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Interest of Youth Living with HIV in Long-Acting Antiretrovirals

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Abstract

Objectives: This study's primary objective was to characterize attitudes to long-acting antiretrovirals (LAARV), among youth aged 13 to 24 years living with perinatally- and non-perinatally-acquired HIV (PHIV and NPHIV, respectively). Secondary objectives included: assessing whether those with detectable HIV RNA PCR viral load had higher enthusiasm for LAARV compared to those with suppressed viral load, and examining characteristics associated with LAARV enthusiasm.

Methods: A cross-sectional survey of 303 Youth Living with HIV (YHIV) followed at four pediatric/adolescent HIV clinics in the USA was performed to determine interest in LAARV, using

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Author Contributions

EDW wrote the protocol, designed and adapted the survey tool, participated in the analysis, and prepared the manuscript for publication. MSR performed data cleaning and key portions of statistical analysis. AA participated in planning, design, and oversight of the study as well as guiding analysis and interpretation of results. CWF and SS served as advisors and provided information about the preceding survey study in adults. RD, ACG, PR, AG, and RC all served as site investigators.

IRB/ Ethics Committee Approval

Procedures followed in this study were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Institutional Review Boards (IRB) at all four institutions reviewed and approved this study. (Note: The University of Maryland's IRB reviewed and approved the study, but that site only recruited one participant, so that participant's data was combined with the data from the Johns Hopkins site, leading to the characterization of four sites mentioned in the text.)

a modified survey instrument previously used in adults. Interest in LAARV across groups was compared. Poisson regression with robust variance was used to determine the impact of various characteristics on interest in LAARV.

Findings: Overall, 88% of YHIV reported probable or definite willingness to use LAARV. The enthusiasm level was similar between PHIV and NPHIV youth ($p=0.93$). Youth with HIV viral load >1000 copies/mL had significantly higher interest than youth with suppressed viral load (PR 1.12 [95% CI: 1.03 – 1.20]; $p=0.005$). Female youth participants who had had past experience with implantable contraceptive methods had a significantly higher interest in LAARV (100% vs 85.5%; $p=0.002$). Proportion of respondents endorsing definite willingness to use was significantly higher with decreased injection frequency compared to increased injection frequency.

Interpretation: YHIV at four urban US pediatric/adolescent HIV clinics had high levels of enthusiasm for LAARV. LAARV should be given high priority as a potentially viable treatment option to improve clinical outcomes in YHIV.

Keywords

Adolescent; HIV; Treatment; Long-Acting Antiretroviral Agents; Patient Acceptance of Healthcare; HIV Care Continuum

Introduction

Youth 13 to 24 years old comprise more than 1 in 5 of all incident US HIV infections, and are a high-risk group for non-adherence to antiretrovirals (ARV).^{1,2} Low rates of being linked to ongoing HIV care for those youth newly diagnosed with HIV is one of many factors leading to relatively low numbers of youth who achieve viral suppression nationwide and globally. Of note, 43% of U.S. youth who get linked to ongoing HIV care fail to sustain viral suppression.¹ Almost half of adolescents who start a first line antiretroviral therapy (ART) regimen fail that regimen and require transition to a second-line regimen.^{1,3} Failure of second-line ART is more likely to be due to non-adherence to medications rather than development of viral resistance.⁴ The overall 44% rate of viral suppression among adolescents and young adults living with HIV is the lowest of all age groups.² As a result, deepening HIV-related disparities in outcomes between youth and adults exist, with youth *per se* emerging as a dominant risk factor for sub-optimal adherence to ART.⁵ Because younger age is a modifiable risk factor with the passage of time, novel and effective strategies to facilitate and improve adherence to ART in youth living with HIV (YHIV) are urgently needed.

Long-acting parenterally formulated nanosuspensions of selected ARV are currently in phase 3 testing for treatment of HIV, and stand to benefit YHIV particularly. Administration of long-acting cabotegravir and rilpivirine, in q 4 week or q 8 week intragluteal intramuscular (IM) injections to HIV-infected, virally suppressed adults, maintains viral suppression as effectively as an oral combination ARV regimen over 96 weeks.⁶ Because of the prolonged pharmacokinetic (PK) “tail” of these compounds (i.e., concentrations after a single injection remain detectable in the body for longer than one year), any treatment regimen involving LAARV requires consistent follow-up in the context of ongoing access to

care.⁷ YHIV including those who struggle with sustaining adherence to oral ARVs may be an ideal target population for such an intervention within the setting of a youth-friendly program.⁸

