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A Binational Study of Patient-Initiated Changes to Antiretroviral Therapy Regimen Among HIV-positive Latinos Living in the Mexico–U.S. Border Region

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Abstract

Research is lacking on factors associated with antiretroviral therapy (ART) sub-optimal adherence among U.S. Latinos, who are disproportionately affected by HIV and face substantial health care barriers. We examined self-reported, patient-initiated changes to ART (i.e., made small/major changes from the antiretroviral drugs prescribed) among HIV-positive Latinos. Trained interviewers administered surveys to 230 participants currently on ART in San Diego, U.S. and Tijuana, Mexico. We identified factors independently associated with ART changes. Participants were Spanish-language dominant (86%), mean age of 41 years, male (77%), and born in Mexico (93%). Patient-initiated changes to ART were reported in 43% of participants. Being female, having 1 sexual partner (past 3 months), 6 years since HIV diagnosis and poor health were associated with increased odds of ART changes. Findings raise concern about sub-optimal adherence among this binational population. Longitudinal studies are needed to further explore adherence barriers and avenues for intervention.

Keywords

Persons living with HIV/AIDS (PLHA); Medication adherence; Latinos; U.S.–Mexico border; Antiretroviral therapy

Introduction

Achieving high levels of antiretroviral therapy (ART) adherence with HIV-positive persons is a critical public health goal. When HIV-positive individuals on ART are able to take their medication as prescribed 95% of the time (optimal adherence), they are more likely to prevent viral resistance, disease progression, transmission, and premature death [1–3]. Barriers to optimal adherence may include medication side-effects [4–9], patient limited knowledge about their HIV disease or treatment [7], and interpersonal and structural barriers such as poor patient-clinician communication [6] and health care access problems [10–12], respectively. In the U.S., sub-optimal adherence is a well-studied area among the general population, with a majority of studies focusing on non-Latino White and African-American populations. There is a dearth of published studies conducted with HIV-positive individuals of Latin American ancestry in the U.S., especially in populations who are Spanish-language dominant and/or immigrants [13, 14]. U.S. Latinos face substantial health disparities that are inextricably linked to poor adherence; they have disproportionately worse health indicators (e.g., faster disease progression) and health outcomes (e.g., AIDS or AIDS-related death) than non-Latino Whites [14, 15]. The gap in scientific knowledge about factors associated with suboptimal adherence for U.S. Latinos living in the U.S.–Mexico border region is exacerbated by a lack of information on HIV-related health care decisions, access to care, treatment-seeking behavior and cultural and environmental factors that may be influenced by proximity to the border [16].

The 2,000-mile U.S.–Mexico border is home to a rapidly growing population characterized by a constant back and forth flow of persons and goods. By 2025 the border population is projected to double from its current 13 million residents [17]. Health issues in the border region, especially HIV/AIDS, which has escalated on both sides of the border [18, 19], are of public health significance to both the U.S. and Mexico. In Southern San Diego County, Latinos comprise 64% of residents [20], yet account for 73% of AIDS cases [19]. San Diego's Latino HIV/AIDS cases are primarily foreign born (>60%) and mostly of Mexican origin [19]. California's Mexican sister state, Baja California, ranks 2nd in HIV prevalence among Mexico's 32 states—the prevalence is driven largely by the HIV increase in Tijuana, the state's largest city [21]. Our earlier work elucidates that many HIV-positive Latinos in the region seek health care services on both sides of the border, which has implications for HIV care continuity and service provision in both countries [22]. Limited information, however, is available on Latino patient decision making around ART adherence in a binational context. The current study explores factors associated with patient-initiated changes to their ART regimen among HIV-positive Latinos in the U.S.–Mexico border region.

Methods

We conducted a cross-sectional study with HIV-positive Latinos recruited from HIV social service agencies or clinics in Tijuana and San Diego from July 2009 to January 2010; half were recruited in Mexico and half in the U.S. Participants were screened for eligibility by trained interviewers. Inclusion criteria were: HIV-positive and of Mexican or other Latin American origin; 18 years old; residing in Tijuana or San Diego for 1 month in the prior year; ability to speak Spanish or English; and able to provide voluntary and informed consent. The current analysis is restricted to 230 participants who reported taking ART medications and who had valid responses for questions regarding patient-initiated changes to their ART regimen. This study was approved by the University of California, San Diego Human Research Protection Program and the Bioethics Committee at the General Hospital in Tijuana.

