Example 1

2. CANDIDATE'S BACKGROUND: My goal in seeking a Mentored Research Career Development Award is to acquire the necessary training, practical experience, and knowledge to become a leading independent clinical investigator in implementing public health interventions to reduce the burden of obesity and diabetes in low-income communities. I propose to investigate the association between food insecurity and the incidence and management of obesity and diabetes using two longitudinal studies. I will then undertake a pilot project to determine whether reducing financial barriers to fruit and vegetable consumption improves dietary intake and diabetes self-management in a clinical population at high risk of food insecurity.

I received my Bachelor of Arts in Biology from Williams College (Magna Cum Laude, 1996) and my Doctor of Medicine from Baylor College of Medicine (Alpha Omega Alpha Honor Society, 2000). I then completed Internal Medicine internship and residency at the University of California San Francisco (2000-2003). I entered UCSF's Fellowship in General Internal Medicine and received a Master's of Advanced Studies in Clinical Research, and then joined UCSF's faculty in 2006. I received a CTSI KL2 award in 2009. This KL2 award has funded additional preliminary research supporting the association between food insecurity and poor chronic disease self-management. However, I must still generate data supporting food insecurity as a causal factor in the development of obesity/diabetes (Aim 1) and poor self-management (Aim 2), and generate pilot data in preparation for submission of an R01-level intervention to shift dietary intake among food insecure patients with diabetes (Aim 3). This application will build on my KL2-funded activities to better position me to obtain R01-level funding.

I have published two first-author publications addressing health literacy as a barrier to behavior change among patients with diabetes, both under the mentorship of Dr. Dean Schillinger (my primary mentor). The first publication, a randomized, controlled trial of screening for limited health literacy in the clinical setting,[1] won the Best Poster Award at California's Society of General Internal Medicine meeting. The second publication relates to the development of written health education material for patients with limited health literacy.[2]

I am part of a national, multidisciplinary team of experts funded by the American College of Physicians Foundation (ACPF) to develop self-managements guides targeted toward adults with limited health literacy (diabetes and COPD, in press; coronary artery disease, in progress). As project site director, I supervise activities related to content development at UCSF, including focus groups, cognitive interviews, photography production, and Spanish translation. I also acted as site director for a feasibility evaluation of the effectiveness of the diabetes self-management guide in association with brief counseling. We enrolled 80 Latino patients with diabetes receiving care in the General Medicine Clinic at San Francisco General Hospital and achieved a 96% retention rate over three months of follow-up. Two manuscripts resulted from this work.[3, 4] I have spoken about behavior change counseling and health literacy at a number of national meetings, including the Joint Commission on Accreditation of Health Care Organization's National Symposium on Health Literacy and Patient Safety (plenary session, 2006), the American College of Physicians National Meeting (workshop, 2007), and the Institute for Healthcare Advancement (plenary, 2007 and workshop, 2008).

My primary research efforts now focus on the role of food insecurity in the prevention and management of obesity and diabetes. Unlike the literature on limited health literacy, which is relatively mature, little literature exists about the clinical and public health impact of food insecurity. I developed experience working with complex survey data using the California Health Interview Survey. This work resulted in a first-author publication and a nomination for the Society of General Internal Medicine's Mack Lipkin, Sr. Award.[5] I applied my skills with complex survey data to the National Health and Nutrition Examination Survey (NHANES) and demonstrated that food insecurity is associated with obesity, diabetes, and hypertension. I presented this work in abstract form at national meetings of the Society of General Internal Medicine (2007 and 2008) and at the American Diabetes Association (2008). This work resulted in two first-author publications.[6, 7] Because I have been unable to find data estimating the prevalence of food insecurity in a clinical population since the early 1990's, I have also added food insecurity measures to studies in San Francisco, Chicago, and Louisiana. Manuscripts from this work are in press or in progress.[8] I have presented abstracts of this work at the Society of General Internal Medicine meeting (2009 and 2010), the UCSF Health Disparities Symposium (2009), the CDC's Diabetes Translation Conference (2010), and the Clinical and Translational Research and Education Meeting (2010). I present my conceptual framework for the association between food insecurity and diet-sensitive chronic disease in an editorial in press at *New England Journal of Medicine.*[9]

