RACIAL ETHNIC MINORITY ISSUES IN HIV/AIDS

REPORT OF A FORUM FOR COLLABORATIVE HIV RESEARCH
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DEPARTMENT OF PREVENTION AND COMMUNITY HEALTH
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This report summarizes the discussions held at the "Racial/Ethnic Minority Issues in HIV/AIDS" workshop held on October 29-30, 2003 in Washington, D.C.

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[*] http://www.hivforum.org/about/sponsors.htm

EXECUTIVE SUMMARY

This report summarizes the proceedings of the "Racial and Ethnic Minority Issues in HIV/AIDS" workshop, sponsored by the Forum for Collaborative HIV Research at the request of the Racial and Ethnic Minorities Section of the Office of AIDS Research, National Institutes of Health. The workshop focused on three major thematic areas, whose interrelatedness was highlighted by the workshop format:

- Prevention
- Treatment
- Vaccines

The concepts of "race" and "ethnicity" are difficult to delineate; it is clear that socio-cultural, environmental as well as genetic factors contribute to racial and ethnic identity, with inter-individual differences regarding the relative importance of each of these factors. Rather than focus on definitions of "race" and "ethnicity", this workshop aimed to decipher and describe the essence of HIV/AIDS associated health disparities experienced by various populations in the context of the following: how these populations self-identify, multi-faceted perspective that affect self-identity, with an ultimate emphasis on pathways of integrated research and policy making designed to alleviate these disparities.

Racial/ethnic minority communities experience disparities in all areas of health and health care. In HIV/AIDS, the burden of disease is carried disproportionately by both men and women of non-Hispanic Black and Hispanic communities, and in every transmission category. Disparities are not unique to non-Hispanic blacks and Hispanics: men and women from the American Indian/Alaskan Native population carry the third largest burden of HIV disease. Among newborns, minority communities also bear a highly disproportionate burden. Across the life cycle, the

disparities are evident at every level: accessing HIV testing, HIV treatment and care, and disease outcome, including higher rates of death.

The following considerations informed the planning of this project:

- research on disparities and ways to resolve disparities cannot be done without gathering data on race and ethnicity
- improvements will not self-generate: measurement and reporting are essential steps in the pathway to improvement
- deeper understanding of the principles that drive disparity will help us find solutions.

All research efforts (including behavioral prevention, treatment and vaccine research) need to be conceptualized and carried out within a framework that reflects the social, economic and cultural diversity within and among communities of color. Only through such comprehensive approaches can the complex interplay of race, ethnicity, culture and health reflecting the "real lives" of individuals belonging to minority communities be understood, and the multitude of interventions available be of benefit.

ENGAGING COMMUNITIES OF COLOR IN RESEARCH

Lack of participation in research contributes to HIV health disparity. Increasing minority communities' participation in research was identified as a major a need to be addressed. This research participation deficit is a multi-factorial problem, and includes mistrust, lack of access to research programs and lack of understanding the research process. Diversity in study populations is important to understand not only from the biologic and behavioral perspective, but foremost at a pragmatic level: the research community needs to understand the needs of individuals and populations at greatest risk of HIV infection.

To overcome this barrier of research non-participation, workshop participants identified areas in which the research community needs to develop strengths:

- A better understanding of the historic realities that contribute to the broken trust vis-à-vis research
- A better understanding of how factors such as racism, stigma and discrimination threaten individual and public health in racial and ethnic minority communities
- More research on what skills and abilities will help individuals from minority communities actively participate in health and health care related activities, including research
- Addressing the ties between economic issues, lack of resources and risk behavior, including an assessment of the impact of disease on minority community economics and social disruption
- Balancing the needs and perspectives of the minority communities against those of the research community
- Identifying, acknowledging and addressing the antecedents of low self-esteem and depression
- Research on how "beliefs" which reflect a high level of mistrust drive health seeking behavior and willingness to participate in research and on how knowledge of those "beliefs" will influence the design of better products and interventions
- Recognition that support for development of cultural competency in research is as necessary in the domestic setting as it is in the resource-limited setting

The theme "broken trust" ran throughout the workshop. Distrust and mistrust toward the medical and research professions is based on specific historic events, such as the Tuskegee Syphilis Study, as much as a collective community experience of a broader historical and personal nature. Institutional characteristics

that foster distrust include lack of expertise in racial and ethnic minorities, resources and capacity, the paucity of minority researchers and leaders, and the lack of positive translation of research findings, e.g. community resiliency or other factors.

PREVENTION RESEARCH

Approaches to prevention research that need to be explored and expanded include:

- Research that addresses the underlying problems that place racial and ethnic minority communities at greater risk for HIV infection, integrating this with research on underlying genetic factors
- Recognition of cross-cutting issues that extend beyond race and ethnicity, especially important in prevention programs for adolescents and family-friendly interventions
- Approaches that avoid further stigmatization and discrimination of communities especially marginalized, such as sexually abused adolescents and transgender individuals
- Recognition of socio-cultural differences in how personal responsibilities vs. societal responsibilities are perceived
- Greater consideration of contextual factors in risk for infection and the inconsistent nature of being or not being "at risk"
- Conceptually innovative approaches such as identifying protective factors within communities at risk
- Greater use of the "negative test result" setting for prevention interventions (e.g. more effective counseling when reporting an HIV-negative status to individuals picking up their test results)
- Development of a longitudinal and sustainable framework for prevention research

The communication of research outcomes and translation of research findings into practice is an essential and fundamental component of the research process requiring contribution from and integration of health communication experts. Carelessness at the level of communication of findings may inadvertently add to the stigma of vulnerable communities and contribute to trust-breaking experiences.

Special issues and problems faced by American Indian/Alaskan Native communities include the especially damaging effects of HIV/AIDS due to the small size of this population, the migration from rural to urban settings which compounds the likelihood of "being missed" in surveillance activities and the significant historical trauma experienced as a people. Appropriate approaches for research within this population will incorporate indigenous ways of knowing and practicing, collaboration with tribes and indigenous entities at a community-based level and recognition of the sovereign status of tribes.

Work with Asian/Pacific Islander and Latino communities reveals the importance of immigration status as a risk factor and the influence of migration (from US to home country) on risk of infection.

TREATMENT ACCESS AND TREATMENT RESPONSE RESEARCH

Studies on access to HIV/AIDS care and treatment have revealed marked disparities, ranging from insurance status to quality of received care and access to clinical research programs. Regardless of the area of the disparity, the final result is the same; poorer treatment outcomes. Worse outcome can also cross generations in the setting of mother-to-child transmission of HIV. System and provider factors, competing subsistence needs, lack of supportive services and case management, general settings of care as well as provider and patient attitudes are included in the explanatory factors for these discrepancies. The long term consequences of this ongoing disparity are lower quality of life, higher number of hospitalizations, and

higher post-hospital risk of death. In summary, vulnerable groups are increasingly at risk for HIV infection, and when they become infected, receive fewer medications, report more barriers to care and have worse health outcomes.

Inadequate recruitment into clinical studies translates into insufficient knowledge and understanding of minority specific concerns (such as potential variation in drug levels, treatment efficacy and toxicities) for the clinical community. Similarly this poor recruitment also means less "first-hand" knowledge about new products and ownership of the research process within minority communities. The cycle of lack of specific information on differential impact of disease by race, gender and/or ethnicity, health system unresponsiveness, worse treatment outcomes, perceived lack of care, and mistrust, drives continuing health disparity. Therefore, the importance of recruitment of minority populations cannot be overstated – not only for the immediate knowledge gain, but for breaking the cycle of broken trust and disengagement. Failure to recruit and retain adequate minority representation in clinical trials contributes to poor science and is indefensible.

Individuals from minority communities need realistic opportunities to join research programs, and these need to be supported by ongoing sufficient resources. Training of minority researchers and leaders in research is essential for a number of reasons, including but not limited to: 1) increasing the overall health literacy of the communities, 2) raising awareness of the positive roles of clinical trials and 3) presenting clinical research and science as viable options within the community for improved health quality and outcomes. Opportunities such as industry sponsored fellow programs and medical research grants need to be pro-actively targeted to minority communities. Industry can also play a role by encouraging and facilitating minority recruitment into their sponsored clinical studies.

A major barrier for integration of prevention and treatment is the perception of many providers that prevention is not within their purview, or the time constraints of clinical practice render it impossible. The gap between what patients need, and

what physicians are able to deliver, needs to be recognized and addressed. Multidisciplinary research into what it takes to change and sustain health care provider behavior is needed, recognizing that the best person to deliver some of these interventions may be an allied health professional. Training physicians to refer appropriately may provide much needed support for integrating prevention into care settings.

Improved integration of prevention and clinical programs at the federal and state levels will help to remedy the problem. The role of research, and opportunities for more effective research, need to be considered in this setting. Patients who have had the best care to date are those that have been included in biomedical research programs. The fact that increased effort is required in recruiting patients needs to be recognized and appropriate funding made available: funding structures need to be revised to remedy the problem at the source in order to break the disparity cycle.

New approaches to integrate prevention with care and treatment that should be considered include:

- Greater emphasis and prioritization of research on the recently infected
- Greater emphasis and prioritization on program implementation in the recently infected to prevent transmission and link them to care
- More models of community based research, where the researchers goes to the community
- Sustainable and long-term commitment to communities where research is being carried out
- Adaptation of treatment guidelines by incorporating information on different models of care for minority communities

VACCINE RESEARCH

The need for diverse research participation is even more critical in vaccine research. Whereas treatment related research needs to discover the potential impact of diverse genotypes on response to a single drug, vaccine research needs to contend with the potential interaction of viral diversity in addition to host diversity. Many genetic factors affecting susceptibility to infection, post-infection disease course and host immune responses have been identified. Key issues in HIV vaccine research include the potential variation in impact due to genetic differences that independently can influence infection and/or disease outcome. Superimposed on the host and virus genetic variables, are other biologic cofactors affecting transmission and susceptibility to infection, such as the presence of sexually transmitted diseases, co-existing illnesses and the relative availability of antiretroviral treatment for break-through infections. Discerning and interpreting racial/ethnic variation in immune response is made even more daunting because of the need to perform vaccine studies internationally. This adds geographic, circumstantial, genetic and virologic variation to the list of confounders. Responsible and ethical research needs to consider the consequences of not recruiting the appropriate populations and the detrimental effect that this can have on communities, such as diminishing the scientific knowledge that is gained through the studies with subsequent diminished benefit to the communities.

