PROJECT SUMMARY/ABSTRACT

This proposal represents a five-year curriculum and research plan designed to transition the candidate to an independent investigator in clinical research. During the five years the candidate will complete coursework relevant to the project and will execute the research plan.

Infection is one of the leading causes of morbidity and mortality in residents of long-term care facilities (LTCFs). As a result, LTCF residents are exposed to large numbers of antimicrobial agents but use of antimicrobials in LTCF residents is often suboptimal due to difficulty in distinguishing acute infection from colonization and due to the increased likelihood of inaccurate or inappropriate antibiotic prescribing in LTCF residents (for example due to increased presence of antimicrobial resistance).

The emergency department (ED) is a common site for treatment of infection in LTCF residents, particularly those most severely ill. Comprehensive programs to address problems of antimicrobial use for LTCF residents in the ED are currently lacking. The **conceptual framework** for the study is borrowed from the literature on antimicrobial stewardship programs (ASPs), empiric antibiotic treatment, and LTCF infection control guidelines. ASPs have been successfully implemented in inpatient populations to improve antimicrobial prescribing practices and outcomes with resulting decreases in resistance and side effects. This study expands their use to a high-risk ED population with the goal of incorporating both improved diagnostic accuracy and empiric antimicrobial prescribing. Current LTCF infection control guidelines recommend that acute infection be diagnosed in LTCF patients only when they meet specific criteria in order to differentiate active infection from colonization and prevent overuse of antibiotics. These guidelines were developed for use in the LTCFs themselves and have not yet been studied in the ED or inpatient settings. As failure to differentiate acute infection from colonization in the ED may lead to inappropriate antibiotic use, validating diagnostic guidelines in the ED setting is an important step towards appropriate antimicrobial stewardship. Another key concept of these studies is efficiency, driven primarily by Health Information Technology (HIT). In an era of limited resources utilizing pre-existing HIT systems and information will allow extension of ASPs to novel clinical settings and populations.

The majority of moderately- to severely-ill LTCF patients receive their initial diagnosis and initiation of antimicrobials in the ED. To improve care of this high-risk population, **our overall objective is to develop and implement an antimicrobial stewardship program (ASP) based on use of health information technology (HIT) for ED LTCF patients that will result in improvements both in accuracy of diagnosis and in correct antimicrobial prescribing**. To achieve this objective, we will conduct two projects with the following Specific Aims:

Specific Aim 1 (ED-observational): To develop a validated definition for acute infection and to identify antimicrobial stewardship needs in ED LTCF patients.

Specific Aim 2 (ED-interventional): To test the effect of implementing a health information technology (HIT)-based ASP for ED-LTCF patients on diagnosis and treatment of acute infection

For Specific Aim 1, the project (**SA1: ED-observational**) will consist of a prospective observational cohort study of ED LTCF patients. It will be used to validate definitions for the presence of acute infection in ED LTCF patients (as distinct from colonization), establish baseline rates of need for ASP interventions, and develop data required to construct specific antimicrobial recommendations and an ASP for ED LTCF patients.

For Specific Aim 2, a prospective, interventional trial (**SA 2: ED-interventional**) will be conducted in which an ASP program tailored to ED LTCF patients will be devised and implemented. This phase will rely on the use of a real-time web-based health information technology (HIT) decision support tool to provide the intervention. It will include factors such as the suggested algorithms for diagnosing an acute infection in LTCF patients, a newly developed antibiotic by site grid, patient specific past culture results, patient specific data on hepatic and renal function with recommended dosing, and formulary restrictions. Outcomes will include accuracy of diagnosis, appropriateness of empiric antibiotics, and ongoing requirements for ASP intervention.

The career development plan will include didactic work in advanced biostatistical techniques useful in conducting these studies. Coursework will also be undertaken in specific aspects of aging studying biology of aging and challenges in aging research. It will also include a significant component studying the application of health information technology including didactic coursework, online coursework, and practical experience to allow completion of the proposed research and position the candidate for further studies.

Based on the results achieved, it will be possible to develop validated and reproducible interventions to improve antimicrobial stewardship in a variety of settings. The proposed projects and career development plan will provide an important initial step towards the ultimate goal of improving care for residents of LTCFs.

Project Narrative Public Health Relevance

This research addresses antimicrobial stewardship in nursing home patients, an important means of combating antimicrobial resistance which is a significant and increasing threat to public health. By developing novel technology-based techniques to improve information available and provide decision support to physicians in emergency department the project will ultimately improve accuracy of antibiotic treatment in elders.