Part 1 Examples

3. CAREER GOALS AND OBJECTIVES: My long-term goal is to develop, implement, and disseminate interventions for reducing the burden of obesity and diabetes in low-income communities. My Master's of Advanced Studies degree in Clinical Research provided me with skills to plan, implement, and analyze data from observational and experimental studies. My KL2 has given me the opportunity to extend my research into the health implications of food insecurity. However, progress toward my career goals requires I develop expertise in three additional content areas: advanced statistical methods, nutrition, and intervention research. The projects proposed in this application and my team of mentors and co-mentors will provide me with this focused, trans-disciplinary expertise. The skills and experience I will acquire carrying out the research in this proposal will prepare me to apply for an R01 grant implementing an intervention to reduce financial barriers to fruit and vegetable consumption in a large, at-risk population of patients with diabetes.

4. CAREER DEVELOPMENT AND TRAINING ACTIVITIES DURING AWARD PERIOD: I will concentrate my training efforts during the period of the Mentored Career Development Award on three areas critical to my success with future independent funding. Each training goal is supported by a member of my multi-disciplinary advisory team and practical experience with a specific project. I will gain experience with advanced statistical methods from each of the three aims proposed in this application, with mentorship provided by Drs. Bibbins-Domingo and Vittinghoff. I will gain experience with nutritional epidemiology, assessment, and policy in Aims 1 and 3, under the mentorship of Dr. Laraia. Finally, I will gain hands-on experience with the implementation and dissemination of interventions with Aims 2 and 3, under the mentorship of Dr. Schillinger.

	Training Goal 1: Advanced Statistical Methods	**Training Goal 2: Nutrition Epidemiology, Assessment, and Policy**	**Training Goal 3: Intervention Research**
Mentorship	Kirsten Bibbins-Domingo, MD, PhD; Eric Vittinghoff, PhD	Barbara Laraia, PhD, MPH, RD	Dean Schillinger, MD (primary mentor)
Practical Experience			
Aim 1: Food insecurity and obesity/diabetes incidence (CARDIA)	•	•	
Aim 2: Food insecurity and diabetes self-management in behavioral intv'n	•		•
Aim 3: Pilot intervention, F&V voucher	•	•	•

4.1 Advanced statistical methods: Experience with advanced statistical methods, including repeated measures and longitudinal data analysis and analysis of RCTs, is critical to my ability to accomplish the projects proposed in this application and to the analysis of future interventions. As part of my Master's degree I completed Biostatistical Methods for Clinical Research I-III, which focused on developing basic skills. However, I need applied experience with specific advanced techniques to be successful at completing the projects proposed in this application and the R01 application to follow. These techniques include, as examples, handling of missing data in repeated measures analyses and time-varying covariates (including dietary intake). I also need experience with applying basic analytic techniques, such as analysis of RCTs, to my own data. Success with the projects proposed in this application and development of the R01 application to follow this K award is contingent on mentorship from more experienced members of the faculty.

This training goal will be supervised by Drs. Kirsten Bibbins-Domingo and Eric Vittinghoff. Dr. Bibbins-Domingo, an internist, CARDIA Investigator, and national expert in the epidemiology of chronic disease disparities, has first-authored multiple manuscripts in the *New England Journal of Medicine* using longitudinal data from CARDIA.[1-3] Dr. Vittinghoff, a biostatistician in the Department of Epidemiology and Biostatistics, has extensive experience working with longitudinal data, including CARDIA. I have worked with Dr. Vittinghoff on a number of other projects as well. [5, 6]

Practical experience: Dr. Vittinghoff will meet me weekly during the data analysis stages of Aims 1 and 3 to assist me with accurately interpreting longitudinal data. Dr. Bibbins-Domingo will meet with me twice monthly during Aim 1 to assist with interpretation of CARDIA data.

4.2 Nutrition epidemiology, assessment, and policy: I have engaged in substantial self-directed study of food insecurity and its effect on dietary intake and health outcomes. This work informed my conceptual model of mechanisms by which food insecurity predisposes adults to chronic disease and poor disease management.[9] It has also given me sufficient expertise to complete three cross-sectional food insecurity analyses.[6-8] However, accurate measurement and analysis of dietary intake is a complex field requiring a substantially richer understanding than I have been able to acquire without formal mentorship and training.

