PRIORITY:

Translating Research From Bench to Bedside to Community

Natural History and Epidemiology

Information Dissemination

AREA OF EMPHASIS

Natural History and Epidemiology

FY 2013 RESEARCH PRIORITIES

- Develop and evaluate novel methods for HIV testing, linkage to and retention in care, adherence to treatment, and monitoring response to care for use in domestic and international settings. This priority activity includes conducting research on: (1) accurate, reproducible, and affordable virologic, immunologic, pharmacologic, and genetic assays, and behavioral assessments; (2) measures of the outcomes of HIV testing programs; (3) accurate and cost-effective point-of-care diagnostics and monitoring technologies; (4) assays to determine HIV incidence at the population level; (5) methods for evaluating the outcomes of viral suppression at a population level; and (6) novel strategies for identifying HIV-infected persons who are unaware of their status.

- Conduct studies that improve the uptake, implementation, and translation of research findings into health care practices involving HIV/AIDS and related conditions. This priority includes implementation science research studies that address the multiple and diverse issues being encountered in the scale-up of prevention and treatment interventions, particularly in resource-limited settings, and evaluative research leading to more effective and cost-effective public health interventions.

- Conduct studies that assess the epidemiologic aspects of HIV infection in aging populations, including risk factors for HIV acquisition and transmission, and the long-term effects of HIV disease and its treatment, in aging individuals.

- Integrate data from clinical trials and observational studies with simulation, mathematical modeling, and other advanced statistical methods with the goal of assessing the short- and long-term effects of preventive and therapeutic interventions, including multicomponent intervention strategies, in domestic and international settings; develop best practices for the collection, analysis, and sharing of data from these studies.

OBJECTIVE–A: Transmission of HIV (Prevention, Risk Factors, and Mechanisms)

Further characterize the relative importance of major risk factors, population-attributable risk, and mechanisms of HIV susceptibility and transmission in domestic and international settings to guide prevention and treatment strategies.

STRATEGIES

- Study the feasibility and acceptability of the seek, test, treat, and retain approach, both alone and in combination with other prevention interventions, in the United States and internationally, using clinical and mathematical models and cost-effectiveness analyses.
- Utilize existing cohorts, and develop new cohorts of selected subpopulations (especially newly emerging, vulnerable groups), to employ novel methods (e.g., social/sexual network analysis, molecular epidemiology and epigenetics, temporal phylogenetic analyses, and geographic information systems), alone and in combination, to further assess the magnitude of HIV incidence and risk factors for HIV transmission.
- Optimize the use of existing cohort data to evaluate the impact of differing demographics (e.g., socioeconomic status, race, ethnicity, gender, age, and sexual orientation) and societal/structural factors (e.g., stigma, community cohesion, and conflict) on the risk of HIV acquisition and to assess the impact of in-country resource capacities, allocation, and availability on HIV progression and outcomes.
- Conduct molecular epidemiology studies to identify and estimate the incidence, prevalence, and correlates of divergent viral genotypes, drug resistance, and neutralization profiles and their temporal trends; characterize how different HIV types, subtypes, and recombinant forms influence routes and modes of HIV transmission; superinfection; natural history; response to antiretroviral therapy (ART), pre-exposure prophylaxis (PrEP), postexposure prophylaxis, and other biomedical interventions; and emergence of antiretroviral (ARV)-resistant viruses.
- Conduct studies on the clinical and public health significance of multiple circulating subtypes and the generation of dual, multiple, and recombinant viruses in population epidemiologic dynamics and their potential implications for prevention and therapy.
- Refine epidemiologic and mathematical models to improve estimates of per-exposure risk of HIV transmission and to develop estimates of population-attributable risk, based on type of sexual and/or other exposure; characteristics of the infected and uninfected partners (e.g., plasma and/or anogenital tract viral load, host genetics, and coinfections); cofactors (e.g., substance use, psychiatric comorbidities, and ART); and biomedical interventions (e.g., oral PrEP, topical microbicides, male circumcision, and vaccines).