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Caterino, Jeffrey M.	POSITION TITLE Assistant Professor of Emergency Medicine and Internal Medicine
eRA COMMONS USER NAME jcaterino	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Dartmouth College , Hanover, NH	B.A.	1995	History
The Pennsylvania State University College of Medicine, Hershey, PA	M.D.	1999	Medicine
Allegheny General Hospital, Pittsburgh, PA	Residency	1999-2004	Combined Emergency/ Internal Medicine

Employment

1999-2004	Resident, Departments of Emergency Medicine and Internal Medicine, Allegheny General Hospital, Pittsburgh, PA. Dennis Hanlon, MD, Residency Director.
2003-2004	Chief Resident, Departments of Emergency Medicine and Internal Medicine, Allegheny General Hospital, Pittsburgh, PA.
2003-2004	Department of Emergency Medicine, The Medical Center, Beaver, PA. John Luellen, MD. Department Chairman.
2004-present	Assistant Professor, Departments of Emergency Medicine and Internal Medicine, The Ohio State University, Columbus, OH. Douglas Rund, MD, Department Chairman. Tenure track.
2005-present	Director, OSU Emergency Department Undergraduate Research Associate Program
2006-2008	Ohio Department of Public Safety, Trauma Committee, Geriatric Trauma Triage Workgroup
2008-2009	Geriatrics Task Force, Society for Academic Emergency Medicine

Honors

1999	Penn State University Medical Student Research Symposium Award
1999	Penn State University Emergency Medicine Faculty Senior Medical Student Award
1999	Society for Academic Emergency Medicine Excellence in Emergency Medicine Award
2001-2002	Emergency Medicine Foundation Resident Research Grant
2002	Finalist, Golden Apple Medical Student Teaching Award, Allegheny General Hospital
2003	First Place Poster, William H. Spivey Research Competition, Pennsylvania ACEP Annual Meeting, Pittsburgh, PA
2003	Second Place Oral Presentation, 2003 Allegheny General Hospital Resident Research Day
2004	Second Place Oral Presentation, 2004 Allegheny General Hospital Resident Research Day
2007	Faculty Researcher of the Year. The Ohio State University Department of Emergency Medicine
2009	Fellow, American College of Emergency Physicians

Professional Societies and Public Advisory Committees

1997-present	American College of Emergency Physicians
1999-present	Society for Academic Emergency Medicine
2004-present	American College of Physicians
2005-present	American Geriatrics Society

Publications

Original Publications
Caterino JM, Holliman CJ, Kunselman AR. Underestimation of disease severity by emergency department patients: implications for managed care. *Am J Emerg Med* 18(3), May 2000: 254-256. PMID 10830677.

Caterino JM, Scheatzle M, D'Antonio J, Forbes MF. Bacteremic elder emergency department patients: procalcitonin and white count. Acad Emerg *Med* 2004; 11(4): 393-396. PMID:

Caterino JM, Emond JA, Camargo CA. Inappropriate medication use among the acutely-ill elderly: A nationwide emergency department study, 1992-2000. *J Am Ger Soc* 2004; 52:1847-1855. PMID: 15507061.

Caterino JM, Scheatzle MS, D'Antonio JAD. Descriptive analysis of 258 emergency department visits by spina bifida patients. *Am J Emerg Med* 18(3), May 2006: 254-256. PMID: 16798148

Caterino JM, Hiestand BC, Martin DR. Quality of care in elder emergency department patients with pneumonia: a prospective cohort study. *BMC Emerg Med.* 2008 Apr 30;8:6. PMID: 18447936.

Caterino JM, Weed SG, Espinola J, Camargo CA. National Trends in Emergency Department Antibiotic Prescribing for Elders with Urinary Tract Infection, 1996-2005. *Acad Emerg Med*; 2009; 16:500-507. PMID:19245373

Caterino JM, Kulchycki LK, Fischer CM, Wolfe RE, Shapiro NI. Risk Factors for Death in Elder Emergency Department Patients with Suspected Infection. *J Am Ger Soc,* 2009; 57(7):1184-90. PMID: 19558478

Caterino JM, Karaman R, Arora V, Martin JL, Hiestand BC. Comparison of Balance Assessment Modalities in Emergency Department Elders: A Pilot Cross-Sectional Observational Study. *BMC Emerg Med* 2009, 9:19. PMID: 19785763

Caterino JM, Vasalek T, Werman HA. Identification of an Age Cutoff for Increased Mortality in Elder Trauma Patients. *Am J Emerg Med;* in press

Caterino JM, Jalbuena T, Bogucki B. Predictors of Acute Decompensation after Admission in Emergency Department Patients with Sepsis. *Am J Emerg Med;* in press

Non-Experimental Articles and Book Chapters
Caterino JM. Pulmonary Medicine. Kahan S, ed. *In a Page Medicine.* Malden, MA, Blackwell Publishing, 2002.

Caterino JM, Kahan S, eds. *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Caterino JM, Zimmerman HW, Driver R, Washington LC. Environmental Emergencies. Caterino JM, Kahan S, eds: *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Caterino JM. Traumatic Emergencies. Caterino JM, Kahan S, eds: *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Perkins J, Kahan S, **Caterino JM**. Resuscitation. Caterino JM, Kahan S, eds: *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Davis M, **Caterino JM**. Opthalmologic Emergencies. Caterino JM, Kahan S, eds: *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Wahan S, **Caterino JM**. ENT Emergencies. Caterino JM, Kahan S, eds: *In a Page Emergency Medicine.* Malden, MA, Blackwell Publishing, 2003.

Caterino JM. Evaluation and Management of Geriatric Infections in the Emergency Department. *Emerg Med Clin N Am* 2008; 26 (2): 319–343. PMID 18406977.

Caterino JM. Sepsis. Katz G, Moseley, M. eds: *Emergency Medicine's Top Clinical Problems.* Irving, TX, Emergency Medicine Residents' Association (EMRA), 2008.