Critically absent from existing data is the youth perspective on LAARV technologies. There is a knowledge gap on the readiness of YHIV to adopt and adhere to LAARV. In order to assess this readiness, we surveyed the interest and attitudes of YHIV towards long-acting modalities of treatment. In addition, we examined the characteristics that confer greater enthusiasm for LAARV, to guide selection of the appropriate sub-populations in which to deploy LAARV. Prior work assessing interest and attitudes to LAARV for treatment among HIV-positive adults found a 73% overall rate of definite or probable willingness to use LAARV among 400 adults with a mean age of 47 years (range 18–71).⁹ More recently, surveys of HIV-uninfected individuals have indicated interest in long-acting injectable forms of pre-exposure prophylaxis (PrEP) against HIV; it is estimated that if a licensed long-acting injectable was available for PrEP, it would increase overall uptake of PrEP by 24.5% compared to oral PrEP.^{10–12} The acceptance of new technologies may differ across the age spectrum, and it is possible that youth may be more willing to adopt new technologies, particularly those that control underlying infection while conferring less intrusion in their daily lives. To our knowledge, this is the first effort to evaluate the attitudes of U.S. youth towards the promising new technology of injectable or implantable LAARV. This will provide the pediatric and adolescent perspective currently absent from discussions about these technologies as well as inform decisions about deployment of LAARV in this key vulnerable population, especially surrounding design of research protocols and sample size and enrollment estimates.

Methods

Interest in LAARV was assessed in a population of 303 YHIV, 13 and 24 years of age, and receiving care at four pediatric & adolescent HIV clinics in the U.S.: St. Jude Children's Research Hospital in Memphis, TN; Emory University-Grady Infectious Disease Program in Atlanta, GA; and the University of Maryland and the Johns Hopkins Hospital in Baltimore, MD. The study was conducted at four sites, however only one participant was enrolled at the University of Maryland site. Therefore, for purposes of analysis and reporting, University of Maryland was grouped with Johns Hopkins into a single group known as "Johns Hopkins". The population included youth with both perinatally (PHIV) and non-perinatally acquired HIV (NPHIV), to assess the impact of mode of HIV transmission and length of time infected on possible pill fatigue and desire for non-daily modalities of HIV-treatment.

Institutional Review Boards (IRB) at all four institutions reviewed and approved this study. Participants gave verbal informed consent at the time of the survey; those below the age of consent gave their assent to participate alongside their guardian's consent. \$10 gift cards were given as compensation for participants' time and participation.

A one-time, cross-sectional Qualtrics® survey with 34 questions was administered on an electronic device to participants in clinic, between January 1, 2016 and April 1, 2017. The survey (Appendix I) was adapted from one previously used in adults.⁹ Demographic

information, mode of HIV acquisition, ARV treatment, variables related to adherence, marijuana, alcohol, and illicit drug use were all collected by self-report. Participants' most recent HIV RNA PCR viral load was ascertained from the medical record for all sites except St. Jude Children's Research Hospital, where (per the requirements of that site's IRB), subjects took an anonymous survey with no link to the medical record, and manually entered their most recent viral load from recall after being reminded about it by study staff prior to taking the survey.

Interest in intramuscular (IM) and subdermal (SD) LAARV (primary outcome), was measured via responses to a question ascertaining likelihood that the youth would use LAARV if it were available, using a four-point Likert-scale. Responses were dichotomized into interested yes/no. Participants who stated that they "definitely would" or "probably would" try LAARV were classified as interested, and those who stated that they "definitely would not" or "probably would not" try the new drug were classified as non-interested. Interest in LAARV should hereafter be understood to refer specifically to intramuscular LAARV, except where subdermal is explicitly stated. Site investigators were blinded to the participants' responses, which were automatically extracted from the online survey form and exported into a data spreadsheet.

Demographic and other baseline characteristics were compared between PHIV and NPHIV participants using a Chi-squared test. The primary outcome (interest in LAARV) was analyzed with Poisson regression with robust variance estimation, in both bivariate and multivariable analyses. Since the prevalence of interest in both groups was more than 15%, Poisson regression instead of logistic regression was used, in order to approximate a Prevalence Ratio from the Relative Risk (RR).^[13]

The impact of relevant variables on youth participants' unadjusted interest level was analyzed using a bivariate analysis. In a multivariable analysis, interest in LAARV was evaluated among youth with PHIV and NPHIV, adjusting for variables that were considered clinically important or found to be significantly associated with the primary exposure (mode of HIV acquisition) in the Chi-squared test at a significance level of $p=0.05$. Statistical analyses were performed with Stata software, version 14.0 SE (Stata Corporation, College Station, Texas, USA).

