PRIORITY:

Translating Research From Bench to Bedside to Community

Natural History and Epidemiology

Information Dissemination

AREA OF EMPHASIS

Natural History and Epidemiology

FY 2012 RESEARCH PRIORITIES

- 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, maintain, and effectively utilize research resources, such as domestic and international observational and intervention studies, collaborative networks, databases, and biological sample repositories from populations experiencing emerging, re-emerging, and ongoing HIV epidemics.

- Encourage development and evaluation of novel methods for HIV testing, linkage and retention to care, and for monitoring response to care for use in domestic and international settings. This priority activity would include conducting research on: (1) accurate, reproducible, and affordable virologic, immunologic, pharmacologic, and genetic assays; (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 initiation of antiretroviral therapy at a population level; and (6) methods for measuring, preventing, and treating comorbidities.

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 populations to guide prevention and treatment strategies.

STRATEGIES

- Utilize existing cohorts, and develop new cohorts of novel subpopulations (especially newly emerging, vulnerable groups), to employ novel methods (e.g., social/sexual network analysis, molecular epidemiology, temporal phylogenetic analyses, and geographic information systems), alone and in combination, to further assess the magnitude of 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) on the risk of HIV acquisition and to assess the impact of in-country resource capacities and availability on HIV progression and outcomes.
- Conduct molecular epidemiology studies to identify and estimate the 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), response to pre-exposure prophylaxis, 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 intervention and therapy.
- Refine epidemiologic and mathematical models to improve estimates of per-contact risk of HIV transmission and to develop estimates of population-attributable risk, based on type of sexual exposure; characteristics of the infected and uninfected partners (e.g., plasma and/or anogenital tract viral load, host genetics, and coinfections); and cofactors (e.g., drug use, psychiatric comorbidities, and ART).
- Examine the test-and-treat concept in the United States and internationally, using both clinical and mathematical models, focusing on test-and-treat both alone as a form of prevention and also as part of a larger scale prevention package.

Strategies Related to Transmission and Its Prevention

- Investigate viral, host, and environmental characteristics that distinguish individuals who have not become infected with HIV despite intensive or prolonged exposure to the virus.
- 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, semen, and mucosal compartments such as the female genital tract and the anorectal mucosa);
  - Host factors such as age, sex, race, socio-economic status, country of origin, hormonal status, strength and breadth of immune response, comorbid chronic diseases, coinfections, and host genetics;
  - Modifiable factors such as diet and nutritional status (including food insecurity); 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 hepatitis;

- 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; and racial/ethnic minorities); and
- Sexual activity, abstinence (including during the postoperative period after male circumcision), pregnancy, sexual networks, partner choice (i.e., serosorting or choosing partners from high–low-prevalence populations), partner concurrency, partner fidelity, duration of partnership, sex trade, control of STIs, hygienic practices such as douching, contraception choices, cultural practices such as the use of traditional vaginal preparations and male circumcision, 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:
  - 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 short- and long-term health of women and their infants, and on the emergence of ARV drug resistance in the mother and in those infants who become infected despite prophylaxis;
  - Studying the safety and effectiveness of sustainable approaches to prevention of MTCT of HIV, including the access and provision of maternal ART, identification of successful breastfeeding weaning strategies, methods for improving the safety of formula feeding, ongoing 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 optimization of ART for prevention of MTCT (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, from maternal testing to receipt of test results, provision of PMTCT regimens, retention in care, and infant testing;
  - Assessing the impact of perinatal treatment and prophylaxis regimens on community-wide HIV resistance to ARVs, future regimens, and costs of care;
  - 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; orphans; and pediatric neurobehavioral development; and
  - Assessing the clinical outcomes, cost, and cost-effectiveness of different strategies for prevention of MTCT.

Strategies Related to Prevention and Treatment

- Conduct epidemiologic modeling studies on the aggregate impact of ART on HIV transmission in the presence or absence of other biomedical and behavioral interventions, particularly in settings with endemic, high-prevalence, and emerging epidemics.
- Study the impact of widespread ART availability, adherence, 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 to assess the clinical (i.e., individual) and public health value of programs to promote widespread, frequent HIV testing with immediate linkage to care and ART.