Strategies Related to Transmission and Its Prevention

- Investigate viral, host, and environmental characteristics that distinguish high-efficiency transmitters and nontransmitters of HIV, through studies of serodiscordant couples, sexual and/or molecular network-based studies, and other strategies.
- Evaluate the risk of sexual and blood-borne HIV transmission in relation to the following:
  - Viral factors such as viral quantity, diversity, coreceptor usage, genotype (e.g., types, subtypes, recombinants, and resistant mutants), and dual virus infections in various body compartments (e.g., blood, saliva, gingival crevicular fluid, and semen), and mucosal compartments such as the oral mucosa, the female genital tract, and the anorectal mucosa;

- Host factors such as age, sex, race, socioeconomic status, functional capacity, hormonal status, strength and breadth of immune response, comorbid diseases, coinfections, transfusion and transplant history, and host genetics;
- Modifiable factors such as diet and nutritional status; geographic location (urban, rural, and mobility); drug, alcohol, and tobacco use and/or treatment; mental health; housing; circumcision status; behavioral interventions; and access to and use of health care;
- Other infections, including *M. tuberculosis* (TB) and drug-resistant strains, multi-drug-resistant (MDR)- and extensively drug-resistant (XDR)-TB, *Plasmodium* sp. (malaria), sexually transmitted infections (STIs), and viral hepatitides;
- Psychological, behavioral, social, cultural, geographic, and structural determinants of susceptibility to HIV acquisition among hard-to-reach and vulnerable populations (e.g., transient and mobile populations, sex workers, injection and noninjection drug users, men who have sex with men [MSM] in developing countries, and racial/ethnic minorities); and
- Sexual activity, abstinence, pregnancy, sexual networks, partner choice (i.e., serosorting or choosing partners from high- versus low-prevalence populations), partner concurrency, partner fidelity, duration of partnership, sex trade, control of STIs, hygienic practices such as douching, contraception practices, cultural practices such as the use of traditional vaginal preparations and male circumcision, venues for meeting sexual partners, and use of drugs/alcohol during sexual activity.

- Further refine the timing, mechanisms, and risk factors in perinatal and postnatal transmission, including HIV testing and treatment of the mother, infant feeding modalities, fertility interventions, child spacing, physiology of lactation, long-term effects of perinatal interventions, maternal and infant genetic variation, and kinetics of viral resistance. These studies include:
  - Assessing the clinical outcomes, cost, and cost-effectiveness of different strategies for prevention of mother-to-child transmission (PMTCT), and determining predictors of success in countries in which the elimination of perinatal HIV transmission is being pursued as a public health goal;
  - Studying practices and barriers to HIV testing of the mother during prenatal care, during labor, and of the infant after birth;
  - Assessing the impact of maternal and infant ARV regimens of different potency and duration on mother-to-child transmission (MTCT) of HIV, on the health of women and their infants, on the emergence of ARV drug resistance in the mother and in those infants who become infected despite prophylaxis, and on programmatic uptake, adherence, and costs;
  - Studying the safety and effectiveness of sustainable approaches to PMTCT of HIV, including the access and provision of maternal ART, successful breastfeeding weaning strategies, improved safety of formula feeding, longitudinal HIV testing of the child, and determining the effects of such approaches on infant morbidity and mortality;
  - Evaluating maternal HIV risks during pregnancy, including the optimization of maternal HIV testing, behavioral and hormonal risks, risk of MTCT during incident infection or after pregnancy, and further optimization of ART for PMTCT;
  - Assessing the impact of maternal and infant adherence to ART on the risk of subsequent ARV resistance, clinical outcomes, and the effectiveness of ART in mothers and their children;
  - Assessing the clinical and economic impact of investments in alternative components of the PMTCT cascade, including maternal testing, receipt of test results, provision of PMTCT regimens, retention in care, and infant testing; and
  - Assessing the impact of perinatal treatment and prophylaxis regimens on community-wide HIV incidence, resistance to ARVs, and costs of care and treatment; assessing the impact of MTCT programs on public health measures, including maternal, paternal, and infant morbidity/mortality rates; overall life expectancy; disability and/or quality-adjusted life years; orphanhood; and pediatric neurobehavioral development.

Strategies Related to Prevention and Treatment

- Conduct studies to assess the individual and public health value of programs to promote widespread, frequent HIV testing, including couples counseling and partner notification with immediate linkage to counseling, care, and ART.

- Assess the efficacy and effectiveness and long-term sustainability of individual and various combinations of prevention strategies (e.g., behavioral changes, partner testing and notification, ART, biomedical interventions, and treatment for coinfections and comorbidities) in different populations.

- Conduct epidemiologic modeling studies on the aggregate impact of ART, oral PrEP, topical microbicides, and male circumcision on HIV transmission in the presence or absence of other biomedical, behavioral, and structural interventions, particularly in settings with endemic, generalized, hyper-endemic, and emerging epidemics.

- Study the impact of widespread ART availability, adherence, pre-ART and ART care, HIV-related comorbidities, and patterns of ARV resistance on HIV prevalence, incidence, community-level viral load, risk behaviors, and the transmission of resistant HIV strains.