The study also examined the impact of young women participants' past experience with intramuscular injectable contraception such as medroxyprogesterone (Depo-Provera, hereafter called Depo) and implantable long-acting reversible contraception (LARC) such as etonogestrel implant (Implanon, Nexplanon), on their willingness to use long-acting technologies.

The continuous predictor variable of age and viral load were categorized into three categories each: 13–16; 17–20; and 21–24 years of age and undetectable (<40 copies/mL), low detectable (40 copies/mL to 1000 copies/mL) and high detectable (>1000 copies/mL), respectively. The race variable was analyzed as a binary variable (African-American vs. Non-African-American).

Role of the funding source

The study sponsors played no role in study design; in the collection, analysis and interpretation of the data; in the writing of the report; or in the decision to submit the paper for publication.

Results

Of the 303 participants enrolled, 79 (26.1%) were PHIV, and 224 (73.9%) NPHIV. Demographics and other baseline characteristics of these patients, split by mode of HIV acquisition, are presented in Table 1a. The Johns Hopkins Hospital had a significantly higher proportion of PHIV (32.9%) compared to the other sites, whereas St. Jude and Emory had a significantly higher proportion of NPHIV (81.2%) (Appendix II, Table 1b). Viral suppression was similar in PHIV and NPHIV. Participants with PHIV were younger compared to the participants with NPHIV (27.8% vs. 1.8% in the 13–16 age group). The majority of participants with PHIV were female (68.4%), whereas the majority of those with NPHIV were male (83.0%). All eight transgender patients belonged to the group with NPHIV. The distribution of race and ethnicity was similar in PHIV and NPHIV participants, with the majority being African-American (87.2% and 87.4%, respectively) and non-Hispanic patients (96.2% and 91.0%, respectively). Ninety-nine percent of PHIV participants and 94.2% of the NPHIV participants received ARV and both groups had a similar distribution of participants who ever missed a pill. Both alcohol and marijuana use were more prevalent in the NPHIV group. (See Table 1a.)

A total of 266 (88.1%) respondents stated that they would definitely or probably try injectable LAARV; 70 (88.6%) participants from the PHIV group and 196 (87.9%) participants from the NPHIV group. The prevalence of interest in LAARV in PHIV and NPHIV participants was not significantly different (PR 0.99 [95% CI: 0.90 – 1.09]; $p=0.86$). While significantly lower compared to injectable LAARV, the overall interest in subdermal implantable LAARV among the youth surveyed was still high (78.7% vs. 88.1%; $p=0.002$.)

In order to get a sense of possible regional differences (Southeast versus mid-Atlantic United States) in youth interest, outcomes were analyzed by site. In the bivariate analysis (Table 2), participants from St. Jude Children's Research Hospital had a significantly lower interest level in LAARV than subjects from the other clinics (81.7% interested at Saint Jude vs. 90.9% at Hopkins and 91.7% at Emory; PR 0.89 [95% CI: 0.80 – 0.99]; $p=0.03$). There was an impact of HIV RNA PCR viral load on interest level; participants with high detectable viral load were significantly more likely to be interested in LAARV (PR 1.12 [95% CI: 1.03 – 1.20]; $p=0.005$) compared to subjects with undetectable viral load. Using bivariate analyses, there was no statistical difference in the proportion interested in LAARV based on age, gender, race, ethnicity, ART treatment, adherence, alcohol use, and marijuana use.

In multivariable analysis (Table 2 & Figure 1), the interest level towards the injectable LAARV between the PHIV and NPHIV groups was identical (PR 1.00 [95% CI: 0.92 – 1.10]; $p=0.93$) after adjusting for viral load, clinic, age, gender, alcohol and marijuana use. The impact of site (St. Jude vs. others) (interest level PR 0.89 [95% CI: 0.80 – 0.99]; $p=0.03$) and viral load level (high detectable viral load versus undetectable viral load) (interest

