PRIORITY:

Reducing HIV-Related Disparities

Special Populations:

- Racial and Ethnic Populations
- Women and Girls
- Research in International Settings

Training, Infrastructure, and Capacity Building

AREA OF EMPHASIS

Racial and Ethnic Populations

FY 2012 RESEARCH PRIORITIES

- Encourage high-risk, high-impact research that explores specific environmental and societal factors, including economic disadvantage, racism, sexism, and homophobia that drive: (1) HIV-risk behavior; (2) HIV acquisition, transmission, and disease progression (including the development of viral resistance); and (3) access to, as well as adoption and retention of, preventive and therapeutic interventions for those at highest risk for HIV infection.

- Fund systems-focused research that examines the impact of policies; organization; financing; and delivery of HIV/AIDS-related prevention, care, treatment, and support services in disproportionately affected racial and ethnic populations, including those at highest risk for HIV infection. This includes operations and policy research with a focus on the impact systems have on the health outcomes of gay men and other men who have sex with men (MSM).

- Expand behavioral, intervention, and implementation research that focuses on HIV-related community capacity, preparedness, and/or response readiness (e.g., readiness to adopt specific prevention intervention measures). This research includes the familial, cultural, and community-level factors and their intersection that affect HIV infection, risk of infection, and related health outcomes in racial and ethnic populations.

- Identify practical and cost-effective HIV prevention interventions for racial and ethnic communities, including for those in a sexual minority within these communities.

- Develop and conduct population-specific primary research that focuses on individual-level determinants of HIV risk and infection, including biologic factors, resiliency, and cultural and social norms, in populations at highest risk for HIV acquisition and in communities disproportionately affected by HIV/AIDS. These communities include gay men and other MSM, sexually active women, transgender women, and drug users.

- Identify factors that increase HIV risk among racial and ethnic minority transgender individuals, and develop, pilot, and test models of HIV prevention that reduce or eliminate those factors.

- Fund basic behavioral, intervention, and implementation research that: (1) identifies the factors that promote treatment readiness and treatment adherence; (2) examines the biological and individual factors that affect treatment complications and outcomes; and (3) explores the intersection of individual, community, and systems-level factors that affect treatment outcomes in racial and ethnic populations, with a focus on disproportionately affected communities.

- Determine the impact of race and ethnicity on HIV progression and disease manifestations in racial and ethnic populations, including indigenous populations such as Native Americans, Alaska Natives, Pacific Islanders, and Native Hawaiians.

- Fund studies that examine the impact of incarceration on HIV stage at presentation for care, as well as stage of other comorbid diseases at presentation.

OBJECTIVE–A: System Determinants of Health

Support systems-focused research that examines the impact of policies, organization, financing, and delivery of HIV/AIDS-related prevention, care, treatment, and support services in disproportionately affected racial and ethnic populations, including those at highest risk for HIV infection. This includes operations and policy research, with a focus on the impact systems have on the health outcomes of gay men and other men who have sex with men (MSM), sexually active women across the lifespan, transgendered women, and drug users.

STRATEGIES

- Identify the synergistic effects of the provision of stable housing, treatment, and prevention interventions upon HIV-risk behavior, disease outcome, and treatment adherence in marginalized and high-risk racial and ethnic populations.
- Develop, pilot, and test synergistic prevention interventions for high-risk HIV-uninfected individuals within health care systems.
- Adapt, test, and evaluate new systems-based HIV prevention interventions in disproportionately affected populations modeled upon widely disseminated, effective private-sector social marketing and health communication strategies.
- Utilize implementation science to identify the necessary components of HIV prevention interventions for efficient and rapid translation into racial and ethnic minority populations.
- Identify and modify system-level factors that create barriers to HIV prevention, care, and treatment for incarcerated racial and ethnic minorities when they are released back into their communities.
- Explore the systems of care available to seasonal workers and what factors facilitate, as well as prevent, engagement in HIV testing, care, and treatment.
- Identify and modify system-level factors that create barriers to HIV testing, care, and treatment for aboriginal individuals, including the role that traditional or indigenous medicine does or does not play.
- Identify venues that can effectively deliver acceptable, efficient, and dependable HIV testing for racial and ethnic populations.
- Examine the influence of bias, prejudice, and homophobia upon health care systems and HIV-testing behaviors among racial and ethnic populations.
- Quantify the impact of insurance payor status on HIV care-seeking behavior, treatment, and treatment adherence, as well as on cost of care and years of life lost, among racial and ethnic populations.
- Study the influence of educational systems, educational levels, and health literacy upon HIV awareness and risk behavior within racial and ethnic populations.

OBJECTIVE–B: Environmental and Social Determinants of Health

Encourage high-risk, high-impact research that explores specific environmental and societal factors, including economic disadvantage, racism, sexism, and homophobia, that drive: (1) HIV-risk behavior; (2) HIV acquisition, transmission, and disease progression (including the development of viral resistance); and (3) access to, as well as adoption and retention of, preventive and therapeutic interventions for those at highest risk for HIV infection.

STRATEGIES

- Explore the effects of poverty, residential segregation, inadequate educational opportunities, incarceration, and health literacy upon HIV transmission among racial and ethnic populations across the lifespan.
- Explore the impact of the intersection of residential segregation, poverty, and community isolation upon HIV acquisition and transmission in racial and ethnic populations.
- Examine the influence of race, ethnicity, language fluency, and gender, independently and collectively, upon the social and cultural contexts of HIV acquisition, transmission, and risk.
- Examine the impact of the intersection of poverty, racism, substance abuse, and historical displacement upon HIV-risk behavior and HIV resiliency in indigenous domestic populations, including Native Americans, Alaska Natives, Native Hawaiians, and Pacific Islanders.
- Develop, test, and evaluate new HIV prevention interventions in racial and ethnic minority populations modeled upon widely disseminated and effective social marketing campaigns.
- Study the impact of social, sexual, and drug networks upon the HIV risk of racial and ethnic youth, especially youth in sexual minority.
- Study the impact of social and sexual networks upon HIV resiliency and risk in racial and ethnic populations.
- Develop culturally and racially appropriate HIV testing and prevention interventions that utilize adolescent and youth culture for dissemination in their social and sexual networks.
- Explore the impact of seasonal population migrations (e.g., migrant workers) upon HIV-risk behavior, comorbid sexually transmitted infections, and disease burden within racial and ethnic populations.
- Identify effective, efficient, and sustainable HIV prevention interventions for rural communities with significant numbers of undocumented immigrants and limited access to health care and health care information.
- Determine the effect of stigma, racism, and racial/cultural stereotyping on access to HIV prevention, care, and treatment.
- Examine the influence of bias, prejudice, and homophobia upon health care providers and HIV-testing behaviors among racial and ethnic populations.

OBJECTIVE–C: Family and Community-Level Determinants of Health

Expand behavioral, intervention, and implementation research that focuses on HIV-related community capacity, preparedness, and/or response readiness (e.g., readiness to adopt specific prevention intervention measures). This includes the familial, cultural, and community-level factors and their intersection that affect HIV infection, risk of infection, and related health outcomes in racial and ethnic populations.

STRATEGIES

- Identify practical and cost-effective HIV prevention interventions for racial and ethnic communities, including for those in a sexual minority within these communities.
- Develop, test, and pilot multidisciplinary HIV prevention and treatment interventions that target intersecting antecedents of HIV transmission (e.g., incarceration and drug use, poverty, and homelessness).
- Develop processes for, and measures of, community leader and community organization engagement that predict and/or facilitate effective community mobilization for evidence-based prevention interventions.
- Identify the factors that consistently predict the level of community readiness to engage with HIV prevention research.
- Study the intersection between community and health organizations required for effective prevention message delivery, including the role of key informants, key community organizations, and the linkages necessary for community acceptance.
- Develop models to incorporate community-initiated HIV prevention intervention and evaluation in community–academic partnerships, especially in communities disproportionately affected by HIV.
- Develop culturally and racially appropriate health information tools and dissemination techniques to increase health information literacy and study its impact.
- Incorporate implementation science in the development of HIV prevention interventions for racial and ethnic populations to facilitate prompt scale-up and delivery of effective interventions.
- Evaluate interventions that incorporate traditional and indigenous medicines and medical practices for prevention of high-risk behaviors.
- Identify what constitutes sexual behavior "norms" in racial and ethnic populations, including sexual minorities.
- Explore the impact of prevalent community-derived interventions in response to HIV transmission (e.g., serosorting).
- Conduct community-based and community-driven participatory research on HIV interventions that incorporate community observations and experiences to: (1) create practical and community-appropriate interventions and (2) facilitate bidirectional transfer of knowledge and observations of interest to both the community and the investigator(s).

OBJECTIVE–D: Individual-Level Determinants of Health

Develop and conduct population-specific primary research that focuses on individual-level determinants of HIV risk and infection, including biologic factors, resiliency, and cultural and social norms, in populations at highest risk for HIV acquisition and in communities disproportionately affected by HIV/AIDS. These communities include gay men and other MSM, sexually active women, transgendered women, and drug users.