This background is critical to my ability to design, implement, evaluate, and disseminate future dietary interventions. This training goal will be supervised by Barbara Laraia, PhD, a nutritional epidemiologist and national expert in food insecurity who co-directs UCSF's Center for Obesity Assessment, Study, and Treatment. She and I have developed a strong working relationship during previous projects.[7]

Coursework: The Public Health Nutrition Program at UC Berkeley's School of Public Health will offer me formal training through the following two classes: (1) *Nutritional Epidemiology* (Public Health 206C, 3 units; relevant to Aim 1): issues in design, analysis, and interpretation unique to nutritional epidemiology; (2) *Measuring Dietary Intake and Nutritional Status* (Public Health 206A, 2 units; relevant to Aims 1 and 3): concepts, methods, and limitations in the determination of nutritional status; methodologies for interpreting data; technical, social, and political implications of nutritional assessments. The UC Berkeley campus is located just across San Francisco Bay from UCSF (15 miles from my office and accessible by rapid transit).

Structured tutorial: Dr. Laraia will complement this coursework with a structured tutorial emphasizing individual-level health outcomes (weekly for 3 months during Year 1). Dr. Laraia has compiled primary research and commentary addressing areas in which I need additional expertise, including statistical and non-statistical methods of correcting for measurement error, dietary aspects of obesity and diabetes prevention and management (including micro- and macronutrients and the glycemic index), meal patterning, sociocultural determinants of food choice, and dietary behaviors prevalent among adults with chronic disease.

Practical experience: Aims 1 and 3 of this proposal include dietary assessment measures. Dr. Laraia will assist me with design of the dietary assessment for Aim 3 and development of the nutritional aspects of the R01 application in Year 4.

4.3 Intervention research: I have had some limited experience with intervention research. I completed Clinical Trials (Epi 205) in 2004, which taught me general principles of trial design and implementation. I also first-authored a randomized, controlled trial manuscript, although the trial was already complete by the time I took over the project at the data analysis stage.[1] Finally, I served as the site coordinator for a small behavioral intervention.[3, 4] This latter experience made me aware of the complexities involved in implementing clinical trials, particularly in safety net settings. If I am going to lead large clinical trials as the PI of an R01-level project, I need to have the practical and applied experience associated with designing and running my own small clinical trial. I have designed this K23 application to provide this practical and applied training. Dr. Schillinger, my primary mentor, will supervise this training goal. He has experience with the development and implementation of numerous clinical trials in the safety net setting.[1, 3, 10-12]

Coursework: I will take two new courses offering training in the specific types of interventions I would like to implement: (1)*Translating Practice into Evidence: Community Engaged Research (*Epi 248, 1 unit): principles and applied methods of community engaged research, including defining community and partnership models, developing and implementing study designs, interpreting and disseminating findings, and scaling-up studies for translational implementation research; (2) *Translating Evidence Into Practice: Individual-Centered Implementation Strategies* (Epi 246, 2 units): developing interventions for individual health behavior change, including behavior change strategies at the individual, interpersonal, and system/community level.

Practical experience: I will obtain practical experience with intervention research as a member of the Investigator Team for Aim 2, which disseminates a self-management intervention into federally qualified health centers. Aim 3 will give me hands-on experience with the design and implementation of my own RCT implemented in a safety-net setting. This project will position me to successfully compete for R01 funding.

4.5 CTSK Scholars Program: I will continue to participate in the Clinical and Translational K Scholars (CTSK) Program, offered by the UCSF Department of Epidemiology and Biostatistics. This program provides clinical and translational research training and mentored support to individuals with career development awards at UCSF. Key program elements include (1) weekly works-in-progress seminars, (2) weekly methodology seminars; (3) expert epidemiologic and biostatistical guidance; and (4) the opportunity to receive extensive one-on-one feedback and suggestions on manuscripts and grant applications.

5. TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH: As part of the Masters Program in Clinical Research, I completed a course entitled "Responsible Conduct of Research". This course is designed to address the requirements of the National Institutes for Health for education of investigators about ethical issues in research involving human subjects. I have also completed on-line training courses required by the UCSF Committee on Human Research on research involving human subjects, laboratory safety, and handling of infectious specimens. I will maintain up-to-date certification throughout the award period.

Example 2

2. CANDIDATE'S BACKGROUND

I graduated *Summa Cum Laude* from Northwestern University, where I studied medical engineering. It was at Northwestern where I first became interested in medicine and research, studying the biomechanics of an intra-thoracic artificial lung. I went on to attend medical school at Northwestern University Feinberg School of Medicine. During this time, I took on leadership and mentorship positions in both university and community organizations. During internship and residency training at the McGaw Medical Center of Northwestern University, I developed a passion for interstitial lung disease. While I was at Northwestern, I sought out the mentorship of Dr. J. Iasha Sznajder, the Chief of the Division of Pulmonary and Critical Care Medicine. With his mentorship, I studied the molecular mechanisms of insulin on the alveolar type II cell and the physiologic effects of insulin in a mouse model. This experience allowed me to gain important laboratory skills and a solid foundation in basic science research. This work resulted in achievement of the top award for basic science research at the Northwestern University Resident Research Symposium.

When I completed residency training, I had a year off before starting my fellowship in Pulmonary and Critical Care Medicine at UCSF. I decided to use this time to further my training in basic science research and the basic mechanisms of lung injury. I approached Dr. Michael Matthay about potential research opportunities (Dr. Matthay is the principal investigator of the NHLBI-sponsored SCCOR grant in translational research in acute lung injury). In his lab, I worked on an endotoxin model of acute lung injury; specifically, investigating the role of priming. During this time, I acquired skills in complex mouse model work, biochemical assays, and cellular analysis. In addition to learning the technical aspects of basic science work, I also learned practical aspects of research in general, including hypothesis generation, execution of study design, problem solving, critical analysis of my findings, and perseverance. My work in Dr. Matthay's lab resulted in a poster discussion session at the American Thoracic Society (ATS) meeting in 2008 and the manuscript is currently submitted to Anatomical Record for review.

While working with Dr. Harold Collard, the director of the UCSF Interstitial Lung Disease Program, I began to learn about acute exacerbations of idiopathic pulmonary fibrosis (IPF). I found this area to be interesting and challenging and felt this area of research integrated my interests in interstitial lung disease and acute lung injury. After learning more about this area, I became interested in the role of gastroesophageal reflux (GER) and secondary microaspiration in patients with IPF. With careful consideration and discussion with several mentors, I decided to pursue further training in clinical research to address this issue. During my last year of dedicated research time, I have accomplished the following goals: 1) Awarded a Ruth L. Kirschstein National Research Service Award investigating the role of microaspiration in patients with IPF; 2) Completed a comprehensive review of the literature resulting in a manuscript that has been accepted to the American Journal of Medicine; 3) Designed and implemented a retrospective cohort study investigating the significance of hiatal hernia in patients with IPF that has resulted in a manuscript that has been submitted to Thorax; 4) Designed and implemented a retrospective cohort study investigating bronchoalveolar lavage pepsin levels in patients with acute exacerbations of IPF that has resulted in a manuscript that has been submitted to the American Journal of Respiratory and Critical Care Medicine; 5) Formed research collaborations both locally (Gastrointestinal Motility group and Lung Transplant group at UCSF) and abroad (acute exacerbation study with Korea); 6) Enrolled in the Master's degree program in clinical research at UCSF where I am obtaining essential skills in epidemiology and biostatistics

3. CAREER GOALS AND OBJECTIVES

My goal is to become an independent clinical investigator and leader in the study of diffuse lung disease. To continue my progress towards this goal, I am proposing an observational prospective study addressing specific hypothesis surrounding the role of gastroesophageal reflux in IPF, a timely and important topic. Specifically, I am interested in studying 3 primary topics: (1) the clinical characteristics of reflux in patients with IPF, (2) the biomarkers of reflux and microaspiration in patients with IPF, and (3) the impact of reflux and microaspiration on outcomes in patients with IPF. The knowledge and experience gained from this proposal will allow me to successfully compete for R01 funding and lead directly to a study validating these findings in a multicenter fashion utilizing the resources of the NIH-funded IPFNet.