On the whole, community participation in vaccine research has been extensive. However, Phase I studies are generally not performed within communities that most need vaccines. A credible commitment to minority communities will require that the research community develop trust within minority communities and engage them from the very beginning of vaccine development programs. While a "community building" perspective will foster community engagement, the research community needs to recognize that in contrast to treatment related research, participation in vaccine studies is based almost entirely on altruism. Altruism is difficult to elicit in populations affected by hopelessness, despair and accumulated experiences of poor treatment. Altruism is hard to elicit when the community has experienced little return on its prior altruistic investments in science. Thus, the

need to address the underlying problems and antecedents of vulnerability cannot be escaped.

In addition to the recommendations already listed for other areas of research, the following communication strategies were discussed:

- Find better ways of explaining to potential trial participants being placed "into an experiment" does not deprive them of their decision making rights
- Recognize and incorporate the values of communities into communications
- Avoid referring to American Indian/Alaskan Native communities as "other"

Other recommendations for vaccine research include:

- The ramifications of seropositivity as a consequence of participation in a vaccine study for racial and ethnic minority subjects require immediate and ongoing attention.
- As with other areas of research in racial and ethnic minority communities, a long term commitment is essential in vaccine research; new funding paradigms may be necessary given current funding cycles
- Behavioral research needs to be fully and consistently integrated into vaccine research

DISCUSSION

Repair of the broken trust between the research and racial and ethnic minority communities will require a concerted effort from the research community, including government agencies, academic researchers, industry sponsors and community leaders. There is a clear need for more opportunities and venues that

facilitate communication of the kind that this workshop provided, between individuals involved in prevention, treatment, and vaccine research. None of the issues and problems raised may be solved by investigators from a single discipline working in isolation.

New areas of prevention research:

Several new areas in prevention research were highlighted during the workshop, including:

- Sustained support for ongoing research of biomedical intervention tools
- Research on best mechanisms to introduce biomedical interventions (e.g. microbicides and vaccines) once they are available
- Research to find ways to ensure that individuals continue to engage in multiple ways of protecting themselves and their partners, given the fact that none of these methods, including vaccines, are going to be 100% effective

BACKGROUND

In 2000 the Racial and Ethnic Minorities Section of the Office of AIDS Research approached the Forum for Collaborative HIV Research to convene a meeting bringing together the various constituencies to discuss the issue of HIV in racial and ethnic minority communities. The Ad Hoc Minority Working Group suggested this format as it was clear that all entities involved in HIV research needed to be present, including the pharmaceutical industry. With a focus on research, the issues to be highlighted included the recruitment and retention of racial/ethnic minorities in clinical trials, challenges to prevention research in racial/ethnic minority communities and the issues surrounding vaccine research in these communities.

The Forum enlisted the help of a planning committee (see Appendix A), representative of the Forum member constituencies to develop a workshop agenda (Appendix B) and recommend participants (Appendix C). The workshop was held on October 29 – 30, 2003.

In consultation with the Office of AIDS Research, three thematic areas were identified as focus points for the workshop:

Prevention – chaired by Dr. Maria Cecilia Zea – George Washington University, graduate of the Center for AIDS Prevention Studies Minority Program.

Treatment – chaired by Dr. William Cunningham – UCLA, co-investigator on the HCSUS study

Vaccines – chaired by Dr. Mark Feinberg – Emory University, currently with Merck Vaccines, former member of the OAR

The vision of the planners was that the key to progress in this area involved recognition of the interrelatedness among these three thematic areas. Consequently, the workshop plan called for specific thematic overview presentations followed by interdisciplinary panel discussions addressing the points of contacts and intersection, interrelationships and common threads among the three areas.

This report summarizes the proceedings of the meeting, emphasizing the research agenda. It does not purport to be a thorough review of all racial/ethnic minority issues, nor of the prevention, treatment and vaccine research areas. Where appropriate, references for overviews and reviews are provided.

Quotations are used throughout the report. If these originate from a published source, the citation is given. Quotations without a reference are comments made by workshop participants.

INTRODUCTION

"*Race, as currently measured in most health studies, reflects a social construct in the minds of Americans that is imprecisely mapped to the differences that exist among us…*" [1]

"*Communities of color present a particular challenge to researchers ….The current literature does not provide sufficient information why minority groups are at increased risk"* [2]

"The statistics about HIV/AIDS have demonstrated clearly that the epidemic has a social face, with focal points increasingly found in communities of color and among the poor" [3]

"*Color does not equal culture, language is not about translation, and enculturation, self and societal acceptance (as well as social involvement and activism) are not easy to come by and may, justifiably, not be desired by a segment of society whose issues and concerns continue to be minimized* " (Workshop Participant)

WHY ARE WE TALKING ABOUT RACIAL/ETHNIC MINORITY ISSUES IN HIV/AIDS?

The statistics are striking: In 2004, 49 percent of the estimated 1.2 million persons in the US living with HIV infection were non-Hispanic blacks. Black males had the largest or second-largest percentage of cases in every transmission category; black females had the larges percentage in every category[4]. Racial/ethnic minorities access testing less often, are more likely to receive their HIV diagnosis late in disease, and less likely to access quality treatment, as will be discussed throughout this report.

Unfortunately, racial/ethnic minority disparities in HIV/AIDS are not an anomaly – disparities exist in every health sector or disease indication where this issue has been examined. Fifty-nine percent of Latinos, 53 percent of African American and 54 percent of American Indian/Alaskan Native were classified as "near poor" or "poor", compared to 25 percent of Whites [5]. Sixteen percent of African Americans, 15 percent of American Indian/Alaskan Native and 13 percent of

Latinos experience fair or poor health, compared with 8 percent of Whites, and the poor health is experienced primarily by the poor [5]. A recent editorial in the New England Journal of Medicine stated: "During the past decade, hundreds of articles have been published documenting the existence of racial and ethnic disparities in health and health care – a data deluge that has led many observers to suggest that it is time to stop documenting disparities and turn our effort to doing something about them"[6].

This project was undertaken with the following considerations:

- research on disparities and ways to resolve disparities cannot be done without gathering data on race and ethnicity
- improvements will not self-generate: measurement and reporting are essential steps in the pathway to improvement
- a deeper understanding of the principles that drive disparity will help us find solutions.

DEFINING RACE AND ETHNICITY

The subject of race and ethnicity in the context of health is a very sensitive one not only due to past abuses and potential future abuses. Much discussion has focused on the respective role of genetic factors, environmental factors and cultural factors in determining risk for disease, post-exposure outcome and treatment outcome [7]. Although specific genetic factors may underlie specific diseases, it is commonly understood that the genetic differences within what we commonly accept as racial categories may exceed genetic differences between racial categories [8].

While the genetic underpinnings of "race" are difficult to define, self-identification as belonging to one particular race or ethnic group has also grown more complex, and this is reflected in official use of the terms "race" and "ethnicity". For example,

the decision to allow "one or more races" was reached by the Office of Management and Budget in 1997 in response to increasing number of children from interracial unions. In some US official documents, up to 63 different racial or ethnic categories are noted; in cases where this is not possible, seven mutually exclusive categories are used, including White alone, Black or African American alone, American Indian and Alaska Native alone, Asian alone, Native Hawaiian and Other Pacific Islander alone, Some other race alone, and Two or more races. The Census Bureau standards for race "generally reflect a social definition of race recognized in this country. They do not conform to any biological, anthropological or genetic criteria". The phrase "Race is a social concept, not a scientific one" gained much acceptance in many academic and social spheres.

However, the concept of race and biologic differences among populations cannot be dismissed. Clear instances of genetic predisposing factors have been identified. Although it may be difficult to ascribe these at the individual level (or individual gene level) to specific races, what has become clearer in recent studies, is the fact that based on an assortment of genes, the human race can indeed be divided into major groups that more or less correspond to the major racial classifications. The concept of "ancestry" is also important to consider in this context [8]. In recent years, the pendulum has swung the other way; the benefit of identifying disease risk and treatment response according to racial categories has started to be recognized in many areas. Nevertheless, it has been noted that race and ancestry are both confounded by the genetic heterogeneity within the groups in addition to the widespread missing of populations that were previously isolated [9].

The planning committee for this project made a conscious decision not to be distracted by focusing attention on definition of "race" or "ethnicity", but rather, make an attempt to decipher and describe the essence of HIV/AIDS associated disparities experienced by various populations in the context of how these populations are racially/ethnically viewed, described and self-identified in the US, from a multi-faceted perspective, including genetics, the socio-cultural factors,

economics and behavioral sciences. Furthermore, the planning committee recommended a focus on finding pathways of research and policy making that would alleviate the severe problem faced by "minority communities" affected by HIV/AIDS in a manner that integrates the behavioral, cultural and biomedical approaches. Only through such comprehensive approaches can the multi-faceted "real lives" of individuals belonging to sometimes hard-to-define minority communities be understood, and will communities benefit from the multitude of interventions available.

HIV/AIDS EPIDEMIOLOGY IN USA: A WINDOW ON HEALTH DISPARITY

The Centers for Disease Control and Prevention released a new report describing the racial/ethnic disparities in diagnosis of HIV/AIDS, based on data from 33 States, gathered between 2001 and 2004 [10]. This report paints an even bleaker picture than the numbers reported in 2003. Blacks predominated among the 1.2 million estimated persons living with HIV as well as among the 157,252 estimated diagnoses of HIV infection. Blacks account for only 13 percent of the population in the 33 States, yet they accounted for 51 percent of diagnoses between 2001 and 2004: 44 percent among males and 68 percent among females. Breaking down the figures further, 70 percent of high-risk heterosexual contact cases and 60 percent of injection drug use cases were in Blacks. The racial disparity was also evident in perinatal transmission: Blacks accounted for 69 percent of the cases.