STRATEGIES

- Develop, pilot, and test synergistic prevention interventions for high-risk HIV-uninfected individuals within health care systems.
- Identify factors that increase HIV risk among racial and ethnic minority individuals in sexual minority, and develop, pilot, and test models of HIV prevention that reduce or eliminate those factors.
- Identify factors that affect an individual's perception of risk within racial and ethnic populations, and determine the effect of those factors upon decisions concerning HIV testing and testing frequency.
- Develop, pilot, and test effective models for increasing the awareness of the benefits of HIV testing in racial and ethnic minority individuals.
- Identify what constitutes sexual behavior "norms" in racial and ethnic populations.
- Identify the behavioral, biological, cultural, and social factors that affect HIV risk, acquisition, and transmission on older women in racial and ethnic populations.
- Conduct basic behavioral research on the determinants of sexual health, as well as HIV risk, in racial and ethnic minority individuals in sexual minority and their social networks.
- Develop, pilot, and test new ecological models of HIV behavioral interventions that incorporate common stressors and experiences for racial and ethnic minority individuals.
- Determine the impact of antecedent personal trauma (e.g., gender-based violence and childhood abuse) upon the adoption and maintenance of HIV prevention strategies in racial and ethnic minorities, with particular attention to adolescents and other individuals in sexual minority.
- Study the biological (including genetic), physiological, and environmental factors that affect HIV acquisition, transmission, and disease progression among racial and ethnic minority individuals.
- Explore the effects of hormone replacement and its biological impact upon racial, ethnic, and sexual minority individuals and the risk of HIV acquisition and transmission.
- Determine the impact of increased education levels on health literacy, HIV awareness, and risk behavior in racial and ethnic minorities.

OBJECTIVE–E: Expanding Research Methods and Measures

Develop and test innovative methods and measures to accurately assess the system, social, community, and individual determinants of HIV risk in racial and ethnic populations, with special emphasis on those underrepresented in current clinical studies.

STRATEGIES

- Recruit and retain racial and ethnic minorities using existing and novel sampling methods to ensure numbers sufficient to provide adequate statistical power to detect racial and gender differences in NIH-sponsored studies, especially Phase III clinical trials.
- Develop novel sampling methods to enhance the proportion of underrepresented populations that are disproportionately affected by HIV infection in clinical and prevention research.
- Develop and standardize assessment tools that are designed for the community in which they are to be used, including rural populations, populations with foreign-born individuals, and racial and ethnic populations at risk for HIV acquisition.
- Develop, pilot, test, and evaluate new measures of HIV-risk behavior that are culturally and contextually appropriate for racial, ethnic, and sexual minority populations.
- Develop novel methods of delivering HIV care and treatment interventions in nontraditional venues for racial and ethnic populations, including those that utilize social networks and technology to enhance community penetration and effectiveness.
- Develop measures to assess the impact of evidence-based quality-of-care and best practices upon HIV disease outcome in racial and ethnic minority individuals.
- Develop novel clinical research methodologies for prospective studies of the effect of racial, ethnic, gender, and sexual orientation differences on HIV transmission, disease pathophysiology, and treatment outcomes.
- Utilize implementation science to identify what determines which HIV prevention interventions are ready or necessary for efficient and rapid translation into the field.
- Evaluate interventions that incorporate traditional and indigenous medicines and/or medical practices that encourage adherence to prevention and/or treatment protocols.
- Develop, pilot, and test models of HIV behavioral interventions that incorporate common resiliency factors for racial and ethnic populations, such as cultural identity, spirituality, family ties, and collectivism.

OBJECTIVE–F: Treatment and Treatment Access

Fund basic behavioral, intervention, and implementation research that: (1) identifies the factors that promote treatment readiness and treatment adherence; (2) examines the biological and individual factors that affect treatment complications and outcomes; and 3) explores the intersection of individual, community, and systems-level factors that affect treatment outcomes in racial and ethnic populations, with a focus on disproportionately affected communities.

STRATEGIES

- Advance the study of the biology of HIV infection among racial and ethnic populations by:
  - Evaluating the effect of race/ethnicity and gender upon immune dysfunction and the development of opportunistic infection;
  - Determining the effect of race/ethnicity and gender upon the individual response to HIV therapy and the development of HIV drug resistance; and
  - Exploring the role of pre-existing health conditions disproportionately found in racial and ethnic minorities, such as cardiovascular disease, diabetes, and hepatitis, upon HIV treatment, disease course, and progression.
- Determine the impact of race and ethnicity on HIV progression and disease manifestations in understudied indigenous populations, including Native Americans, Alaska Natives, Pacific Islanders, and Native Hawaiians.
- Identify successful interventions to increase access to care and quality of care in racial and ethnic communities, and assess the impact of increased care upon HIV transmission in these communities.
- Examine the intersection of race, gender, and socioeconomic factors upon seeking, accessing, and remaining in HIV care and treatment.
- Develop and evaluate therapeutic strategies for preventing and treating complications of HIV infection, particularly those complications more prevalent among racial and ethnic populations.
- Develop novel multidisciplinary interventions that target the barriers to HIV care and treatment.
- Evaluate models for HIV prevention, care, and treatment that utilize comprehensive, culturally and contextually appropriate interventions for HIV-infected individuals in disproportionately affected communities.
- Identify community and environmental factors that can facilitate seeking and remaining in care.
- Strengthen—through enhanced research collaboration—nontraditional community partners for the conduct of treatment and treatment adherence research in racial and ethnic populations.

OBJECTIVE–G: Comorbidities—The Intersection of Multiple Health Disparities

Expand the study of the interrelationship between HIV infection and comorbid conditions as they affect: (1) access to appropriate care and treatment, (2) adherence to treatment, (3) retention in care, and (4) health outcomes for racial and ethnic populations.

STRATEGIES

- Examine the impact of alcohol, drug use, and chronic medical and neuropsychiatric comorbidities on care-seeking behavior.
- Examine the impact of substance abuse and chronic mental health comorbidities upon retention in care and HIV morbidity in racial and ethnic populations.
- Determine the impact of treatment interventions upon progression of HIV disease and HIV-associated coinfections and comorbidities, including hepatitis B infection and hepatitis C infection, tuberculosis (TB), and HIV-associated malignancies, in racial and ethnic individuals.
- Determine the roles of providers and patients, individually and collectively, in the success or failure of HIV treatment interventions, transmission of HIV resistance, and ultimate HIV disease progression in racial and ethnic minorities.
- Examine the impact of incarceration upon HIV stage at presentation for care, as well as stage of other comorbid diseases at presentation.
- Evaluate the impact of underlying cardiovascular, endocrine, metabolic, neurologic, psychiatric, and renal disorders upon treatment acceptance, treatment effectiveness, and HIV disease progression.
- Examine the resurgence of sexually transmitted infections within racial and ethnic communities and the impact of such resurgence upon treatment options and HIV morbidity and mortality.
- Explore the impact of late testing and combination antiretroviral therapy on the progression of opportunistic infections among racial and ethnic minorities, especially hepatitis B infection, hepatitis C infection, TB, and HIV-associated malignancies.
- Develop effective interventions to decrease the risk factors associated with the development of HIV-associated malignancies among racial and ethnic minority individuals living with HIV infection.

AREA OF EMPHASIS

Women and Girls

FY 2012 RESEARCH PRIORITIES

- Design and conduct studies that integrate the biological, behavioral, and social sciences to explain factors that influence HIV risk, pathogenesis, and prevention in women, girls, and infants.
- Define and analyze normal and abnormal female genital tract and anal/rectal immune function and their impact on HIV risk and acquisition.
- Define and analyze the impact of aging on HIV risk, pathogenesis, and prevention in women compared with men.
- Develop and study interventions to prevent intrapartum and breastfeeding-related mother-to-child HIV transmission.
- Define and study interventions to affect maternal factors that contribute to mother-to-child HIV transmission.

OBJECTIVE–A: Determinants of HIV Transmission

Elucidate the biologic determinants of HIV transmission; define the mechanisms by which innate and adaptive viral and host immune factors influence HIV transmission, acquisition, and resistance to infection in non-pregnant and pregnant women and girls across the life cycle.

STRATEGIES

- Evaluate the role of viral characteristics and host immune function on HIV transmission, acquisition, and resistance to infection.
- Investigate the relationship of age and endogenous and exogenous hormone status on HIV transmission, acquisition, and resistance to infection.
- Evaluate the role of oral, anal/rectum, and genital tract physiology, innate and adaptive immunity, microbiology, and concomitant infections on cellular mechanisms on HIV transmission, acquisition, and prevention.
- Study genetic factors and the impact of host factors, including anatomic/physiologic changes, non-hormonal and hormonal contraception use, and vaginal and rectal practices, on HIV transmission, acquisition, and resistance to infection.
- Study the impact of other sexually transmitted infections (STIs) and syndromic or disease-specific STI treatment and exposure to semen on HIV susceptibility, transmission, acquisition, and resistance to infection.
- Study the impact of antiretroviral therapies (ARTs) on genital tract and anal/rectum viral dynamics and vertical and sexual HIV transmission, acquisition, and resistance to infection.
- Identify and study appropriate animal models to explain host-viral-immune interactions and mechanisms of infection.
- Develop standardized assays to investigate host, viral, and immune factors.
- Develop standardized techniques for sampling upper and lower genital tract, anus/rectum, and oral mucosa that are minimally invasive or noninvasive and do not promote HIV acquisition.