- Conduct studies of male circumcision as an HIV risk-reduction strategy, including:

  - Assessing the impact of adult male circumcision on HIV incidence in circumcised men and their partners, and on sexual behavior and attitudes, in the domestic and international setting;

  - Evaluating prevention and risk-reduction approaches in the context of adult male circumcision, particularly those based on combinations of known methods, including reproductive health, partner reduction, condom use, and STI control; and

  - Assessing the effect of male circumcision on HIV transmission to uninfected female and male partners, with consideration of the timing of male circumcision and other factors that increase or decrease transmission.

OBJECTIVE–B: Disease Progression (Including Opportunistic Infections and Malignancies)

Use epidemiological research in domestic and international settings to identify the effectiveness, impact, and interactions of HIV-related therapeutics (e.g., ART and opportunistic infection [OI] prophylaxis), biological factors (e.g., age, host genetics, coinfections, comorbidities, HIV types and subtypes, and viral genetic variation), and behaviors (e.g., health care system use; adherence; sexual activity; and smoking, alcohol, and drug use) in relation to HIV progression, response to ART, and development of non-AIDS-defining chronic conditions, as indicated by virologic, immunologic, and clinical outcomes.

STRATEGIES

Strategies Related to Disease Progression and Response to ART

- Develop new interval-based or standard-of-care cohorts and maintain long-term followup of existing cohorts to determine the changing spectrum of HIV disease; identify highly exposed uninfected persons, long-term non-progressors, and elite suppressors; and evaluate interventions, especially in aging and minority populations, in resource-limited countries, and in emerging epidemic zones.

- Characterize short- and long-term consequences of recent HIV infections, including the roles of host and viral genetic characteristics and differences by route of exposure, and continue to characterize the epidemiology of HIV disease and AIDS among those early in infection, those with minimal or no exposure to ART, those with virologic and/or immunologic responses to ART, and those who have experienced ART failure.

- Determine, using different epidemiologic study designs, the effects on disease progression of cumulative and current ART exposure to specific drugs; classes of drugs; drug combinations, including drugs for coinfections; and treatment strategies and laboratory monitoring overall and by sex and age groups.

- Characterize global patterns of innate and acquired viral resistance to ART and how these patterns are influencing the long-term effectiveness and cost-effectiveness of monitoring strategies and therapies.

- Characterize the changing spectrum of clinical outcomes, causes of morbidity and mortality, complications of ART, (e.g., cardiovascular disease), and cost patterns associated with evolving therapeutic strategies, domestically and internationally, in relation to person, medication, and system-level factors.

- Use observational studies in resource-limited settings to estimate the HIV prevalence, incidence, and correlates of treatment failure in first-line, second-line, and subsequent treatment regimens.

- Assess the effect of ART on the incidence, pathogenesis, and presentation of cancers in the domestic and international settings, and use mathematical models to project the frequency, outcomes, and costs of treatment for these cancers.

- Define the prevalence, incidence, predictors, potential treatments, and consequences of diabetes and other diseases (e.g., cardiovascular, musculoskeletal, skin, renal, oral, and liver disease) in HIV-infected individuals. Use mathematical models to project the frequency, outcomes, and treatment costs of these comorbidities in HIV survivors.

- Characterize the long-term effect of HIV infection on the central nervous system, including the effect of viral burden in the cerebrospinal fluid, its effect on white matter degeneration, and the role of ART in reducing the neurocognitive burden of disease, and differentiate these changes from other neurocognitive diseases, such as dementia and Alzheimer's disease.

- Evaluate and characterize immune reconstitution inflammatory syndrome (IRIS), including modifiable (e.g., the microbiome) and nonmodifiable predictors of immune recovery, and determine best treatment practices for IRIS in diverse populations.
- Define the prevalence, incidence, and determinants of HIV-associated neurologic, behavioral, and psychiatric manifestations and their relation to HIV disease progression and response to ART.