- Conduct research to increase the uptake of and adherence to all steps of the testing and treatment process (testing, linkage to care, initiation of ART, and adherence to ART), with the goal of reducing community-level viral loads.

- 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 male circumcision delivery models with respect to safety, acceptability, cost-effectiveness, and long-term impact on HIV transmission;

  - 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 transmission to uninfected female and male partners, with consideration of the timing of male circumcision.

- Develop and evaluate the effectiveness of individual-, couple-, network-, and community-based interventions for HIV-infected and at-risk persons and their partners to sustain behavioral change and prevent acquisition and transmission of HIV, especially in racial and ethnic minorities, injection drug users, and men who have sex with men (MSM).

- Assess the effectiveness and long-term sustainability of various combinations of prevention strategies (e.g., behavioral changes, ART, biomedical interventions, and treatment for coinfections and comorbidities).

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 and response to ART, 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 host and viral genetic characteristics and differences by route of exposure, and continue to characterize the natural history 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, overall and by age group.
- Investigate the effect on disease progression of viral factors, including viral type, subtype, and genetic variation; fitness; viral tropism; and innate and acquired genotypic and phenotypic resistance to ARVs.
- 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 these therapies.
- Characterize the changing spectrum of clinical outcomes, causes of morbidity and mortality, complications of ART, and cost patterns associated with evolving therapeutic strategies, domestically and internationally.
- Use observational studies in resource-limited settings to estimate the HIV prevalence, incidence, and correlates of treatment failure.
- Assess the effect of ART on the incidence, pathogenesis, and presentation of cancers in 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, and liver disease) in HIV-infected individuals. Use mathematical models to project the frequency, outcomes, and costs of treatment for these comorbidities in HIV survivors.
- Characterize in a prospective manner 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 the spectrum of malignancies not associated with HIV that may develop in HIV-infected patients who have responded to ART and thus are living longer with immune deficiency.

- Investigate the role of risk factors such as chronic inflammation in the development of malignancies and metabolic, cardiovascular, bone, renal, and liver disorders in HIV-infected individuals and appropriate controls, and how cumulative and current ART use might mediate or mitigate the effects of chronic inflammation.

- Establish standards in different regions of the developing world 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 viruses, and helminthic infections) on such standard values.

- 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 outcomes related to methods of integrating TB and HIV care 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 use and abuse, illicit drug use, 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.

- Identify, characterize, and determine 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 cancer and high-grade dysplasia in HIV-infected women and in MSM.
- Evaluate the effectiveness of HPV vaccines among HIV-infected individuals (female and male) from geographically diverse regions.
- Evaluate different cervical dysplasia and cancer identification methods in HIV-infected women for sensitivity, specificity, cost-effectiveness, and appropriateness.
- Assess the effect of primary care screening and interventions (e.g., statin use; hypertension management; smoking cessation; treatment of depression, STIs, and viral hepatitis; and cancer screening and treatment) on HIV disease outcomes, survival, and costs of care. Use these assessments to guide the development of improved interventions and to inform recommendations for adoption and prioritization of primary care guidelines tailored to patients living with HIV infection.
- 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 MTCT and Pediatric HIV Infection

- Assess the implications and outcomes, including uptake, of different strategies of prevention of MTCT on transmission and costs of care in HIV-infected mothers and their infants.
- Evaluate the differences in adherence, treatment response, 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 pediatric populations 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, and how these may be affected by biomedical and behavioral interventions.
- 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, and dyslipidemia), as they affect disease outcomes and survival.

- Study the incidence and determinants of physical, neurologic, and cognitive decline in aging HIV-infected individuals and the effect of frailty and functional impairment on HIV, ART, 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, and mortality in older versus younger adults receiving ART to refine treatment guidelines for older HIV-infected patients.

Strategies Related to Adherence, Linkage to Care, Retention in Care, and Quality of Life

- Elucidate the effects of HIV infection on pain and sleep disturbances, including prevalence, possible immunological and endocrine mechanisms, associations with HIV outcomes, possible changes with ART, and influence on quality of life and physical and mental health.