Katz G, Moseley M, **Caterino JM.** A Physician Led Intervention Improves Coding Distribution and Reimbursement in an Academic Emergency Medicine Group. *Physician Executive: Journal of Medical Management;* in press.

Research Support

Ongoing

"Novel techniques for identification of antimicrobial resistance patterns and prediction of susceptibility in long term care facilities." The Ohio State University Department of Emergency Medicine Strategic Initiative Grant. Role: Principal Investigator, 7/01/2009-6/30/2010. Project goals: To characterize and identify antimicrobial resistance patterns in LTCF patients presenting to the ED with focus on differences from the general hospital population.

"Infected elders in the ED: Outcome and processes of care." Clinical Research Loan Repayment Program, NIH. Role: Principal investigator. 7/01/2006-6/30/2010.

"Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) U01 (University of Massachusetts, Primary Site). NIMH, NIH. Role: Subcontract Site -9/30/09-5/31/14 Project goals: Develop a standardized ED screening for suicidal ideation and test whether it increases detection of suicidal ideation/ behavior compared to usual care.

Completed

"Evaluation of serum procalcitonin in systemic bacterial infections among emergency department patients 65 years of age and older." Emergency Medicine Foundation Resident Research Grant. 2001-2002. Role: Principal investigator. Project goal: A prospective observational study which identified laboratory and clinical predictors of bacteremia in elderly ED patients.

"Infected elders in the ED: Outcome and processes of care." The Ohio State University Strategic Initiative Grant. Role: Principal investigator. 3/01/2006-2/28/2007; renewed for 6/01/2007-5/30/2008 and for 7/01/2008-6/30/2009. Project goals: To identify geriatric-specific predictors, including functional status, of adverse outcome in Emergency Department patients admitted with severe infections. Provides additional funding for protected time required by the AGS Jahnigen Grant.

"Usefulness and Accuracy of the Field Glasgow Coma scale in Elderly Trauma Victims", Ohio Department of Public Safety Trauma Grant,. Role: Principal investigator. 9/01/2007-9/30/2008. Project goals: To determine the optimum age cutoff for identifying elderly trauma victims. To determine the usefulness of GCS as a criterion for trauma center activation in injured elders and to identify areas for intervention to ensure its accurate use.

"Validation of the Simplified Motor Score in a State Trauma Registry", Ohio Department of Public Safety Trauma Grant, Role: Principal Investigator, 9/01/2008-8/31/2009.Project goals: To evaluate the utility of the Simplified Motor Score as compared to the Glasgow Coma Score in Ohio trauma patients, with special focus on elderly trauma victims.

*"Predictors of Clinical Course in Infected ED Elders".*American Geriatrics Society/John A. Hartford Foundation. Dennis W. Jahnigen Career Development Scholars Award. 7/01/2007-6/30/2009. Project goals: To identify geriatric-specific predictors, including functional status, of adverse outcome in Emergency Department patients admitted with severe infections.

RESEARCH PLAN

Section 10: Specific Aims Infection is one of the leading causes of morbidity and mortality in residents of long-term care facilities (LTCFs)(1). As a result, LTCF residents are exposed to large numbers of antimicrobial agents. Use of antimicrobials in LTCF residents is often suboptimal for several reasons. First, it is often difficult to ensure that an acute infection is actually present given the common presence of chronic colonization with pathogenic microorganisms in LTCF residents (2). Second, elders are at particularly high risk of inaccurate or inappropriate antibiotic use due to several factors such as increased antimicrobial resistance (complicating antibiotic choice) and need for dose-adjusted antibiotics (e.g., due to renal dysfunction) (1;3).

   Infection may be treated in several clinical arenas including the LTCF itself, the emergency department (ED), and the inpatient setting. Comprehensive programs to address problems of antimicrobial use for LTCF residents in the ED are currently lacking. The **conceptual framework** for the study is borrowed from the literature on **antimicrobial stewardship programs (ASPs)**, empiric antibiotic treatment, and LTCF infection control guidelines (1;4). ASPs have been successfully implemented in inpatient populations to improve antimicrobial prescribing practices and outcomes with resulting decreases in resistance and side effects (4). This study expands their use to a high-risk ED population with the goal of incorporating both improved diagnostic accuracy and empiric antimicrobial prescribing. Regarding accuracy of diagnosis in acute infection, current LTCF infection control guidelines recommend that acute infection be diagnosed in LTCF patients only when they meet specific criteria in order to differentiate active infection from colonization and prevent overuse of antibiotics (2). These guidelines were developed for use in the LTCFs themselves and have not yet been studied in ED or inpatient settings. As failure to differentiate acute infection from colonization in the ED may lead to both overuse of antibiotics and to failure to search for alternative diagnoses, validating diagnostic guidelines in the ED is an important step towards appropriate antimicrobial stewardship.

