through the online response form, but due to the format and text size limitations, we would like to expand on the proposed priorities for the bBSSR OppNet. All of the opportunities we list below refer to scientific research of at least 3-5 years duration.

CHALLENGE 1: BEHAVIORAL AND SOCIAL SCIENCES RESEARCH IN PATIENTS WITH SICKLE CELL DISEASE (SCD).

1a). Anxiety and Depression in SCD.

Opportunity: Individuals with sickle cell disease are at increased risk for anxiety and depression, compared with individuals of comparable cultural and economic backgrounds. There is a need to understand which individuals are vulnerable to developing mental health symptoms by identifying individual differences in physiological responses to the stress of the diagnosis, the experience of pain, repeated medical procedures and life threatening complications.

By determining which individuals are most vulnerable to developing mental health symptoms, interventions can be more effectively targeted, because these individuals in turn are more likely to exhibit increased frequency and intensity of pain. Follow up on such observations of changes in hippocampal volume for some patients with stroke on Magnetic Resonance Imaging (MRI) is needed to determine how the regulatory functioning of the hypothalamic-pituitary-adrenal (HPA) axis might be disrupted by other pathophysiological processes in sickle cell disease.

Outcome Measures: Patient satisfaction, reduced anxiety and depression, reduced pain, absence of medical care.

1b). Pain and SCD.

Opportunity: There is still a great deal that needs to be understood about the pain experience in SCD. Using such technologies as fMRI could help identify different pain syndromes and particularly inform treatment of chronic pain syndromes as some may have a greater component of depression and others may have a greater component of anxiety.

Outcome Measures: Quality of care measures, patient satisfaction, reduced pain.

1c). Race and Ethnicity in SCD.

Opportunity: Sorting out the social constructs of race and ethnicity and how these have contributed to the many disparities in the quality of care available to patients with SCD needs to be addressed. Social science research of how discrimination alters patient interaction and compliance will be of great benefit to understanding health care disparities.

Outcome Measures: Quality of care measures, patient satisfaction, absence of medical care.

1d). Adherence to treatment in SCD.

Opportunity: There is a need to understand issues that affect adherence with treatments. Strategies to improve adherence must incorporate potential neurocognitive challenges such as poor memory and executive functioning.

Outcome Measures: Adherence measures, patient satisfaction, provider satisfaction, absence of medical care.

1e). Quality of Life Tools in SCD.

Opportunity: The disease-specific measure of quality of life in sickle cell disease will be available for use soon. Standardizing a measure that can be used internationally is the obvious next step that would greatly benefit from additional basic behavioral and social sciences research.

Outcome Measures: Quality of life measures, reduced morbidity and mortality.

1f). Education and Employment in SCD.

Opportunity: Chronic illness, particularly in sickle cell disease, is dramatically worsened by lack of education opportunities and employment. Systematic interventions need to be implemented on the level of improving school and employment experiences as a means of improving overall quality of life for people with SCD.

Outcome Measures: Quality of life measures, socioeconomic measures, reduced morbidity and mortality.

CHALLENGE 2: BEHAVIORAL AND SOCIAL SCIENCES RESEARCH IN PATIENTS WITH THALASSEMIA.

2a). Adherence to Iron Chelation Therapy in Patients with Thalassemia.

Opportunity: Data from numerous studies demonstrate that the regular use of iron chelation therapy delays or prevents the accumulation of transfusional iron and the onset of iron-induced cardiac failure or arrhythmias. As a result, patients with thalassemia who regularly use iron chelation therapy have the potential for a vastly improved quality of life and normal or nearly normal lifespans. However, the development of these effective chelators, even those that are orally active, has not been matched by a rate of adherence that is necessary to achieve the long-sought benefits. The issue of adherence was felt by many to be one that would disappear as the oral chelators replaced the parenteral agent deferoxamine that required nightly infusions. Adherence, however, remains a major problem which, perhaps, should not be so surprising given the known problems of adherence with medication for hypertension, chronic renal disease and other disorders in which no immediate clinical benefits (*i.e.*, relief of symptoms) are visible to the patient. Thus, patients with thalassemia, particularly adolescents and young adults, continue to accumulate iron, to develop heart disease and to die prematurely despite drugs that are capable of preventing all of these unfavorable outcomes. Research on the behavioral and social aspects of adherence to treatment is urgently needed for the patients with thalassemia.

Outcome Measures: Compliance measures (*e.g.*, electronic pill counters), better control of iron stores and reduction of morbidity and mortality.

2b). Transition Pediatric to Adult Care and Better Provision of Care to Adults with Thalassemia and Other Blood Disorders.

Opportunity: Numerous factors contribute to the difficulties in providing comprehensive care to adults with thalassemia and other blood disorders such as sickle cell disease, hemophilia, Diamond Blackfan Anemia, chronic Idiopathic Thrombocytopenic Purpura, and hypercoagulable disorders. The problem is particularly challenging not only because of the severity of the underlying chronic disease but also because of the many associated problems that require substantial care coordination and the input of numerous subspecialists. Social science research to develop novel effective programs of transition from pediatric to adult-centered care and to enhance the effectiveness of both pediatric and adult-centered care delivery systems is a critical need recognized in all thalassemia centers nationally and internationally.

