MIGRATION AS A NOVEL RISK FACTOR FOR HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) FAILURE IN HIV-POSITIVE ADULTS

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STUDY PURPOSE AND RATIONALE

The proposed study tests the hypothesis that HIV-positive Dominicans and Dominican-Americans who migrate while taking Highly Active Antiretroviral Therapy (HAART) have higher rates of treatment failure.

The HIV epidemic in the United States affects an estimated 1.1 million adults and adolescents leading to significant morbidity and mortality and placing an enormous burden on the nation's health care systems[1]. HAART has greatly improved the lives of people living with HIV/AIDS and its survival benefit has been clearly documented[2,3]. Consequently, identifying the risk factors for HAART failure—and structured interventions to combat these risk factors—has been of great importance in fighting the HIV epidemic. Research since the introduction of HAART has identified a number of key risk factors for HAART failure such as inadequate treatment with antiretroviral medications (ARVs), high risk behavior in populations with known ARV resistance, and poor adherence to medications which is strongly linked to comorbidities such as depression, substance abuse, and other psychiatric disorders[4,5,6]. A recent study shows that HIV-positive immigrants living in France reported more difficulties adhering to their HAART regimen when traveling to their native countries in Africa[7]. Factors such as stigma, a break in daily routine, difficulty obtaining medications, and lack of support systems might contribute to poor adherence while away from home. These data suggest that migration may play a key role in treatment failure—leading to greater morbidity and mortality—but further studies examining the interplay between migration and HAART outcomes are lacking.

Studying the role that migration plays in the HIV epidemic in the United States—with its large foreign-born and migrant populations—is especially important. The epidemic has proved to be extraordinarily dynamic since it was first recognized in the country in 1981 and recent population studies suggest that HIV continues to grow faster in minority populations—where individuals are more likely to be foreign-born—than in Caucasians. The latest Center for Disease Control (CDC) data shows that the incidence of HIV in black Americans and Hispanic/Latino Americans is approximately eight and three times higher respectively than in white Americans[8]. Within these minority communities, especially high rates of new HIV cases are being found in migrant populations, especially those from Central America, South America, and the Caribbean, and the HIV epidemic has long been shown to affect migrant populations disproportionately[9].

It would be fair to say that the epicenter of the HIV epidemic in foreign born and migrant populations is New York City, which has more immigrants, ethnic minorities, and HIV-positive individuals than any other city in the United States, as well as a rate of HIV incidence that is three times the national average[10]. New York City is an ideal place to study migration and outcomes of HAART treatment not only because of the abundance of potential subjects, but also because of the potential consequences that migration may be having on the epidemic. Columbia Presbyterian Medical Center (CUMC) is especially

engaged in the health care of HIV-positive patients and migrant populations due to its location in the Washington Heights neighborhood of northern Manhattan. The Washington Heights community is 71% Hispanic and 51% foreign-born, with most individuals coming from the Dominican Republic were the prevalence of HIV is estimated to be 1.1% in adults[11,12]. A recent community survey estimated that 15% of people in Washington Heights had traveled to the Dominican Republic in the previous six months, indicating that high rates circular of migration are present[13]. The adult HIV outpatient clinic at CUMC, which serves an estimated 1,200-1,400 patients, is reflective of this population with approximately 500 patients who identify as Dominican or Dominica-American.

In summary, the HIV epidemic in the United States is large and it continues growing at faster rates in minority and migrant populations. Improving the response to HIV in these communities is crucial now and will become increasingly crucial in the future given the trajectory of the epidemic. The proposed study seeks to identify migration as a novel risk factor for HAART failure. If migration is indeed a risk factor for HAART failure then further interventions may be developed to blunt its consequent negative impacts on the morbidity and mortality in HIV-positive patients. CUMC is an ideal setting for such a study given its service to a large number of HIV-positive patients in a community with high rates of migration.

STUDY DESIGN AND STATISTICAL PROCEDURES

Study Type:

This study is a retrospective cohort study.