Strategies Related to Comorbidities

- Expand research on the spectrum of HIV-associated malignancies and on malignancies not associated with HIV that may develop in HIV-infected patients who have responded to ART and are living longer with immune deficiency.
- Identify effective and cost-effective screening strategies for such malignancies in HIV-infected populations.
- Investigate the role of risk factors such as chronic inflammation in the development of malignancies and metabolic, cardiovascular, musculoskeletal, renal, and liver disorders in HIV-infected individuals, and how cumulative and current ART use might mediate or mitigate the effects of chronic inflammation.
- Establish standards in different resource-limited regions affected by the HIV epidemic for lymphocyte subsets, activation markers, and hematologic and clinical chemistries, and determine the influence of endemic diseases (e.g., malaria, TB, hepatic and herpes viruses, and helminthic infections) on such standard values.
- Assess the ability of health care systems in resource-limited settings to screen, diagnose, and treat AIDS-defining and non-AIDS-defining malignancies.
- Investigate TB/HIV interactions, including the effects of dual infection on the infectiousness and progression of both TB and HIV, and the effect of various treatment strategies on disease control and TB drug-resistant strains.
  - Investigate new approaches to successful diagnosis and linkage to and retention in care of patients in high-prevalence settings who are coinfected with HIV and TB.
  - Develop novel TB diagnostics for use with HIV-infected patients in order to rapidly identify undiagnosed active TB, latent TB, and MDR/XDR-TB in HIV/TB-coinfected populations.
  - Investigate the MDR/XDR-TB epidemic, evaluating risk factors for MDR/XDR-TB prevalence, incidence, therapeutic options, and clinical outcomes among HIV-infected patients.
  - Investigate the prevalence of disseminated (miliary) disease, including cerebral TB, its impact on everyday function, disease progression, and therapeutic options among HIV-infected patients.
  - Assess methods of integrating TB and HIV diagnostics and care and their effects on survival, quality of care, cost, and cost-effectiveness of care.
  - Investigate the feasibility, effectiveness, and cost-effectiveness of treating latent TB on the epidemiology of HIV/TB coinfection in endemic countries.
  - Conduct implementation science research to understand barriers to implementation of preventive therapy and treatment of active TB in HIV/TB-coinfected patients.
- Evaluate the clinical and economic impact of treatment of smoking; alcohol and illicit drug use, abuse, and dependence; and mental health disorders on the effectiveness and consequences of ART, HIV disease progression, development of comorbidities, and mortality.
- Support research efforts to link existing databases (e.g., cancer, TB, transplant, and mortality) to enhance the understanding of HIV/AIDS outcomes in populations and in standard-of-care cohorts.
- Study the frequency, changing manifestations, and effects of HIV-related respiratory disease (e.g., recurrent bacterial pneumonia; drug-resistant TB, MDR-TB, and XDR-TB/HIV cases; immune reconstitution syndromes affecting the lungs, including sarcoidosis and other immune-mediated and

smoking-related diseases; HIV-related pulmonary hypertension; accelerated emphysema; and lung cancer) on morbidity, mortality, and HIV disease progression, in both untreated patients and those receiving ART.

- Study the emergence and reemergence of infectious diseases and the clinical and epidemiological characteristics of antimicrobial-resistant infections in HIV-infected populations (e.g., MDR-TB, sulfa-resistant malaria, antibiotic-resistant pneumococcal pneumonia, cotrimoxazole-resistant *Pneumocystis jirovecii* pneumonia, methicillin-resistant *Staphylococcus aureus* [MRSA] infections, and lamivudine-resistant hepatitis B virus [HBV] infections).
- Estimate the prevalence of specific human papillomavirus (HPV) types associated with cervical and anal cancer and high-grade dysplasia as well as oral cancer in HIV-infected individuals.
- Evaluate different cervical and anal dysplasia and cancer identification and treatment methods in HIV-infected individuals for sensitivity, specificity, cost-effectiveness, and appropriateness in both international and domestic settings.
- Evaluate the effectiveness of HPV vaccines among HIV-infected individuals (female and male) from geographically diverse regions.
- Assess the effect of primary care screening and interventions (e.g., statin use; hypertension management; smoking cessation; alcohol/drug use screening, treatment of depression, STIs, and viral hepatitis; and cancer screening and treatment) on HIV disease outcomes, survival, and costs of care.
- Investigate hemostatic disturbances in HIV-infected individuals and the role of coagulation and fibrinolytic mechanisms in risk of vascular events and other complications.
- Examine the impact of cryptococcal disease on early mortality in international settings, and evaluate potential effective and cost-effective strategies for prevention and early detection of cryptococcal disease in HIV-infected individuals.

Strategies Related to Mother-to-Child Transmission and Pediatric HIV Infection

- Evaluate the differences in adherence, treatment response, drug resistance, and HIV outcomes between adolescents, adults, and perinatally infected children; in behaviorally acquired versus perinatally infected adolescents; and in adolescents treated in pediatric versus adult HIV treatment centers.
- Investigate the long-term outcome of complications due to HIV and ART use in HIV-infected children as these children reach adolescence and adulthood.
- Assess the long-term impact of *in utero* HIV and ART exposure in HIV-uninfected infants and children born to HIV-infected mothers.
- Study the effect of the health status of HIV-infected mothers and of ART during pregnancy, lactation, and early child life on survival, quality of life, and care costs of their HIV-infected and -uninfected children and on maternal outcomes.
- Study HIV-infected and -uninfected children and adolescents to determine factors related to impaired growth and neurodevelopment; cognitive, behavioral, and psychomotor development; impact of other childhood infectious diseases and nutritional status; and safety and efficacy of immunizations.
- Develop appropriate epidemiologic and surveillance studies to assess the immunologic responses to routine vaccinations of childhood and adolescence and the need for altered vaccine schedules in HIV-infected youth.
- Assess the risk factors for acquisition and natural history of HPV infection, and the impact of HPV vaccines in HIV-infected children and adolescents.

