Sexually Transmitted Infections Clinics as Strategic Venues for Targeting High Risk Populations for HIV Research and Sexual Health Interventions

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Puerto Rico has one of the highest incidence rates of HIV in the U.S. Concurrent with increases in sexually transmitted infections (STI), an increasing share of the new infections in PR are associated with sexual transmission. Much of the available research on sexual risk in PR derives from STI/HIV surveillance data. There is limited social and epidemiological research on sexual risk in PR, particularly in hidden and often hard-to-reach populations at high risk. Despite the absence of substantial resources that most epidemiological studies require, a research collaboration was initiated in 2007 between researchers in the School of Public Health at the University of Puerto Rico and the Centro Latinoamericano de Enfermedades de Transmisión Sexual (CLETS), one of the largest publicly funded centers for STI/HIV screening and treatment in the San Juan metropolitan area. Structured as a case study in the development of community-based research collaborations, this paper describes the early history and development of the project, including formative research, recruitment and training of students, and evolution in the study design that contributed to the current configuration of the ongoing "Core" study. Preliminary data are presented, highlighting data from a number of subpopulations that may contribute to our understanding of the role of behavioral risk in the STI/HIV epidemics in PR. More generally, the paper may guide the development of similar collaboration elsewhere in the Caribbean where HIV risk is increasing but where resources for research in high risk settings and groups are scarce. [PR Health Sci J 2011;30:101-108]

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Despite a decline in rates of HIV in the United States (U.S.) as a whole, Puerto Rico (PR) has one of the highest overall HIV incidence in the U.S. (45.0 per 100,000 population), twice that of the 50 U.S. states as a whole and 1.5 times that of the overall U.S. Hispanic population (1). Although the early HIV epidemic in PR was principally associated with high risk heroin injection practices, recent reports highlight the growing importance of sexual transmission in new HIV infections in PR, (2, 3) including high rates of co-morbid sexually transmitted infections (STI) (4, 5).

HIV and other STI confer substantial negative consequences for both the individual and the community and there is an urgent need to develop targeted behavioral and medical interventions to reduce risk. However, the development of targeted interventions in PR is limited, at least in part, by the relative dearth of detailed information about the context in which behavioral risk is situated, particularly in hidden and often hard to reach populations.

In 2007, researchers from the School of Public Health at the University of Puerto Rico began a strategic research collaboration with the clinical staff of Centro Latinoamericano de Enfermedades de Transmisión Sexual (CLETS), Department of Health, San Juan, Puerto Rico; †Puerto Rico Comprehensive Cancer Center, School of Medicine, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico; §National Development and Research Institutes, Inc.

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Enfermedades de Transmisión Sexual (CLETs), one of the largest publicly funded centers for STI/HIV screening and treatment in the San Juan metropolitan area. The basic concept for the study involved the introduction of a “Core” epidemiological study that would serve as the basis for a detailed profile of behavioral risk within the clinic population, including targeted subgroups in which there is limited research in PR but that may be of particular importance for intervention development since they represent critical groups in which many of the new infections are being seen (see Figure 1).

Figure 1. Core Study

Organized as a case study in community-based health research, (6-8) this paper describe the history and elaboration of the study, including the evolution of the design and methods that are being applied. Additionally, we highlight preliminary findings on particular issues and sub-populations that may be contributing to continued growth of the STI/HIV epidemic in PR and in which intervention development is urgently needed. It is hoped that the paper may guide similar efforts in settings where there is evidence of increased HIV risk but where resources for research, particularly in hidden, high risk populations, remain scarce.

Pre-Research, Formative Activities

Following a series of preliminary planning meetings between the research team and senior clinic staff, the initial step for preparing the study began with formative interviews amongst medical and support staff (9, 10). These interviews were primarily intended to inform the research team’s understanding of the types of data about the clinic population that already existed and the types of research procedures that could be introduced within the clinic environment without causing serious disruption of ongoing clinic activities.