Interviewers administered a structured questionnaire based on questions drawn primarily from the Physician-Patient Relationship Quality Measure [23], the 2008 HIV Cost and Services Utilization Study [24], the Center for Epidemiologic Studies Depression Scale (CESD-10) [25], and our prior work with HIV-positive Latinos and high-risk populations in the U.S.-Mexico border region [22, 26]. Surveys were administered in rooms that allowed for participant privacy and took ~35–40 minutes to complete. All participants were given a \$20 incentive upon survey completion.

Our primary outcome variable was patient self-initiated ART regimen changes using two questions from the Self-reported Adherence Measure [23]. For this analysis we chose to assess global adherence using a 4-week recall period which may be conceptually easier to understand for patients and has provided reliable estimates of adherence [27–29]. The questions were, During the past 4 weeks how often did you: “make small changes from the antiretroviral drugs your doctor prescribed?” and “make major changes from the antiretroviral drugs your doctor prescribed?”, with the following response options: “many times, sometimes, few times and not at all.” The two questions were recoded into one dichotomous variable: “made changes” (made small or major changes: many, some and few times) versus “did not make changes” (small or major changes: not at all).

We examined the extent to which participants who reported ART regimen changes differed in the following domains: (a) sociodemographic and border crossing activity (e.g., number of round-trips in last 6 months, primary reasons for crossing); (b) binational care seeking practices and HIV-testing history (e.g., time living with HIV, HIV-related medical visits, medical insurance); (c) barriers to care (e.g., deportation, depression); (d) patient-clinician relationship (e.g., “how is the doctor who takes care of your HIV at helping you solve problems you have taking your antiretroviral medicines the right way?”); (e) use of complementary and/or alternative medicine (e.g., herbs/plants, home remedies, meditation); (f) perceived health (e.g., “how would you rate your health during the past 6 months?”); (g) stigma (e.g., “some people act as though it's my fault I have HIV”, “I feel guilty because I have HIV”); and (h) HIV-related risk behaviors (e.g., unprotected sex, drug use). Participants were asked about use of specific drugs (e.g., cocaine, methamphetamines, heroine, ecstasy, ketamine, and marijuana). For analysis purposes, we defined low self-rated

health as “very poor,” “poor,” or “fair.” We also created two variables “current drug use,” defined as any drug use in the last 3 months, and “anytime drug use,” defined as ever having used drugs.

We compared participants who reported making changes to ART with those who did not make changes. Univariate associations between the outcome and covariates were explored using *t*-test or χ^2 (df). Logistic regression examined factors independently associated with increased odds of making changes to ART. An initial multivariate model was developed by manually entering factors associated with the outcome at the univariate level ($P < 0.10$). Factors were then manually removed by *P*-value; the final model contained only variables significant at $P < 0.05$.

Results

Participants were 41 years old (SD = 10), 77% male, born in Mexico (93%) and Spanish-language dominant (86%). A majority (60%) had not completed high school or equivalent and almost half (47%) reported being unemployed. A quarter (25%) reported drug use in the last 3 months and 58% reported ever having used drugs. Participants had been living with HIV for an average of 6 years (SD = 5). We found no significant differences between individuals who were recruited in the U.S. and those recruited in Mexico by gender, marital status, socio-economic status, years living with HIV, or patient-initiated ART regimen changes. Significant differences between study groups ($P < 0.05$) were found for age and educational attainment; persons recruited in Mexico were younger and had lower educational attainment (data not presented).

In terms of border crossing activity, 124 participants (54%) had made at least one round-trip in the last 6 months, of those reporting at least one round trip, half reported that they crossed the U.S.-Mexico border 18 times in the last 6 months (IQR = 8,36). The most frequently mentioned reasons for crossing were: health care (66%), medications (64%); and socializing (58%) and participants could choose multiple reasons. Interestingly, 32% of participants reported concern about crossing with their HIV medications because of the authorities.