OBJECTIVE–B: Biomedical and Behavioral Prevention Interventions

Conduct and support basic, translational, preclinical, and clinical biomedical and behavioral intervention research to prevent HIV and other STI transmission, acquisition, and resistance to treatment in pregnant and non-pregnant, HIV-infected and -uninfected women and girls across the life cycle.

STRATEGIES

Joint Biomedical and Behavioral Strategies

- Support an integrated approach to HIV, STI, and pregnancy prevention research that includes linked behavioral and biomedical studies that consider the social context of the population in which the interventions will be applied.
- Support research to understand how the organization, financing, management, cost-effectiveness, and cost-utility of health care, including reproductive health and social services, affect HIV risk, transmission, acquisition, and resistance to infection.
- Analyze the impact of community-level sociologic and behavioral norms on the acceptability and efficacy of and adherence to biomedical and behavioral HIV/STI prevention interventions.
- Analyze the impact of HIV prevention interventions conducted in males on HIV and STI acquisition in females.
- Develop and evaluate methods to access, recruit, and retain women and girls who are demographically representative of the populations at risk for HIV infection into separate and integrated biomedical and behavioral prevention intervention studies.
- Develop and assess the effectiveness of utilizing multiple prevention approaches, including biological, behavioral, and community-level strategies, both individually and in combination, as a potential means for preventing HIV and other STI transmission and acquisition.
- Support research to identify effective methods to improve the translation, dissemination, and increased adoption of effective HIV prevention technologies by women and girls and by their communities, health care providers, and prevention services providers.
- Support research to understand the impact of HIV-related policies and policy changes on HIV-risk behavior and transmission.
- Support research to identify and develop methods to overcome barriers to enrolling girls under the age of 18 and from racial and ethnic populations and other hard-to-reach populations into HIV biomedical and behavioral prevention intervention trials.
- Support research to evaluate the differences between trial participants and their in-trial behaviors and the general community in which HIV prevention interventions will be used.
- Develop and evaluate biomedical and behavioral interventions that target HIV-serodiscordant couples to prevent HIV and STI transmission and prevent or allow pregnancy.
- Investigate the interaction between HIV-risk perception, sexual behaviors and activity, and age of sexual debut on the use of HIV prevention methods.
- Develop, implement, and evaluate biomedical and behavioral HIV/STI prevention interventions that identify and decrease the role of violence, power discordance, intimate partner substance use, and economic survival sex on HIV/STI risk.
- Discover, develop, and conduct preclinical and clinical evaluation of new and current biomedical and behavioral prevention interventions to reduce the transmission and acquisition of HIV and STIs during pregnancy and breastfeeding.
- Conduct research to understand the impact of pregnancy intention and obligation for individuals, couples, and communities on the use of HIV prevention technologies and behaviors.

Biomedical Strategies

- Investigate the interaction between HIV, its treatment, and aging and age-related comorbidities.
- Develop novel interventions that prevent or treat the comorbidities related to the long-term sequelae of HIV infection or its treatment.
- Discover, develop, and conduct preclinical and clinical evaluation of new and current biomedical prevention interventions to reduce the transmission and acquisition of HIV superinfection and other STIs among HIV-infected women and girls.
- Evaluate the impact of biomedical prevention interventions on upper and lower genital tract and anal/rectal physiology, microbiology, mucosal integrity, and innate and adaptive immunity on the risk for the transmission or acquisition of HIV and other STIs.
- Evaluate the impact of endogenous and exogenous hormones on upper and lower genital tract and anal/rectal physiology, microbiology, mucosal integrity, and innate and adaptive immunity on the risk for the transmission or acquisition of HIV and other STIs.
- Develop and study the efficacy of contraceptive and non-contraceptive biomedical interventions to prevent HIV and other STIs.
- Determine how mode of delivery, rheologic properties, and contraceptive efficacy of biomedical HIV/STI prevention interventions affect and improve acceptability and adherence.
- Analyze the interaction between HIV, STIs, trauma, sexual practices, contraception, and female genital mutilation, and how the presence of STIs and their specific or syndromic management affect upper and lower genital tract and anal/rectal physiology, microbiology, mucosal integrity, innate and adaptive immunity, and risk for HIV acquisition and transmission.
- Study the impact of biomedical interventions to prevent mother-to-child transmission, including antiretrovirals (ARVs), cesarean section, and breastfeeding interventions, on maternal morbidity and mortality and on long-term morbidity and mortality.
- Develop treatment and technological interventions to prevent mother-to-child breastfeeding-related HIV transmission.

Behavioral/Sociological Prevention Strategies

- Conduct and support behavioral intervention research to address the female- and couple-specific psychological, social, environmental, economic, and cultural dynamics that affect HIV risk, acquisition, and transmission.
- Identify and study the impact of population-level and community-level social, economic, educational, and behavioral interventions on HIV acquisition and prevention.
- Investigate changes in HIV-related risk and prevention behaviors as a function of developmental and life-course events, such as adolescence, childbearing, sexual partnership choice and change, HIV treatment, menopause, aging, and the presence or absence of family, social, and economic support.
- Develop innovative prevention strategies targeting male partners whose behaviors confer risk for HIV transmission to female partners, particularly in populations/areas with elevated HIV prevalence.
- Develop, implement, and evaluate culturally focused behavioral prevention interventions for populations traditionally perceived to be at low risk for HIV infection, such as middle-aged and older women, college students, persons with physical and mental disabilities, women who have sex with women, residents of rural areas, Asian/Pacific Islanders, Native Americans, and Alaskan Natives.
- Study the impact of macro events and social unrest such as (but not limited to) natural disasters, trauma, war, and refugee status on HIV risk behaviors and acquisition for women and girls globally.
- Conduct basic research to understand the dynamics of gender-specific stigma/discrimination associated with HIV/AIDS and to inform the development of structural interventions to reduce HIV/AIDS-associated stigma.

- Support behavioral and social science intervention research to reduce stigma and sex-related inequalities that may increase transmission to women.
- Develop and evaluate interventions to reduce or prevent adverse psychological, social, and economic consequences for women and girls infected with or affected by HIV/AIDS.

OBJECTIVE–C: Biology of HIV Disease

Study the biology of HIV infection in pregnant and non-pregnant women and girls across the life cycle, including the viral life cycle, disease progression, clinical manifestations, coinfections, sexual dimorphism, and other conditions.

STRATEGIES

- Develop and evaluate innovative and rapid testing strategies in diverse settings to identify acute and chronic HIV infection in women and girls.
- Identify the mechanisms that mediate virus/host interactions and affect disease progression.
  - Determine the HIV viral dynamics, tissue distribution, and replication in blood and in all viral reservoirs specific to females in varied racial and ethnic populations across the human life cycle.
  - Investigate the role of cofactors and mediators of disease progression in both early- and late-stage disease, including:
    - Endogenous and exogenous hormones, puberty, pregnancy, aging, autoimmune diseases, and other concomitant diseases;
    - Opportunistic infections (OIs), other coinfections, HIV superinfection, HIV treatment, intermittent ART and monotherapy for the prevention of perinatal transmission, and genetic factors; and
    - Nutrition, biological indicators of stress, substance use, HIV-related and unrelated medication use, and complementary and alternative treatments.
- Develop approaches for identifying, recruiting, enrolling, and retaining recently exposed and newly HIV-infected women and girls for studies on the biology of HIV infection and prevention.
- Elucidate the sex-specific etiologies and pathogenic mechanisms of HIV disease manifestations in women and girls.
  - Investigate HIV-specific and therapy-associated metabolic and body composition changes at varied stages of HIV infection and at varied ages.
  - Study HIV-specific alterations of puberty, the menstrual cycle, fertility, menopause, and sexual function.
  - Conduct studies on the gynecologic (gyn) manifestations of HIV disease and the impact of HIV on the efficacy of gyn disease treatment.
  - Investigate risks for and novel characteristics and interactions, pathogenesis, screening treatments, and outcomes of HIV-related preneoplastic and neoplastic conditions, including human papillomavirus (HPV), specific to women and girls.
  - Study and outline the female-specific neurological and neuropsychological manifestations of HIV disease and underlying cofactors that affect these manifestations.
  - Investigate the impact of aging, menopause, and perimenopause on HIV disease manifestations and progression.
  - Investigate clinical manifestations and morbidity related to HIV and HIV-related therapies in pregnant, peripartum, and postpartum women.
  - Investigate the impact of HIV and related coinfections and therapy on fetal, infant, and childhood development.
  - Evaluate the impact of HIV and HIV-related therapies on breast milk quantity and quality, and on the development of breastfed infants.

- Explore the role of pharmacogenetics on variations in the course of HIV disease and outcomes of ARV therapies in women and girls.
- Study the impact of HIV infection and disease progression on women's and girls' sexual development, reproductive health, and reproductive decisionmaking.
- Examine the association between sex-specific physical and psychosocial consequences of HIV disease and the initiation and maintenance of HIV-related care.

OBJECTIVE–D: Treatment and Care of HIV Disease

Conduct basic, translational, preclinical, and clinical research to inform the diagnosis, care, and treatment of HIV-infected women and girls across the life cycle, including puberty, pregnancy, and menopause. Emphasis should be on the inclusion of vulnerable and marginalized populations like adolescents and racial and ethnic minorities.

