Scale and significance of the problem

New pathogens, therapeutic advances, devices, and diagnostics continually transform medical care and affect research directions. While many of these changes are incremental, others have a substantial, far-reaching and rapid impact. Comprehensive planning for paradigm-changing advances, when possible, can mobilize the full range of expertise available in a complex institution like UCSF and in our community partners. Systematic planning can identify new research opportunities, reduce institutional costs and improve patient care. The advantages of program planning can extend beyond UCSF to the wider community and our state and country. UCSF created a highly regarded example of response to the HIV epidemic that showed the benefit of a broad mobilization, but that model took years to accomplish and was largely reactive rather than intentional. UCSF is now acting in a more coordinated manner with newer opportunities including the incorporation of genomics and information technology in what is being termed precision medicine.

One healthcare challenge that can serve as exemplary for other implementation opportunities is the treatment of hepatitis C virus (HCV) infection. HCV is a large epidemic-more than 200 million cases worldwide- causing substantial morbidity and mortality. HCV treatment has had limited success as the available drugs are toxic, difficult to administer and of modest potency. New drug development, however, has been dramatic. Drugs in advanced stages of approval have, in early clinical trials, achieved a near 100% cure rate after only 12 weeks of oral administration with minimal side effects. As these drugs are approved over the next 1-2 years, they will predictably cause a rapid explosion of demand for HCV treatment despite the estimated cost of $70,000 for each case. Responding optimally to this challenge will have far-reaching benefits to UCSF and will provide a unique opportunity to design the types of investigative and implementation teams for similar emerging challenges, positioning UCSF as a leader in a new era of healthcare and in the application of an array of potent new technologies. Lessons learned in this demonstration project can be projected to apply to pending breakthroughs including the discovery of effective drugs to prevent or treat Alzheimer’s disease and the identification of genetic causes of common diseases with resulting targeted interventions.

Current approaches (nationally)

Each major academic medical institution follows scientific trends and responds to new challenges and opportunities. Few have a record as established as UCSF in creating models that combine research with novel medical care systems. No other medical university is, as far as is known, responding as yet in a comprehensive manner to the HCV treatment revolution.

HCV infection in the US affects several key populations. Users of injection drugs are very heavily affected doe to parenteral exposure in the sharing of injection supplies. Those transfused with blood before routine blood bank screening in the early 1990’s are a second key target population as are Vietnam era military veterans who, for as yet unknown reasons beyond injection drug use have high HCV prevalence rates. For these reasons, screening recommendations have until recently focused on histories of exposure risk but are now extending to population-based screening particularly based on birth-year cohorts.

HCV treatment until recently was with a combination of parenteral alpha interferon and oral ribavirin. Side effects including depression and anemia were extremely common precluding use in those with underlying mental health diagnoses and many other medical conditions. Response rates were poor, especially in certain HCV strains and host genotypes. Treatment was expensive and side effects often required hospitalization adding to overall cost. As a result of all these issues, treatment demand was low, few were offered therapy and only a small portion of the infected population was screened and diagnosed. Because chronic HCV infection often causes a progression of hepatic disease, HCV infection is the most common cause of liver transplantation in the US. HIV infection, a common co-pathogen with HCV, accelerates the natural history of HCV-induced liver disease and liver failure and hepatic cancer are now among the most common causes of mortality in HIV infected persons.

HCV treatment advances have been well described in the medical literature. In contrast to the existing drugs that act through indirect immunologic pathways, new agents, termed direct acting antiviral drugs or DAA’s, are targeted to known steps in the HCV viral lifecycle. The first two approved agents, HCV protease inhibitors bocepravir and telapravir, showed considerable activity but are limited by significant drug-drug interactions and variable effects in different HCV strains. Newer DAA’s, nearing approval, are potent in some cases across the HCV strains, are active even after prior interferon-based treatment failure, are convenient in oral formulation and have minimal toxicity. As the HCV genome is not incorporated in the host genome, the infection is curable in contrast to HIV and cure rates with combinations of new DAA’s approaches or achieves 100% in relatively small early clinical trials. These startling results are driving the FDA approval process and the first of the newer DAA’s are expected to be approved later in 2013 with subsequent approvals anticipated in 2014 and beyond. The imminent approval of new and frame-shifting HCV drugs will certainly lead to an explosion of demand for diagnosis, staging and treatment, at first focused on those with moderate to advanced liver disease. As each cure is anticipated to cost in the range of $70,000, planning for this surge in demand is critical but there is no evidence that other academic medical centers have mounted such a response.