Strategies Related to Aging

- Investigate the relationship between HIV infection and the spectrum of physical and mental health outcomes that increase with aging (e.g., cancer, renal disease, cardio- and cerebrovascular disease, pulmonary disease, diabetes, hypertension, arthritis, osteoporosis, anemia, metabolic disorders, dyslipidemias, and oral diseases), as they affect disease outcomes and survival.

- Study the incidence and determinants of physical, neurologic, and cognitive changes by age group and by duration of HIV infection among HIV-infected individuals and the effect of frailty and functional impairment on HIV, ART use and response, and self-care behaviors.

- Study the epidemiologic association between immunologic and virologic responses to treatment and adverse effects of HIV and ART in aging populations, including those with coexisting morbidities and/or who receive numerous medications.

- Examine the impact of polypharmacy in elderly HIV-infected patients, including its effect on adherence and prioritization of the most critical drug regimens.

- Evaluate immunologic and virologic measures of HIV disease progression, ART-related toxicities, development and progression of comorbid conditions, and mortality in older versus younger adults receiving ART to refine treatment guidelines for older HIV-infected patients.

OBJECTIVE–C: Methodologies

Develop and evaluate methods and resources for HIV/AIDS epidemiological and clinical studies that use culturally appropriate approaches; incorporate new laboratory, sampling, and statistical methods with information systems; and better integrate research findings into clinical practice and regional, national, and international policies and guidelines.

STRATEGIES

- Evaluate and promote the use of multiple study designs that incorporate appropriate ethical, cultural, and policy context for studies of HIV disease prevention, diagnosis, and treatment and AIDS in diverse domestic and international populations.
- Evaluate study designs, including adaptive trial designs, to more efficiently assess the effectiveness of prevention and treatment interventions.
- Develop and assess strategies to increase the participation of underrepresented groups in epidemiology, prevention, and therapeutics research.
- Continue to support local, regional, and international collaborations to integrate, harmonize, and utilize existing data for rigorous scientific investigations.
- Capture and utilize data from large U.S. and international HIV screening programs, such as blood donor screening programs, to monitor incidence and temporal trends, viral genotypes, drug resistance, and neutralization profiles.
- Ensure that the population composition of domestic epidemiological studies accurately represents populations at risk for and affected by HIV/AIDS, such as older Americans, persons from geographical regions most affected by the epidemic, adolescents and young adults, MSM, racial and ethnic populations, drug and alcohol users, and persons affected by other comorbidities.
- Ensure that studies reflect the needs and priorities of the countries or regions in which they are conducted and produce results that are quantifiable and applicable to diverse circumstances and geographic areas.
- Promote the development and dissemination of simple point-of-care tools appropriate for both industrialized and resource-limited settings to standardize the diagnosis and monitoring of treatment-limiting or life-threatening complications of chronic HIV infection and ART.
- Explore expanded utilization of new diagnostics designed for use at the point of care (e.g., low-cost mobile devices or inexpensive disposable diagnostics), which have potential to address access, disparity, and confidentiality issues for people at risk for or infected with HIV disease, especially in underserved areas and in stigmatized populations.
- Investigate the use of Internet-based methods of recruitment, risk assessment, and preventive interventions for HIV.

Strategies Related to Natural History/Diagnosis and Monitoring

- Further develop epidemiologic, laboratory-based, and simulation modeling methods in conjunction with prospective cohort studies, domestically and internationally, to monitor HIV incidence, response to ART, and the incidence of complications related to chronic use of ART, including:
  - Develop and test methods to produce accurate, reproducible, and inexpensive virologic, immunologic, bacteriologic, pharmacologic, neurobehavioral, and genetic assays suitable for large-scale epidemiological research and surveillance in developing nations. Emphasis should be on simple and reliable staging of disease progression for the initiation and monitoring of ART and OI prophylaxis, viral hepatitis testing, HIV resistance testing, TB screening, and assays for STIs and other coinfections.