STRATEGIES

- Assess novel case-finding approaches, including social- and risk-network-based strategies to identify undiagnosed HIV infection in women and girls at risk.
- Develop and evaluate innovative strategies in diverse settings to identify and link HIV-infected women and girls to care and treatment services, including cancer prevention and screening services.
- Study the impact of receiving an HIV-positive test result on HIV-risk behaviors, seeking access to and participating in treatment and care, and reproductive decisionmaking.
- Study the effectiveness and reasons for the success and failure of new and existing therapeutics in treatment-naive and treatment-experienced women and girls.
- Evaluate the short- and long-term effects of anti-HIV therapy on morbidity and mortality among women and girls across the life cycle.
- Study interventions and other factors that affect adherence to HIV therapeutic regimens and to medical care.
- Evaluate the impact of comorbidities and mental health disorders on access to health care and the enrollment of women and girls in clinical trials.
- Develop and evaluate strategies to increase the participation of women and girls in HIV treatment clinical trials.
- Support multidisciplinary research to identify unmet needs and elucidate barriers for women and girls to achieving optimal HIV/AIDS care, support, treatment, and prevention services.
- Conduct research to optimize the diagnosis and treatment of opportunistic infections and other HIV-related comorbidities and coinfections in women and girls.
- Explore the role of pharmacogenetics, pharmacokinetics, pharmacodynamics, ARV activity, and the toxicity of therapeutic agents on general health and on HIV disease progression in women and girls as compared with males across the life cycle.
- Investigate the medication interactions of ARVs, and of ARVs with other HIV-related and -unrelated therapies, specifically in women and girls.
- Evaluate the interaction and pharmacokinetics of ART and hormonal contraception when used simultaneously.
- Measure the quantity, frequency, and impact of alcohol, tobacco, and other substance use in women and girls in HIV-related therapeutics trials.
- Study the effects of ART on HPV-associated disease.
- Study the effect of the HPV vaccine on HIV disease and the reduction of HPV-related lesions in HIV-infected women and girls.
- Study viral-specific and ART-associated changes in the onset of puberty, the menstrual cycle, fertility, and sexual function and dysfunction.
- Study the effect of ARVs and other HIV-related therapies on HIV viral dynamics, tissue distribution, and replication in blood and viral reservoirs in women of varied race and ethnicity across the life cycle.

- Study how treatment interventions in acute and chronic HIV infection, including treatment during pregnancy, affect short- and long-term HIV disease progression.
- Design and evaluate effective models for service delivery that improve access and adherence to care.
- Identify appropriate female-specific HIV quality-of-care indicators and study the impact of implementing quality-of-care guidelines on the community- and country-level health status of women and girls.
- Study the impact of stigma on access to and use of health services and HIV treatment.
- Study the impact of access to care for women on family health.
- Support research to understand the impact of policy and policy change on the delivery and utilization of HIV/AIDS-related services, HIV-risk behavior and transmission, and HIV/AIDS disease outcomes in women and girls.
- Develop and evaluate accessible assisted reproductive technologies designed to assist in meeting fertility desire without vertical or horizontal HIV transmission.

OBJECTIVE–E: Ethical Issues

Conduct and support research, training, and education on ethical issues that affect the access to and participation of women and girls in HIV/AIDS-related research.

STRATEGIES

- Develop and evaluate methods to facilitate obtaining fully informed consent from potential clinical trial participants.
- Investigate the unintended social and community consequences of policies and practices (including research practices) that provide special benefits, including treatment for HIV-infected individuals.
- Investigate unintended harmful and beneficial consequences for women and girls, their families, their partners, and their communities as a result of participation in research studies.
- Examine the ethical risks and benefits of studies that involve treatment versus observation of women and girls.
- Investigate the ethical impact within a community of studies in which clinical trials provide the only access to therapeutics for women and girls.
- Assess the potential risks and benefits for women and girls living where community-level epidemiological research is being conducted.
- Study the ethical issues related to HIV-specific diagnostic and therapeutic strategies implemented during pregnancy and lactation.
- Study the ethical issues related to providing family planning services and breastfeeding alternatives in communities where these interventions may not be acceptable.
- Study the ethical issues related to the participation of women and girls in clinical trials.

AREA OF EMPHASIS

Research in International Settings

FY 2012 RESEARCH PRIORITIES

- Develop in-country leadership and support sustainable capacity in HIV/AIDS research in low- and middle-income countries through strengthened research training in all relevant disciplines, by building research infrastructure, and through implementation and evaluation of new training methodologies (such as Web-based distance learning), in collaboration with other partners.

- Design and evaluate effective and sustainable biomedical and behavioral interventions at multiple levels (including complex, combined approaches), with a particular emphasis on social and structural interventions and implementation science, to prevent HIV transmission.

- Identify more effective care and treatment approaches, integrated with prevention and operational strategies based on implementation science research, to reduce HIV-related morbidity and mortality.

- Develop, refine, and validate assays and approaches to identify recent HIV infection, and develop cross-sectional measures of incidence densities across HIV-1 subtypes, host populations, and epidemic stages.

OBJECTIVE–A: Capacity Building

Develop a sustainable, collaborative research environment by utilizing existing scientific and public health structures and enhancing in-country capacity.

STRATEGIES

Site Development

- Assess existing international study sites supported by the NIH, and, as needed, further develop sustainable sites, or establish new in-country sites as rapidly as possible to address urgent and emerging scientific opportunities, while coordinating with ongoing NIH-funded research programs.
- Enhance capacity for the conduct of basic and applied prevention and treatment research, with emphasis on maintaining and developing both Good Laboratory Practice and Good Clinical Practice requirements for large-scale clinical trials, through:
  - strengthening laboratory capacity through the provision of required equipment and human resource development, with appropriate quality assurance and training;
  - developing diagnostic and clinical capabilities through research training and "hands-on" research experiences;
  - developing affordable alternatives to viral load, CD4+ cell counts, resistance testing, and other expensive laboratory tests used for monitoring treatment efficacy and toxicity;
  - developing alternative technologies and assays for the diagnosis and monitoring of HIV-related coinfections (e.g., tuberculosis) in resource-limited settings, with a goal to be more affordable, simpler (i.e., not requiring electricity, refrigeration, and/or computer), requiring less operator training, and environmentally more durable (i.e., withstanding high ambient temperature, humidity, and dust) than current technologies;
  - enhancing existing anatomic pathology and histopathology laboratory practices to develop more accurate (differential) diagnosis, ascertainment, and research capabilities of HIV-associated comorbidities, particularly in regions such as sub-Saharan Africa;
  - supporting the analysis of scientific and research-based international databases and developing common laboratory information management systems;
  - enhancing capabilities in medical records management, data analysis, and biostatistics;
  - addressing barriers in maintaining, optimizing the use of, and ensuring human subject protections related to repositories of biological specimens in resource-constrained countries;
  - developing and testing strategies that support the recruitment and retention of participants in prevention, treatment, and care studies;
  - optimizing epidemiological assessments of targeted at-risk populations, including refining respondent-driven sampling, venue-time sampling, and Internet-based sampling, among other approaches to population-based recruitment of hard-to-reach populations;
  - enhancing the ability to ensure protection for human subjects involved in research and the ethical conduct of research, including informed consent and issues specific to women, children, adolescents, and the elderly, as well as vulnerable populations, including injection drug users, men who have sex with men, prisoners, and others at risk.
  - strengthening the capacity of institutional review boards (IRBs), including information-sharing between IRBs, updates on recent development, and building capacity for IRBs for review and monitoring of approved protocols;
  - addressing regulatory issues and oversight mechanisms related to biomedical and behavioral clinical research;

- conducting research on the feasibility, success, and sustainability of rapid scale-up of pilot projects and/or early Phase I and II trials to large research studies (including Phase III trials) and on how to apply and implement research findings in intended populations;
- enabling communities to participate in the development and design of HIV-related research (including clinical trials) as well as in the translation of research results into community-relevant programs, standards of care, and practices;
- enhancing mechanisms for information exchange among investigators, including enhanced electronic communication;
- strengthening library services and access to scientific resources; and
- strengthening capabilities of in-country staff in financial/grants management, administrative practices, and scientific/peer review.

- Build global capacity to conduct implementation science (i.e., operational) research, including outcome and cost-effectiveness studies and modeling, to rapidly address emerging priorities in prevention, treatment, and care.
- Conduct studies on HIV incidence and feasibility, using appropriate incidence measures (e.g., population-specific assays), in order to identify sites suitable for the conduct of efficacy trials of HIV prevention, treatment, and care interventions.
- Foster regional approaches to research in order to enhance communication, avoid duplication of effort, achieve economies of scale, help establish new collaborations, and address common issues and needs (i.e., gap analysis) related to HIV-related research among countries in a given region, such as:
  - conducting regional meetings and training workshops;
  - facilitating the sharing of resources across regional sites; and/or
  - developing regional centers for advanced medical technology and/or training in foundation specialties (e.g., pathology, cytology, and radiology) to build workforce capacity.