level PR 1.09 [95% CI: 1.01 – 1.18]; $p=0.03$) remained significant even after adjusting for the above-mentioned variables. (Table 2 & Figure 1). Participants who used marijuana more than six months ago were found to be more interested in LAARV compared to those who never used or used in the past 6 months (PR 1.15 [95% CI: 1.01 – 1.31]; $p=0.03$). (See Figure 4). On the other hand, alcohol consumption was associated with borderline (non-significant) decreased interest, both in recent (PR 0.93 [95% CI: 0.86 – 1.01]; $p=0.09$) and past users (PR 0.86 [95% CI: 0.73 – 1.00]; $p=0.06$) as compared to never users. Possible interactions between marijuana use and alcohol use were explored, but no significant association was found. Furthermore, mode of acquisition, age, gender, race, ethnicity, and self-reported adherence level were not significantly associated with the participant's interest level.

Participants were queried about their level of concern about side effects of LAARV, and overall 52.9% of the respondents were very concerned or somewhat concerned about the potential side effects. Those who were interested in trying LAARV were less worried about side effects compared to those who were not interested (see Figure 2). Eighteen participants (51.4%) from the binary non-interested group responded that they were very concerned about the side effects, whereas 77 participants (29.4%) from the interested group expressed concern about side effects, and this difference was statistically significant ($p=0.05$).

We investigated the impact of young women participants' past experience with intramuscular injectable contraception such as Depo and implantable LARC such as etonogestrel implant (Implanon, Nexplanon) on their willingness to use long-acting technologies. As shown in Table 2B, there was a greater willingness to use IM LAARV among those female participants who had previously used implantable long-acting reversible contraception (LARC), than among those who had never used LARC (14/14 (100%) versus 59/69 (85.5%); $p=0.002$). Likewise, there was a borderline significant increase in interest in SD implantable LAARV among those participants who had used LARC in the past (13/14 (92.9%) versus 54/69 (78.3%); $p=0.081$). In participants with past use of IM injectable contraceptive technologies, there was no difference in enthusiasm for either IM or SD implantable LAARV as compared to those with no past use of IM injectable contraception.

With respect to the timing of injections, interest level in intramuscular LAARV was found to increase with a decrease in frequency of injections. Only 49.6% of participants had probable or definite willingness to use LAARV when the injections were proposed once a week, 56.3% when once every two weeks, 86.1% when once a month, 86.8% when once every two months, and 90.2% when once every three months; many of these step-wise differences were significant (see Figure 3a). When only *definite* willingness to use was assessed, a significantly higher proportion of respondents were willing to use IM LAARV if injection frequency was q3 months than q2 months, and q1 month was preferred over either q2 weeks or q1 week, but the enthusiasm for q 2 months and q monthly was not statistically different (see Figure 3b).

Discussion

Survey results indicate that the majority of YHIV surveyed are interested in taking LAARV to control their HIV. There was no difference in interest level between participants with PHIV and NPHIV. Several behavioral and clinical characteristics were associated with a higher likelihood of interest in LAARV in youth. Of note, participants with high-detectable viral load (indicating a degree of difficulty in adhering to their daily pills) were more enthusiastic about trying LAARV (which does not require daily pills) than participants who had attained and sustained virologic control on their current oral regimen. Those who have trouble adhering to daily oral pills represent an ideal target population for LAARV. Prior work has uncovered a panoply of reasons cited by YHIV for missing medications over the past month—forgetting, not being physically near medication, getting busy with other things, reluctance to be witnessed taking pills, etc.¹⁴ All of this should point to the need for HIV suppression approaches that do not require youth to take daily pills.

Finding that almost 90% of the participants in our study were interested in trying injectable LAARV to control their HIV is encouraging evidence that LAARV may be a welcome strategy for achieving and maintaining viral suppression in this age group. The high enthusiasm was consistent with a previous cross-sectional study in New York among young men who have sex with men, where investigators also found that more than 80% of the participants were interested in the injectable LAARV of pre-exposure prophylaxis (PrEP) for HIV.¹¹ In another similar study in adults, the interest level towards long-acting injectables was found to be 73%.⁹