- Maintain and effectively utilize ongoing and newly developed cohort studies, domestic or international specimen repositories, and databases for interdisciplinary HIV-related studies to address short-, medium-, and long-term outcomes. Collaborative studies between cohorts and nested studies that utilize these resources should be particularly encouraged.
- Identify and/or develop uniform assessment tools to measure host and environmental characteristics, including substance abuse and mental health, which may affect immediate and longer-term HIV-related health outcomes. Assessment tools should be both culturally appropriate and scientifically valid and made available for other researchers to assess, validate, and use.
- Develop new and evaluate existing assays to accurately measure HIV incidence at a population level, using rapid, inexpensive, and reproducible measures, including methods appropriate for international populations and measures integrated into point-of-care testing.

Strategies Related to Research on Design and Analysis of Epidemiologic Data

- Develop new epidemiological designs and statistical methods, including development of informatics tools and simulation, to better characterize transmission dynamics and monitor long-term trends in disease progression and development of toxicities in the setting of potent ART.
- Continue to develop and improve upon quantitative methods for making effective and appropriate use of data from local, State, and national HIV/AIDS surveillance systems and from large observational, cross-sectional, and cohort studies, such as:
  - Assessing costs of care for HIV disease management and treatment of comorbidities, both domestically and internationally;
  - Methods for inferring causal effects of nonrandomized exposures (e.g., treatment and policy changes);
  - Methods for estimating incidence rates in cross-sectional samples;
  - Validation of methods for imputing ART status in HIV surveillance registries that do not collect information on ART use;
  - Methods for sampling hidden populations (e.g., venue-based, Internet-based, snowball, mixed method, respondent-driven, and time-location sampling);
  - Methods for standardizing the reporting of results from studies that are Internet-based or use respondent-driven sampling;
  - Models and inferential methods for characterizing multiple/comorbid disease processes and events;
  - Methods for linking cohort data to health care utilization and cost data to address health policy questions;
  - Methods for compiling and linking blood donation data across blood centers, and estimating trends in incidence and transfusion-transmitted risks for HIV;
  - Methods for simultaneously addressing more than one hypothesis or intervention, including the use of factorial randomized trials and quasi-experimental designs;
  - Methods for collecting and analyzing spatio-temporal data (including geo-sentinel mapping), especially as they relate to transmission and spread of HIV infection;
  - Methods for multilevel analysis of population-based HIV/AIDS surveillance data; and
  - Methods to assess the role and effectiveness of social media use in different populations to enhance HIV prevention, care, and treatment.
- Encourage research on innovative design and analysis through interdisciplinary collaboration between methodologists from different fields, such as epidemiology, biostatistics, econometrics, computer science, biomathematics, decision sciences, implementation science research, health services research, behavioral and social sciences, and demography.

- Conduct studies that make innovative use of existing data (e.g., cohorts, surveillance data, routinely collected service delivery data, blood donor screening programs, and data from monitoring and evaluation systems) for well-designed, rigorous analyses, hypothesis generation, and hypothesis testing.
- Design data collection and evaluation to accurately assess "community viral load."
- Promote collaborative studies using genetic epidemiology methods (e.g., genome-wide association studies applied to large, diverse populations to elucidate mechanisms of HIV infection, disease progression, and complications.

Strategies Related to Interventions

- Study and evaluate prevention packages that combine multiple strategies into one intervention, especially those that combine behavioral, biological, and/or structural interventions.
- Develop studies to compare the effectiveness, efficacy, and cost-effectiveness of various HIV prevention strategies (e.g., opt-out testing, secondary prevention, oral PrEP, topical microbicides, male circumcision, and immediate ART) between populations with generalized versus concentrated epidemics.
- Assess optimal algorithms for HIV diagnosis, including point-of-care algorithms, and strategies for diagnosis of acute HIV infection.
- Assess the effectiveness and outcomes of clinical and/or laboratory monitoring for the initiation, monitoring, and switching of ART, particularly in resource-limited settings, including laboratory monitoring with new methods that are technologically appropriate, cost-effective, and affordable in various international settings.
- Use appropriate clinical and laboratory definitions of short- and longer-term ART failure, and mechanisms for monitoring drug resistance evolution in HIV types, subtypes, and variants in domestic as well as international populations.
- Develop, evaluate, and promote new, improved, and cost-effective methods and strategies to prevent HIV transmission via blood transfusion, as well as other medical interventions and iatrogenic exposures in developing countries, including instrument sterilization.
- Assess the impact and cost-effectiveness of different strategies for HIV testing and counseling and linkage to/maintenance of care for different populations, including adolescents, older adults, racial and ethnic populations, and populations in diverse domestic and international settings.
- Develop strategies to validate the use of surrogate markers for HIV acquisition and/or transmission risk, including use of behavioral measures and biomedical markers.
- Assess the effectiveness of strategies designed to reduce the impact of comorbidities, including smoking cessation, medication-assisted treatment for substance abuse, hepatitis C virus treatment, vaccination against HBV and HPV-16/18, and cytologic screening for cervical and anal cancers.
- Adapt interventions initially developed in older adults to HIV-infected individuals with multiple comorbidities, functional impairments, polypharmacy, cognitive decline, and/or who are at risk of adverse outcomes common in geriatric populations (e.g., falls, fractures, and functional decline).