Collaboration and Coordination

- Ensure the leadership role of in-country investigators, community-based and indigenous leaders, and other stakeholders in countries where studies take place by involving them in all stages of the research, including conceptualization of the research question, study design, development of protocols, study implementation, data collection and analysis, publication, and presentation of research results to government and other relevant stakeholders and audiences.
- Encourage the integration and coordination of research projects being conducted by NIH-funded U.S. researchers in resource-limited countries with established in-country programs, while collaborating with local investigators on strategic planning for research, to ensure project relevance and to optimize the research effort.
- Encourage the continued development of research collaborations between international and U.S. investigators, and encourage U.S. researchers to participate at the developing country research site to better understand the challenges of conducting research and providing care and services in such settings.
- Coordinate with other U.S. Government agencies, foreign governments, and international organizations to help identify and support priorities for research infrastructure and capacity building in developing countries.
- Explore and assess the efficacy of collaborations with non-physician health professionals (e.g., nurses, pharmacists, and health aides) and community members (including faith and religious communities, elders, indigenous/traditional healers, student leaders, peer educators, and at-risk populations) to identify practices that may add value in treating and preventing diseases in diverse geographical settings and to facilitate their involvement as partners in AIDS research, prevention, and care, including the optimization of antiretroviral (ARV) rollout in settings with limited numbers of physicians and/or resources.

Ethical Issues

- Ensure that research projects are designed to benefit the communities in which the research is being conducted by addressing locally relevant scientific questions.
- Enhance the capability of institutions in resource-limited settings to conduct independent scientific and ethical reviews, while ensuring timeliness of the review process.
- Ensure education/cross-fertilization between resource-limited countries' ethical review committees and U.S. IRBs, and educate U.S. IRBs about culturally relevant issues in developing countries.
- Identify ways to improve the application of ethical principles in the conduct of research in varied cultural settings by encouraging countries to develop their own set of ethical guidelines and procedures, to include the principles of respect for persons, beneficence, and justice, and the application of informed consent, assessment of risks and benefits, and selection of subjects.
- Ensure that ethical review mechanisms, such as informed consent forms, are relevant and appropriate to the country where the research is conducted and are placed in an appropriate cultural context (including low literacy and local languages).
- Ensure that all research is conducted in accordance with international standards of human rights principles and in accord with the dignity of persons.

Technology Transfer and Translation of Research Results

- Ensure that research results are provided to and understood by participants and the community in which the study is conducted, as well as to the community's health professionals and relevant Ministry of Health personnel.
- Develop effective technologies to enhance communication of research results and translation into prevention, treatment, and care programs.
- Provide improved access to information concerning treatment and prevention guidelines and research results through enhanced information technology.
- Transfer clinical, laboratory, and public health technologies that may be sustained and used for implementation of prevention, symptoms management, clinical training, and patient care programs after research studies are completed.
- Support operational research based on implementation science and innovative research designs not limited to randomized clinical trials (RCTs).

OBJECTIVE–B: Mentoring and Training Investigators

Develop an in-country community of investigators committed to a culture of leadership in research through providing sustainable mentoring for junior investigators and career development opportunities for new, mid-career, and senior investigators.

STRATEGIES

- Provide sustainable research career development opportunities, with incentives for working in-country, for new, junior, mid-career, and senior investigators in resource-limited international settings.
- Provide opportunities for new, junior, mid-career, and senior investigators from developed countries to spend significant amounts of time working with investigators in developing countries.
- Develop in-country training partnerships, and support "south-to-south" training to enable investigators to obtain training appropriate for the areas in which they will work by (1) developing a cadre of in-country scientific professionals, and (2) providing opportunities to enable trained investigators returning to their home countries to serve as training resources for others.
- Continue to support research training, both in-country and in the United States, of clinicians (including non-physician professionals, such as nurses, midwives, and pharmacists), social and behavioral scientists, clinical pathologists, biostatisticians, public health professionals, community health workers, and other researchers from developing nations to enhance the conduct of research on HIV/AIDS, other sexually transmitted infections (STIs), and HIV-related coinfections, malignancies, and comorbidities.
- Provide training in data collection, management, and analysis for in-country research personnel.
- Provide training in the ethical conduct of research, including application of informed consent, establishment of community advisory boards, and other topics related to the protection of human subjects.
- Develop and provide training at international sites conducting vaccine studies on the role and responsibilities of an institutional biosafety committee.
- Enhance training in implementation science research (i.e., translational, operational, and health services research), including training in cost-effectiveness analysis.
- Provide training in all aspects of grantsmanship, including preparation of grant proposals, registration for electronic submission, grants management, reporting requirements, research administration, and fiscal accounting.
- Support research efforts to develop and assess the impact of novel training technologies with applications in low-resource settings, such as Web-based and distance learning, video conferencing, handheld platforms, and other innovative training tools.

OBJECTIVE–C: Structural Interventions

Conduct studies to identify effective structural and policy interventions to address the AIDS epidemic.

STRATEGIES

- Determine barriers and facilitators to acceptance of voluntary counseling and testing (VCT), and develop more comprehensive and integrated health system-level approaches to the provision of VCT, including:
  - assess new VCT approaches for effectiveness and cost-effectiveness with regard to reducing risk from sexual behaviors and substance use in settings with varying levels of HIV seroprevalence;
  - assess approaches to integrate VCT into other existing health services, including family planning, maternal and child health care, and child immunization services; and
  - change community norms for seeking VCT that encourage knowledge of one's status, help mitigate social harm, and reduce HIV stigma.
- Identify the most effective and sustainable strategies for schools, leisure locations, and worksites to support behavior change interventions.
- Investigate the effectiveness of community-based and community-level HIV prevention programs, including prevention education and strategies to evaluate, replicate, and extend effective behavioral interventions.
- Evaluate the various approaches used by different countries for implementing structural interventions and investigate how these approaches may be systematically facilitated.
- Investigate the effectiveness of structural interventions for HIV, STI, and tuberculosis (TB) prevention, treatment, and care among incarcerated populations.
- Evaluate the effectiveness of interventions targeted to drug users and other at-risk populations.
- Develop and test strategies for encouraging voluntary and safe partner notification within the context of families and couples counseling.
- Evaluate the effectiveness and consequences of expanded access to male circumcision programs to implement such expanded interventions.
- Assess and determine optimal combinations of different interventions for specific populations at high risk, as no single intervention is likely to eliminate HIV transmission in all groups.
- Conduct empirical data analysis and modeling to determine required coverage levels for different interventions in order to attain basic efficiencies and maximal effectiveness for specific populations.
- Assess and determine optimal methodologies for evaluation of various structural interventions and their impact, encouraging the use of innovative study designs not limited to RCTs.

OBJECTIVE–D: Interventions to Alleviate Stigma and Discrimination

Develop and test interventions that address the issues of sex/gender, age, power relationships, stigma, and discrimination.

STRATEGIES

- Conduct research on sex/gender identity and age differences and their impact on inequities in access to and use of resources, prevention and care services, and adherence issues, particularly in settings where rights of minorities or vulnerable populations are limited and/or where stigma persists.
- Evaluate the relationship between new technologies and structural interventions (e.g., male circumcision) and gender and power relationships.
- Encourage analysis of sex/gender and age differences in all relevant HIV-related research.
- Study age-, sex-, and gender-related social, behavioral, and biological factors affecting susceptibility to HIV infection and its acquisition or transmission, including:
  - use of medications and/or contraceptives;
  - presence of gender-specific conditions, such as human papillomavirus (HPV) infection and cervical cancer;
  - intimate partner violence; and
  - the conflicting demands of childbearing and avoidance of disease.
- Study how HIV infection psychologically affects women, including their role as heads of households and/or caregivers, their reproductive health requirements, and family support.
- Evaluate strategies to reduce stigma related to choice of infant-feeding modality by HIV-infected women.
- Develop interventions to mitigate the negative social consequences, stigma, and discrimination associated with HIV and AIDS, with particular emphasis on children infected with or affected by HIV.
- Design and evaluate strategies to reduce stigma and discrimination and increase willingness of individuals to enter into voluntary counseling and testing; identify, accept, and implement alternative infant-feeding practices; receive and adhere to antiretroviral therapy (ART) and anti-TB drug regimens; and participate in HIV/AIDS research studies.
- Support the training of community leaders to become role models in the implementation of such strategies and interventions.
- Develop and strengthen innovative research methods, including measures and study designs, for investigating the impact of stigma and discrimination (and interventions to decrease stigma) on HIV prevention, care, and treatment-seeking behavior.
- Evaluate attitudes (e.g., stigma) of health care providers regarding HIV-infected individuals and the effect of these attitudes on provision of care and treatment.
- Study how stigmatization within small social networks (e.g., ostracism and interpersonal violence) can be minimized in order to increase utilization of counseling, testing, and ART, and to reduce further transmission.

OBJECTIVE–E: Prevention of Risk Behaviors in Social Settings and Networks

Study the significance of interactions among individuals in groups engaging in various risk behaviors, and develop and evaluate interventions and strategies to prevent HIV-risk behaviors in social settings and high-risk networks.