   The majority of moderately- to severely-ill LTCF patients receive their initial diagnosis and initiation of antimicrobials in the ED. To improve care of this high-risk population, **our overall objective is to develop and implement an antimicrobial stewardship program (ASP) based on use of health information technology (HIT) for ED LTCF patients that will result in improvements both in accuracy of diagnosis and in correct antimicrobial prescribing**. To achieve this objective, we will conduct two trials. The first (**SA1: ED-observational**) will consist of a prospective observational cohort study of ED LTCF patients. It will be used to validate definitions for the presence of acute infection in ED LTCF patients (as distinct from colonization with microorganisms), establish baseline rates of need for ASP interventions, and develop data required to construct specific antimicrobial recommendations and an ASP for ED LTCF patients. This will be followed by a second trial (**SA 2: ED-interventional**) in which an ASP program tailored to ED LTCF patients will be devised and implemented. This phase will rely on the use of a real-time web-based health information technology (HIT) decision support tool to provide the intervention. A key concept of these studies is efficiency, driven primarily by Health Information Technology (HIT). In an era of limited resources, utilizing pre-existing HIT systems and information will allow extension of ASPs to novel clinical settings and populations. The proposed studies will have the following Specific Aims and Hypotheses to meet the overall objectives:

Specific Aim 1 (ED-observational): To develop a validated definition for acute infection and to identify antimicrobial stewardship needs in ED LTCF patients.

   Hypothesis 1a: In ED LTCF patients, current diagnostic guidelines developed for use in LTCFs demonstrate good or very good agreement with ultimate determination of presence of acute infection by subsequent treating physicians.

   Hypothesis 1b: In ED LTCF patients, ED physician diagnosis of acute infection demonstrates fair or worse agreement with currently available LTCF diagnosis guidelines.

   Hypothesis 1c: A clinically significant portion of ED LTCF patients with infection (>20%) would benefit from action through an ED-based ASP program.

Specific Aim 2 (ED-interventional): To test the effect of implementing a health information technology (HIT)-based ASP for ED-LTCF patients on diagnosis and treatment of acute infection

   Hypothesis 2a: Implementation of an ASP will improve the accuracy of diagnosis of acute infection in ED LTCF patients.

   Hypothesis 2b: Implementation of an ASP will increase the percentage of patients receiving appropriate empiric antibiotic therapy in ED LTCF patients.

   Hypothesis 2c: Implementation of an ASP will decrease the percentage of patients requiring pharmacist review and recommendation of empiric antibiotic therapy in ED LTCF patients.

Candidate's Background

My current goal of developing a clinical research career in the study of infectious disease in elders is attributable to a continuum of experiences over my career. I consciously chose to study at a liberal arts college to ensure a broad base in my education. This led to my matriculation at Dartmouth College and major in History. My first clinical research experience was with an emergency physician Jim Holliman, MD at the Penn State College of Medicine which awakened an unexpected interest in clinical research. I completed a clinical research project which consisted of a survey of ED patients to determine if they were able to correctly stratify the urgency of their presenting medical condition. This was my first exposure to constructing a focused scientific enquiry, designing an appropriate study, and interpreting data. Through it, I acquired not only an appreciation for the difficulty and complexity of clinical research but also for the sense of accomplishment with completion and publication of such a project. This experience led to my desire to continue with clinical medical research as a key element in my career.

The next step in career evolution came through clinical time spent in my dual emergency/internal medicine residency. The broad exposure of a dual residency helped me to appreciate the important role that decisions made in individual clinical settings play in ultimate patient outcome. For example, ED antibiotic choice strongly shapes an admitted patient's hospital course. This clinical experience prepared me for studying patients across care continuums. During residency, my particular interest in geriatrics and infectious disease started as the result of work undertaken for a grant from the Emergency Medicine Foundation. In conducting a study to identify markers of bacteremia in elders, I had my first exposure to the inadequacies in the geriatrics literature and the need studies conducted by investigators with geriatrics expertise became clear.

After residency, I continued working clinically in both the ED and inpatient internal medicine setting, reinforcing the observations I had made during residency. I have also come to realize that one of the most effective ways to improve care is to develop automated processes of care. As part of medical center committees responsible for creating and implementing guidelines for both sepsis and pneumonia, I have noted the tremendous investment of resources required to identify deficiencies and implement change. Such resources will not be available in many institutions, particularly long-term care facilities (LTCFs). This has led to my interest in leveraging already existing information using health information technology (HIT) resources and applying it to a variety of clinical settings.

My clinical research experience has continued its geriatric focus, including through an American Geriatrics Society Jahnigen Career Development Award. We are conducting a clinical study attempting to identify the role of functional status in predicting outcome in infected elders. Conduct of this study has reinforced my appreciation for the complexity of caring for elders with infection and of the paucity of current data. In examining the large number of variables that affect outcome, the need for an HIT solution to improve patient care has become even more apparent. This project has allowed me to form contacts within the Medical Center and demonstrated the power of an intra-departmental team for advancing research. These include a number of specific relationships to be relied upon going forward, including with the mentors on this proposal.

Both in residency and at Ohio State, I have sought out additional training in clinical research methodology. During residency, this included a 6-month "mini-fellowship" in clinical research which provided initial formal training in the design and conduct of clinical research as well as basic biostatistics. However, the initial work towards the MPH degree has resulted in great increases in my knowledge of study design, including significant training in statistical methods.

In conclusion, by virtue of previous clinical and research experiences I have developed a strong, sustained clinical research program focused on infectious diseases in elders. I have obtained both practical and theoretical experience in the conduct of clinical research and biostatistical analysis. A team of collaborators has been developed which will be of significant benefit for the proposed projects. The proposed series of projects and career development activities will ideally position me to advance to becoming an independent investigator in the study of infectious disease in elders.