Information from these interviews guided the initial planning study procedures, including approaches to sampling, the types of research interviews that could be practically implemented, preliminary consideration of selection of the types of assessment measures that could be employed, and the types of research staff and associated research training that would be required to support these activities. It became apparent, for example, that the processes within the clinic-including intake, clinical assessment, clinical treatment, and documentation-were much more complex than the research team had initially appreciated and that implementation of the research study would require coordination amongst a much larger group of individuals (reflecting different roles within the clinic) than had been anticipated. Additional interviews amongst individuals with different roles within the clinic, including security guards, intake personnel, case managers, and medical records personnel, were required in order to obtain a better understanding of the daily operation of the clinic and to establish more effective and efficient study procedures within the context of the clinic’s service delivery and available resources. The interviews were mostly informal and extended through the initial period of the study implementation. These interviews also served to establish the foundation of a relationship between the research team and the clinic staff and significantly contributed to the development of trust, rapport, and mutual cooperation between the two.

Following the initial interviews with clinic staff, we conducted informal interviews with a small number of patients in the clinic while concurrently conducting targeted observations in the patient waiting room and adjacent public areas within the clinic. These activities included an informal census that served to document the size and general demographic characteristics of clinic population. The informal census was not intended to yield a formal estimate of the size of clinic population but rather to provide a general estimate of the size of the daily client burden so that research procedures could be appropriately scaled. For example, it was determined that an average of 95 patients attend on the clinic every day, including both men and women and spanning a wide age range, and this served to guide decisions related to sampling and staffing.

Research Capacity-Building and Training

The next step in preparing for the implementation of the study involved two simultaneous activities, recruitment and training of research staff to assist in the data collection and development and pilot testing of study procedures and instrumentation. Over a period of 20 months, a total of 22 undergraduate and 8 graduate students were recruited as research interviewers as part of an independent study practicum in research, with ongoing recruitment of new students every semester and during the summer session. The training and orientation program reflected strategic contributions from members of the interdisciplinary research staff, including medical anthropology, clinical psychology, public health education, and epidemiology. In brief, the training consisted of approximately 16 hours of didactic and
practical preparation in key research methodologies, including an introduction to research in public health, and introduction to social and behavioral research in HIV and the history of this kind of research in the epidemiology of HIV, an overview of the current epidemiology of HIV and STI in the U.S., and a profile of HIV and STI in PR. Also included was a detailed training of the history and importance of ethical conduct in research involving human subjects.

In addition to providing specific guidance on procedures establishing informed consent and for the protection of confidentiality, particular attention was given to the fact that the target population was involved in highly stigmatized behavioral activities, and consequently that substantial care was required in conducting inquiry on these topics, including strategies of managing embarrassment and shame, and also in recognizing signals of emotional distress and the potential need for crisis intervention.

Following the preparatory training, students participated in mock-interviews that were served to provide them with practical experience in the use of study procedures and instrumentation and also to insure that they were fully prepared to manage the types of challenges that accompany research on sensitive and highly stigmatized activities.

The didactic training included substantial review of prevailing concepts of how and why people use drugs (particularly drug injection) and why they engage in sexual risk, both of which were intended to serve as a foundation that would encourage students to assess their own values about these issues, including deontological and consequentialist approaches.

The didactic training also included substantial review of biological concepts, including the consequences of perinatal HIV infection in the current population of young men and women who are at especially high risk for HIV infection, as well as a discussion of the epidemiology of HIV in PR, including the current epidemiology of HIV and STI in the U.S., and a profile of HIV and STI in PR.

However, evidence from the preliminary activities and piloting showed that the population available in the clinic could support recruitment of a broader and more complex sample, including women and non-injecting drug users. Second, after the study began, emerging HIV surveillance data showed higher rates of new infection in older age cohorts. Consequently, a decision was made to broaden the target population groups and inclusion criteria, to recruit both men and women, and to eliminate the age boundary for study eligibility. Additionally, and like many other studies of sexual practices, (11) our initial review of the condom use data suggested that our questions were not eliciting reliable self-report data. Based on feedback from interviewers, it became clear that a narrow focus on condoms necessarily did not serve to capture the full range of alternative strategies (other than condom use) that were being employed in reducing risk for pregnancy and or disease transmission.

In an effort to accommodate expansion of the study to include both men and women and a broader age range, and also to improve the reliability and scope of the sexual risk assessments, the research team conducted extended meetings in order to plan and develop the needed changes in instrumentation. Three major changes were made in the sexual risk assessments. First, the questions were revised and focused on a broader range of practices and options surrounding oral sex, ejaculation in penetrative sex, including insemination, early withdrawal, and condom use.