STRATEGIES

- Develop and test sustainable interventions at multiple levels (e.g., individual, couple, group, and society) that address multiple risk factors of HIV acquisition and transmission, targeting both HIV-infected and -uninfected individuals in specific populations.
- Develop and test prevention strategies that reflect regional aspects of the epidemic.
- Define sexual and substance use behaviors and their predictors in HIV-infected populations, and design and test interventions to reduce the risk of HIV transmission.
- Develop and test prevention strategies that address relationships between substance use and sexual transmission of HIV.
- Study risk behaviors and prevention of such behaviors among individuals with perinatally acquired HIV who are surviving into adolescence and young adulthood.
- Study the movement of the HIV epidemic across borders and regions, and evaluate the effects of various policies and structural interventions related to migration and immigration on HIV transmission.
- Identify the most effective strategies to reach and prevent HIV transmission among mobile or at-risk populations.
- Develop analytical tools and support innovative methodologies, including ethnographic studies, to better understand and evaluate risk behaviors within social networks.
- Investigate the role of mental health conditions (e.g., depression) and use of psychoactive substances in promoting or facilitating high-risk sexual behaviors that reduce the efficacy of prevention strategies.
- Determine the factors involved in high-risk social networks (e.g., drug and alcohol users and individuals with physical and/or mental disabilities) that influence the rates and patterns of HIV infection, and design prevention programs based on these results.
- Encourage molecular epidemiology studies of viral diversity in the context of social networks.
- Investigate the processes through which some social network interventions become self-sustaining forces for risk reduction and the frequency of this occurrence.
- Devise strategies to prevent substance use initiation, dependence, and transition to riskier drug practices, such as initiating drug injection and sharing of injection equipment.

OBJECTIVE–F: Biomedical Prevention Interventions

Develop and evaluate the application of complex and combined biomedical prevention interventions and strategies.

STRATEGIES

- Evaluate techniques for detection of acute HIV infection, and study the effects of early identification of potential HIV transmitters on HIV infection spread in different settings.
- Utilize population-based studies to examine basic scientific questions about HIV infection, mechanisms of transmission, and host responses, including viral evolution, viral diversity, human immunology, and mucosal factors in transmission.
- Study the risk of transmission of drug-resistant strains of HIV.
- Develop and evaluate methods for increasing access to, acceptability of, and adherence to biomedical interventions, including treatment as prevention.
- Study and integrate the behavioral aspects of complex, combined biomedical interventions and strategies.
- Conduct research on how best to deliver prevention education in the care and treatment setting, targeting interventions to both HIV-uninfected and -infected individuals.
- Conduct research to better understand coverage of available prevention interventions and barriers to their access.

Male Circumcision

- Determine the durability of effectiveness (i.e., sustainability) of circumcision in reducing HIV transmission risk in men.
- Study the effectiveness of male circumcision for reducing HIV transmission from men to women and from men to men.
- Develop and evaluate innovative strategies for the safe and effective delivery of male circumcision and other male-oriented prevention services to prevent or reduce HIV transmission.
- Determine the factors affecting acceptability of male circumcision.
- Study the sociocultural aspects that may inhibit or encourage the use of male circumcision.
- Study the technical training and implementation requirements for widespread uptake of male circumcision interventions.
- Determine the cost-effectiveness of male circumcision in limiting transmission and curtailing the expansion of the epidemic.
- Evaluate whether circumcision is associated with behavioral disinhibition.

Antiretroviral Use

- Determine the effectiveness of pre- and postexposure ARV prophylaxis in prevention of sexual and blood-borne HIV transmission, while continuing to study and monitor drug resistance.
- Determine the most effective ARV agents, formulations, or combinations of agents to reduce transmission risk.
- Focus on compartments including ARV optimization in genital secretions and in the anorectal and gut mucosa.
- If proven effective, determine the social, cultural, and practical factors affecting ARV use and/or providing barriers to implementation of pre- and postexposure prophylaxis.

HIV Vaccine Development

- Continue the accelerated efforts toward development of HIV vaccine candidates suitable for use around the world, and foster the development of vaccines to optimize characteristics appropriate for broad international use, including low cost, ease of production and administration, and stability.
- Define immune approaches that will provide specific and sustained protection against HIV transmission; develop the products necessary to achieve these goals; and develop the capacity to evaluate their safety in human subjects.
- Provide a scientific knowledge base (HIV incidence, viral subtypes, major histocompatibility types, and natural history) to guide decisionmaking regarding identification of potential international clinical trial sites and the conduct of vaccine clinical trials in these sites according to the highest clinical and ethical standards.
- Identify suitable populations of adults, adolescents, and children to enroll in clinical trials of candidate vaccines, while ensuring equitable and appropriately representative gender balance in enrollment.
- Conduct Phase I, Phase II, and Phase III clinical trials of suitable HIV candidate vaccines in diverse international settings for safety, immunogenicity, and efficacy, with appropriate surrogate markers and measures of correlates of protection.
- Enlist the participation of local community representatives in the development of appropriate clinical trial protocols, as well as responsive mechanisms to inform and educate the participating individuals; establish networks within the community that will effectively address the social and medical concerns of the participants; and establish mechanisms to provide ongoing information and open discussions concerning the scientific rationale of the study.
- Examine relevant behavioral issues related to the conduct of HIV vaccine research and its acceptability in diverse populations.
- Conduct research on the potential social and economic effects, including cost-effectiveness, of the use of HIV vaccines.

Microbicides and Barrier Methods

- Discover and develop candidate microbicides (including ARV-based microbicides) and other physical/chemical barrier methods to prevent sexual HIV transmission.
- Conduct Phase I, Phase II, and Phase III clinical trials of suitable candidate microbicides in diverse international settings for safety and efficacy.
- Develop appropriate biological and surrogate markers of safety or protection.
- Determine the efficacy and use of prevention interventions, including microbicides and other physical/chemical barrier methods (particularly female-controlled methods), and determine the factors affecting their use and acceptance.
- Study the sociocultural aspects that may inhibit or encourage microbicide use and barriers to adherence.
- Study the sociocultural and behavioral concerns related to partner involvement and acceptance of microbicide use or covert use in the absence of partner willingness or acceptance.
- If found to be effective in preventing HIV transmission/acquisition, determine the cost-effectiveness of microbicides and other physical/chemical barrier methods in limiting transmission and curtailing the expansion of the epidemic.

STIs and Other Diseases

- Determine the efficacy and cost-effectiveness of syndromic management of STIs among HIV-infected individuals to prevent HIV transmission.
- Improve clinical management of viral STIs in HIV-infected individuals, emphasizing coinfections with herpes simplex virus (HSV)-2 and HPV.
- Identify gender-related biological factors affecting susceptibility to HIV infection, including the use of hormonal contraceptives and the presence of gender-specific conditions such as HPV infection, cervical cancer, and genital ulcer disease.

- Examine how coinfection with other endemic diseases affects HIV transmission, acquisition, and disease progression.
- Determine the role of sexually transmitted coinfections on HIV transmission, acquisition, and disease progression.

Substance Abuse

- Develop and evaluate innovative, culturally relevant, contextually appropriate alcohol and drug abuse treatment programs for their utility as HIV and hepatitis C virus (HCV) prevention approaches in different international settings.
- Develop and evaluate approaches for drug and alcohol abuse programs among HIV- and HCV-coinfected patients to improve adherence with drug/alcohol treatment strategies.
- Develop and evaluate approaches to integrate risk-reduction prevention strategies for drug and alcohol use into HIV treatment and primary care settings.
- Develop and evaluate innovative strategies for identifying "hidden populations" of young, older, and out-of-treatment drug users, including those in high-income social strata.

Mother-to-Child Transmission: Considerations for the Mother, Child, Adolescent, and Family

- Develop and evaluate strategies:
  - for primary prevention, i.e., prevention of HIV acquisition by adolescent girls and women;
  - to evaluate reproductive decisionmaking and improve reproductive health in serodiscordant couples, including HIV-risk reduction during *in vitro* fertilization; and
  - for prevention of unintended pregnancy by HIV-infected adolescent girls and women, and study factors associated with unintended pregnancy.
- Investigate the mechanisms of and risk factors for *in utero*, intrapartum, and postnatal mother-to-child transmission (MTCT) of HIV.
- Develop new effective, safe, and feasible strategies to further decrease vertical transmission of HIV, particularly postnatal (breast milk) transmission, or provide alternatives to currently identified effective strategies.
- Further evaluate and adapt known efficacious interventions in infants, mothers, or both to prevent MTCT (i.e., ARV prophylaxis, cesarean section before labor and before ruptured membranes, complete avoidance of breastfeeding, exclusive breastfeeding, and ARV prophylaxis to breastfeeding infants and/or lactating mothers).
- Evaluate the effects of perinatally acquired HIV infection in adolescent girls who become pregnant and receive treatment regimens to prevent MTCT.
- Evaluate acquisition of HIV infection during pregnancy:
  - quantify more precisely the risk of MTCT when maternal HIV infection is acquired during pregnancy; and
  - develop strategies for detecting or reducing maternal incident infection during pregnancy.
- Investigate the unique immune status of pregnant women and their infants and develop passive and active immunization interventions to interrupt HIV transmission.
- Evaluate risk factors for and strategies to reduce the morbidity and mortality associated with HIV infection in pregnant and postpartum women and their HIV-exposed infants, including:
  - maternal and infant nutrition during the peripartum and postpartum periods; and
  - the association of maternal HIV disease stage and mortality of both HIV-infected and -uninfected children.

- Investigate the effect of ARV regimens used for prevention of MTCT, including repeated interventions, on subsequent response to ARV used for treatment in mothers and infants, if infected despite prophylaxis.

- Conduct implementation science research on identifying barriers to developing effective strategies for scale-up and delivery of successful interventions for prevention of MTCT of HIV, in view of the new World Health Organization (WHO) recommendations on prevention of MTCT and infant feeding.