Lifelong daily or nearly daily dosing of currently available oral ART is very difficult to maintain, especially for younger participants, as borne out in the poor rates of viral suppression in this group.³ Unsurprisingly, a gradient of interest in long-acting technologies was demonstrated among youth respondents, with steadily and significantly increasing interest level as injection frequency declined, as shown in Figure 3. This aligns with data showing a high level of interest towards LAARV associated with less frequent dosing than the currently available oral ART.¹⁵ This finding (prospective hypothesized adherence) also corroborates that of previous studies where a linear decrease in actual adherence with increasing number of doses per day has been observed.^{16–18} A previous study among gay and bisexual men also revealed that fewer men found long acting injectable PrEP to be acceptable when the frequency of administration was every month rather than every three months.¹⁹ This finding was echoed in our study, which found that interest in LAARV increases in a gradual gradient with increased spacing in between injections from q week to q 3 months, and that fewer youth found q1 month injections acceptable than q3 month injections. This makes a strong case for shoring up efforts to arrive at an injectable product with a q3month injection frequency, which would also have parallelism with Depo injection frequency. However, while every 3 month injection frequency would be desirable if available, it is worth noting that the steepest step-off in acceptability occurs with injection frequencies more frequent than once a month (i.e., once a week or once every 2 weeks). Any injection frequency once monthly or less frequently was associated with an acceptability > 85% in these youth respondents.

The findings on the impact of past experience with long-acting contraceptive technologies on young women's willingness to use LAARV imply an increased willingness to use *both* IM and SD LAARV among participants with past LARC use. These individuals may represent a niche population of early adopters of new technologies. That a similar finding was not observed among Depo users should not detract from the observation of extremely high rates of interest in IM LAARV among both Never Depo (87.9%) and Ever Depo (88%) groups.

Youth were specifically asked about their concerns. Those who were interested in trying LAARV were less concerned about the possible side effects of IM and SD long-acting drugs compared to those with lower interest. A breakdown of the specific concerns of youth is displayed in Figure 4. In total, about half of the respondents in our study were worried about the potential side effects of the new drug. The interested group was found to have less concern about the side effects than the non-interested group. This study mirrors the findings of prior survey findings in adults where only 48% of overall participants were concerned with the side effects of IM LAARV.⁹ Conversely, a high proportion (87.8%) of respondents in a previous survey study in young men who have sex with men (MSM) voiced concern about the side effects of injectables.¹¹ The reason for this difference is not clear, but differing study populations is most likely: there was a quite narrow age distribution (mean age of 21.2 years (SD=0.8)) and high level of educational attainment in the previous study.

There is dramatic import to society of this inquiry into youth readiness for LAARV. The fact that the previously discovered high enthusiasm rate for LAARV in adults is not only replicated in youth, but increased, makes the strong case for the further study and eventual implementation of LAARV treatment strategies broadly in youth with HIV. The increased interest in LAARV among respondents whose HIV is uncontrolled is an important observation given that adherence to currently available ARV is likely to be sub-optimal.^{20,21} A more nuanced understanding of the characteristics associated with a greater interest level in LAARV may assist in planning future clinical studies and ultimately in choosing appropriate youth sub-populations for deployment of LAARV.

There were several limitations of this study. Firstly, only HIV positive individuals engaged in care were surveyed. Findings could have been different in individuals not receiving care. However, youth who do come to clinic but do not take daily pills precisely represent the population that may benefit from LAARV, (i.e., their engagement in care despite adherence difficulties opens up the way for health-setting-administered ART, which is only user-dependent in the sense that the patient must show up to clinic, and also demonstrates a possible willingness/ likelihood to return for subsequent injections.) Therefore, gauging the opinion of these youth about LAARV is most important. Secondly, dichotomizing the outcome variable interest level into "interested" and "non-interested" and the quantitative adherence into "ever missed" and "never missed" might have resulted in a loss of questionnaire specificity. Thirdly, social desirability bias may have played a role in participants' responses, particularly in self-reporting of risky behavior and interest level in non-anonymized surveys. Fourthly, participants were not given information about the prolonged length of time that injectable ART remains detectable in bodily fluids, or about the safety and efficacy implications of this prolonged PK tail; this might potentially have

some impact on willingness to take up such technologies and could be viewed as a limitation of the study. Finally, the sample size was not large enough to perform certain subgroup analyses of interest. Future studies should target a larger sample size of populations not engaged in care, explore youth interest in LAARV as PrEP, and should incorporate detailed non-theoretical acceptability assessments among youth participants receiving LAARV in clinical trials.