I have made progress in developing my clinical research skills, but there are four important areas where I require additional training, mentoring, and experience: (1) multi-disciplinary collaboration with clinical and basic scientists, (2) the design and implementation of prospective study design with involvement in the IPFnet,

(3) advanced study design and biostatistical methodology, and (4) focused mentorship and career development through the UCSF Clinical and Translational K Scholars (CTSK) program. In the following section, I present a detailed career development plan designed to enable me to acquire the additional training and mentored research experience I need to address these deficiencies and compete successfully for R01 funding, thereby achieving independence as a clinical investigator.

4. CAREER DEVELOPMENT/TRAINING ACTIVITIES DURING AWARD PERIOD

(1) Coordination of multidisciplinary research teams: I have had exposure to the disciplines of gastroenterology, radiology, and pathology throughout my medical school, residency, and fellowship training. In addition, I have had laboratory experiences during college, residency, and fellowship that have provided a broad understanding of laboratory technique and animal models of human disease. Although I have the basic foundation in these areas, I need more formal training in 4 key areas to successfully execute Aims 1 and 2 of my research plan. Effective clinical research requires close collaboration with a multidisciplinary team of clinical and basic researchers. It is critical that I develop an in-depth understanding of the relevance, potential contributions, and important limitations of various fields of clinical and basic science. This area does not lend itself to didactic coursework, so I have made the following plans to address this need:

Tutorials: I will work closely with my sponsor and primary mentor, Dr. King, on issues particular to collaboration and effective coordination of multidisciplinary teams. In addition, I have developed four tutorials with specific curricula in the areas of clinical medicine.

Gastroenterology tutorial (John Cello, MD): I will study gastroesophageal reflux disease with Dr. Cello, a renowned expert in the field of gastrointestinal disorders. The specific objectives of this tutorial are to understand the epidemiology, diagnostic evaluation, and management of gastroesophageal reflux disease. In addition, it will be important for me to understand the current literature on the diagnosis and clinical characteristics of gastroesophageal reflux disease, recognizing the limitations of the technology, which will be particularly important in successfully achieving Aim 1. I will meet with Dr. Cello monthly for the first year and every other month during the second and third year. During these meetings, we will accomplish several goals, including review of relevant literature, observation of endoscopy and 24-hour pH monitoring with manometry, and interpretation of pH and manometric recordings.

Basic science tutorial (Michael Matthay, MD): I will meet with Dr. Matthay, an internationally recognized expert in acute lung injury, from both a basic science and clinical research perspective, once a month to troubleshoot laboratory methods and discuss progress on my research project. This is particularly relevant to achieving Aim 2 of the research plan, which requires an understanding of the biologic mechanisms of lung injury, inflammation, and repair in the development of fibrosis. Dr. Matthay and I will also review the relevant literature in the field and discuss the advantages and disadvantages of various laboratory techniques.

Radiology tutorial (Wayne Webb, MD): I will study high-resolution computed tomography (HRCT) scanning of the chest with Dr. Webb, an internationally recognized expert of this field. The specific objectives of this tutorial are to understand the technical aspects and limitations of HRCT, to identify the typical radiographic pattern seen in IPF, and to understand the literature supporting the use of HRCT for diagnosis and management of IPF. Achieving these objectives will be particularly important in not only expanding my ability to recognize radiographic IPF but also in achieving Aim 1 of the research proposal, which uses radiologically diagnosed hiatal hernias as a risk factor for GER. This will be accomplished through review of a large number of HRCT images available electronically through Dr. Webb. I will meet with Dr. Webb monthly during the first year and quarterly during the second and third years of the research award. During these meetings, we will review cases that I have interpreted and discuss relevant literature.

Pathology tutorial (Kirk Jones, MD): I will study the preparation and interpretation of surgical lung biopsy specimens through structured tutorials with Dr. Jones, a recognized expert in this field. The specific objectives of this tutorial include understanding the technical aspects of tissue preparation and confidently identifying typical usual interstitial pneumonia, the histopathologic pattern seen in IPF in addition to recognizing signs of aspiration related lung disease. This tutorial is essential to achieving Aim 2 of the research plan, which requires an understanding of histopathologic signs of lung injury, inflammation, and repair. This tutorial will consist of reviewing a large number of cases with Dr. Jones on six occasions during the first two years of the award.