An even more striking picture emerges from specific studies. For example, in a National HIV Behavioral Surveillance System study of men who have sex with men (MSM) in five US cities, 46 percent of the black MSM were HIV-positive; only 67 percent were aware of their infection status [11].

Figures 1 and 2 depict the average annual rates of HIV diagnoses according to distinct transmission categories for males and females, respectively. Among both males and females, the second highest rate was seen in Hispanics. Interestingly, the estimated annual percentage change was negative for most categories, but positive for Asian/Pacific Islanders (8.1 for males and 14.3 for females) and American Indian/Alaskan Native (2.4 for males and 4.8 for females).

Figure 1: Rates in Males According to Transmission Category

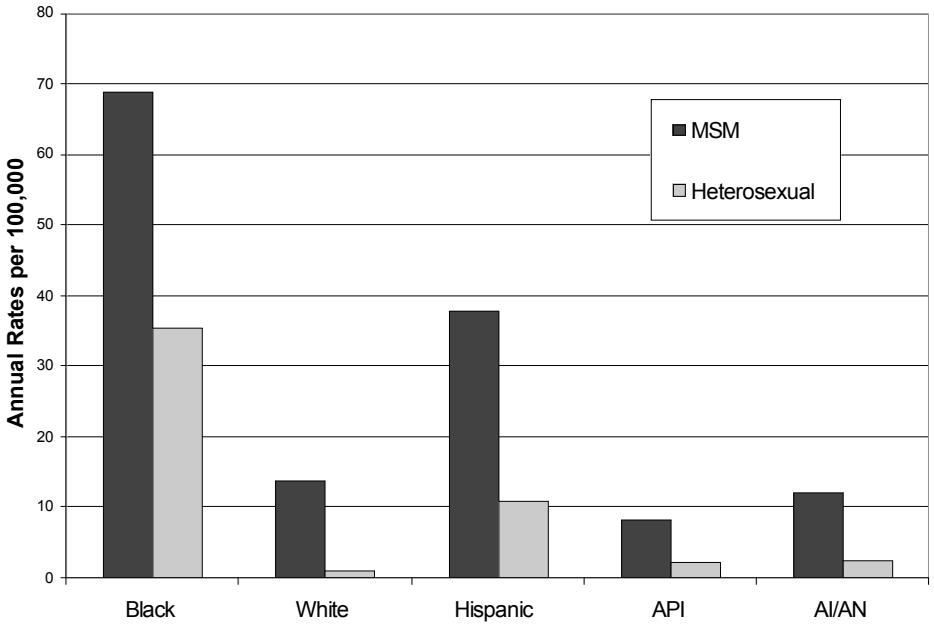
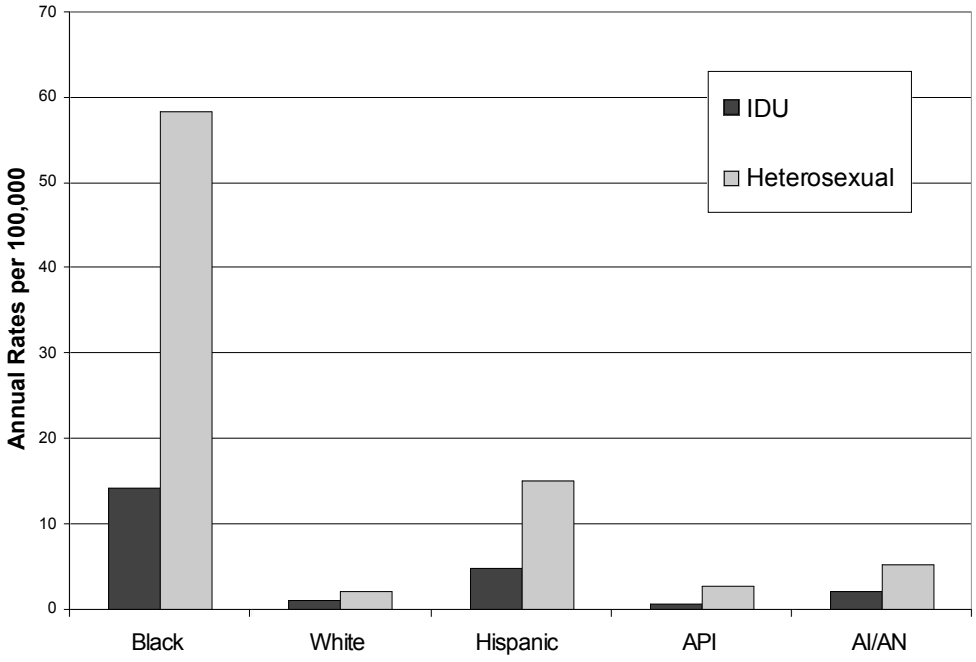


Figure 2: Rates in Females According to Transmission Category



Figures 1 and 2 are derived from data presented in [10]

The disparities are also evident in disease outcome. While the proportion of deaths in Whites decreased, it increased in Black HIV-positive populations through 2001. Estimated survival after diagnosis was significantly shorter in Blacks compared to Whites.

The CDC initiated a new strategy to combat these statistics, with four priority areas:

- Make voluntary HIV testing a routine part of medical care
- Implement new models for diagnosing HIV infections outside medical settings
- Prevent new infections by working with persons diagnoses with HIV and their partners
- Further decrease perinatal transmission

With respect to eliminating racial/ethnic disparities, the CDC launched the Minority HIV/AIDS Research Initiative, funding investigators specifically working with African American and Hispanic communities. Additionally, the CDC provides research fellowships for HIV prevention in communities of color and directly funds Community Based Organizations to help reach African Americans at greatest risk.

Disclosure of HIV status among young Latino MSM – a prevention research perspective

Dr. Maria Cecilia Zea is a Professor of Psychology at The George Washington University. She was a recipient of the Collaborative HIV Prevention Research in Minority Communities Program [12]. Dr. Zea's research program, focused on Latino gay men, helps to illustrate some of the important parameters in prevention research in specific populations [13] [3]. One of Dr. Zea's studies was on disclosure of serostatus among HIV-positive Latino gay men from New York City and Washington, DC. Participants were diverse in terms of country of origin (including South America, Central America, Mexico, the Caribbean and USA) and demographic factors (nearly 20% of participants had less than a high school education and over 70% received less than $800.00 in monthly income)[14].

Disclosure of HIV status is an important prevention tool. The process of disclosure is complex, and there are many factors that promote or preclude disclosure of seropositive status. Similarly, there are potentially negative and positive consequences of disclosing one's serostatus to different targets. Degree of disclosure seems to be moderated by ethnic group. For example, Latinos disclose less frequently than Anglo men [15] [16].

In Dr. Zea's and colleagues' studies, predictors of disclosure included socio-cultural factors, such as socio-economic status, acculturation level, experiences of stigmatization and discrimination for being gay and for being Latino. These socio-cultural factors create the context within which individuals decide or not to disclose. Individual psychosocial factors, such as anticipated negative consequences of disclosure, emotional closeness to target, target's knowledge of sexual orientation, and self-efficacy for disclosure also played a role in disclosing serostatus. Finally, HIV-related factors such as stage of illness and time since diagnosis also influenced decision to disclose.

Rates of disclosure to the different components of the social network differ[14]. In studies by Zea and colleagues, Latino men are more likely to disclose seropositive status to their main partners and to their friends than to their parents; moreover, they are more likely to disclose to mothers than to fathers [14]. Disclosure to mother was significantly associated with emotional closeness and the mother's knowledge of the participant's sexual orientation. Disclosure to the father, on the other hand, was significantly associated with the level of US acculturation, in addition to emotional closeness and the father's knowledge of sexual orientation. The strong association of disclosure with the target's knowledge of one's sexual orientation supports the concept that the stigma associated with gay sexual orientation may act as an obstacle to disclosure among Latino gay men. While emotional closeness was important for disclosure within the family setting, it was not as important in disclosure to friends[14].

Disclosure consequences included mental health outcomes, with findings indicating that those who disclosed were less depressed, had greater self-esteem, and were more satisfied with the social support they received from others[14]. Disclosure of serostatus *per se* did not predict sexual risk but, rather, disclosure is indispensable to establish seroconcordance between partners, which in turn strongly predicts sexual risk [17].

This vignette of a research program illustrates the importance of recognizing the socio-cultural and individual characteristics and variables within specific populations, as well as the interconnectedness of antecedents and consequences of disclosure of HIV status.

The first concept to internalize when considering research of any type within racial/ethnic minority populations is that regardless of how these are classified, not any one population within a category will be homogenous. The simplified classification of "minority populations" does not acknowledge the multi-faceted character of populations within a very diverse social, cultural, economic and to some extent genetic, context. Characterization based on any one single of these components will lead to an incomplete, distorted view. Nevertheless, the research community needs to work with data, such as surveillance data collected by the CDC that does not reflect the nuances of real populations. It is hoped that the CDC's move toward more universal acceptance of name-based reporting will help to ameliorate this problem by providing more efficient linkages among the various datasets and improving the quality of reporting.

> *"The research community has to be able to get its head around, and acknowledge the fact, that perceived and experienced poverty, racism, discrimination, and stigma keeps people of color away from behavioral and clinical research, just as it continues to put people at risk for HIV in the first place"*

The research community needs to develop a greater level of understanding of the context in which people of color live. The extent to which layers of culture, generations of experience, multiple – and at times competing and contradictory – perceptions of self and self-within-society underlie attitudes towards health and research, cannot be overstated. Acknowledgment by the research community that there is more to a person of color than skin color is an absolute prerequisite for research of the cultural and societal context on risk for HIV infection, and the readiness of people of color to enroll in clinical trials.