Conclusion

The vast majority of youth participants reported moderate or high interest in using LAARV. The enthusiasm among both PHIV and NPHIV youth for LAARV was identical. The interest also was not significantly impacted by other factors except for the clinic location, viral load, and marijuana use. Among patients who both have adherence difficulties *and* are engaged in care, these findings suggest that LAARV would be equally acceptable in all patients with HIV in this age group. If long-acting ART strategies are not ultimately deployed in populations with poor adherence, they will fall far short of their intended mark and fail to help the very populations they stand to benefit the most. *In sum*, youth ages 13 to 24 *who are struggling to adhere to oral daily medications* are a vulnerable niche population in whom LAARV could serve as a critical strategy to improve clinical outcomes. The current study suggests that implementation of this strategy was acceptable for such high-risk youth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Rudy BJ, Lindsey JC, Flynn PM, et al. Immune reconstitution and predictors of virologic failure in adolescents infected through risk behaviors and initiating HAART: week 60 results from the PACTG 381 cohort. *AIDS Res Hum Retroviruses*. 2006;22(3):213–221. [PubMed: 16545007]
2. Prevention CfDCa. Diagnoses of HIV infection in the United States and dependent areas, 2016 In. Vol 28 HIV Surveillance Report, 20162017.
3. Ryscavage P, Anderson EJ, Sutton SH, Reddy S, Taiwo B. Clinical outcomes of adolescents and young adults in adult HIV care. *J Acquir Immune Defic Syndr*. 2011;58(2):193–197. [PubMed: 21826014]
4. Levison JH, Orrell C, Gallien S, et al. Virologic failure of protease inhibitor-based second-line antiretroviral therapy without resistance in a large HIV treatment program in South Africa. *PLoS One*. 2012;7(3):e32144. [PubMed: 22427821]
5. Irene Hall ELF H, Rhodes Philip. Differences in Human Immunodeficiency Virus Care and Treatment Among Subpopulations in the United States. *JAMA Intern Med*. 2013;1337–1344. [PubMed: 23780395]
6. Margolis DA, Gonzalez-Garcia J, Stellbrink HJ, et al. Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial. *Lancet*. 2017;390(10101):1499–1510. [PubMed: 28750935]
7. Landovitz RJ, Kofron R, McCauley M. The promise and pitfalls of long-acting injectable agents for HIV prevention. *Curr Opin HIV AIDS*. 2016;11(1):122–128. [PubMed: 26633643]
8. Griffith DC, Agwu AL. Caring for youth living with HIV across the continuum: turning gaps into opportunities. *AIDS Care*. 2017;29(10):1205–1211. [PubMed: 28278569]
9. Williams J, Sayles HR, Meza JL, et al. Long-acting parenteral nanoformulated antiretroviral therapy: interest and attitudes of HIV-infected patients. *Nanomedicine (Lond)*. 2013;8(11):1807–1813. [PubMed: 23611617]
10. Meyers K, Wu Y, Qian H, et al. Interest in Long-Acting Injectable PrEP in a Cohort of Men Who have Sex with Men in China. *AIDS Behav*. 2017.
11. Meyers K, Rodriguez K, Moeller RW, Gratch I, Markowitz M, Halkitis PN. High interest in a long-acting injectable formulation of pre-exposure prophylaxis for HIV in young men who have sex with men in NYC: a P18 cohort substudy. *PLoS One*. 2014;9(12):e114700. [PubMed: 25502768]
12. Oldenburg CE, Le B, Huyen HT, et al. Antiretroviral pre-exposure prophylaxis preferences among men who have sex with men in Vietnam: results from a nationwide cross-sectional survey. *Sex Health*. 2016.
13. Barros AJ, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC medical research methodology*. 2003;3:21. [PubMed: 14567763]
14. Hosek SG, Harper GW, Domanico R. Predictors of medication adherence among HIV-infected youth. *Psychol Health Med*. 2005;10(2):166–179. [PubMed: 25705113]
15. Mack N, Evens EM, Tolley EE, et al. The importance of choice in the rollout of ARV-based prevention to user groups in Kenya and South Africa: a qualitative study. *Journal of the International AIDS Society*. 2014;17(3 Suppl 2):19157. [PubMed: 25224616]
16. Cromer BA, Steinberg K, Gardner L, Thornton D, Shannon B. Psychosocial determinants of compliance in adolescents with iron deficiency. *American journal of diseases of children*. 1989;143(1):55–58. [PubMed: 2910045]
17. Farmer KC, Jacobs EW, Phillips CR. Long-term patient compliance with prescribed regimens of calcium channel blockers. *Clinical therapeutics*. 1994;16(2):316–326; discussion 271–312. [PubMed: 8062325]
18. Jacobs J, Goldstein AG, Kelly ME, Bloom BS. NSAID dosing schedule and compliance. *Drug intelligence & clinical pharmacy*. 1988;22(9):727–728. [PubMed: 3215123]