Career Development/Training Activities During Award Period

The candidate's ultimate career goals is to use the health information technology (HIT) resources of a large medical center to increase the accuracy of diagnosis of acute infection and to improve antimicrobial prescribing for long-term care facility (LTCF) patients across a variety of clinical settings. The proposed projects are designed to validate diagnostic guidelines and establish an Antimicrobial Stewardship Program (ASP) for LTCF patients presenting to the emergency department (ED). Eventually, the goal is to expand a similar computerized decision-support ASP to other clinical settings such as the LTCFs themselves. To implement these plans will require the candidate to acquire additional experience and training in several areas. This training, when combined with the preliminary data obtained in this grant, will allow the candidate to design and implement future studies in this area as well as be competitive in applications for external funding.

The candidate's **first career development goal** is to **obtain additional formal training in the design and conduct of clinical research in elders** as a means towards more completely studying antimicrobial stewardship in LTCF residents. This will include training in advanced epidemiologic and biostatistical methods as well as training in biology and issues of aging. The **second career development goal** is to **develop new skills in using medical informatics and health information technology (HIT)** as tools towards developing systems for implementing antimicrobial stewardship. Both goals will be accomplished by relevant training in ethical conduct of human subjects research.

Table 1: **Main career development goals and the associated supervisors**.

Career Development Goal	**Mentor/Supervisor**
• Acquiring skills in the design and conduct of clinical research in LTCF relating to acute infections including ethical conduct and statistical analysis • Acquire skills and knowledge in specific aspects of clinical research in aging adults • Acquire statistical skills useful for future interventional trials in LTCF residents (e.g. group randomized design)	• **Kurt Stevenson, MD** (Mentor and sponsor): Study design and progress, coursework • **Stanley Lemeshow, PhD**: (Co-Mentor): Study design and Progress, data analysis, biostatistics coursework • **Gowrishankar Gnanasekaran, MD, MPH** (collaborator): Specific aspects of aging research • **Carson Reider, PhD** (collaborator): Ethical conduct of research
• Acquiring skills in integrating, utilizing, and developing health information technology systems	• **Kurt Stevenson, MD, MPH** (Mentor and sponsor): Study design and Progress, techniques of HIT utilization • **Tara Borlawsky-Payne, MA** (collaborator): HIT and informatics utilization

Goal 1 - Formalized research training: For the first goal of formalized research training, the candidate will take course work from the College of Public Health. Drs. Stevenson and Lemeshow, the mentors responsible for supervising this goal, have combined expertise in epidemiology, outcomes research, and clinical prediction modeling, and are well-positioned to facilitate the Candidate's growth. Dr. Stevenson, the primary mentor, holds an additional appointment in the College of Public Health, teaches a class on ID epidemiology, and will serve as the candidate's academic advisor. Dr. Lemeshow, Dean of the College of Public Health, will also supervise completion of the coursework. Under an American Geriatrics Society Jahnigen Career

Table 2: MPH coursework completed by Winter 2010	
PUBH-BIO 701: Design and Analysis of Studies in the Health Sciences PUBH-BIO 702: Design and Analysis of Studies in the Health Sciences II PUBH-BIO 703: A problem-oriented approach to biostatistics	PUBH-EPI 710: Principles of Epidemiology PUB HLTH 793 Indiv. Studies in Public Health PUBH-EPI 711: Epidemiology I PUB HLTH 685 Field Experience in Public Health PUBH-BIO 606: Applied Logistic Regression PUB HLTH 850 Seminar in Clinical Investigation

Development Grant, the candidate is currently pursuing coursework towards a Master of Public Health in Clinical Investigation. By winter of 2010, the candidate has completed 42 credit hours of the 60 needed for the degree (Table 2). Coursework completed during the K23 will result in completion of the MPH degree.

Formal coursework is outlined in Table 3 and includes elements designed to advance knowledge in **biostatistics, aging, and HIT**. The **biostatistics** focus will be on developing expertise in techniques useful for designing and conducting studies of antimicrobial stewardship among ED and LTCF patients. They will facilitate both analysis of the current proposal's data as well as the design and conduct of future studies. Infectious Disease Epidemiology will aid in the interpretation and data analysis phase of the current study. Future studies of LTCF patients will include longitudinal outcome measures as well as involve multiple LTCFs.

Group-Randomized Design will be crucial to the conduct of future interventional trials of ASPs in LTCFs where the intervention is stratified at the level of the institution. Outcomes in LTCF patients will be measured over time, therefore a class in Applied Survival Analysis is planned. In the end, the candidate will have developed expertise to conduct interventional trials using HIT in LTCF patients and to study outcome measures over time.

Coursework in **aging research methods** is designed to provide exposure to various elements important to the candidate's research. Two courses (Anth 820.18 and 640.05) will provide knowledge in aspects unique to geriatric research such as concepts of frailty, senescence, environment, and epidemiology of aging. Specific coursework in the management in the long term care environment will inform the candidate's future work intending to involve LTCFs directly. Finally, completion of a course in pharmaceutical care is directly relevant to study of the currently proposed antimicrobial stewardship program.