Second, and based on other studies which have shown greater reliability in the use of event questions in eliciting reliable data on self-reported condom use, (12) we added a series of questions about recent “events” in which the subject engaged in a particular type of sexual exchange (e.g., last penetrative sex with new partner, etc.).

Third, the informed consent process was changed from verbal to written informed consent. The initial decision to frame the study as an anonymous interview was based on uncertainty about the relative receptivity of the clinic population in relation to research within the clinic environment. Accordingly, the initial concept for the study was purposefully designed to be as minimally intrusive as possible and since no identifying information was being collected, only verbal consent procedures were employed. However, our experience in conducting the pilot studies indicated that participation rates were quite high, that subjects were willing to respond to sensitive questions if they were asked in a careful and respectful manner, and indeed that they often volunteered unsolicited information about their clinical status, including information about their STI and HIV status. This suggested that it would be feasible to include selected biological indicators in the research design. While the original instrument included modules on self-report history of and HIV and other STI, the shift to written informed consent permitted the addition of a targeted chart review component in which a member of the research team extracts selected clinical

Development, Pilot Testing, and Refinement

Following the initial formative assessment, the research team began development, pilot-testing, and refinement of the survey measures and related data collection procedures. Over a six month period, and based on continued discussion with clinic staff, input obtained from conducting mock-interviews, and initial data collection experiences, and review of the initial data from early interviews, three inter-related changes were made to the overall study design.

First, the initial study had been conceptualized as a way of gathering preliminary data for research studies of young men (age 15-39) with a history of drug use (particularly heroin injection), reflecting our initial interest in youth and young adult populations as well as the significance of this age group and behavioral risk in the history of the HIV epidemic in PR.
information from the patients’ clinic chart, including current diagnosis with a broad range of STI and HIV. This in turn required a change to written informed consent. Additionally, it became apparent that the brief nature of the interview limited the level of detail that could be included in the Core interview and that it would be useful to have a mechanism for recruiting particular subgroups for participation in follow-up research --- a goal that would also require written consent.

Collectively, these changes in the design required revision of the study recruitment procedures and behavioral instrumentation, additional pilot-testing, and additional review by the Human Research Subjects Protection Office of the University of PR - Medical Sciences Campus. The final design involves random selection of subjects from the clinic waiting room, a brief screener interview that includes details of study participation, and an assessment of eligibility (including a formal demonstration of capacity for consent), and written informed consent for voluntary participation in the study. Study participation includes a brief behavioral survey interview that is conducted by a member of the research team and permission to extract selected clinical information from their patient chart.

The instrument that is used to guide the behavioral survey interview is divided into four sections: The first section, Socio-Demographic Characteristics, includes questions on date of birth, education, sources of income, sexual self-concept and identification, history of incarceration, military service, and history of suicide. Section 2 includes a detailed assessment of drug use, including lifetime exposure to a broad range of substances, the year that the individual first used the substance, age at first injection, use of drugs in the 90 days prior to the interview, and injection in the past 90 days. Section 3 involves an assessment of sexual risk included onset of oral, vaginal, and anal sex, sexual practices and partners in the last 90 days, experience in buying or selling sex, participation on group sex in the last year, and details of the last sexual event. The fourth and final section includes questions about health history and utilization of health services, including the subjects’ purpose for visiting the clinic, self-reported history of STI, Hepatitis B Vaccination, and history of pregnancy.

In addition to the self-reported behavioral and self-reported history of STI diagnosis, a limited set of clinical data for each subject is recovered from the Targeted Chart Review process that includes documentation of current STI (including Syphilis, Chlamydia, Gonorrhea, Herpes, Hepatitis B, Hepatitis C), HIV status, and clinical indicators of HIV disease (including current CD-4 count and viral load).

Preliminary Findings
The primary objective of this paper is to elaborate the development of the research collaboration in an STI clinic environment and it is beyond the scope of a single research article to provide a complete description of the data set. However, by way of illustrating the types of data that the collaboration is yielding, in this section we provide a preliminary profile of the overall clinic population. Additionally, we highlight preliminary findings on behavioral risks in a number of subgroups that may be contributing to continued high STI/HIV incidence and in which intervention research is urgently needed.