19. Parsons JT, Rendina HJ, Whitfield TH, Grov C. Familiarity with and Preferences for Oral and Long-Acting Injectable HIV Pre-exposure Prophylaxis (PrEP) in a National Sample of Gay and Bisexual Men in the U.S. *AIDS and behavior*. 2016;20(7):1390–1399. [PubMed: 27000145]
20. Murphy DA, Wilson CM, Durako SJ, Muenz LR, Belzer M, Adolescent Medicine HIVARN. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. *AIDS care*. 2001;13(1):27–40. [PubMed: 11177463]
21. de Jong BC, Prentiss D, McFarland W, Machekano R, Israelski DM. Marijuana use and its association with adherence to antiretroviral therapy among HIV-infected persons with moderate to severe nausea. *Journal of acquired immune deficiency syndromes (1999)*. 2005;38(1):43–46. [PubMed: 15608523]

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Figure 1: Adjusted Prevalence Ratio of High Interest in LAARV by Participant Characteristics. Reference values for each category: Perinatal Acquisition; Viral Load Undetectable; Clinic: Emory; Age category: 13–16 years old; Gender: Male; Never Used EtOH; Never Used Marijuana. Interest in LAARV defined as “Probably would use” or “Definitely would use”, as compared to “Definitely would not use” or “Probably would not use”.

Figure 2a:
 Gradient of Definite or Probable Willingness to Use Increases with Decreased Injection Frequency

	<i>Q 1 week</i>	<i>Q 2 weeks</i>	<i>Q 1 month</i>	<i>Q 2 months</i>	<i>Q 3 months</i>
<i>Q 1 week</i>	NA	0.83 (p=0.407)	7.14 (p<0.001)	8.55 (p<0.001)	11.19 (p<0.001)
<i>Q 2 weeks</i>		NA	6.34 (p<0.001)	7.77 (p<0.001)	10.43 (p<0.001)
<i>Q 1 month</i>			NA	1.51 (p=0.130)	4.36 (p<0.001)
<i>Q 2 months</i>				NA	2.86 (p=0.004)
<i>Q 3 months</i>					NA

Figure 2b: Proportion of Definite Willingness to Use Is Higher with Decreased Injection Frequency Compared to Increased Injection Frequency

Z-scores are displayed in table for a two sample proportion test (p values in parentheses).

Significant values are in bold. The injection frequencies specified in the column headings are what is being compared to row headings (the reference).

a. By Viral Suppression **b. By Marijuana Use** **c. By Site** **Figure 3: Comparison of Interest in LAARV by Various Characteristics**

* $p < 0.05$; significance tested by adjusted Poisson regression, robust variance. In Figure a), Viral loads were one-time, cross-sectional viral load results most proximal in time to the survey. Undetectable HIV viral load was defined as <20 copies or <40 copies, depending on site; Low detectable as $>UD$ and <1000 ; High detectable >1000 copies. For Figures b) and c), a binary interest level outcome was used, where Interested was “Probably would or Definitely would use” and Not Interested was “Definitely would not use” or “probably would not use”.

Figure 4: Youth Preference for intramuscular (IM) over subdermal (SD) Implantable LAARV

* t-test for proportions: $p=0.002$

Table 1.