- Evaluate strategies to ensure linkage of sites (and information from sites) conducting prevention of MTCT with sites providing ART treatment for mothers and with infant/child health clinics.

OBJECTIVE–G: Treatment Research

Develop and evaluate the most effective, setting-specific strategies for care and treatment of HIV and HIV-related conditions and their sequelae among HIV-infected and HIV-affected children, adolescents, and adults at all stages of the life course.

STRATEGIES

- Characterize the clinical course of HIV infection in diverse geographic settings.
- Conduct research on biological, behavioral, and psychosocial effects related to the treatment and care of HIV disease among children and adolescents (both horizontally and perinatally infected).
- Develop and evaluate suitable and sustainable approaches for the diagnosis of HIV infection, especially for children under the age of 18 months.
- Collaborate with clinicians from resource-limited countries to identify, recruit, and retain individuals with acute and early HIV infection in treatment research programs.
- Identify affordable, safe, and effective ARV regimens, including timing of initiation and durability of initial treatment, and study the cost-effectiveness of starting early treatment.
- Determine the role of pharmacogenetics/pharmacokinetics and identify appropriate ARVs that can be used in specific populations (e.g., children, adolescents, and adults at all life stages) in resource-constrained settings.
- Develop appropriate pharmacovigilance systems to evaluate short- and long-term effects of treatments provided to HIV-infected individuals (including special populations such as children, adolescents, pregnant women, and alcohol and substance users).
- Determine the efficacy of ARV regimens on various clades prevalent around the world.
- Conduct studies, including clinical trials and operational research, on the quality of treatment, its effectiveness, and its efficacy.
- Develop and evaluate suitable and sustainable approaches to monitoring the effectiveness and safety of HIV treatment, especially with regard to affordable technologies to measure CD4+ cell counts and viral load (on appropriate alternatives) and validate low-cost monitoring technology.
- Assess the cost-effectiveness of ARVs in resource-limited settings and determine the minimal level and methods of targeted drug resistance monitoring necessary in those failing therapy and in pregnant women.
- Evaluate and monitor treatment effectiveness, adherence, drug–drug interactions, drug resistance, and toxicity of ARVs and prophylaxis medications against major coinfections in pediatric, adolescent, and adult populations (including over age 50 and pregnant women) in resource-constrained settings.
- Examine the effectiveness of a variety of approaches to the administration of therapy (e.g., directly observed therapy, directly delivered therapy, or directly administered ART).
- Develop and test region-specific strategies, including promotion of treatment literacy for health care workers, people living with HIV/AIDS, and family and community members, to support adherence to medication regimens in adults, adolescents (including those who acquired HIV through perinatal transmission), and children to enhance therapeutic outcomes and limit the development of drug resistance.
- Conduct community-based studies that assess the effect of community mobilization on VCT and treatment success.

- Assess the effect of nutritional status and nutritional interventions on patient survival and the efficacy and tolerability of ART, including measuring the rate of immune system deterioration.

- Develop culturally appropriate mechanisms to identify persons for whom treatment is indicated and to overcome factors such as stigma and discrimination, which can forestall testing and limit the provision of treatment and care.

- Develop, evaluate, and implement programs to prevent discrimination in the provision of ARV treatment, and determine whether expanded ART care leads to a decrease in HIV-associated stigma.

- Support the long-term followup of children exposed to ART *in utero* and/or postpartum to evaluate possible late effects of ARV exposure.

- Identify and study conditions that emerge as a consequence of ART and longer survival, such as malignancies, neurological and neuropsychological conditions, and metabolic and nutritional dysfunctions.

- Develop and evaluate strategies to initiate and provide care to targeted groups of individuals such as health care workers, security forces, and teachers.

- Develop and evaluate public health models, such as family and community models of care, for infants to older adults that integrate HIV/AIDS care and other existing health services in a single setting to maximize outcomes and avoid duplication of effort.

- Evaluate the effectiveness of different approaches to task shifting for HIV care and treatment from physicians to non-physician staff.

OBJECTIVE–H: Endemic Diseases, Comorbidities, and HIV

Study the interactions between HIV infection, endemic diseases, and the entire spectrum of comorbidities (including alcohol and substance use, psychiatric illness, and other organ system disorders), with a particular focus on diseases that affect HIV care, and develop strategies to optimize their integrated prevention, diagnosis, treatment, and care.

STRATEGIES

- Define the spectrum, incidence, and risk factors for HIV-related sequelae (e.g., coinfections such as TB, HCV, and HPV, malignancies, and organ system-specific manifestations such as renal and urologic diseases; musculoskeletal and skin disorders; and neurological and neuropsychiatric conditions) in adult, adolescent, and pediatric populations specific to individual regions in diverse geographic settings.
- Investigate sustainable strategies for preventing, treating, and monitoring responses to treatment of endemic diseases in HIV-infected adults, adolescents, children, and infants in resource-constrained settings.
- Develop simple clinical algorithms for guiding initiation of prevention or treatment of HIV-related coinfections, opportunistic infections (OIs), and comorbidities.
- Identify affordable strategies to target high-risk patients for initiation of prophylaxis for HIV-related coinfections, OIs, and comorbidities.
- Develop and test new, low-cost, effective, and rapid diagnostic tools and drug susceptibility tests for comorbid diseases, including TB and malaria.
- Examine the role of coinfections and other endemic diseases and their treatment in modulating HIV infection or disease, including risk of acquiring and/or transmitting HIV infection, disease progression, and the use of ART.
- Determine the effect of ART on susceptibility to infection with endemic diseases, and on their natural history.
- Determine the effect of ART on the efficacy of treatment and prophylaxis for other endemic diseases.
- Investigate drug–drug interactions of ARVs and drugs used to prevent and treat endemic infections and/or other manifestations of such endemic infections.
- Assess the burden of TB and the relative importance of reactivation versus *de novo* infection in HIV-coinfected individuals in various settings.
- Develop and study strategies for primary and secondary TB prevention, including prophylactic regimens in HIV-infected patients.
- Develop and study feasible and effective strategies for prevention of transmission of drug-susceptible and drug-resistant TB in community and health care settings.
- Determine optimal ways of integrating treatment for HIV disease with prevention of and treatment for OIs, endemic diseases, and comorbidities, especially TB, including clinical research to assess clinical outcome and operational research to determine cost-effectiveness.
- Determine the safest and most efficient treatment modalities for endemic diseases (e.g., TB, HCV, HIV-associated cancers, and malaria) in HIV-infected adult, pediatric, and adolescent populations, including pregnant women.
- Assess the impact of available antibiotic treatment and prophylaxis regimens to optimize therapeutic approaches for TB and other endemic coinfections in the context of ART, including new therapies for TB and new approaches to administering drugs in HIV-infected adult, pediatric, and adolescent populations, including pregnant women.

- Develop new agents and therapeutic strategies to treat drug-sensitive and drug-resistant TB (including multi-drug-resistant [MDR]-TB and extensively drug-resistant [XDR]-TB).

- Investigate behavioral and cultural factors related to endemic coinfections, within the context of HIV, and develop strategies to enhance and monitor adherence to therapy and prophylaxis for endemic coinfections in HIV-infected individuals.

- Develop methods to monitor the development of resistance to ARV and anti-TB drugs in clinical study participants.

- Determine the safety and effectiveness of available immunizations for endemic pathogens in diverse HIV-infected populations.

- Conduct studies to better understand the role and mechanism of reinfection and/or superinfection with HCV in coinfected individuals.

- Develop and test the feasibility of low-cost assays for early diagnosis of viral cancers, particularly cervical cancer, non-Hodgkin's lymphoma, and Kaposi's sarcoma, and utilize these to develop adequate clinical approaches to the management of such cancers in regional settings.

OBJECTIVE–I: Integrated Prevention and Treatment

Evaluate the impact of prevention and treatment programs on the HIV epidemic, including the integration of comprehensive prevention and clinical care in existing health service delivery programs related to HIV/AIDS.

STRATEGIES

- Assess the social, psychological, societal, and economic impact of ART on risk behaviors, HIV transmission, and prevalence, including associated behavior change, in individuals (including children), families, and various communities.
- Determine how availability of ART affects utilization of VCT and entry into care and treatment in various communities.
- Determine how availability of ARV prophylaxis for prevention of MTCT affects entry into antenatal care (ANC) and utilization of VCT within ANC.
- Develop effective strategies to integrate the delivery of HIV care with other medical and social services, while enhancing and optimizing linkages among interdependent programs, such as those for control and management of TB and other comorbid conditions, alcohol/substance abuse or dependence treatment programs, maternal and child health services and family planning, and support services for the elderly.
- Evaluate the interactions of ARVs with alcohol, psychoactive drugs, or medications used for the treatment of substance abuse, and investigate the effects of these comorbid conditions (and their integrated treatment) on HIV disease progression, adherence to treatment regimens, and clinical outcomes.
- Determine how ART affects breastfeeding behaviors.
- Identify comorbidities in HIV-exposed, uninfected infants and young children, using appropriate control populations, in resource-constrained settings.
- Study the direct effects of ART on HIV transmission (e.g., by evaluating the effectiveness of specific ART strategies in curtailing HIV transmission in HIV-serodiscordant couples).
- Consider the implications of ART use for prevention in settings where ART is not available for all those infected individuals who meet WHO eligibility criteria.
- Develop biomarkers that can serve as surrogates for measurement of HIV-risk behaviors and can be used to predict and monitor rapid escalation of HIV subepidemics (i.e., in local areas or in high-risk groups).
- Integrate operational and health services research with clinical research to facilitate the translation of research findings to clinical practice and public health programs and to provide information to inform the scale-up of HIV prevention, care, and treatment programs.
- Develop and test optimal strategies to integrate ART treatment programs with region- and/or country-specific cancer services for diagnosis and management of HIV-associated malignancies to allow a continuum of care and enhanced outcomes of comprehensive HIV care.
- Develop demonstration programs that simultaneously address prevention, care, and treatment.
- Examine the potential use of HIV therapeutic vaccines.
- Develop links with other agencies and organizations to integrate research with service programs and to develop multidisciplinary prevention research in multiple settings, including medical treatment and community support and care organizations.
- Develop strategies to control the HIV epidemic and strengthen existing infrastructure that simultaneously address multiple health outcomes.