Table 3: Proposed Public Health curriculum to accomplish career development goal #1				
	Autumn Quarter	**Winter Quarter**	**Spring Quarter**	**Summer Quarter**
1st year		BMI-710: Introduction to clinical informatics	Anth 820.18: Research issues in gerontology	
2nd year			PUBH-EPI 815: Infectious Disease Epidemiology	
3rd year		PUBH-HSMP 841: Long-term care management	Anth 640.05: Biology of Senescence	
4th year		PUBH-BIO 605: Applied Survival Analysis	Pharmacy 760: Geriatrics -- Pharmaceutical Care	
5th year		PUBH-EPI 821: Design and Analysis of Group-Randomized Trials		

Goal 2 – To develop skills in medical informatics and health information technology (HIT): The growing availability of large HIT database infrastructure provides an opportunity to facilitate investigations of AR by integrating information and providing analyses across a spectrum of clinical settings. The goal is to develop skills in use of medical informatics for clinical research. This goal will be under the overall supervision of Dr. Stevenson who has extensive experience in using IT across a variety of clinical settings, including LTCFs. Tara Borlawsky-Payne from the OSUMC CCTS' Bioinformatics Core will serve as a collaborator in the mechanics of using and developing HIT systems.

Three methods will be used to acquire the relevant expertise. **First**, the candidate will complete the course "BMI-710 Clinical Informatics" which is taught by Dr. Philip Payne, director of the CCTS BMI and which covers the design, implementation, and management of clinical information systems. **Second,** three training classes offered through the IW will be completed which will cover the type of data stored in the IW, data sources, demonstration of the IW query tool, queries and sub-queries, and use of order entry data including the type of data stored and practice queries. **Third,** the candidate will acquire additional didactic training by attending the annual meetings of the American Medical Informatics Association (AMIA) and will take part in AMIA online educational courses such as the AMIA 10x10 program, a distance learning program which utilizes curricular content from existing informatics training programs and which covers "areas such as electronic and personal health records, health information exchange, standards and terminology, and health care quality and error prevention." (www.amia.org/10x10). Course specific to medical informatics utilization are offered. **Fourth,** additional training in HIT skills will be obtained during the conduct of the proposed project which will provide significant experience in using HIT for data queries and constructing custom applications incorporating multiple data applications. The project experience will provide the candidate with familiarity with the advantages and problems inherent in creating novel health information technology systems involving multiple clinical sites and health systems. This will provide a model for future endeavors of the candidate.

In conclusion, the accomplishment of these career objectives will take focused effort and support over a five-year period. The career development plan will provide expertise based on classroom work in biostatistics, aging, and HIT as well as practical use of HIT systems. The mix of skills obtained by the conclusion of this funding period complement each other and will allow the Candidate to function as an independent clinician scientist in the area of AR in elders with focus on using HIT to identify problems and effect change. The Candidate's long-range objective will be to maintain NIH funding after this period (via R01) and sustain continued studies in this area. The proposed schedule of research activities is noted in Table 4.

Table 4: **Proposed schedule** for the accomplishment of the Specific Aims in the context of the Career Development objectives.

	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**

Clinical trials	Conduct of Specific Aim 1				Write RO1 based on preliminary data
			Conduct of Specific Aim 2		
Career development	College of Public Health statistical and aging coursework				
	Informatics course		AMIA courses and conferences		
	Protection of human subjects training				

Mentoring Plan

The candidate's mentoring plan includes the assignment of both specific responsibilities and time expectations from each of the mentors. The combined mentors have the expertise to design, conduct and interpret clinical research in the study settings as well as ensure the proper training of the candidate. The mentors include individuals possessing expertise in antimicrobial stewardship both in acute care settings and LTCFs (Dr. Stevenson); in the statistics required for logistic regression analysis (Dr. Lemeshow); in the integration of HIT with clinical research (Ms. Borlawsky-Payne); and in ethical issues (Dr. Reider).

Dr. Kurt Stevenson will serve as the primary mentor and sponsor for the candidate. He will oversee the conduct of the clinical trials including design and data analysis. He will be directly responsible to ensure the selected didactic curriculum meets the career development goals and be responsible to mentoring the candidate regarding career advancement within the institution. Dr Stevenson brings extensive experience in epidemiologic research including the study of AR among elders, use of LTCFs in clinical research, and use of HIT resources to integrate data from multiple institutions including LTCFs. He has previously received funding to carry out several multi-center projects with characteristics similar to those proposed here. These include a multi-center study of 77 rural hospitals to assess infection control and microbiology lab practices (4). They also include a CMS-funded project to improve antimicrobial use in 17 LTCFs, and a CDC-funded project to conduct surveillance for drug-resistant organisms at 51 rural hospitals (5;6). Dr Stevenson is head of the OSUMC Antimicrobial Stewardship Program and the PI of the Ohio State Health Network Infection Control Collaborative (OSHNICC), a federally funded multi-center project (CDC Prevention Epicenters) using OSU HIT systems to connect rural acute-care hospitals with a tertiary-care center for purposes of infection surveillance. Thus, Dr. Stevenson has the expertise both to guide the proposed clinical projects and to oversee the training program of the candidate. In addition, Dr. Stevenson has an extensive record of actively and effectively mentoring junior investigators (junior faculty, fellows, residents, MPH and medical students) which will serve the candidate well.