Baseline characteristics stratified by mode of HIV acquisition

Variable	Perinatal (PHIV) n (%)	Non-Perinatal (NPHIV) n (%)	Total N	P-value [†]
Clinic			303	0.01
Emory	34 (43.0%)	99 (44.2%)		
Johns Hopkins [*]	26 (32.9%)	40 (17.9%)		
St. Jude	19 (24.1%)	85 (37.9%)		
Viral Load			289	0.69
Undetectable	53 (67.9%)	132 (62.6%)		
Low Detectable	8 (10.3%)	24 (11.4%)		
High Detectable	17 (21.8%)	55 (26.1%)		
Age Category			296	<0.001
13–16 years	22 (27.8%)	4 (1.8%)		
17–20 years	27 (34.2%)	71 (32.7%)		
21–24 years	30 (38.0%)	142 (65.4%)		
Gender			303	<0.001
Male	25 (31.6%)	186 (83.0%)		
Female	54 (68.4%)	30 (13.4%)		
Transgender M-F	0 (0.0%)	8 (3.6%)		
Race				0.96
African-American or black	68 (87.2%)	194 (87.4%)	300	
Non-African-American	10 (12.8%)	28 (12.6%)		
Hispanic or Latino				0.13
No	76 (96.2%)	202 (91.0%)	301	
Yes	3 (3.8%)	20 (9.0%)		
Missed Pills			303	0.76
Never missed	26 (32.9%)	78 (34.8%)		
Ever missed	53 (67.1%)	146 (65.2%)		
Alcohol Use			295	<0.001
Never Used	38 (49.4%)	53 (24.3%)		
Past 6 months	25 (32.5%)	137 (62.8%)		
Not in the past 6 months	14 (18.2%)	28 (12.8%)		
Marijuana Use			302	0.01
Never Used	34 (43.0%)	57 (25.6%)		
Used in past 6 months	30 (38.0%)	124 (55.6%)		
Used > 6 months ago	15 (19.0%)	42 (18.8%)		

[†] P-values based on Chi-square test

^{*} Since only one patient was enrolled at the University of Maryland, this participant was included as a Johns Hopkins participant for the purposes of analysis.

Table 2.

Crude and adjusted Prevalence Ratio (PR) and 95% Confidence Interval of the interest level in Intramuscular LAARV by Poisson Regression with robust variance

Variable	Crude		Adjusted*	
	Prevalence Ratio(95% CI)	P-value	Prevalence Ratio(95% CI)	P-value
Mode of HIV Acquisition (n= 302)				
Perinatally	Ref		Ref	
Non-perinatally	0.99 (0.90 – 1.09)	0.86	1.00 (0.92 – 1.10)	0.93
Clinic (n= 302)				
Emory	Ref		Ref	
Johns Hopkins *	0.99 (0.90 – 1.09)	0.86	0.97 (0.89 – 1.07)	0.58
St. Jude	0.89 (0.80 – 0.99)	0.03	0.89 (0.80 – 0.99)	0.03
Viral Load (n= 288)				
Undetectable	Ref			
Low Detectable	0.98 (0.84 – 1.15)	0.83	1.00 (0.86 – 1.16)	0.99
High Detectable	1.12 (1.03 – 1.20)	0.005	1.09 (1.01 – 1.18)	0.03
Age Category (n= 295)	Ref		Ref	
13–16 years	1.21 (0.97 – 1.50)	0.09	1.18 (0.93 – 1.51)	0.18
17–20 years	1.14 (0.92 – 1.42)	0.24	1.10 (0.87 – 1.40)	0.42
21–24 years				
Gender (n= 302)	Ref		Ref	
Male	1.00 (0.91 – 1.10)	0.96	1.04 (0.94 – 1.15)	0.42
Female	0.99 (0.76 – 1.30)	0.96	0.95 (0.67 – 1.35)	0.78
Transgender M-F				
Race (n= 299)	Ref			
African-American or black	1.02 (0.90 – 1.14)	0.80		
Non-African-American				
Hispanic or Latino (n= 300)				
No	Ref			
Yes	0.88 (0.71 – 1.10)	0.26		
Missed Pills (n= 302)	Ref			
Never missed	0.96 (0.89 – 1.04)	0.35		
Ever missed				
Currently on HIV Drugs (n= 302)				
No	Ref			
Yes	1.04 (0.82 – 1.32)	0.73		
Alcohol Use (n= 294)				
Never	Ref		Ref	
Past 6 months	1.00 (0.91 – 1.09)	0.90	0.93 (0.86 – 1.01)	0.09

Variable	Crude		Adjusted*	
	Prevalence Ratio(95% CI)	P-value	Prevalence Ratio(95% CI)	P-value
Not in past 6 months	0.95 (0.83 – 1.10)	0.50	0.86 (0.73 – 1.00)	0.06
Marijuana Use (n= 301)				
Never				
Past 6 months	Ref			Ref
Not in past 6 months	1.08 (0.97 – 1.20)	0.14	1.10 (0.98 – 1.24)	0.09
	1.07 (0.94 – 1.22)	0.28	1.15 (1.01 – 1.31)	0.03

* Adjusted for the variables identified as statistically significant in table 1 (P-value is <0.05) and those were considered clinically relevant. N=274 for the adjusted analysis.

* Since only one patient was enrolled at the University of Maryland, this participant was included as a Johns Hopkins Hospital participant for the purposes of analysis.