Up to December 2010, a total of 779 individuals have participated in the study, including 461 men and 318 women. Study participation is high, with 78% of those who were screened and deemed eligible, agreeing to participate. Mean age of males is 35.9, ranging from 16.5 to 79.5 years (SD=13.3). Mean age of females is 32.5, ranging from 16.2 to 78.3 years (SD=13.1). The majority (84.1%) were born in PR, one fifth (20.2%) have less than 12 years of education, and more than a third (42.4%) are unemployed. Most (70.9%) are unmarried while about a third (29.1%) are married or living with a consensual partner. Most (81.0%) identified themselves as heterosexual, 13.0% as homosexual, gay or lesbian, and 6.0% as bisexual. More than half of the men (56.0%) and over a quarter of the women (26.1%) have a history of illegal drug use and over a quarter (29.1%) of the men and 10.8% of the women have a history of injected drugs. Of those who have ever used any type of drug (excluding alcohol, tobacco, and marijuana), a third (34.0%) are currently using one or more drugs, and of these, nearly one fifth (17.9%) are currently using injecting drugs. Within the overall sample, 37.1% of men and 27.0% of women are living with HIV.

With a general interest in understanding high HIV incidence rates in PR, we summarize preliminary data on key issues and subpopulations that may be contributing to continued increases in HIV incidence.

Onset of Sex, Age Discordance, and Early Sexual Health Intervention
Generally, the available literature on early sexual debut suggests that early sexual initiation is associated with a wide range of poor sexual health outcomes, including increased risk for STI and HIV (13, 14). Generally consistent with earlier population studies of sexual debut in PR, (15) mean age of first sex among men in the study is 15.1 years and mean age of first sex among women is 15.8 years.

Somewhat unique in our sexual risk data, however, is the fact that we also collected information on characteristics of their current sexual partners, including age. Over a third (40.1%) of the young women (16-29 years) has a current sexual partner who is at least 5 years older. Age discordance is generally associated with disparities between sexual partners in sexual decision-making, notably in condom use, (16, 17) and this may be contributing to increasing rates of STI and HIV among young women in PR. These findings amplify earlier longstanding recommendations for the need for early sexual health education in PR and the need for targeted health promotion interventions for high risk youth and young adult populations (18, 19).
Men Who Have Sex with Men (MSM)

Surveillance data in PR show that MSM are disproportionately affected by STI and HIV and that they also account for an increasing number of new STI and HIV infections (2, 20). For example, Syphilis rates among males in PR are six times the rate among females, and have increased substantially among men since 2001 when their distribution by gender was almost equivalent. The increase in the incidence ratio between males and females has been attributed to sharp increases in Syphilis among MSM (21, 22).

Consistent with these overall trends in the epidemiology of STI and HIV in PR, MSM in the Core study evidence high levels of behavioral risk. Nearly a third (30.4%) of the men reported having had sex with another male in their lifetime. Of these, two thirds (65.0%) have had sex with another male within the last 90 days (with a mean number of 3 sexual partners, SD=4). 18.7% had receptive unprotected anal intercourse (UAI) and 26.4% had insertive UAI. Self-reported history of an STI diagnosis among MSM is high, including Syphilis (30.8%), Gonorrhea (16.5%), genital warts (14.3%), and Herpes (14.3%). As might be expected given that the clinic is also a key HIV treatment provider, over half of the MSM self-reported having HIV infection (50.5%). Over half (55.9%) of the HIV+ MSM are sexually active in the last 90 days, 10.9% had receptive UAI and 15.2% had insertive UAI.

Findings suggest the need to develop HIV and STI prevention interventions targeted to MSM in PR. Research is needed to fully describe the behavioral and social factors that contribute to HIV/STI risks among MSM in PR. Particular attention should be given to the role of local culture on sexual partnering practices and sexual risk and to the role of stigma as a barrier to health seeking and serostatus disclosure (23, 24).

Sexual health promotion interventions, including HIV and STI prevention strategies among MSM must consider not only the behavioral components that may place MSM at risk but also the social and structural contexts that may constrain safe sex decision making. Moreover, given the increased prominence of MSM in the emerging epidemiological data on STI/HIV in PR, (25) there is an urgent need for interventions among HIV+ MSM.