The candidate and Dr Stevenson have collaborated on several research projects and OSUMC clinical epidemiology projects over the past 4 years. In the area of research collaboration, Dr. Stevenson has served for the past two years as the primary mentor on the candidate's Dennis W. Jahnigen Career Development Award. In his role as mentor, Dr. Stevenson has overseen the coursework for the candidate's MPH degree. He has also overseen the design, conduct, and analysis of the related clinical research project (see Preliminary Studies section). As a planned continuation of this mentoring relationship, the candidate has been incorporated as a key component of Dr. Stevenson's recently submitted K24 mentoring grant application. As a result, the candidate's current proposal is heavily integrated with Dr. Stevenson's ongoing work. The candidate's proposal provides a novel and significant extension of the current inpatient antimicrobial stewardship work by incorporating the ED, specifying LTCF patients, and providing real-time IT based clinical decision support. Clinical projects have included collaboration on the OSUMC Antimicrobial Management Committee and various University Health Consortium sepsis initiatives. Through these previous collaborations, an extensive mentoring relationship has already been developed.

To achieve an appropriate level of supervision, Dr Stevenson agrees to **meet with the candidate every two to four weeks** and be available to the candidate *at all times* as necessary during the clinical study's execution. Examples of Dr. Stevenson's planned role in mentoring include: **a)** study design, specifically epidemiologic and practical considerations, **b)** statistical analysis, data interpretation, and manuscript preparation, **c)** utilization and integration of clinical research with HIT systems such as the IW, **d)** designing future studies and preparing future grant applications, and **e)** assuring the academic productivity and the ultimate promotion of the candidate. Dr Stevenson's extensive activity and experience in the areas addressed in this proposal are critical to ensuring the proper design and execution of the research trial and in securing an adequate educational and mentoring experience for the candidate. This collaboration with Dr. Stevenson will facilitate the candidate's successful transition to independent investigator status.

Stan Lemeshow, PhD is the Dean of the School of Public Health and Director of the Center for Biostatistics at the Ohio State University. Dr. Lemeshow will serve as the **co-mentor and the primary consultant for**

biostatistics to oversee the statistical aspects of the clinical trial including study design and data analysis. In addition, he will provide direction in selecting appropriate coursework to meet the career development goals. Dr Lemeshow brings with him extensive experience in outcomes research and in mentorship of junior faculty. He is a world-renowned expert on the use of logistic regression, particularly in the development of outcome-assessment models. For example, he has been integral to the development of two of the major severity of illness measurement tools used in ICU research (MPM and SAPS II). Dr Lemeshow also commands the full resources of the School of Public Health to assist in the educational and research objectives of the candidate. His extensive experience will ensure that the studies are well thought out and interpreted. The candidate and Dr. Lemeshow have an established relationship through interactions in the MPH degree program. The candidate has completed two courses with Dr. Lemeshow including Design and Analysis of Studies in the Health Sciences and Advanced Logistic Regression. This has resulted in the establishment a professional and collaborative relationship which will facilitate the proposal. To ensure oversight of the Candidate and the research plan, Dr Lemeshow will **meet with the Candidate monthly** to review the research plan and analysis.

Tara Borlawsky-Payne, MA will serve as a collaborator on this project in the areas of biomedical informatics and health information technology. Ms. Borlawsky-Payne is an Instructor in the Department of Biomedical Informatics and the Knowledge Engineer for the CCTS' Biomedical Informatics Core. She has particular expertise in the construction of surveillance systems for nosocomial infections having collaborated extensively with Dr. Stevenson over the past several years. These systems are similar to the proposed decision-support algorithms and so this past experience places her in an excellent position to guide the candidate through the training and research aspects of the proposal. Her specific role will include aiding the candidate in understanding and utilizing the HIT systems at OSUMC including REDCap, the information warehouse, and enterprise electronic medical record system and in the design of the proposed decision-support tool. Due to the intensive informatics nature of the project, Ms. Borlawsky-Payne will meet **every other month** with the candidate. These meetings will be more frequent in periods where design and implementation of specific IT aspects of the study is necessary, for example during design of the clinical decision support tool.

Gowrishankar Gnanasekaran, MD, MPH will serve as a collaborator on the project bringing specific expertise in health issues in older adults and LTCF patients. Dr. Gnanasekaran is an Assistant Professor of Internal Medicine who is board-certified in both Internal Medicine and Geriatrics. His clinical and research expertise extend to the specifics of disease in an elder population. He will meet with the candidate **every other month** to review aging-specific aspects of the research, to suggest new methodologies, variant ways of considering data, and additional aspects of infection in elders which will inform the conduct and analysis of the research.

Carson Reider, PhD will serve as a consultant in the area of human subjects protection. As the Research Subject Advocate for the CCTS, Dr. Reider has extensive experience in the area of human subject protection. He has a long track record in the education and oversight of investigators, particularly junior investigators, and study personnel. He has worked with the candidate on the current Jahnigen Grant. Through **quarterly meetings**, Dr. Reider will be responsible for overseeing ethical conduct of the research, ensuring completion of the relevant portions of the training plan, and focusing on issues of consent in impaired persons.