(2) Design and implementation of prospective studies and involvement with the IPFNet: My experience has been restricted to retrospective cohort studies; I have had little training in the methodology of prospective

cohort studies. To achieve Aim 3 of my research plan, I need to learn how to manage the longitudinal aspects of a cohort study design, including how to minimize loss to follow-up. Training in this area will be essential to my development as a clinical investigator. To address this need, I have made the following plans:

Coursework: In addition to completing the Master's program in clinical research through the UCSF Department of Epidemiology and Biostatistics, I will take another elective course called "Measurement in Clinical Research (EPI 225)". This course covers issues related to the identification, review, selection, and adequacy of outcome measures in clinical research.

Tutorials: I will work closely with my mentor, Dr. King, on issues particular to prospective clinical research. Dr. King will help me get involved in the IPFNet by including me in IPFNet conference calls and expanding my role as a site investigator in studies sponsored by the IPFNet. In addition, I will also participate in study visits and data collection of IPFNet studies. Lastly, I will have the opportunity to attend investigator meetings during which I will network with other IPFNet investigators. Dr. King will provide structured tutorial in subjects relevant to prospective cohort studies, such as successful subject recruitment, effective organization of study design, mechanisms to minimize loss to follow-up, and data collection. I will continue to meet with Dr. King to discuss these issues as well as my overall progress with my research project and career plans every two weeks. I will also participate in weekly interstitial lung disease lab meetings, as well as attend international meetings to present my research and learn about the work of others.

(3) Advanced study design and biostatistical methodology: I have had basic training in biostatistics and epidemiology during undergraduate coursework, medical school, residency, and fellowship. To further my training in biostatistics and epidemiology, I have enrolled in the Master's degree program in clinical research provided through the UCSF Department of Epidemiology and Biostatistics. My coursework and degree will be complete in June 2011. Advanced training, particularly through applied mentorship, will solidify my understanding of the advantages and disadvantages of various study design and biostatistical methods. This is a critically important skill for clinical investigators to master and will help me analyze the data obtained in all three aims of the research proposal. To address this need, I have made the following plans:

Coursework: I will complete my Master's degree coursework and take two elective courses through the UCSF Department of Epidemiology and Biostatistics to explore advanced topics in statistical methodology:

• BIOSTAT 210 Biostatistical Methods for Clinical Research IV (Fall, 2 units): This course is designed to cover topics related to individual students' research projects. In addition, it covers survey analysis, nonparametric regression techniques, and repeated measures analysis.

• BIOSTAT 226 Biostatistical Methods for Clinical Research V (Winter, 2 units): This course covers advanced topics related to the design and analysis of randomized clinical trials, as well as issues related to bioinformatics.

Tutorial: Dr. Mark Pletcher will provide structured mentorship in prospective study design methodology, data retrieval and entry, data preparation, and measurement of outcomes and endpoints. We will also cover the topics of power calculation, data preparation, descriptive statistics, two-group comparisons, regression, and time-to-event analysis. We will meet in person quarterly to discuss biostatistical principles relevant to my proposed and future research projects, including topics not covered in my coursework.

(4) CTSK Scholars Program: I will participate in the Clinical and Translational K Scholars (CTSK) Program, offered by the UCSF Department of Epidemiology and Biostatistics. The purpose of this program is to provide clinical and translational research training and mentored support to individuals with career development awards at UCSF. Key program elements include (1) weekly works-in-progress seminars, (2) weekly methodology seminars; and (3) expert epidemiologic and biostatistical guidance and the opportunity to receive extensive one-on-one feedback and suggestions on manuscripts and grant applications.

5. TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH

As part of the Masters Program in Clinical Research, I completed a course entitled "Responsible Conduct of Research". This course is designed to address the requirements of the National Institutes for Health for education of investigators about ethical issues in research involving human subjects. I have also completed on-line training courses required by the UCSF Committee on Human Research on research involving human subjects, laboratory safety, and handling of infectious specimens. I will maintain up-to-date certification throughout the award period.