Proposed approach and why it is innovative

UCSF has responded previously and well to new epidemic diseases. UCSF through San Francisco General Hospital created a model of tuberculosis care in the early part of the last century, we have hosted an innovative approach to sexually transmitted infections and our HIV model is still accepted as an international standard. UCSF has a broad array of expertise available for emergent health care demands. Our basic scientists value a translational disease-focused application to discovery, our clinicians and clinical investigators explore new treatment modalities, our population-based investigators collect and analyze needed data and our social scientists and community engagement efforts allow us to focus our work carefully and solicit the active partnership of affected populations. Each element of this investigative and implementation team is available to important emergent healthcare priority and opportunity, certainly including a model of response to new HCV therapies, the focus of this proposed project.

The HCV treatment revolution is a rare example of an increase in care demand that is predictable in advance, allowing the design of optimized systems of care and research organization to monitor, evaluate and adjust the screening of patient populations, to stage underlying liver disease and to initiate therapy when indicated. As each of the three primary UCSF-related medical centers; Parnassus, San Francisco General Hospital and the VA Medical Center have large but demographically distinctive patient populations and payment systems, comparing experience through data sharing will enrich the development of the HCV response model and increase its generalizability. Linking the information collected across UCSF with data from the network of the five University of California medical centers through the UC BRAID system of CTSI with 12 million covered lives will further strengthen the lessons learned from this project, representing an innovative use of “big data” in healthcare.

The HCV model project will be dynamic. As drugs are approved and as demand for care increases, the team will monitor data from each medical center to compare population screening rates and success in each step of the treatment “cascade” familiar from the HIV experience. Information sharing in real time will be used to shorten time from diagnosis to staging and treatment and causes for treatment adherence problems and cases of drug failure and/or drug resistance. The project will be innovative and outward looking in working from the start with community members and with experts at UCSF expert in engaging the very different communities most affected by the HCV epidemic. The project will also closely evaluate economic data and medical center impact to adjust the treatment caseload and shift care tasks as indicated by ongoing experience. For example, if ease of therapy and side effects allow, employing fewer specialists and more non-physician providers than is possible with current HCV treatments may reduce cost of care.

The HCV project will continually attend to how the systems found effective might be similarly deployed against other health care imperatives, particularly as the entire structure of American healthcare adjusts to the rollout of the Affordable Care Act. The overriding aim of the project is to gain insights from HCV that are generalizable across very different patient populations and payment systems and to improve care outcome of other diseases as newer technologies continue to be developed.

Potential partners

The HCV project will grow from an established group of HCV treating physicians that has been meeting in a cross-campus dialog initiated by the AIDS Research Institute at the request of the Chair of the Department of Medicine. This core group includes specialists in hepatology, infectious diseases, HIV/AIDS and general internal medicine from each of the three UCSF affiliated medical centers as well as basic scientists and epidemiologists. To the core, the HCV projects will add:

* **Information technology** specialists who will develop systems to collect and compare data across medical centers locally and Statewide through UC BRAID
* **Public health** experts knowledgeable about the network of community clinics and agencies already or potentially involved in HCV care
* **Members of communities** affected by HCV for input in the project design and execution
* **Community engagement** experts to help increase the project impact by increasing screening and treatment uptake and participation rates in treatment trials
* **Communication** experts, particularly in social networking, to convey developments to and invite input from the broader community
* **Economists** who with **pharmacists** will model and follow the costs of new care approaches and the impact on other medical center missions
* **Medical center** leaders who will help determine positive and negative aspects of increasing HCV care delivery. Space, workforce and incurred costs may, for example, be offset by an influx of insured persons who remain as primary care patients following HCV cure.
* **Implementation scientists** who will work with epidemiologists, economists and others in monitoring the project and in dynamic adjustments as data is collected and analyzed.
* **Global health** experts who will participate and consider project applications in middle and lower income countries many of which are heavily affected by the HCV epidemic

Projected impact (estimate resources needed)

The potential impact of creating a model of HCV care is difficult to estimate as the prevalence of the infection in covered patient populations is largely unknown. San Francisco General cares for a large population infected from injection drug use and those infected sexually. The VA Medical center has large numbers infected in the Vietnam era and at Parnassus HCV is the cause of more than 50% of liver transplant recipients. The cost of new HCV treatments will be a serious challenge to an enclosed pharmacy benefits system like the VA while the impact at SFGH will be primarily determined by the decision of MediCal to support or limit HCV treatment coverage. At Parnassus, private insurance coverage as well as MediCal policies will affect impact. Whatever the situation at specific medical centers, “getting it right” by developing the data needed to optimize and individualize a model system will reduce costs and improve care outcomes. The project will have an impact beyond San Francisco through the UC BRAID component and to other countries through the involvement of global health leaders. Most importantly, the project will provide a structure for an effective academic medical center response to future health challenges and opportunities.

Ideally, funds for the project would be used for the time of the faculty and staff on the outlined team. Costs of care are not part of this project but creating the data systems at the heart of the project would require support.