Most participants had medical insurance in the U.S. (65%) or in Mexico (57%), and 24% reported having medical insurance in both countries. Almost all (93%) reported an HIV-related visit in the last 6 months and a majority (85%) reported positive attributes about their HIV care provider such as demonstrating compassion during their visits or explaining their test results in a comprehensible way. Almost all participants (97%) believed in ART efficacy and were able to fill their ART prescriptions at their last clinical visit (99%). Almost all participants (92%) did not stop taking ART due to side effects, 40% reported having made small changes to ART regimen and 19% reported having made major changes in the last 4 weeks.

Univariate Analyses

We compared characteristics among participants who reported making changes (small or major) to ART regimen (43%) with those who did not (57%). Individuals who reported having made changes to ART were more likely to be females (30 vs. 18%, $\chi^2 = 4.12[1]$, $P <$

0.05), ever used illicit drugs (67 vs. 48%, $\chi^2 = 8.14[1]$, $P < 0.01$) and perceived low self-rated health (47 vs. 25%, $\chi^2 = 7.59[1]$, $P < 0.01$). Additionally, persons who reported making changes to ART regimen were also significantly more likely to report use of herbal or plant-based complementary and alternative medicine (37 vs. 24%, $\chi^2 = 4.28[1]$, $P < 0.05$), and reported “always”/“often” when asked how often they experienced specific instances of HIV-related stigma e.g., “People have told me that getting HIV is what I deserve for how I lived” (34 vs. 20%, $\chi^2 = 5.76[1]$, $P < 0.02$). Participants reporting self-initiated changes to ART were less likely to report that their HIV clinician was “excellent”/“very good”/“good” at helping them to solve problems they have taking ART medications (69 vs. 81%, $\chi^2 = 4.21[1]$, $P < 0.05$). We found no significant differences between those who reported making changes to their ART regimen and those who did not by: age, marital status, educational attainment, employment, depression symptoms, medical insurance status and border crossing patterns. Additional characteristics by ART changes are presented in Table 1.

Multivariate Analysis

In the final multivariate logistic regression model (Table 2), factors associated with increased odds of making changes to their ART regimen as prescribed by their physician included: being female (adjusted odds ratio [AOR] = 2.15, 95% confidence interval [CI]: 1.03–4.48), reporting 1 (AOR = 2.42, 95% CI: 1.21–4.83) or 2 current sexual partners (AOR = 3.33, 95% CI: 1.47–7.53), living 6 years with HIV (AOR = 1.99, 95% CI: 1.08–3.60), and low self-rated health (AOR = 2.50, 95% CI: 1.32–4.72).

Discussion

Our study revealed that sub-optimal adherence remains a complex and pervasive problem that will require continued public health ingenuity to address, particularly among U.S. Latino populations, where disparities in adherence and other key health indicators persist. Our model revealed significant disparities in ART adherence by sub-groups, with Latina women being twice as likely to report self-initiated changes to ART compared to Latino men. Further, persons living with HIV for fewer years, those with relatively poorer self-perceived health status and those who reported one or more sexual partner were more likely to report having made changes to their ART regimen. Considerations of these findings follow.

Poorer ART adherence among women is consistent with other studies that have looked at gender disparities in health access and health outcomes among individuals living with HIV in the U.S. [30–32]. In Tijuana, Mexico, Viani and colleagues reported gaps in care for HIV-positive women who did not receive timely prenatal care and clinical intervention to prevent mother-to-child-transmission of HIV, contributing not only to poor health outcomes for the women, but for their children as well [33]. HIV-positive Latina women living in the U.S.-Mexico border region may face additional barriers to optimal ART adherence when life, care giving and/or work responsibilities may include navigating activities in a binational context. Future studies should explore adherence barriers specific to women and the nature and context of caretaking responsibilities (e.g., number of family members under participant's care, HIV status of those persons, etc.). In prior work with binational

populations, we and other colleagues have reported that living in the border region or being in the U.S. and having close ties with Mexico impacts health behavior in a variety of ways [16, 22]. For example, an HIV-positive Latina woman may reside on one side of the border and obtain medications on the other side, which can represent a burden due to border crossing delays that can range from 2 to 3 hours or longer. The relative importance of border-related factors, such as perceived stress of crossing with one's ART medications, is an area ripe for study in the U.S.-Mexico border region.