Strategies Related to Implementation

- Evaluate the various operational strategies that can be employed for the implementation and dissemination of efficacious, preventive (e.g., male circumcision, oral PrEP, and topical microbicides), or therapeutic interventions, and evaluate countrywide ART programs, including the use of implementation science research and integrated observational databases, to evaluate effectiveness at community and population levels.
- Evaluate novel methods for rapid dissemination of successful and reproducible findings for implementation into the field, and improve understanding of how to efficiently deliver effective interventions, develop standardized

methodologies to transfer interventions from one setting or population to another, and make informed choices among different interventions.

- Design and implement evaluations of both targeted and large-scale HIV testing and treatment programs, with attention to clinical outcomes, HIV incidence rates, viral resistance, long-term dynamics of the HIV epidemic, and comparative costs for the programs relative to present-day strategies.

- Utilize implementation science to improve the operations and efficiency of a proven strategy or treatment and to determine to what degree it is applicable across a broad range of target populations.

- Evaluate the long-term clinical and public health impact, cost, and health care utilization ramifications of different strategies for care, including treatment of HIV-associated conditions and comorbidities, ART, and complications of ART.

- Support implementation science studies and population-based research necessary for translating epidemiology findings into guidelines for health care practices.

- Assess the use of "community viral load" (CVL) as a population-level marker of program effectiveness. Establish the CVL sensitivity, specificity, and predictive value in tracking the epidemic, allocating resources, and evaluating the effectiveness of HIV prevention and treatment efforts.

- Support the use of implementation science to investigate barriers and facilitators to the efficient implementation of empirically tested prevention and adherence strategies in different environments.

- Design and evaluate implementation of system-level approaches for management of complex HIV-associated comorbidities in settings or populations with resource-limited available care.

- Evaluate different models of approaching a continuum of screening, prevention, treatment, and care and the impact of expanded intervention availability, access, and coverage in various settings and populations.

AREA OF EMPHASIS

Information Dissemination

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE–A: Disseminate Information to All Constituencies

Support the effective dissemination, communication, and utilization of information about HIV infection, AIDS, coinfections, opportunistic infections, malignancies, and clinical complications to all constituent communities of the NIH, domestically and internationally.

STRATEGIES

- Rapidly disseminate new basic, translational, and clinical research findings, including information on the potential implications for HIV prevention, care, and treatment, using existing and innovative methods.
- Promote study designs that include plans for dissemination of appropriate and relevant findings to study participants, health care practitioners, community representatives, policymakers, program administrators, and the public, while ensuring that confidentiality of efficacy and safety data is maintained during the conduct of clinical trials.
- Facilitate the update and dissemination of HIV prevention and treatment guidelines based on the latest clinical research findings.
- Utilize computer and other information dissemination technology (including the Internet) to disseminate up-to-date HIV and AIDS information; information about HIV therapeutic, vaccine, microbicide, and other prevention trials; and information about HIV training programs.
- Expand access to and education about state-of-the-art treatment and patient management guidelines, including information on clinical trials, using multiple technologies such as online access and voice access *(AIDSinfo)*.
- Widely disseminate information concerning specimen repositories, including existing repositories, specimens available, and relevant information concerning cohorts, contact information, and the process for obtaining access to samples.
- Collect, archive, and promote the use of existing data from NIH-supported basic and applied research for secondary data analysis, including rapid development of public use datasets that can be used for secondary data analysis in NIH-supported studies, especially baseline survey and HIV/STD (sexually transmitted disease) incidence data.
- Widely disseminate experimental findings regarding AIDS-related studies using nonhuman primates, as well as information concerning the availability of animals for AIDS-related studies.
- Improve current techniques and develop and evaluate new techniques for the two-way communication of information to scientific and lay audiences, particularly to hard-to-reach populations, including information about the importance of clinical trials participation, ongoing clinical trials, and trial results.
- Improve outreach and support access to AIDS information resources (including computers) by community groups, health care providers, and community-based AIDS service organizations, including those serving racial and ethnic populations.