AREA OF EMPHASIS

Training, Infrastructure, and Capacity Building

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE–A: Research Training

Provide training in biomedical, social and behavioral, and intervention research on HIV and its associated complications, coinfections, and comorbidities, with an emphasis on multidisciplinary research in gender-diverse and racially and culturally diverse and marginalized populations domestically and in developing countries with high HIV incidence and/or high prevalence of HIV infection.

STRATEGIES

- Increase opportunities for prebaccalaureate, undergraduate, predoctoral, doctoral, postdoctoral, and advanced research training across a broad range of AIDS-related scientific disciplines, and support research to better understand the barriers and incentives along the research career pathways for investigators.
- Expand the NIH AIDS Loan Repayment Program to encourage promising U.S. scientists and physicians from disadvantaged backgrounds and from racial and ethnic populations to pursue HIV-related research careers.
- Establish mentoring networks to improve the supply of trained mentors for the development and retention of new investigators in all aspects of AIDS research, and support research that develops an evidence-based approach to effective mentoring so that future mentoring programs can build on the knowledge base of educational and social science research.
- Enhance programs to improve recruiting, training, mentoring, and retaining investigators in AIDS research, especially those from diverse scientific backgrounds, including biomedical, behavioral, and social scientists.
- Provide new incentives and research training opportunities to attract newly trained investigators and established researchers from other fields to pursue AIDS research.
- Support the development and sharing of novel techniques from relevant research fields to the HIV field, including structural biology, computational biology, and systems biology to understand HIV-associated disorders. Encourage and facilitate collaborative and interdisciplinary research in these areas.
- Implement new research training programs for non-physician professionals (e.g., physician assistants, nurse practitioners, and laboratory staff) in resource-limited settings and at domestic sites to increase the diversity of the pool of AIDS researchers.
- Develop collaborative evaluation research programs to assess the efficacy of strategies to shift HIV care tasks in resource-limited settings to non-physician-professional trained individuals.
- Strengthen cultural competency training and ethics training for the conduct of HIV/AIDS research in vulnerable populations, in both domestic and international settings.

- Expand training programs to increase the capacity for basic and clinical research on HIV and HIV-related complications, coinfections, and comorbidities in domestic and resource-limited countries, including tuberculosis, hepatitis B virus, and hepatitis C virus.
- Develop research training programs in the area of blood safety to develop improved blood screening strategies and technologies and appropriate use of transfusions.
- Support training programs for pediatricians in HIV prevention, diagnosis, manifestations, complications, and treatment.
- Support training opportunities for HIV prevention researchers interested in adding specific methodological skills to their research expertise (e.g., methods to conduct cost-effectiveness analyses, measurement of biologic outcomes in behavioral intervention studies, appropriate use of behavioral and social science measures in clinical trials, ethnographic and other qualitative methods, and network analysis).
- Support training programs for veterinarian scientists conducting AIDS research using animal models, including nonhuman primates (NHPs).
- Provide training in Good Laboratory Practices/ Good Clinical Practices for staff in domestic and international settings where clinical research on HIV/AIDS is being conducted.
- Support training opportunities in the use of advanced computer and information technologies for HIV-related biomedical and behavioral research, and support access to appropriate tools and equipment at the end of training.
- Support analysis of distance learning used to teach research and research-related topics, to assess and better understand the acquisition of research skills and competency.
- Develop new models of integrated training and mentoring that focus on the protection of human and animal subjects in AIDS research.
- Support training programs for personnel in institutions in resource-limited settings to strengthen the administrative and financial management capacity needed to conduct AIDS-related research.
- Expand programs that provide support for international AIDS researchers trained in NIH-sponsored programs to continue their studies in their home countries.
- Expand programs that utilize the infrastructure at NIH-sponsored AIDS clinical trial sites for training programs in the design and conduct of clinical research.
- Further develop, validate, and utilize experimental animal models, *ex vivo*, and theoretical/mathematical models to study the transmission and establishment of HIV/SIV (simian immunodeficiency virus) infections, with emphasis on models of direct relevance to human HIV infection and models that address important issues not readily approachable in human subjects.

OBJECTIVE–B: Infrastructure Development

Establish and maintain the appropriate infrastructure needed to conduct HIV research domestically and internationally, with emphasis on populations of high prevalence.

STRATEGIES

- Enhance and improve research capacity and infrastructure to advance research on HIV and HIV-associated coinfections, comorbidities, and other complications.
- Enhance and improve the infrastructure to conduct clinical trials of prevention and therapeutic strategies in domestic and international sites, including laboratory capacity, trained scientists and other personnel, appropriate participant cohorts, and establishment of local institutional review boards to address bioethical issues.
- Support the infrastructure necessary for producing AIDS vaccine candidates under Good Manufacturing Practices for preventive and therapeutic vaccine clinical trials.
- Develop, maintain, and effectively utilize domestic and international cohorts, repositories, and nested studies among populations experiencing emerging and ongoing HIV epidemics, and maintain updated databases, allowing their broader and more efficient use by the scientific community, when appropriate.
- Establish and support quality-controlled repositories, biobanks, and well-characterized panels of reagents to ensure access by qualified scientists to human blood and tissue specimens from clinical trials and cohorts. Improve and disseminate the process of requesting, prioritizing, and receiving these specimens to allow timely and equitable access.
- Promote Internet connections, cell-phone-based communication, and online social networks, including those with virtual worlds for training, infrastructure, and treatment. Ensure availability of pertinent information technology at health science centers, hospitals, outpatient clinics, community-based organizations (CBOs), and other access points, both domestically and internationally, for HIV-related research and patient care.
- Develop statistical sampling methodologies, data collection protocols, and statistical analysis tools that are easy to use and adaptable to different settings; facilitate efficient statistical analysis and report generation and enhance standardization, when appropriate, in the context of AIDS research.
- Promote research in, and application of, medical informatics (e.g., high-performance computing) for AIDS research and clinical practice in resource-limited settings, both domestically and internationally.
- Develop efficient and effective systems for collecting and managing HIV/SIV/SHIV (chimeric simian/human immunodeficiency virus) multiple-center and single-site clinical and animal model trial data, and ensure timely and accurate dissemination of clinical and animal model trial information.
- Increase collaborations between CBOs and other Government-supported health care service providers and academic researchers to improve the quality and capacity of HIV/AIDS research in health care service settings.

DOMESTIC

- Support enhanced research infrastructure at U.S. minority-serving institutions to improve capacity to support AIDS research.
- Support HIV/AIDS research planning and organizational initiatives targeting domestic minority institutions and minority-serving communities, with emphasis on initiatives that develop academic–community partnerships.
- Expand opportunities for institutions serving specific diverse populations at risk for HIV/AIDS to develop equal and productive partnerships with U.S. majority institutions.

- Develop programs to sustain human capacity and to link U.S. AIDS research scientists, industry partners, and relevant institutions with each other and with investigators and institutions in both resource-developed and -developing countries.

- Develop strategies to promote the infrastructure for bidirectional translational science by enhancing national capacity for clinical and translational HIV research; supporting team-building, consortium collaborations; and facilitating the use of national data-sharing HIV networks.

- Support and expand adequate facilities and resources, including BSL-2/3 (Bio Safety Level 2/3) facilities for studies in NHPs, and provide appropriate ethical and procedural training to house and breed NHPs for use in AIDS research.

- Expand the breeding of genetically defined specific pathogen-free NHPs, with emphasis on Indian-origin rhesus macaques.

- Develop and characterize appropriate reagents for use in HIV-related research conducted in different species of macaques and other NHPs.

- Support programs that enhance the current AIDS research infrastructure, such as the Centers for AIDS Research, the Research Facilities Improvement Program, and the National Primate Research Centers.

- Support the Biomedical Technology Research Centers Program for structural studies of HIV proteins and host proteins.

INTERNATIONAL

- Enhance and improve research capacity and infrastructure in resource-limited settings with high HIV incidence, with particular emphasis on facilities for research on HIV prevention, therapeutics, and behavioral interventions.

- Enhance coordination and collaboration among NIH-supported investigators, other U.S. Government agencies, and other international agencies conducting HIV/AIDS research in the same countries.

- Develop and improve conventional and electronic systems for documentation of medical care and tracking of HIV/AIDS in low-resource settings to improve epidemiologic research.

- Increase population-based cancer registration in resource-limited countries to allow for a better understanding of cancer rates in HIV-infected persons in these locations.