Outcome Measures: Patient satisfaction, provider satisfaction, missed appointments, absence of adult medical care.

CHALLENGE 3: BEHAVIORAL AND SOCIAL SCIENCES RESEARCH IN ELDERLY PATIENTS WITH ANEMIA.

Background: Multiple studies have now confirmed that anemia is common in the elderly. The prevalence of anemia is approximately 10% in community-dwelling men and women aged 65 and older, rising to 20-30% in those aged 85 and above. The prevalence of anemia in nursing home residents has been reported to be even higher, ranging between 48 and 63%. The United States population as a whole is both expanding in size and aging. In 2006, those aged 65 and older were estimated to comprise approximately 12% of the United States population (that is, 37 of 299 million total population). By 2030, this proportion is estimated to rise to approximately 20% of the U.S. population (that is, 71 of 363 million). Thus, in the year 2030, we can reasonably anticipate that approximately 7.1 million adults over the age of 65 will be anemic.

3a). Anemia and Impaired Physical Performance.

Opportunity: Recent studies have highlighted the association between mild anemia and even low-normal hemoglobin values in persons 65 and older and poor outcomes, including impaired performance-based mobility function, increased frailty, muscle weakness and increased falls. Behavioral and social aspects of these findings are not well understood, and should be studied.

Outcome Measures: Physical performance measures, reduced morbidity and mortality.

3b). Anemia and Impaired Cognitive Function.

Background: Recent evidence suggests anemia negatively impacts cognitive function in the elderly. In one study in community-dwelling women between the ages of 70 and 80, the presence of mild anemia (hemoglobin between 10 and 12 g/dL) was associated with significantly worse performance on the Trail Making Test Parts B and A, measures of executive function. In one of the larger cross-sectional studies conducted to date, Lucca et al., investigated the association of anemia and mild grade anemia with cognition, mood, and quality of life (QoL) in 170 community-dwelling elderly adults with mild anemia and 547 non-anemic controls, all between 65 and 84 years of age. After adjustment for a large number of demographic and clinical confounders, mild anemia was significantly associated with poorer performance in measures of selective attention. Further, when anemia was defined as 0.2 g/dL above the WHO criteria, those who were mildly anemic performed worse than non-anemic elderly persons on all cognitive measures, including those of memory function, delayed recall, recognition, attention and selective attention and cognitive flexibility.

Data also suggest that anemia may have long-term effects on cognitive function. In a longitudinal study of 1,435 Swedish men and women aged 75 to 95 years, the diagnosis of anemia at baseline in cognitively intact elderly patients (Mini-Mental Status Examination score ≥ 26) was associated with a significantly increased risk of developing dementia over approximately three years of follow-up when adjusted for sex, age, education, and MMSE score. However, when adjustments were made for chronic diseases, inflammation, and nutritional status, statistical significance was not reached. In an additional study in 1,744 community-dwelling men and women aged 71 to 102 years, the presence of anemia at baseline was associated with significantly lower cognitive function, as measured by the Short Portable Mental Status Questionnaire (SPMSQ).

Opportunity: Arguably, cognitive impairment may be the single most powerful deterrent to quality of life for those over age 65. Reducing cognitive impairment and delaying the onset of Alzheimer's disease have significant clinical and economic benefits. While the development of cognitive impairment in the elderly is likely due to a multiplicity of environmental and genetic factors, only very few of such factors are amenable to intervention. Understanding the basic biologic and behavioral mechanisms that underlie cognitive dysfunction in the anemic elderly patient is a pre-requisite to determining whether interventions aimed at correcting or improving anemia will also have a positive impact on cognitive decline and any underlying brain pathophysiology.

Outcome Measures: Cognitive function measures, reduced morbidity.

3c). Anemia in the Elderly and Morbidity and Mortality

Opportunity: Multiple studies have shown an association between anemia in the elderly and increased mortality. In a Dutch study of community-dwelling men and women aged 85 and older, anemia was associated with an increased mortality rate over a 10-year period, even after adjustments for functional impairment and associated diseases. In the Framingham study, there was increased mortality in men with a hematocrit of less than 42% and less than 39% in women compared to those with higher values. Basic behavioral and social mechanisms of this association need to be studied with the goal of reducing the morbidity and mortality of these patients.

Outcome Measures: Reduced morbidity and mortality.

ASH will be happy to provide further information and discuss these challenges with you. Please contact ASH Scientific Affairs Manager, Ulyana Desiderio, Ph.D., at (202) 776-0544 or udesiderio@hematology.org for any additional information.

Sincerely,

A handwritten signature in black ink that reads "Hal E. Broxmeyer". The signature is written in a cursive, flowing style.

Hal E. Broxmeyer, PhD

President