> "*What we don't need is more research to tell us that racism, stigma, discrimination, and homophobia are real and contribute to HIV risk. We don't need more research that tells us that people of color live at the crossroads of context.* "

Panelists voiced the need to engage in research that helps to further our understanding of *how* factors such as racism, stigma and discrimination threaten not only individual health, but also public health. Research needs to address how attitudes within minority communities contribute to the "living at the crossroads" problem and help identify what skills and abilities will help individuals from minority communities to move into a more favorable context. This approach will require the development of innovative intervention models, but it is a prerequisite to engaging minority communities in clinical and/or behavioral research programs.

> "*How is it that people at the bottom of the socio-economic status end up being infected*?"

The research community has not addressed the ties between economic issues, lack of resources, and risk behavior sufficiently. To what extent is "sex for housing" or "sex for food" responsible for risk behavior in immigrant populations? Prevention needs to include an assessment of the impact of economics, social disruptions upon racial/ethnic minority communities.

Unless the approach to clinical research is informed by the reasons why it is being done, it will be difficult to engage communities. The research community needs to ask questions such as: what is the purpose of research on people of color? Is it to help people of color understand their world and live their lives? A thorough look at questions such as these will naturally lead to questions regarding *who* is actually doing the research, who the community partners are, and the appropriate dissemination strategies (see section below: Broken Trust).

The needs of the research community need to be balanced against the needs of the communities. Panelists expressed that this is often not perceived to be the case. For example, the frequent lumping together of "minorities, women and drug users" does not reflect the necessary level of understanding by the research community that although all of these populations may be underserved, they are not "one" community.

> "*Individuals who are depressed tend to participate in unprotected sex and individuals who are struggling with issues of self-esteem don't see the need to protect themselves, because if they're worth nothing, why would they protect themselves?"*
>
> "*What needs to be done to turn the tide to where a community initiates and takes hold of the problem and moves it forward*?"

Given the significant role that low self-esteem and depression play in the context of HIV/AIDS, it is important to identify the antecedents of low self-esteem and depression. Poverty is an amplifying factor for this cycle, as are other structural factors including racism and experiences of discrimination, which may also be ethnic in origin. Sexual risk taking is clearly connected to depression. It is important to recognize that issues of oppression and discrimination play a central role, not just in African Americans, but also in American Indian/Alaskan Natives, Asians, Hispanic/Latinos, and other immigrant groups. Conversely, in some groups, over-confidence may contribute to risk.

Another factor not frequently discussed is the pervasive denial that exists in many minority communities, and the impact of that denial. In addition to more minority researchers, effective engagement of community leaders, including churches, is needed.

APPROACHES TO PREVENTION RESEARCH

One approach to answering the question "Why are particular groups at increased risk for HIV infection?" is to address the underlying problems, such as drug use (and reasons for drug use), economic vulnerability, etc. These approaches need to be developed further, and integrated with research on the underlying genetic factors

that determine risk. This latter point raises an important question: given the detrimental effects of marginalization, discrimination and stigmatization, how can we study genetic variables without adding to stigmatization and other types of discriminatory problems? Another related question that needs to be addressed is: how do we keep people uninfected while we solve the underlying problems?

Cross-cutting issues extend beyond race and ethnicity. For example, in approaching prevention for adolescents, family-friendly prevention methods or peer-based interventions are applied. The appropriateness of the family based interventions will depend on the type of family environment and the cultural values around families in specific cases. Peer-based interventions will also vary according to the cultural context. In situations where family, friends and society have failed -- as frequently found with gay and lesbian youth, street kids, and sexually abused adolescents -- approaches need to be developed without further stigmatizing communities and populations.

Another area displaying cross-cultural variation is how personal responsibilities are viewed in relation to societal responsibilities. This is particularly relevant in "prevention for positives" programs.

> "*It takes two or more for infection to occur. We haven't studied enough which factors play a role in whether certain risk behaviors are enacted or not in a relationship*"

Traditionally, risk measurement and intervention development has occurred at the level of the individual, rather than in a relational context. "Riskiness" has also been attributed to a person as a consistent variable, not recognizing that most individual's behavior is never 100% risky or 100% non-risky. The contextual factors contributing to risky vs. non-risky behavior decisions need to be considered in prevention interventions. These will include factors such as disclosure of HIV status and power differential between partners. How do these contextual factors

facilitate and increase the potential for structural barriers such as racism, discrimination, poverty, oppression, and colonial trauma to do harm?

Receipt of "negative test results" is another neglected area in prevention research. The new prevention guidelines do include the setting of individuals returning for their test results, which provides an opportunity for prevention interventions. Screening is not carried out for the purpose of finding positives only; people participate in screening programs to confirm that they are negative.

TRANSLATION OF RESEARCH FINDINGS INTO PRACTICE

> "*Researchers need to think about the relatively resource-poor setting of the community-based organizations and physician's office where the real interventions are going to take place. The prevention research literature is full of very elegant interventions – and it's very nice that they worked – but totally unrelated to the reality of where 99.9% of people with HIV or at risk for HIV are going to be reached*"
>
> "*We are very readily giving money to work in communities, to work on cultural norms, to pay attention to making sure that our behaviors are appropriate in countries outside the US. We are not given any dollars to do that work in the US….*"

The CDC has been grappling with the issue of interventions that work in certain circumstances, but are difficult to translate into a large enough scale to make a difference. The efficacious interventions need to work in the long-term. As HIV/AIDS has transitioned into a chronic disease, we need sustainable interventions, practical enough for government agencies implement and fund over a long period of time. The example of ACTG 076 – the first study to document prevention of mother-to-child transmission through a biomedical intervention, is frequently cited as a turning point in prevention research [18]. Biomedical interventions may be easier to implement than behavioral interventions; nevertheless this example provides an interesting case study of translation of research findings into policy. As has been pointed out, the original findings of the study were not that "brilliant"; yet the resulting policies have more or less

eliminated the mother-to-child transmission route for the US and other developed countries. Panelists encouraged workshop members to consider ways to make optimal use of the biomedical context for prevention programs. Examples include the use of emergency rooms and other high risk settings for testing. Evidence supports the notion that knowledge of one's status supports the appropriate behavior change [19].

The intersection between quality research and media is crucial in the translation of research findings to communities. Carelessness at this juncture may result in re-stigmatization of sectors of communities. This was clearly evident in the communications of the VaxGen trial results as outlined later and the ensuing community response. Educational materials addressing issues at the level of people, as opposed to individual risk or individual responsibility, need to be developed

> "*We wouldn't expect McDonald's to run the same ad for 20 years; we don't expect Coca-Cola to put up the same poster for 20 years*."

We need to recognize that the "Coca-Cola model" has survived because of its effectiveness. Experts in health communication and media communication need to be brought to the table to integrate more effective communication models.

<u>Pigeon-hole approach will not work</u>

> "*The African American men are saying we have a lot of funding and research for men who have sex with men, women, children, etc but nothing for heterosexual men*"

Prevention *is* an integral part of treatment (see below), but funding needs to be available to make this possible in the treatment setting. Translation of research finding into practice requires the necessary infrastructure. Practicing clinicians need to know what messages, what approaches work for different communities. The group approach will work with some communities [20] but not others, who need an individual approach, possibly including their partners. Thus, expecting group discussions to work with communities that "don't do groups" will be a waste of resources.

Prevention training for the treatment setting should not be limited to physicians with HIV expertise. Everyone in the clinical team, including other clinicians, nurses, case managers needs to be trained and involved in the effort. Combining prevention training with regular community forums, where patients and their families participate, has proven to be effective in encouraging testing and dispelling myths regarding treatment.

SPECIAL ISSUES FOR AMERICAN INDIAN/ALASKAN NATIVE POPULATIONS

The American Indian/Alaskan Native community has the third highest rate of infection. Because the population is so small to begin with, the absolute numbers are low. However, the potential for great devastation is that much bigger.

In approaching prevention research, panelists called for theoretical, conceptual and methodological innovation, addressing population based issues and forging new partnerships. Examples from the American Indian/Alaskan Native populations serve to illustrate these points. Theoretical and conceptual innovation will incorporate indigenous ways of knowing, thinking, behaving, practicing. Much health knowledge already exists within the community, but this resource has not been tapped effectively. Individuals with expertise in both western medicine and traditional medicine, as well as expertise in how to bridge these, exist, and they need to be involved at a more significant level. Integrated approaches will focus on multiple levels of pathways and mechanisms: from environmental structural levels down to individual factors.

Another example of conceptual innovation relates to the question: what helps specific individuals do well? Although the detrimental effects of racism, discrimination and oppression are well known, not everyone that is exposed does poorly. Yet research targeted at identifying protective factors that help buffer the

effects of trauma (this may be historical trauma, intergenerational trauma, microagressions) is not being carried out. Linkages to the field of post-traumatic stress syndrome should be explored in this context.

Progress in this area will require methodological innovations and new sampling strategies. Researchers need to develop models and measures that reflect the reality of individual communities. Examples include measures for historical trauma and protective factors (e.g. traditionality, spiritual coping). Due to active migration of Native American/Alaskan Natives driven by poverty, relocation and termination policies at the federal level, more than half of the population now lives in urban settings. As a result, this population does not cluster by neighborhood and thus misses being identified by normal survey techniques, with the effect of being marginalized even further. Yet identification of these communities in urban settings is essential for the longitudinal studies required to identify multi-level causal pathways. For example, preliminary data indicates that women are affected in much greater numbers than expected, illustrating the need for the new sampling approaches. What effects the frequent back and forth migrations between urban settings and reservations, has not yet been addressed.

In terms of new partnerships, the research community needs to collaborate more with tribes and indigenous entities at a community-based level. The sovereign status of tribes is not always recognized. Mechanisms to award more control over grant processes to tribes by providing resources and opportunities need to be explored. The implications extend beyond the immediate research goals. The significance of such a collaborative approach is particularly evident in the context of tribes beginning to contract more of their own health care. Tribal leaders will need to have the information of how HIV/AIDS is affecting their community in order to make the appropriate decisions regarding their community's health care.