Our finding that Latino participants who were diagnosed with HIV 6 years were more likely to report making changes to their ART may be because these individuals are also less experienced with HIV treatment and more prone to poorer adherence. In recent qualitative interviews conducted by members of our study team with HIV care providers on both sides of the U.S.-Mexico border, providers commented that some recently-diagnosed patients appeared to have more problems with adherence than patients who have been on treatment for longer periods (unpublished data). To this effect, a recent study of ethnic/racial differences in ART adherence and treatment outcomes found that upon ART initiation, Latinos were younger, had known about their HIV status for less years and reported less prior use of ART than non-Latino Whites [34]. At 24 months after ART initiation, this same study reported that adherence was lower in Latinos compared with non-Hispanic Whites (64.2 vs. 70.1%, $P < 0.001$), however, no significant differences between groups were observed in clinical outcomes such as time to AIDS hospitalization or death [34]. Future studies with border populations should gather longitudinal data on treatment experience and biomarkers (e.g., viral load) in order to elucidate potential confounders between years since diagnosis and adherence.

Individuals with poor perceived health status were also more likely to make changes to their ART regimen. Similar to our finding, Cardarelli and colleagues [35] reported that individuals who perceived their health as fair or poor were several times more likely to have poorer adherence to their antiretroviral medications. This implies that general health status may serve as a proxy for stress, depression and other psychosocial variables that negatively impact adherence and health [36]. It is also likely that suboptimal adherence has led to the progression of HIV and consequently general poor health. Longitudinal studies are needed to determine the direction of this relationship.

Four factors that were significant at the univariate level, that have also been found to predict poor adherence in other studies, merit further exploration: use of complementary and alternative medicine, patient-provider communication, HIV-related stigma and having ever used drugs. Use of certain types of complementary and alternative medicine has been associated with poor adherence [37]. Findings from our prior work with border populations living with HIV indicate that individuals do cross from the U.S. to Mexico to obtain medications [38]. While most patients reported having an overall positive and trusting relationship with their HIV care providers, univariate results suggest that this may not be sufficient for a patient to have high ART adherence. Further research should focus on patient-provider communication surrounding adherence problem solving in the context of the overall patient provider relationship. Although HIV-related stigma was not significant at the multivariate level, the pervasive nature and potential health impact of HIV-related

stigma among persons living with HIV merits continued measurement and monitoring if we are to understand how to eliminate stigma. Perhaps measuring individual resilience to HIV-related stigma, including healthy coping strategies that we did not measure in our study, may help us better understand the relative impact of HIV-related stigma on persons living with HIV. Use of illicit drugs and alcohol has been shown to negatively impact adherence [39–42]. It is possible that drug use was underreported in our study, which may explain why it did not reach significance in the final model. Future adherence studies in this region should continue to probe regarding use of illicit drugs, given that Tijuana and San Diego are located on a major drug trafficking route [43].