Setting:

All participants will be recruited from the adult HIV clinic at Harkness Pavilion in the Columbia University Medical Center. This clinic cares for a wide range of HIV-positive adults and accepts both private and government insurance, including forms of AIDS Drug Assistance Program (ADAP) insurance which provides coverage to previously indigent patients who are diagnosed with HIV. Many of the patients come from the surrounding neighborhoods of northern Manhattan and the western Bronx. These neighborhoods are especially burdened by the HIV epidemic and are home to large numbers of Dominican-Americans, many of whom migrate frequently.

Entry Criteria:

Patients will be eligible for the study if they meet the following criteria 1) enrolled in the adult HIV clinic at CUMC 2) age 18 years or older 3) self-identify as Dominican or Dominican-American 4) have initiated or re-initiated (after a break of more than three months) HAART between nine months and two years prior to the date of the interview 5) are fluent in either Spanish or English

Study Protocol:

Eligible participants will be identified on a daily basis by chart review of the patients who will be seen in clinic that day. Eligible patients will be approached in private, after being seen by the triage nurse prior to their appointment. Language fluency and self-identity as Dominican or Dominican-American will be confirmed. Informed consent prior to study

participation will be obtained. Participants will undergo a brief interview (Appendix A). Data collected will include the following

--basic demographics: age, sex, current marital status, level of education, country of birth, spoken language ability (English), written language ability (English), estimated household income

--HIV information: mode(s) of HIV transmission, ARVs prior to HAART by an HIV specialist, ARVs prior to HAART from another source

--comorbidities and support: current depression, substance abuse, number of people who know of HIV diagnosis

--migration history: country of birth, time since immigration to US (if applicable), trips outside of New York metropolitan area in previous two years (frequency, when left, when returned, amount of time away, location visited, purpose of trip, who accompanied by)

Following the interview a chart review will be conducted which will extract the following information:

--HIV information: initial HAART regimen, HIV drug resistance panels, last CD4 count prior to initiation of HAART, all subsequent CD4 counts, last viral load prior to initiation of HAART, all subsequent viral loads, documentation of WHO stage IV disease,

At least two research assistants will be involved in the data collection. The interviewer will be blinded to the results of the pre-interview and post-interview chart review and the chart reviewer will be blinded to the results of the interview.

Study Groups:

Participants will be divided into two groups: migration and no migration. The migration group will be defined as meeting the following criteria after the initiation of HAART but before evidence of treatment failure: traveling more than 50km away from home for seven days or more.

Primary Outcome:

The main study outcome will also be binary: treatment failure or no treatment failure. Treatment failure will be defined per World Health Organization guidelines[14]. Failure will include meeting any of the following criteria between 6 months after the initiation of HAART and the end of the study period (the day of the interview): recurrent or new WHO stage IV disease, CD4 count below level at which HAART was initiated, CD4 count dropping >50% below peak level on treatment, CD4 <100 after >6mo of treatment, viral load >10,000 copies/ml.

Secondary outcomes:

In addition to comparing the basic demographic information between the two groups, the following risk factors for treatment failure will also be analyzed to look for potential confounders: English language ability, household income, ARV use prior to HAART, depression, substance abuse, number of people who know of participant's HIV diagnosis, initial HAART regimen, last CD4 count prior to HAART, last viral load prior to HAART. The following factors will also be analyzed to further investigate the hypothesized difference in treatment failure between the migration group and the no migration group: duration of migration, frequency of domestic and international migration, reason for migration.