Migration and Immigration

Migration and self-identification within a particular racial/ethnic construct is also a major factor within the Asian/Pacific Islanders (API) population. Rarely do individuals identify themselves as "Asian". Furthermore, over 65% are foreign born. In other words, studies or programs that categorize solely on race/ethnicity will completely miss the "immigration factor". The statistic of "1%"for HIV/AIDS in the US API community belies the fact that the MSM community is disproportionally affected, and that migration to their countries of origin during holidays provides opportunities for infection.

> "*Public health researchers and epidemiologists are not seriously looking for ways to find a way to study the surveillance issues of how migrations are contributing to risk*"

Migration and foreign-born status is also a factor in Latino populations, where one out of 6 children of Latino descent are foreign born, and migrations between the US and the Caribbean and Latin America may substantially affect HIV prevalence in this community. In all of these communities, poverty is a major driving force for migration. These nuances will not be revealed if classification is based solely on race/ethnicity. A recent article in the Los Angeles Time highlighted the increasing HIV prevalence among Latina immigrants in California [13, 14, 21]. By the end of 2005, about 30% of HIV-positive women were Latina, compared with 36% who were Black. Stigma associated with HIV and the community's religious and cultural stance on homosexuality contributes to the non-disclosure of HIV status to the women's families and friends. Fear of deportation contributes to delay in seeking care for many immigrants.

Migration and immigration issues are further complicated by legal and ethical concerns. Disclosure of one's immigration status can be threatening both to the community members and the researcher. Yet, if immigration status is one of the key factors related to risk, scientists will need a way to address this in their research program.

BROKEN TRUST

> "*This is work that must be done, and it can only begin with an acknowledgment that we are dealing with real people who have real and complex lives*"

The fact that people of color are, in general, distrustful of the medical profession has been clearly and extensively documented. Although "Tuskegee" is often cited as the root-cause for the distrust [22] [23], evidence shows that broader historical and personal experiences are also important factors [24].

Unfortunately, many other institutional characteristics compound, rather than ameliorate, the distrust. For example, the lack of expertise, resources, capacity and dedicated staff within minority organizations available for grant writing, research and evaluation feeds into the limited number of people of color actually conducting research. Other barriers include the absence of translation of positive research findings into practice and the ineffective dissemination of evidence-based HIV prevention models to community leaders at all levels. The Collaborative HIV Prevention Research in Minority Communities Program, at UCSF-CAPS, provides an interesting model for engaging and developing investigators of color and improving the quality of research in communities of color [2] [12]. The program includes grant funding, a structured summer program, individualized long-term research collaborations, access to behavioral science expertise, and internal peer review of all programs. Another outcome was the network of HIV prevention investigators of color. The program has resulted in an impressive number of multi-year grants and publications [12]. This model should be replicated across agencies and institutes.

The impact of lack of trust extends beyond the individual patient – physician relationship. For example, communities have rejected name-based reporting because of lack of trust in the government.

> "*So the things that people believe affect what happens to them, as greatly as the information we provide them*"

A recent study revealed that a significant proportion of African Americans believe that an HIV vaccine exists, but is being kept secret by the government [25]. The research community has not fully addressed the questions:

- How does this belief regarding the socio-political structure drive health seeking behavior?
- How does belief regarding HIV affect the willingness to seek testing, treatment, or participation in vaccine trials?

- How will we use effective marketing techniques to reach out to the community?
- How will our knowledge of community's beliefs alter our design of better products, services and treatments?

The "beliefs" moreover need to be seen the context of reality. Historical reality and actual experiences that communities have endured lead to the realistic and justifiable mistrust towards research. Whether the scientific issue is Tuskegee, smallpox blankets, tuberculosis experimentation, involuntary sterilization – the impact of these events, (and some in the not so recent past) will be long-lasting, passed down through oral history for generations. A policy of "active repair" of these deep wounds, as opposed to passive waiting, needs to be developed.

FOCUS ON HEALTH CARE DISPARITIES

HCSUS 1994-1999: Disparities Documented

The HIV Care and Services Utilization Study (HCSUS) is a key and unique source for information on HIV/AIDS health care disparities in the US [26]. As the first major research effort to collect information on a nationally representative sample of individuals in care for HIV infection, it provides policymakers with information on health care services received as well as the costs. HCSUS serves as a research model bridging across federal agencies and non-governmental organizations. HCSUS was funded through a cooperative agreement between the Agency for Healthcare Research and Quality and RAND, a private nonprofit research institution. Additional funding and in-kind support was also provided by the Health Resources and Services Administration, the National Institutes of Health (including National Institute of Mental Health, National Institute on Aging, National Institute on Drug Abuse, National Institute on Dental Research, and National Institute of Allergy and Infectious Diseases), the Office of Minority Research, and the Office of the Assistant Secretary for Planning and Evaluation.

HCSUS collected information starting 1994 through 1999 only. Given the recent expansion of the epidemic into new demographics and the rapid pace of changes in treatment standards, we are left with a critical information gap. The type of information collected through a HCSUS like mechanism is pivotal for policy development and participants noted the inadequacy of information currently available at the national level. The CDC Morbidity Monitoring Project (MMP) [27] may provide a potential new source for health services utilization in the US. The MMP is designed to collect information from HIV-positive individuals receiving care from randomly selected providers. The project plans to provide ongoing, population-based state and national estimates of morbidity, the impact of treatments, adherence to antiretroviral medications, utilization of health care, risk behaviors, and quality of life among HIV-positive individuals [28].

Dr. William Cunningham provided a comprehensive overview of the disparities revealed by HCSUS [26] including a description of the disparities, the factors explaining these, and the health consequences as a result of disparities.

As a whole, the HIV population reflected in HCSUS – a national representative sample – differed from the general population in several ways: they were half as likely to be employed, to have a household income above the 25th percentile, or to have private insurance [29], but had similar levels of education. The adult HIV-positive population in care was three times as likely to be insured by Medicaid and nine times as likely to have Medicare coverage. Within in this general "adult HIV-infected population in care", striking differences were observed according to

racial/ethnic, gender an geographic lines. For example, women were twice as likely as men to have household incomes less than $5000.00 or to have private insurance. Non-Hispanic Whites comprised 70 percent of those with private insurance, 30 percent of those on Medicaid and 41 percent of those without insurance. In contrast, non-Hispanic Blacks comprised only 15 percent of those with private insurance, 48 percent of those on Medicaid and 37 percent of those without insurance [29]. Quality of HIV care was inferior for Blacks and Latinos compared to Whites, for those on Medicare and Medicaid compared to those privately insured, and women compared to men, even after adjusting for CD4 cell count (a measure of disease state) [30]. For example, in an multivariate analysis, the odds ratios for less than two office visits in the preceding six months, for one or more emergency department visit without associated hospitalization and for not receiving a protease inhibitor or non-nucleoside reverse transcriptase inhibitor by the end of 1996 (when these were included in standard of care) were significantly higher for Blacks and Latinos compared to Whites. Analyses using other indicators for quality of HIV care, including types of expenditure (for medication vs. hospital care) [31], ever using highly active antiretroviral therapy [32], access to opportunistic infection preventive medications [33], or greater than 3 months delay from diagnosis to first HIV medical care [34]confirmed the picture already presented.

System and provider factors (described above), competing subsistence needs [35], lack of supportive services and case management[36], general settings of care as well as provider and patient attitudes [37, 38] are included in the explanatory factors for these discrepancies.

One additional factor was investigated in HCSUS: access to clinical trials and experimental medications [39]. This is an important parameter, not only because of the access to new (and hopefully improved) drugs per se, but because it indicates that the acceptance of new and innovative therapies within minority communities is slowed, and reflects on the difficulties of recruiting minorities into clinical trials,

with the ensuing consequences, as discussed below. Non-Hispanic Blacks and Hispanics were less likely to participate in clinical research programs (odds ratio for participation 0.50, 95% confidence interval 0.28-0.91; 0.58, 95% confidence interval 0.37-0.93, respectively) and to have received experimental medications than Whites (odds ratio 0.41, 95% confidence interval 0.32-0.45; 0.56, 95% confidence interval 0.41-0.78, respectively). Participation in clinical studies was associated with a higher level of trust in the provider.

Although HCSUS data indicated that the degree of disparity narrowed over time, disparities did not disappear [32]. The long term consequences of disparity are lower quality of life, higher number of hospitalizations, and higher post-hospital risk of death [40]. In summary, vulnerable groups are increasingly at risk for HIV infection, receive fewer medications, report more barriers to care and have worse health outcomes.

FOCUS ON HOST GENETICS AND PHARMACOGENOMICS

Pharmacogenetic and pharmacogenomic studies focus on the genetic basis underlying differences in drug response (including efficacy as well as toxicity) in individual patients. The genetic basis for racial/ethnic differences in treatment response may be difficult to discern because of the fact that genetics are so imprecise in determining "race" and "ethnicity", as discussed above (see Introduction). Nevertheless, emerging data indicate that genetically-based differences frequently may sort according to racial lines. Examples of relationships between host genetic polymorphisms and treatment response include the CCR5 chemokine receptor polymorphism, drug transporter polymorphisms such as MDR1, polymorphisms influencing drug metabolism, such as CYP2D6 [41]. Examples of polymorphisms associated with differential drug toxicity responses include the HLA-B*5701, DQ3 and DR7 loci and abacavir hypersensitivity and the SRECBP-1C locus and hyperlipidemia [41].

The case of abacavir hypersensitivity is perhaps the best known for its association with "race". Approximately 5 to 9 percent of Whites experience a hypersensitivity reaction that can be life threatening. Caucasians are significantly more likely to encounter this toxicity; the risk for occurrence is reduced by 40 percent in persons of African descent [42, 43].