Sexual Health among People Living with HIV

Improvements in HIV treatment in recent years have reduced mortality and morbidity among people living with HIV infection and also contributed to substantial improvements in daily functioning and quality of life (26, 27). This has also allowed HIV+ individuals to remain sexually active for a longer period of time (28, 29). Consistent with these overall trends, HIV+ men and women in the sample are sexually active, with 60.8% of the HIV+ men and 47.7% of the HIV+ women reporting having had two or more sexual partners in the last 90 days. Of those, 26.6% of men and 48.7% of women had unprotected sexual intercourse in their last sexual encounter. These data support the urgent need to develop effective sexual health interventions among HIV+ individuals, including sexual risk reduction and partner disclosure.

Gaps in Continuity of HIV Care Following Release from Prison

Studies in 2008 showed that nearly 7% of adult men and 14% of adult women imprisoned in PR had HIV infection, (30) a dramatically higher rate compared to the U.S. as a whole and one of the highest rates in prison populations worldwide (31). Substantial progress has been made within the PR Correctional System in increasing HIV detection at intake and also in the provision of HIV treatment while inmates are in custody (32, 33). However, there has been little attention to the development of mechanisms to engage HIV+ inmates in community-based HIV care following release from prison, with the result that many of those who have initiated care while incarcerated are at high risk for falling out of care after their release.

To date, and despite its potential importance for understanding the continuing epidemic in PR, there has been no assessment of the rate of treatment discontinuity among HIV+ prisoners released from prisons in PR. Preliminary data from the Core study indicate that nearly a quarter of the men (23.7%) and 9.1% of women have a history of at least one incarceration. Among those with any history of incarceration, two thirds (68.0%) of men and 27.6% of women reported two or more incarcerations. Among those with a history of incarceration, 43.0% of men and 37.9% of women are living with HIV.

With an interest in understanding barriers to enrollment in community-based care following release from prison, we examined data from 10 (8 men and 2 women) who self-reported being HIV-positive and also had a history of incarceration and calculated the interval between their release from prison and their enrollment in HIV care at CLETS. On average, there was a four year gap between release from prison and enrollment in HIV care at the CLETS clinic. This is consistent with information from qualitative interviews among clinic staff who reported that HIV+ patients who had a history of incarceration typically appeared for HIV treatment only after the development of advanced HIV disease, typically via referral following hospitalization for HIV-related opportunistic infection.

The extended interval between release from prison and initiation of community-based care following release may be expected to contribute to increased poor health outcomes at an individual level, including increased morbidity and mortality. It also contributes to poor community level outcomes in the form of increased risk for secondary transmission to drug and sexual partners, a fact that may partially explain high HIV incidence rates in PR. There is an urgent need to develop interventions to retain HIV+ prisoners in community-based care following release from prison, an outcome that may be expected to
Contribute to improved individual clinical benefit as well as reduction in community-level HIV incidence.

**Unmet Mental Health Needs**

It is well established that populations at high risk for HIV and STI are at disproportional risk for mental health problems (34, 35). Suicide has been documented as a major public health challenge in PR (36) and there is growing evidence that diagnosis with HIV may pose significant risk for suicide (37, 38).

Within the overall Core sample, nearly a fifth (19.3%) of the HIV+ men has a history of suicide, with a mean age of 32 at first attempt. Of those HIV+ men with a history of suicide, nearly half (48.1%) have had multiple attempts and a third (30.8%) have attempted within the last 2 years. Over a third (34.9%) of the HIV+ women has attempted suicide, with a mean age of 29 years at first attempt. Of those HIV+ women with a history of suicide, 59.1% have had multiple attempts and 27.3% have attempted within the last 2 years.

These preliminary findings support the urgent need for research on the mental health needs of people living with HIV and the need to advance individual, social, and structural interventions to reduce stigma and promote HIV-related coping skills in this vulnerable population. Particular attention should be given to the use of STI clinics as platforms for comprehensive care of co-existing medical conditions, including mental health distress and related risks.

**HBV and Other Preventable Infections**

Behavioral risk in many high risk populations are often compounded by structural health disparities in access to health resources that may exacerbate HIV transmission risk and also contribute unnecessarily complication in options for clinical care (39, 40). One example is Hepatitis B infection (HBV) which is associated with exposure to infectious blood or body fluids (41). Infection with HBV can result in liver disease and liver cancer—that is not always amenable to treatment (42). Importantly, HBV infection is preventable by vaccination and is especially important in groups in which behavioral risk associated with HBV transmission are prevalent, notably IDUs and MSM (43). However, significant gaps in vaccination coverage exist, particularly among ethnic and racial minority populations (44).