Statistical Analysis:

Power calculations: Analysis for the primary outcome, which is binary, was conducted using the chi-squared test for two groups. The estimated rate of treatment failure in the no migration group is 0.25 (published studies for HIV treatment failure in the United States after 1-2 years of HAART range from 20-40%). The estimated effect in the migration group is 0.20 with a hypothesized increase in failure. As a result, the estimated rate of treatment failure in the migration group is 0.45. It is also estimated that the number of patients classified to the no migration group will be twice as large as those classified to the migration group. When aiming for 80% power with a 0.05 probability of a type I error, the number of participants in the no migration group will be 144 and the number of participants in the migration group will be 72.
Other statistical analysis: Data from this cohort study will be used to calculate the relative risk of treatment failure based on migration status. Relative risks for the secondary outcomes will also be calculated. The secondary outcomes and demographic information will also be compared between the migration and no migration groups to adjust for both potential confounders and to look for possible explanations of the hypothesized difference in treatment failure rates.

STUDY PROCEDURES
Data from the study will be generated by both a single survey of the participant and a chart review. Study subjects will not undergo any additional medical procedures, lab work, imaging studies, or physical examinations.

STUDY DRUGS OR DEVICES
There are no study drugs or devices.

STUDY QUESTIONNAIRES
Please see Appendix A below.

STUDY SUBJECTS
Study subjects are HIV-positive adult patients seen in the HIV clinic at Harkness Pavilion in the Columbia University Medical Center. To participate in the study they must provide informed consent and they must meet the inclusion criteria detailed above in "Study Design and Statistical Procedures."

RECRUITMENT
Participants will be recruited from the adult HIV clinic at Harkness Pavilion in the Columbia University Medical Center. Please see "Study Design and Statistical Procedures" above for an explanation of the inclusion criteria and recruitment methods.

CONFIDENTIALITY OF STUDY DATA
All efforts will be made to ensure patient confidentiality. Potentially eligible patients identified prior to clinic visits will be assigned a study number. That study number will be the only unique identifier recorded on the interview data sheet (no name, date of birth, contact information, medical record number, etc.). Interview data sheets will be kept in a secure location in the clinic and electronic information extracted from the medical record will be stored on secured computers at CUMC.

POTENTIAL RISKS

Participants will only undergo a brief interview and the study coordinator will then conduct a chart review. The study organizers do not foresee any potential risks to the study participants.

POTENTIAL BENEFITS

There is no anticipated benefit to study participants aside from the greater societal interest in improving understanding of how migration and HIV treatment success may be interrelated.

ALTERNATIVES

No feasible alternative exists to collecting both medical and migration information in this study population.

Appendix A

INTERVIEW DATA SHEET

[The first two entries will be completed by the researcher who identifies potential study participants. The rest will be filled out by the second researcher during a Spanish or English language interview]

Study number: _____

Date HAART was initiated: _____

Age: _____ years

Sex: M / F

Current marital status: single / married

Time since immigration to US: N/A _____ years

Level of education: primary not completed / primary completed / high school not completed / high school completed / college not completed / college completed / advanced degree completed

English spoken language ability (self-assessment): none / little / some / a lot / fluent

English written language ability (self-assessment): none / little / some / a lot / fluent

Estimated household income: _____ USD

Country of birth: DR / US / _____

Mode(s) of HIV transmission (all applicable): heterosexual / homosexual / perinatal / blood transfusion or surgical procedure / IVDU / don't know

Depression (PHQ-9 score): ____ / 27 *[For questions involved in PHQ-9 see: http://www.patient.co.uk/showdoc/40025272/]*

Substance abuse (current): none / EtOH / IVDU / _____

ARVs before HAART by HIV specialist: Y / N

ARVs before HAART from another source: Y / N

Number of people who know of HIV diagnosis: _____ people

----------Migration History----------

Travel further than 50km from home since the date HAART was initiated: Y / N

Migration #1 *[information below completed for each migration event since start of HAART]*

Time away from home: _____ days / weeks / months / years

Date left: _____

Date returned: _____

Place(s) traveled to: _____

Purpose of trip: business / vacation / visiting family

Accompanied by: spouse / other family / friends / nobody

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[12] Dominican Republic Fact Sheet. In: Joint United Nations Programme on HIV/AIDS; 2006

[13] Personal communication, unpublished results

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