- Develop studies on the impact of routine, voluntary HIV testing, point-of-care rapid testing, home-based testing, and Internet-based test notification, and their roles in different prevalence settings in increasing linkage and access to care, retention in care, and improving HIV-related outcomes.

- Examine predictors of successful care outcomes, including linkage to and retention of HIV-infected patients in care, from the time of HIV testing through ART provision and patient followup.

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 and AIDS in diverse domestic and international populations.
- 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.
- Use mathematical models to assist in trial design to project value of information and to assess which trials are most feasible and cost-effective.
- When feasible and appropriate, involve representatives of the community and study participants in all phases of research planning, design, management, approval, and reporting, and promote and support academic/community-based research collaborations.
- Assess different strategies to improve community education about research and community involvement in planning, interpretation, implementation, and dissemination of research.
- Promote study designs that provide the highest degree of human subject protection and benefit possible, according to U.S. Government requirements, as well as local requirements in the case of international research.
- Promote the development and dissemination of simple point-of-care tools appropriate for both industrialized and resource-limited settings to standardize the objective 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 remote or otherwise underserved areas.

Strategies Related to Natural History/ Pathogenesis

- 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, 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.

- Develop assays to distinguish between serological changes induced by HIV vaccine candidates and those induced by HIV infection in countries where nucleic acid tests are not readily available.

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;

  - Methods for sampling hidden populations (e.g., venue-based, Internet-based, snowball, mixed method, respondent-driven, and time-location 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 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, especially as they relate to transmission and spread of HIV infection; and

  - Methods for multilevel analysis of population-based HIV/AIDS surveillance data.

- 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.

- Support studies that make innovative use of existing data (e.g., cohorts, surveillance data, routinely collected service delivery data, and data from monitoring and evaluation systems) for well-designed, rigorous analyses, hypothesis generation, and hypothesis testing.

- 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 the various operational strategies that can be employed for the implementation and dissemination of efficacious, evidence-based preventive or therapeutic interventions (e.g., male circumcision) and to evaluate countrywide ART programs, including the use of implementation science research and integrated observational databases, to evaluate treatment effectiveness and cost-effectiveness at the individual, community, and population levels.

- Improve understanding of how best to disseminate effective interventions, deliver effective interventions most efficiently, transfer interventions from one setting or population to another, and make informed choices among available interventions.

- Study and evaluate prevention packages that combine multiple strategies into one intervention, especially those that combine behavioral, biological, and structural interventions.

- Develop studies to compare the effectiveness, efficacy, and cost-effectiveness of various HIV prevention strategies (e.g., opt-out testing, secondary prevention, and immediate ART) between populations with generalized versus concentrated epidemics.

- Assess the optimal algorithms for HIV diagnosis in patients, including strategies for identification of acute 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.

- Develop and refine simulation and modeling strategies to assess the costs and impacts of a variety of interventions on HIV transmission, cofactors of HIV infection, and community-wide morbidity and mortality.

- Assess the effectiveness of strategies designed to reduce the impact of comorbidities, including smoking cessation, vaccination against HBV and HPV-16/18, and cytologic screening for cervical and anal cancers.

Strategies Related to Implementation

- Design and implement evaluations of 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.
- Assess the impact and acceptability of routine, voluntary HIV testing programs and new models for point-of-care testing and results notification, including issues such as stigma and confidentiality.
- Support HIV policy research, including studies of laws and economics, necessary for translating epidemiological and clinical studies into policy to improve health and to make cost-effective clinical and policy decisions.
- Assess the impact of strategies for managing HIV coinfections in international settings using modeling and other integrative methodologies.

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, 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 current 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.
- Widely disseminate experimental findings regarding AIDS-related studies using nonhuman primates, as well as information concerning the availability of animals for AIDS-related studies.
- Collect, archive, and promote 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.
- 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 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 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 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.

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, and other international AIDS agencies or societies on information/communication efforts, including information about international clinical trials.
- 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.