Nearly two thirds (59.4%) of the men in the Core study have not been vaccinated against HBV or do not know if they have been vaccinated against HBV. Similarly, half (49.7%) of the women have not been vaccinated against HBV or do not know if they have been vaccinated. Even allowing for some errors in recall, it seems likely that there are substantial gaps in HBV vaccination in this population, noteworthy given that one or more behavioral risk factors associated with HBV transmission are evident (45). Innovative approaches are needed to identify, engage, and retain high risk adults in HBV vaccination (46). Many of these individuals, both men and women, would also benefit from human papilloma virus (HPV) vaccination (47, 48).

**Summary**

This paper described the development and evolution of a research collaboration between the University of PR and CLETS, a publicly-funded center for STI/HIV screening and treatment in the San Juan metropolitan area. The paper showed that research collaborations in these types of service settings are possible, and particularly when integrated into practical research training programs for students that they can yield important social and epidemiological data about hidden, hard-to-reach populations even in the absence of large amounts of external funding.

Key issues in advancing this kind of collaboration included the need to build the study design and scope of the study as an iterative process, rather than one that could be fully conceptualized and instituted a priori. Allowing time for effective relationships to develop between research and clinic staff was a particularly important requirement.

We acknowledge that like many studies of out-of-treatment or quasi-treatment populations, that the sample available in a STI clinic poses multiple and sometime paradoxical limitations. On the one hand, STI clinic populations are likely to over-represent particular types of health outcomes and alone such data cannot be used to infer trends in overall prevalence and incidence at a population level. STI clinics and similar types of service environments also often have somewhat tenuous relationships with the populations they serves, with high risk for abandonment of care. Finally, these types of environments are notoriously underfunded and understaffed, providing multiple and complex clinical services in a context with limited time and resources. Each of these factors places practical limits on the types of study designs and research complexity that can be accommodated.

On the other hand, STI clinics and similar types of service environments attract large numbers of individuals who are at high risk for multiple, often complexly-related, poor health outcomes. As such, these environments provide the opportunity to recruit important study groups, notably “hidden” populations that are often difficult to recruit or identify using population-based approaches, particularly in the absence of significant resources. Similarly, research in these settings may facilitate intervention development, pilot-testing, and implementation in critical risk groups that may actually serves as ideal platforms in which to formulate and test targeted interventions. In summary, research collaborations like this one may represent important opportunities for understanding HIV risk and related health disparities among high risk groups and also as ideal setting for developing health promotion interventions in these vulnerable populations.
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Resumen

Puerto Rico (PR) tiene una de las tasas de incidencia de VIH más altas en EEUU. Simultáneo al aumento en infecciones transmisibles sexualmente (ITS), una parte creciente de nuevas infecciones se asocia con transmisión sexual. La mayoría de las investigaciones en PR sobre riesgo por contacto sexual surge de estudios de vigilancia de VIH/ITS. En PR existen pocas investigaciones sociales y epidemiológicas sobre riesgos por comportamientos sexuales con poblaciones en alto riesgo y de difícil identificación y acceso. A pesar de contar con recursos limitados, en el 2007 se inició una colaboración para realizar investigación entre la Escuela Graduada de Salud Pública de la Universidad de PR y el personal clínico del Centro Latinoamericano de Enfermedades de Transmisión Sexual (CLETS), una de las clínicas públicas más grandes del área metropolitana de San Juan dirigida al diagnóstico y tratamiento de ITS/VIH. Estructurado como un estudio de caso sobre el desarrollo de colaboraciones para investigación en comunidad, este artículo describe los inicios y desarrollo del proyecto, que incluye investigación formativa, reclutamiento y capacitación de estudiantes, y cambios al diseño que contribuyeron a la configuración del estudio “Medular”. Se presentan datos preliminares y se destacan algunos sobre varias subpoblaciones, que pueden contribuir a nuestra comprensión del rol de los comportamientos de riesgo en las epidemias de VIH/ITS en PR. Este artículo puede servir de guía para el desarrollo de colaboraciones en otras regiones del Caribe donde el riesgo de transmisión de VIH aumenta, pero escasean los recursos para investigación con poblaciones y escenarios de alto riesgo.

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