- Work with community-based organizations (CBOs), nongovernmental organizations (NGOs), and local agencies to develop and promote effective methods of information dissemination on treatment, prevention, and research in target populations to increase awareness and clinical trial participation and to reduce stigma.
- Support dissemination of research findings to community representatives, study participants, health care practitioners, payors, policymakers, AIDS community organizations, and the public, in culturally and linguistically appropriate ways.
- Develop and disseminate educational information to enhance understanding of HIV and basic and clinical research processes by health care providers, community-based AIDS service organizations, social service organizations, policymakers, and persons with HIV and AIDS.
- Develop and disseminate information resources about HIV prevention, microbicide, vaccine, and treatment clinical trials, including cancer trials, to increase awareness about research in these areas and the importance of supporting and participating in clinical studies.
- Evaluate the effectiveness of communication efforts by appropriate means, including obtaining feedback from target audience members through methods such as usability testing of paper and computer interfaces (see *www.usability.gov*) and information dissemination intermediaries, such as journalists and health educators.
- Promote wide dissemination of the annual *Trans-NIH Plan for HIV-Related Research* and other HIV-related reports as they become available.
- Promote and enhance the exchange of scientific information and communication between public and private research enterprises, such as enhancing communication with the pharmaceutical industry concerning research on the development of therapeutics, vaccines, and microbicides, and working with industrial scientists to make information concerning basic science and HIV protein structures available to the general scientific community.
- Communicate and exchange information internationally on topics such as prevention and treatment; patient management, including comorbidities and prevention guidelines; and research results that improve the care of HIV-infected individuals, including those in developing countries.
- Support the exchange of basic and applied research information at community, regional, national, and international conferences and workshops.
- Support the cross-collaborations of HIV and AIDS information providers to develop more integrated and comprehensive information dissemination approaches.
- Provide support for online access to presentation materials and other information (e.g., slides, graphics, and plenary presentations) from scientific meetings.
- Develop HIV/AIDS training materials using a variety of current technologies most appropriate for specific audiences, as well as materials adapted for local languages.

OBJECTIVE–B: Develop New Communication Strategies

Support research to identify existing gaps in communication approaches, identify and evaluate existing strategies, and develop and test new and innovative communication strategies that will improve access to and use of state-of-the-art HIV information by all relevant target audiences, domestically and internationally.

STRATEGIES

- Continue to assess the changing information needs and resources used by various audiences, including biomedical and behavioral research communities, health care providers, service providers, persons living with HIV and their advocates, at-risk populations, scientific and lay media, and the general public.
- Identify obstacles to information dissemination and develop, test, and evaluate possible ways to overcome these obstacles.
- Develop, test, and evaluate innovative strategies for effectively reaching specific audiences (e.g., racial and ethnic populations, adolescents, drug users, other hard-to-reach populations, and health care providers) with relevant HIV information.
- Investigate how and under what circumstances different communication and dissemination strategies influence the adoption of scientifically based HIV behavior-change interventions and clinical practices in specific audiences.
- Promote the use of new technologies and evaluate their effectiveness for disseminating basic and clinical research findings.
- Work to reduce communication gaps between academic researchers and treatment providers so that research results are more effectively disseminated to providers and that research agendas reflect the needs of practicing clinicians.
- Work to facilitate effective dissemination and understanding of relevant prevention research results to HIV prevention workers and to those in community-based and other settings.

OBJECTIVE–C: Coordination and Collaboration Efforts

Develop, implement, and evaluate methods of coordination and collaboration on HIV/AIDS communication activities across NIH Institutes and Centers (ICs), among other Federal and non-Federal groups, and with international partners.

STRATEGIES

- Promote and foster information dissemination regarding research and programmatic efforts across the ICs, among U.S. Government agencies, and with international partners.
- Promote collaboration among all ICs in providing information about their HIV/AIDS clinical trials to *AIDSinfo* and *ClinicalTrials.gov*.
- Build and enhance partnerships among CBOs/NGOs and basic, clinical, and behavioral researchers to encourage exchange of information and experience.
- Continue collaborations with the Joint United Nations Programme on HIV/AIDS, the Pan American Health Organization, the International AIDS Society, and other international AIDS agencies or societies on information/communication efforts, including information about international clinical trials and training opportunities.
- Collaborate with public and health sciences libraries, health care providers, AIDS Education and Training Centers, and community-based HIV/AIDS service organizations to facilitate access to needed information and disseminate NIH HIV-related reports.
- Expand collaboration to include academic, medical, and other communities, as appropriate, in the dissemination of NIH HIV-related reports.
- Expand the development and sharing of HIV/AIDS resources on the Internet to facilitate national and international research collaboration and data sharing.