There are important study limitations that bear discussion. Our measure of medication adherence did not allow us to quantify participant understanding of “small” or “major” changes to their ART regimen and whether the changes were discussed with their provider. Study authors selected these measures in order to simplify adherence questions for participants, an approach that is supported by the literature, where more global measures of adherence have been shown to accurately assess adherence [27, 28]. The measure also did not include questions surrounding reasons for suboptimal adherence which may be better explored through qualitative data collection. Future adherence research in the border region would benefit from qualitative interviews with patients and providers in order to better understand and explore suboptimal adherence. Future research should also include more precise measures of adherence (e.g., missed doses) and use biomarkers such as viral load in addition to self report. The observational, cross-sectional design employed by this study did not permit assessment of changes in adherence behavior over time or the ability to understand potential temporal relationships between barriers to adherence and actual adherence. Our work, however, lays the groundwork for prospectively studying factors associated with underlying causes of suboptimal ART adherence among Latinos living with HIV in the border region. Another study limitation is that the surveys were administered in locations where patients received services, which may have led to socially desirable responses on topics such as opinions of care provision and drug use. Efforts to mitigate response bias included securing a private room to conduct the survey and extensive interviewer training on administering informed consent. Further, participants were forthcoming on other sensitive topics such as deportation, which increases our confidence in sincerity of responses. This study may suffer from selection bias in that it does not represent the experiences of HIV-positive Latinos in very poor health or those who were not receiving clinical care. Therefore, themes such as complementary and alternative medicine use and adherence behaviors may be underestimated. Future studies should attempt to recruit HIV-positive individuals who are no longer engaged in clinical care, although efforts to locate these individuals are labor and resource intensive [44].

We found several encouraging health indicators among this largely binational, HIV-positive Latino study population, including majority reporting overall good health, positive disposition to seek HIV care, generally positive patient–provider relationships, high patient treatment optimism and limited reports of stopping medications due to side effects. These findings merit acknowledgment that public health efforts in both the U.S. and Mexico are on the right track, but substantial work remains to be done. To our knowledge, this is the first report of poorer adherence among HIV-positive Latina women in a binational context,

where health is impacted by border crossing and binational health utilization practices such as use of complementary and alternative medicine [22, 38]. As the HIV epidemic becomes feminized, improved understanding of female patient decisions to alter ART regimens becomes imperative. From a global perspective of understanding “shared” border populations, this study can inform future health care access and ART adherence research in the U.S.-Mexico and other border regions, particularly in regions where the health of women living with HIV is understudied. As success is achieved in engaging newly infected populations into care, continued efforts to understand and address existing and emerging barriers to adherence will be needed. This is particularly important when considering that more persons will be on treatment for longer periods of time and may face different adherence barriers than persons who have been on ART for fewer years [45]. Also important is our continued understanding of adherence among foreign-born Latinos who may face different barriers to care continuity than U.S. -born Latinos. To date, studies with persons living with HIV in the U.S.-Mexico border region have been largely based on populations recruited in the U.S. or Mexico. A major strength of this study is that we successfully recruited from both countries simultaneously, which allowed for a more comprehensive picture of HIV-related health behavior in this rapidly growing region. Our findings underscore the need for continued, meaningful binational collaboration between researchers, health care practitioners and health policymakers in order to effectively address barriers to adherence and improve the health of shared populations living with HIV in the U.S.-Mexico border region and beyond.

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Table 1

Characteristics of Latinos living with HIV in the Tijuana-San Diego border region by self-initiated ART regimen changes