The team of mentors has extensive collaborative experience. Drs. Stevenson and Ms. Borlawsky-Payne have worked extensively on the OSUMC Antimicrobial Stewardship Program resulting in several joint publications and an ongoing relationship using BMI HIT resources to facilitate antimicrobial stewardship at OSUMC. Drs. Lemeshow and Ms. Borlawsky-Payne are collaborators on Dr. Stevenson's Epicenter project. Dr. Stevenson also has an appointment to the College of Public Health of which Dr. Lemeshow is the Dean. To ensure that the group is coordinated in advancing the candidate's research plan and career, a **quarterly mentor meeting will take place involving the candidate and both mentors (Drs Stevenson and Lemeshow) with other collaborators involved as necessary.** At these meetings the candidate will report progress on training and clinical research goals, will submit written goals for the upcoming quarter, and will review progress on the previous expectations. The review will focus the candidate on achieving the specific aims of his research and career development plan. This plan represents will result in the Candidate's growth professionally and, given the prior relationships of the people involved is highly likely to be successful.

Description of Institutional Environment
The research environment in which this proposal will be executed is active and vibrant. The proposal utilizes the combined resources of the Department of Emergency Medicine, Department of Clinical Epidemiology, the Center for Clinical and Translational Sciences (Biomedical Informatics and Research subject advocate), Information Warehouse, and the College of Public Health. The candidate has previously established working relationships and collaborations with all of the entities involved in this work on his current American Geriatrics Society grant as described above. The assembled group of mentors has a long track record of advising young investigators and will be able to provide access to the resources and expertise for successful completion of the proposed studies and career development plan. The CCTS' Biomedical Informatics Core (especially Ms. Borlawsky-Payne) and Research Subject Advocate will serve as invaluable resources in data management and ethical conduct of research as evidenced by their current collaborations with the candidate. Likewise, the mentoring planned with Drs. Stevenson and Lemeshow through the Department of Clinical Epidemiology and the College of Public Health respectively will provide the background for successful completion of the clinical research and biostatistical portion of the proposal. The primary mentor, Dr. Kurt Stevenson has extensive experience in study of antimicrobial resistance and infection control. This includes the conduct of several funded multi-center trials in long-term care facilities. At OSUMC, he currently heads the Antimicrobial Stewardship Program and the CDC-funded Epicenter, which studies techniques of infection control and limiting spread of AR at multiple small, rural hospitals using the OSU information warehouse as a central data repository. Dr. Stevenson also has extensive experience mentoring young investigators. Dr. Lemeshow as Dean of the College of Public Health has extensive experience in mentoring young investigators. He is an international expert on conducting the analyses described in the projects. Dr. Gnanasekaran brings expertise in clinical geriatrics as well as clinical research in elders.

The Department of Emergency Medicine's clinical site is a strong clinical environment with over 70,000 patient visits yearly, almost 7% of whom are elders. The Department is a strong supporter of clinical research and junior investigators. **The department as part of its commitment to the candidate has recognized clinical geriatrics as one of four areas of emphasis in its expansion of its clinical research programs.** In 2007-2008, department investigators have 22 publications, over 20 abstracts at national meetings, and over $400,000 in total external research funding. The Department actively supports young investigators through protected research time and an internal grant mechanism, the Strategic Initiative Grants, of which the candidate has received several. These grants are used to provide seed money to young investigators as well as provide additional support required to meet the requirements of externally-funded training grants. An estimated $150,000 will be made available in FY2010. In support of clinical research, the Department supports a full-time research coordinator and full-time research nurse. In addition, the Department supports the Undergraduate Research Associate program. The success of this program is shown by the fact that, during winter quarter 2009, over 200 patients were consented and enrolled in ED clinical trials over an 8 week period. All together, this represents a formidable display of assets and a core of people to nurture the scientific environment in which the Candidate is developing. The Department has successfully supported multiple research fellows over the past decade. These efforts demonstrate the financial and infrastructure commitment of the Department to young investigators to nurture career development awards.

The Ohio State University provides excellent resources for the candidate's didactic training. These resources have already been and will continue to be made available to the candidate. Dr. Caterino has devised a detailed plan in conjunction with Drs. Stevenson and Lemeshow that includes extensive coursework following a stepwise progression of expertise. The College of Public Health has the necessary resources to ensure that this program is successfully carried out. Additional components of the plan such as BMI Core of the CTSA-funded CCTS have extensive experience in facilitating clinical research and in mentoring young investigators. The candidate will have the statistical expertise, information technology systems, database support, and human subject protection support to successfully complete the proposed research. He has already demonstrated the ability to successfully access these resources. This has included MPH classes through the College of Public Health, use of the CCTS's informatics and research subject advocate, and use of the information warehouse for current clinical projects. These experiences have established the candidate's successful ability to access and use the available resources.

Interactions with other investigators are a key component of developing into an independent investigator. The candidate has successfully completed collaborations with investigators at other institutions, boding well for his ability to successfully collaborate. The team assembled for this project is an interdisciplinary one providing

ample opportunity for growth and intellectual development. As part of the career development portion of this proposal, the candidate will attend the Annual Meetings of the American Geriatrics Society, the Society for Academic Emergency Medicine, and the American Medical Informatics Association.   Additional conferences at OSUMC will be attended to facilitate learning in key study areas and to ensure continued integration with research efforts at OSUMC. These will include: monthly emergency medicine journal club, monthly antimicrobial management committee meetings, and bimonthly statistics lectures sponsored by the Center for Clinical and translational Sciences. The CCTS also has an increasing calendar of courses in bioinformatics which would be open to the candidate.