Drug metabolism exhibits significant interindividual variation. For example, many genetic variants of the enzyme CYP2B6 of the cytochrome P450 family, responsible for efavirenz metabolism, exist, with potential associated functional differences [44]. Differences in drug plasma levels due to differences in drug metabolism may affect efficacy as well as toxicity and tolerability. One of the CYP2B6 polymorphisms occurs more frequently in Blacks than in Whites and is associated with a three-fold higher plasma concentration of efavirenz and with increased central nervous system side effect [45]. These are but few examples of instances where genetics and treatment response intersect[46, 47]. For a full review, see [48] .

The field of HIV pharmacogenetics and pharmacogenomics is in its infancy at this stage, but there are strong prospects for the move from "bench to bedside" for pharmacogenomic testing in HIV therapy [44]. The few examples of relationships between genetic polymorphisms and phenotypic characteristics cited above underline the need to ensure adequate diversity in clinical trials. Most likely, most genotypic-phenotypic relationships will not be traceable to single genetic loci but rather, on multiple genes and multiple polymorphisms. These will not be discernible if clinical trials do not include sufficiently diverse populations. Diverse populations will not be enrolled however, unless the basic disparities described above and below are addressed.

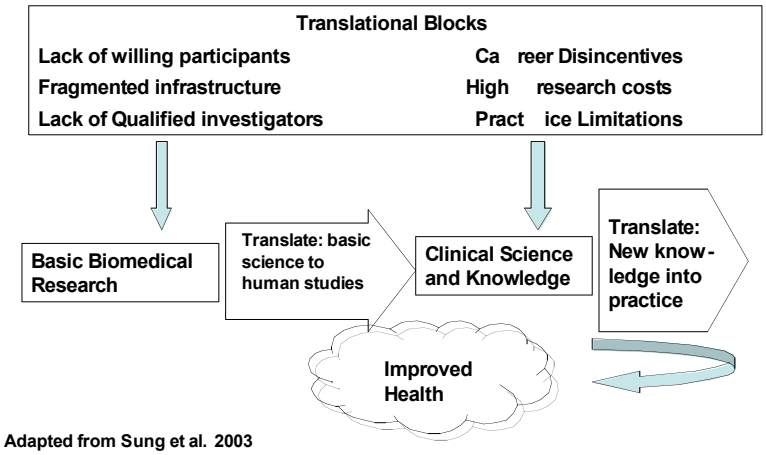
"*Alleviating these disparities in clinical research participation by ensuring adequate representation in clinical studies from among age, sex and culturally diverse groups is essential to developing treatments that will benefit the diverse US populations ....The effective recruitment of sufficient numbers of clinical study participants may ultimately hinge on the willingness and ability of the scientific community to actively engage study participants in every stage of research.."[49]*

The model outlined by Sung and colleagues (cited above; also see Figure 3) points to multiple translation blocks in the clinical research continuum [49]. These blocks – e.g. lack of willing participants, lack of qualified investigators, career disincentives, and lack of funding – provide succinct research topics to address in the context of encouraging minority populations to participate in clinical research. Data already exist illustrating some of the key points, as for example, the importance of concordance between investigator and research participant [38].

RELATIONSHIP BETWEEN CLINICAL RESEARCH AND ACCESS TO QUALITY CARE

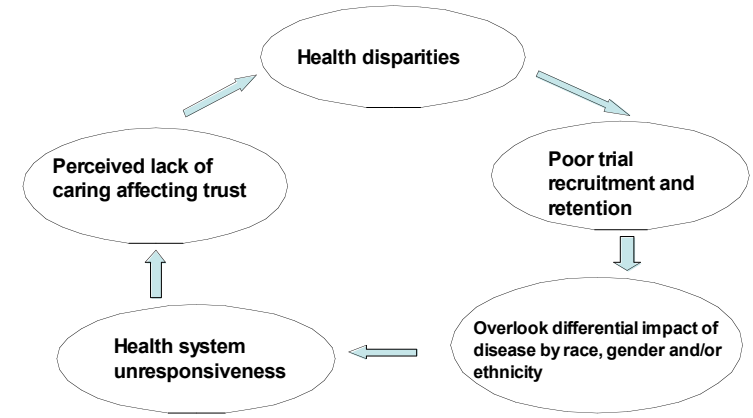
One model to relate clinical research and quality health care is illustrated in Figure 4. Poor recruitment into clinical trials means that potentially significant differences in terms of disease impact or treatment response will be overlooked. Thus ignored, minority community specific concerns cannot be responded to by health systems. The cycle continues by reinforcing mistrust through perceived lack of care, discouraging participation in clinical research. Therefore, the importance of recruitment of minority populations cannot be overstated – not only for the immediate knowledge gain, but for breaking the cycle of broken trust and disengagement (see section Prevention Research/Broken Trust). Individuals from minority communities need realistic opportunities to join research programs, and these need to be supported by sufficient resources [50] [2]

Figure 3: Clinical Research Continuum



Adapted from Sung et al. 2003

Figure 4: Breaking the Cycle
Increasing Participation and Community Trust



Adapted from V Cargill presentation 2003

PACTG 316 provides a stark example of downstream effects of disparities in accessing research and quality care[51]. This international study was designed to investigate the effectiveness of nevirapine, in addition to "standard antiretroviral therapy" in prevention of mother-to-child transmission. Overall, the transmission rate was very low (1.5 percent); however, most transmission events occurred in

Black, non-Hispanic or Hispanic women. In a sub-analysis restricted to participants from the US and Puerto Rico, all transmissions occurred in women identified as Black or Hispanic. Maternal status (CD4 cell count, viral load levels) was also more favorable in White women compared to minority women. Furthermore, white women were more likely to be on treatment before pregnancy; minority women initiated treatment during pregnancy, and were more likely to receive treatment regimen not including protease inhibitors. In fact, race/ethnicity was a predictor of maternal viral RNA levels at the time of delivery. A striking finding of the study was that the reason cited for not starting treatment prior to pregnancy (ie – minority women) was "not knowing their diagnosis", taking us back to the discussions of the importance of testing and diagnosis in all population. An earlier, cross-sectional survey of child-bearing women in California and pediatric AIDS cases similarly documented racial/ethnic based disparity in accessing care during pregnancy and delivery. Most of the HIV-positive specimen in this study originated from newborns of African-American mothers (37.7 percent), followed closely by Latina mothers (35.1 percent). The absence of zidovudine treatment for the prevention of mother-to-child transmission, on the other hand, was highest for Latina and African-American women [52].

Thus, the disparity experienced by the mother at the level of testing and diagnosis as well as accessing quality care translates into unfavorable biomarkers not only for the mother's health, but also for future generations.

This case-in-point reveals several avenues that might be pursued. For one, cross-study databases within national clinical trial networks may be useful for analysis of toxicity, treatment response, and other outcomes by demographic groups. Second, as mother-to-child transmission research wanes in the US, cohort studies will gain in significance to delineate race and ethnicity effects in women, particularly around the time of pregnancy and birth. Non-HIV cohorts should be examined for usefulness in this context, for example cohorts of peri-menopausal women at risk for HIV infection followed long terms; currently no HIV data is captured in these

studies. Other cohorts of interest include cardiovascular disease cohorts and diabetes cohorts.

Adherence

Adherence is central to treatment effectiveness. Just as researchers need to learn that "risk behavior" is not 100% present or not present, researchers should think of adherence as a continuum rather than an all-or-none behavior. The all-or-none approach may in fact be a barrier to accessing therapy. The approach to adherence research has also followed along the "one size fits all" concept. Knowledge of communities is essential in designing adherence promoting interventions. For example, programs in Hawaii have demonstrated the need to engage and involve family members in discussions of treatment with patients [53, 54].

Role of industry

Many companies have fellow programs. There is recognition that these should be more pro-actively engaged in recruiting minority fellows. This is also true for medical research grants. Industry can be more pro-active in ensuring the appropriate representation in industry sponsored clinical trials. The industry has some "weight" with respect to selection of clinical research sites and contributing to "capacity building" in primarily minority communities.

Role of FDA

The FDA calls for monitoring, collecting, displaying and analyzing clinical trial data by race and ethnicity. It is within the FDA's interest to point to any safety or efficacy concerns in sub-populations. The FDA can also use Phase 4 (or post-marketing) commitments to request additional studies that the pharmaceutical sponsor should pursue. However, these commitments are essentially "good faith" commitments rather than binding in the regulatory context. Of interest, the information on phase 4 commitments is now available to the public on the FDA's website.

The FDA also has the mechanism of meta-analysis across studies to look for race/ethnicity effects in efficacy and safety.

> "*HIV/AIDS treatment includes focusing upon behavior change, bolstering coping resources and making lifestyle choices that promote healthy living*"[55]

> "*Treatment must focus on more than pharmacological interventions; treatment must address those attitudes and behaviors that give rise to a successful disease outcome. These are the same attitudes and behaviors by the way, that affect disease transmission*"

The areas of intersection are many. As noted above, biomedical interventions are – or are perceived to be by the research community – simpler to implement. Post-exposure prophylaxis is of course an immediately obvious example. Concerns have been raised regarding the potential disinhibitory effect that widely available access to non-occupational post-exposure prophylaxis may have. In San Francisco, post-exposure prophylaxis has been generally found to be safe, efficacious, and not necessarily associated with increases in sexual risk taking [56]. However, non-occupational post-exposure prophylaxis is not as simple (or devoid of behavioral influences) as might be assumed at first glance. For example, in studies or programs in which individuals are required to self-initiate prophylaxis, self-initiation will depend on an individual's recognition and appreciation of what constitutes events of significant exposure risk. Preliminary data indicates that in real life, exposure events are not readily identified as "risk" events, thus minimizing any potential effect that post-exposure prophylaxis might have [57].

The disinhibitory effect of antiretroviral treatment is frequently touted as a reason why risky exposures continue to take place [58] [59]. Panelists argued that this area of research is not as clear as some may think. The link between treatment and risk of infection (or alternatively, preventing the risk of infection) is not that clear; people's beliefs about antiretroviral therapy and viral load may promote unprotected sex [60].