Characteristics	Total (N = 230)	Did not make ART changes (N = 132)	Made ART changes (N = 98)	χ^2 (df) ^a	P-value
Demographics					
Mean age (SD)	41 (10)	41 (10)	40 (10)	0.33 (228) ^b	0.74
Male	177 (77%)	108 (82%)	69 (70%)	4.12 (1)	0.04
Female	53 (23%)	24 (18%)	29 (30%)		
Spanish language dominant	197 (86%)	115 (87%)	82 (84%)	0.54 (1)	0.46
Single/separated ^c	153 (67%)	93 (70%)	60 (61%)	2.15 (1)	0.14
Less than high school education	137 (60%)	75 (57%)	62 (63%)	0.97 (1)	0.33
Unemployed	108 (47%)	62 (47%)	46 (47%)	0.00 (1)	0.99
6 years since HIV diagnosis	115 (50%)	59 (45%)	56 (57%)	3.48 (1)	0.06
Binational care seeking practices and HIV testing					
One HIV-related visit in the last 6 months	203 (93%)	116 (92%)	87 (95%)	0.52 (1)	0.47
Able to fill ART prescription	224 (99%)	127 (96%)	97 (99%)	1.51 (1)	0.22
Had US and MX medical insurance	54 (24%)	34 (26%)	20 (20%)	0.90 (1)	0.34
1 round trip border crossing in the last 6 months	124 (54%)	70 (53%)	54 (55%)	0.09 (1)	0.76
Reasons for crossing the border ^d					
Healthcare	81 (66%)	45 (66%)	36 (67%)	0.00 (1)	0.96
Medication	78 (64%)	44 (65%)	34 (63%)	0.03 (1)	0.84
Socialization	71 (58%)	39 (57%)	32 (59%)	0.05 (1)	0.83
Barriers to HIV care					
Prior deportation from the U.S.	55 (24%)	28 (22%)	27 (28%)	1.06 (1)	0.30
Concerned about crossing the border w/HIV meds	73 (32%)	37 (29%)	36 (37%)	1.87 (1)	0.39
Felt depressed in the past week	99 (43%)	54 (41%)	45 (46%)	0.68 (1)	0.41
Provider attributes "The Doctor is good at..." ^e					
Helping solve problems w/taking ART	175 (76%)	107 (81%)	68 (69%)	4.21 (1)	0.04
Understanding the problems w/taking ART	186 (81%)	112 (85%)	74 (76%)	3.17 (1)	0.08
Demonstrating care, compassion	198 (86%)	116 (88%)	82 (84%)	0.83 (1)	0.36
Explaining test results in a comprehensible way	199 (87%)	116 (88%)	83 (85%)	0.49 (1)	0.48
Complementary and alternative medicine					
Use of herbs/plants	68 (30%)	32 (24%)	36 (37%)	4.28 (1)	0.04
Use of vitamins/supplements	160 (70%)	88 (67%)	72 (74%)	1.51 (1)	0.22
Perceived Health ^e					
Good	151 (66%)	99 (75%)	52 (53%)	7.59 (1)	<0.01
Fair	79 (34%)	33 (25%)	46 (47%)		
HIV-related stigma ^f					
People act as though it's my fault that I have HIV	82 (36%)	37 (28%)	45 (46%)	7.84 (1)	<0.01

Characteristics	Total (N = 230)	Did not make ART changes (N = 132)	Made ART changes (N = 98)	χ^2 (df) ^a	P-value
People told me HIV is what I deserve for how I lived	59 (26%)	26 (20%)	33 (34%)	5.76 (1)	0.02
People with HIV are treated like outcasts	130 (58%)	69 (52%)	61 (65%)	3.57 (1)	0.06
I feel guilty because I have HIV	77 (33%)	38 (29%)	39 (40%)	5.06 (1)	0.08
Risk behaviors					
Sex partners in the last 3 months					
0	89 (39%)	59 (45%)	30 (31%)	4.94 (2)	0.08
1	92 (40%)	49 (37%)	43 (44%)		
2+	49 (21%)	24 (18%)	25 (25%)		
Ever traded sex for money, alcohol or other drugs	52 (23%)	24 (18%)	28 (29%)	3.47 (1)	0.06
Ever used illicit drugs ^g	130 (58%)	64 (48%)	66 (67%)	8.14 (1)	<0.01

^a χ^2 : Chi-square statistic (degree of freedom)

^b *t*-Statistic

^c Single/separated vs. married/with partner

^d Participants who reported crossing the border (*n* = 124)

^e “Good” (includes good/very good/excellent) vs. “Fair” (includes fair/poor/very poor)

^f Participants who reported “always/often” when asked how often they experienced specific instances of HIV-related stigma

^g Includes: cocaine, methamphetamines, heroine, ecstasy, ketamine, and marijuana

Table 2

Factors independently associated with patient-initiated ART regimen changes among Latinos living with HIV in the Tijuana-San Diego US-Mexico Border Region

Variable	Adjusted odds ratio	95% Confidence interval
Female ^a	2.15	1.03-U8
Living 6 years with HIV ^b	1.99	1.08-3.60
Rate health as fair in the last 6 months ^c	2.50	1.32-4.72
Having 1 sex partner ^d	2.42	1.21-4.83
Having 2 + sex partners ^d	3.33	1.47-7.53

^a Male

^b 6 years

^c good

^d 0 sex partners