Treatment gives hope. The quality of life can be improved. This positive message needs to be emphasized and incorporated into stepped-up testing/diagnosis efforts. A possible avenue – not much explored currently – is the notion of partnering newly infected individuals with treatment savvy mentors. On the other hand, clinicians and researchers need to understand that patients with low-paying jobs will resist taking medication that may interfere with their ability to perform physically demanding work. The fact is that many patients do not enjoy benefits such as compensation for time off due to sickness. Discussions and interventions that are rooted in the reality of people's lives will be more effective in building trust and more effective in integrating prevention in the treatment setting.

There is another side to the issue: provider acceptance of responsibility for prevention interventions. According to a HRSA sponsored study, clinicians can be divided into those who accept prevention as integral to their work, and clinicians who do not[61]. On the other hand, patients in clinical care clearly expressed their need for assistance in reducing risk behavior and interpreted physician's reluctance to engage in the topic as a lack of understanding of the struggles they face. This gap between what patients want and what physicians are able to deliver -- needs to be recognized and addressed. Interestingly, physicians are not all "one group" either. For example, a recent study revealed that infectious disease trained physicians were less likely to integrate prevention counseling in their clinics than non-infectious disease trained physicians [62]. Research into what it takes to change and sustain health care provider behavior is needed. Furthermore, training physicians to refer appropriately may provide much needed support for integrating prevention into care settings. This approach is included in the new prevention guidelines, but practical approaches will need to be worked out for individual settings[63].

Participants related the gap between what patients want and physicians are able to provide to the historical tradition of relegating prevention to "public health". Improved integration of programs at the federal and state level needs to occur to remedy the problem. The new prevention guidelines integrating the programs of

two agencies are a step in the right direction. However, what is missing in the integrated picture is the research angle. Participants reiterated the point that patients who have had the best care to date are those that have been included in biomedical research programs, which ties back into the problem of the lack of minority researchers. Thus, the communities that most need to be recruited, and retained, in clinical research are those most reluctant to participate; meaning that the effort required on the part of minority and majority clinical researchers is profound. Many of these clinical researchers lack the funding to effectively build research infrastructure and effectively implement a research program. Funding structures need to be revised to remedy the problem at the source in order to break this cycle (see also section Treatment Research/Imperative for Clinical Research and Figures 3& 4).

> "*Using treatment for pre or post exposure prophylaxis is maybe more difficult than trying to target those who are already infected in smarter ways than we are doing. What we need is research, care, epidemiology – all silos coming together around the issues of identifying where the greatest risk of transmission is, and devising strategies that will minimize this*".

The risk for transmission is highest during the acute infection period, as documented in the US as well as Europe [64]. This presents a window of opportunity that should not be missed. Although recently infected individuals characteristically will not be aware of their infection, efforts to identify them, diagnose and counsel need to be generated. For example, viral load testing rather than antibody testing will allow diagnosis [65]. Research to develop these strategies – where and how will they be most effective – should be prioritized.

The treatment and research paradigms have depended on models requiring patients to come to a clinic. Some psychosocial studies have reported relative success using models where researchers go out into the community instead. The bridging of treatment and prevention may benefit by consideration of this model. This will require letting go of some assumptions regarding how treatment (clinical), behavioral and psychosocial models operate. Additional models that should be

explored include integrating health clinics into business and corporations. For example, the business sector has recognized the need to emphasize exercise, and "exercise at work" has become the norm in many corporate settings.

> "*Panels designing the treatment guidelines have emphasized setting the bar so high and they haven't really talked about what you do if someone doesn't want to jump that high. Do you offer them whatever they are willing to take or do you just let them go home and suffer the natural history of HIV disease*?"

Models for incorporating HIV treatment directly in community settings (away from clinics) exist and these pilot studies need to be expanded in more areas. One such model is the San Francisco based community "store-front site", where since 1996, over 6000 individual HIV tests have been performed [66, 67]. The clinicians and researchers have slowly established a reputation within the community and positive word-of-mouth communication has resulted in increased attendance and willingness to participate in projects. Trust can be established allowing sufficient time. The more traditional "fly in" or "drive by" research approach is not conducive to building trust.

In addition to more minority researchers, we need to bring more sectors of the racial/ethnic minority communities to the table, including community leaders, churches, employers and schools. For example, participating in research may require more frequent clinic visits; individuals at the lower end of the socio-economic scale do not enjoy the privilege of taking time off. However, if employers were convinced that participating in clinical research is a "good thing" -- that it contributes to the well being of communities -- they might be willing to encourage and accommodate clinic visits. The time off for military service provides an example of employers support for social good.

New models may also require lowering the bar: frequently, physicians' attitudes reflect that patients need to demonstrate total and complete commitment to a complicated regimen prior to initiating treatment. For many patients, raising such

expectations is a non-starter. Too often, patients are encountered in emergency treatment settings, with frequent prior interactions with clinicians, which for whatever reasons did not produce a prescription for antiretrovirals. The fear that imperfect adherence will lead to drug resistance has become a predictor for complete non-adherence i.e. not ever starting treatment. More research into different approaches for care is needed and the outcomes of this research needs to be incorporated into treatment guidelines.

The "Racial & Ethnic Minority Issues" workshop took place soon after the dissemination of the Vaxgen gp120 Phase III trial results [68, 69]. Overall, the trial did not show any protective benefit. However, results from a sub-analysis purporting that minority populations may have been protected as a result of vaccination, were released, leading to headlines such as "*Vaccine for AIDS appears to work. Blacks, Asians receive the most protection*" in the lay press. The myriad of problems with this study (including how the results were communicated) offer a kaleidoscope view of the issues associated with vaccine research. The poor representation of racial and ethnic minorities in the study resulted in the inability to look at potentially protective effects in sub-populations in any meaningful, scientifically appropriate way. The headlines claiming effectiveness for Blacks fuelled the beliefs that effective vaccines are being kept from this population. Most of all, the trial illustrates the complexity of vaccine research communications. Responsible and ethical research needs to consider the consequences of not recruiting the appropriate populations and the detrimental effect that this can have on communities.

Diversity is important to understand not only from the biologic perspective, but foremost at a pragmatic level: the research community needs to understand the needs of individuals and population at greatest risk of HIV infection.

> "*With drugs, it is commonly an issue of a single agent interacting with individuals of diverse genotypes. With vaccines, it is a single immunogen interacting with diversity at the levels of both the host and the virus. With drugs, variable effects are often evident coincident with drug exposure. With vaccines, outcomes may only be apparent some variable time after immunization*" [70]

The barriers to HIV vaccine research have been reviewed elsewhere [71, 72]. Many genetic factors affecting susceptibility to infection, disease course post-infection

and host immune responses have been identified (reviewed in [73, 74]). Some of the key issues in HIV vaccine research include the potential variation in impact due to genetic differences that on their own can influence infection and/or disease outcome. Superimposed on the host and virus genetic variables, are other biologic cofactors affecting transmission and susceptibility to infection, such as the presence of sexually transmitted diseases, co-existing illnesses and the relative availability of antiretroviral treatment for break-through infections.

Whether all these questions can be answered through studies in domestic populations is highly questionable. However, conducting studies in geographically, circumstantially, genetically and virologically distinct environs will add additional layers of difficulty in interpreting results and discerning racial and ethnic variations in response. The only way forward is to conduct early phase vaccine clinical trials in populations and locales as diverse as possible.

> *"One key lesson for future efficacy trials is writ large already: the participation of both men and women from diverse ethnic backgrounds is vital, not just from a perspective of equity, but to ensure that comparisons of vaccine effects by gender and race can me made with confidence"[75]*

The obstacles to be overcome include those discussed throughout the report:

- Disenfranchisement
- Mistrust
- Misperceptions
- Intimidating study procedures
- Proportionate representation in clinical trials
- How to engage racial and ethnic minorities in the AIDS vaccine development process

<u>Moving forward</u>

With this background, panelists engaged in an interdisciplinary discussion.

> "*We want our communities to come along with us and do science with us. Are we willing to think about how we change science to be more in line with the community*?"

Panelists expressed the view that the National Institute of Allergy and Infectious Diseases has in fact taken lessons learned previously in prevention and treatment, and incorporated these into their vaccine research program in innovate ways. Community representatives join the protocol teams at the very beginning stages. Furthermore, the community representatives are trained in investigative approaches to maximize their understanding and their input into protocol design. Protocol designs have been changed based on community input. The real hurdle is the complexity of bringing social science and behavioral science into the research protocols when testing new vaccines.

The sampling problems relating to Native American/Alaskan Native communities mentioned above (see Section: Prevention Research) are also relevant here. Panelists reiterated the need for appropriate sampling strategies to ensure adequate representation of Native American/Alaskan Native individuals. Of major concern is the question whether the vaccine trials will indeed continue to be carried out in the US. If so, then the centers that have traditionally carried out the research need to reverse the trend of weak relationships with native communities. Partnering between minority institutions with majority institutions will be very important and needs to be fostered.

Communication

- The research community needs to find better ways of explaining to potential trial participants that they are indeed being "put into an experiment", even though they do retain the autonomy in decision making. Honest and open communication is essential. Researchers need to explain "what is being done with their blood" to communities being recruited for vaccine trials.

- Researchers will need to learn to work with values of communities. For example, the success of recruiting to vaccine trials in Thailand, where the

Buddhist approach supports the notion of doing something good for all of society.

- Vaccine research necessitates increased access to treatment. The research community needs to demonstrate that commitment in real terms.

- The perception of commitment is difficult to generate if American Indian/Alaskan Native communities keep being referred to as "other"

WHAT ARE THE PLANNING NEEDS?

"*There are lots of meetings for planning for the scientists for phase III trials. There is no real planning going on for community participation*"

"If we really want to fix this, it needs to be a twenty or really a forty year plan, a two generation plan to address some of the underlying issues in a more robust way."

Panelists agreed that vaccine research will require a long term commitment to communities, something that is difficult to achieve given funding cycles. Partnering with agencies and entities and organizations within the community commitment needs to be considered as a way to alleviate this problem.

Volunteering for vaccine trials brings with it a high likelihood of seroconverting. The legal issues regarding HIV seropositivity due to vaccine studies have been largely ignored. For example, the package insert for rapid HIV testing does not provide information specific for individuals who participated in vaccine trials. Leadership in this area needs to be generated (e.g. working with insurance companies).

Our current epidemiology methodology keeps us from looking at the communities of color and looking specifically at some of the high incidence rates in the US. The US needs to invest in these communities as it is investing in other countries.

> "*Biomedical prevention has only gone so far and we need to move into modern medical prevention. Behavioral prevention research and biomedical intervention research need to go hand in hand*"

Panelists stressed that behavioral research needs to be included in vaccine trials. Every vaccine trial should include a wealth of behavioral research, and all trials mined for behavioral outcomes. This should happen consistently.

Much has been learned regarding the effect of antiretroviral treatment on transmission, including studies of behavioral disinhibitory effects. HIV vaccine researchers need to tap into this resource to plan research around how vaccines may affect behavior and risk taking.

A problem is that much of the phase I work has not been done in the communities that will need the vaccines the most. Vaccine researchers need to set up shop in the communities at the very beginning of research, not "drop in" at the Phase III stage. Researchers have been reluctant to engage minority communities earlier on because it is easier to work with communities that the research communities are familiar with. If minority communities are being asked to trust researchers, researchers will need to develop trust towards minority and disenfranchised communities.

> "*What does it take to get you to participate in effective behavior change, what does it take to get you involved in clinical trials? Those are the questions I am not sure we are asking. We determined that folks are not participating, but we haven't determined why*"

> *"It seems to me that if you want to know what folks need, you might ask them"*

> "*Because we are not only working prospectively, we are also working retrospectively*"

The issue of how race, ethnicity and culture play into building of trust towards research is especially relevant in the area of vaccine research [76, 77]. The potential of raising false hopes is particularly dangerous in this setting. The effectiveness of treatment is so clearly documented – we know that treatment works; we have drugs that have prolonged many patients' lives. In the vaccine field, researchers face the challenge of needing to explain that we (the research community) don't know if it will work, thus compounding the scientific complexity with researchers' uncertainty. The scientific community needs to revisit this issue on a regular basis, with the hope of eventually developing a more systematic approach to the problem.

As for all research, the research community needs to face the fear and mistrust within communities and this may be especially so for vaccine research, given the beliefs already rooted in sectors of society (see above) and vaccine-specific issues that arise. For example, within the Native American/Alaskan Native communities, issues around what is being "done with my blood" are substantial. Careful and detailed explanations as to what the actual research plans are need to be provided and community input sought at all stages of vaccine research.

> "*Actually involve the community directly, from the beginning……. so that these fears can be addressed head on, not shied away from*"

Involving the community means more than simply requesting consent. For the Native American/Alaskan Native communities, it means tapping into their traditional strengths that helps them respond to dangerous circumstances as well as their trans-generational knowledge. Such approaches will benefit not only the communities, but also enrich the research community.

"The power of oral history combined with biomedical investigative techniques was displayed during the 1993 Hanta virus epidemic in Navajo country. In June of 1993, 15 tribal healers met with IHS and CDC biomedical professionals to discuss possible causes of the "mystery illness". To the Navajo, any excess is a form of disharmony. Excess rain and snow had fallen that winter and brought an abundance of pinion nuts and new vegetation. Navajo oral tradition mentions three times that this has happened in recent history: 1918, 1933, and 1993. Many Navajos died of sudden and powerful diseases each time. Elders cited the abundant pinion crop and a high rodent population as the cause. This reference led investigators to find the answer to the "mystery illness" within a matter of days by testing rodent feces and urine samples. This is a clear argument for the holistic thinking that combines not only traditional medicine, but also tribal oral history, with Western medical practice for the wellness of an indigenous population." From the paper commissioned by Health Canada "The Health Status of Indigenous Women of the U.S.: American Indian, Alaska Native And Native Hawaiians."
http://www.epa.gov/OSP/tribes/sciinf/waysknow.htm

There are questions that arise in the context of a less than 100% effective preventive vaccine:

- What are the issues around childbearing? This is especially relevant as the burden of disease is transitioning more and more to female populations (including in the American Indian/Alaskan Native populations).
- How does vaccine research and implementation interact with other health problems of prime concern in Native American communities, such as diabetes?

ENGAGING MINORITY COMMUNITIES IN VACCINE RESEARCH

Successful examples of community engagement have approached research from a "community building" perspective. Rather than focus solely on public health issues around HIV/AIDS, community building approaches focus on advancing the health of the community within a political and organizing context. People in communities are really interested in how the community survives. Organizations should think about how to link the historic black and other civil right experiences in discussions on advancing health care.

On the whole, people participate in vaccine research based on altruism. Altruism is based on motivation, but also requires hope. As discussed above (see Section: Prevention Research), minority populations affected by HIV/AIDS are often characterized by hopelessness and despair. This is a world completely foreign to academic, industry or agency researchers, and the question of how people get to that level of hopelessness and despair, and what will bring them out of it, will be unfamiliar, but needs to be asked. How can the research community hope to engage minority communities without addressing these questions?

Panelists cited anecdotal experiences with individuals that managed to make the transformation. The "transformation" appears to be embedded in a spiritual component.

> "*Maybe we need to do more research in understanding the transformation of the mind of individuals, the integration of sort of the spiritual health and the physical health into the individual well being. Because, there is a piece missing there that is not easy to understand*"

SUMMARY AND DISCUSSION

> "*The sense of broken trust is so underlying to all the areas we talked about…..one thing that absolutely needs to be addressed…*"
>
> "*If I have to summarize this in one word, I would say 'weaving*'".

It will take a concentrated effort to find a way to repair the trust, not only in HIV/AIDS but in disparities in all other areas of healthcare. The effort needs to emanate from government agencies, the academic research community as well as industry sponsors.

The need for much more communication of the kind that this workshop provided, between individuals involved in prevention, treatment, and vaccine research was clearly expressed. None of the issues raised during the workshop will be solved by investigators from a single discipline working in isolation. Active engagement is needed in building bridges between these disciplines.

Focusing on areas of particular concern to minority communities may help address the trust gap. For example, defining predictors of toxicity will help demonstrate to minority populations that the scientific community is doing its part of finding ways to minimize or even avoid the toxic effects of drugs. This approach could perhaps provide a wedge to rebuild the broken trust.

Another viewpoint expressed illustrated the potential effect that current events have on supporting or negating trust towards research. Trust will not easily develop in an atmosphere of "cultural assault on science and medicine", as the severe research budget cuts have been interpreted by some. The handling of the anthrax exposure – the differential treatment of Senate members and staff compared to postal workers – provided another example of clearly apparent disparity.

Several new areas in prevention research were highlighted during the workshop, including:

- Biomedical intervention tools, including pre-exposure prophylaxis
- Research on best mechanisms to introduce biomedical interventions (e.g. microbicides) once they are available
- Research to find ways to ensure that individuals continue to engage in multiple ways of protecting themselves and their partners, given the fact that none of these methods, including vaccines, are going to be 100% effective

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APPENDIX B: AGENDA

Session I: Prevention

Topic	*Speakers/Panelists*	*Moderator*
Welcome and Introductions		
Plenary Overview: Epidemiology of HIV-1 in the United States	Allyn Nakashima	Veronica Miller
Presentation of Research: Racial and Ethnic Minorities and HIV	Maria Cecilia Zea	
Question and Answer Session		
Panel Discussion One: "Where does prevention research need to go? What are the priorities for racial and ethnic minorities?"	Kate MacQueen, William Strain, Karina Walters, Frank Wong, Maria Cecilia Zea	Jeff Levi
Panel Discussion Two: "Relationship between treatment and prevention"	Tommy Chesbro, Robert Grant, George Roberts, Anita Vaughn, Steve Wakefield	Laura Cheever
Panel Discussion Three: "Interaction between behavioral prevention research and vaccine research"	Cornelius Baker, Stephen Oxendine, Carlos del Rio, Karina Walters	Frances Priddy

Session II: Treatment

Topic	*Speakers/Panelists*	*Moderator*
Plenary Overview: Race and Ethnicity Issues in Access to Care and Treatment	William Cunningham	Tom Kresina
Question and Answer Session		
Panel Discussion: "Where are the research gaps regarding mechanisms for providing access and care to minorities?"	Omobosola Akinsete, Jennifer Kates, Sana Loue, Carlos Del Rio	John Palen
Plenary Overview: Race and Ethnicity Issues in Treatment Response and Toxicity	Scott Penzak	Lauren Wood
Question and Answer Session		
Panel Discussion: "Opportunities for investigating race and ethnicity dependent differences in treatment response, toxicity, etc. Relationship between clinical research and access to quality care"	David Bangsberg, Arlene D. Bardeguez, Vicky Cargill, Coleen Cunningham, Elaine Daniels, Christopher Dezii, Daniel Montoya, Kim Struble	Rich D'Aquila

Session III: Vaccine Research

Topic	*Speakers/Panelists*	*Moderator*
Plenary Overview	Mark Feinberg	Chad Womack
Comments on the importance of minority involvement in trials and the recruiting of volunteers from minority communities	Barney Graham	
Question and Answer Session		
Panel Discussion: Maximizing representation of racial and ethnic minorities in clinical trials	Naihua Duan, Bonnie Mathieson, Steve Wakefield, Carol Weiss, Chad Womack, Lauren Wood	Barney Graham
Final Discussion Round	Conference Co-Chairs, Vicky Cargill, Michelle McMurry	Veronica Miller

APPENDIX C: PARTICIPANTS

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