Supplemental Digital Content 1

Methods

Study design and objectives

The HPTN074 was designed as multi-site, two-arm, randomized vanguard study to define the feasibility of a future randomized controlled trial.[1] The study was implemented in Indonesia, Ukraine and Vietnam to 1) assess HIV incidence among injection partners, and 2) define the potential for enrollment and retention of Index participants, HIV-infected People Who Inject Drugs (PWID), and their HIV-uninfected injection partners. The study objectives also included the assessment of the feasibility, barriers, and uptake of the integrated intervention. The effect of the integrated intervention was measured by comparing self-reported ART initiation and use, viral suppression, and self-reported MAT initiation and use between experimental and standard of care (SOC) arms.

Study intervention

Index participants in the intervention arm received a standard harm reduction package plus an integrated intervention.[1] The integrated intervention incorporated: 1) systems navigators to facilitate engagement, retention, and adherence in HIV care and MAT; 2) psychosocial counseling using motivational interviewing, problem solving, skills building, and goal setting to facilitate initiation of ART and MAT, and if started, medication adherence. Indexes in intervention arm received a minimum of two psychosocial counseling sessions and were offered additional booster sessions,

approximately one month and three months after enrollment and later, within the follow-up period, upon respondent's request.

Analytic approach

Depression symptoms were measured at baseline and follow-up visits using the PHQ-9 inventory, directly translated into the local languages (Ukrainian, Vietnamese, and Bahasa Indonesia). PHQ-9 collects self-reported responses about problems bothering the person over the past two weeks and was demonstrated to be a reliable and valid measure of depression severity validated in Vietnam and Indonesia. [2-5] This scale was not validated in Ukraine where, however, it is recommended for application by national clinical guidelines.[6]

Study outcomes of self-reported ART, viral suppression (HIV RNA <40 copies/mL, measured by the HPTN Laboratory Center), and self-reported MAT were described previously.[1, 7] Participants who died before the given study visit were considered not on ART or MAT, and not virally suppressed. Daily IDU practice was defined as self-reporting IDU on 28 or more days in the past month. Participants who died before the given study visit were counted with daily IDU users.

Subgroup analyses of adjusted probability differences by baseline depression were evaluated for each outcome using a statistical interaction term. To assess the association between baseline depression and the outcomes controlling for potential confounding variables, marginal structural models were fit using inverse probability weights (IPWs) for baseline depression exposure with robust variance estimates.[8] In analyses of the effect of intervention according to depression subgroup, marginal structural models were fit using IPW for treatment arm exposure. IPWs were estimated using logistic regression, both overall, and within site for site-specific analyses. Analyses of the association between baseline depression and 12-month outcomes were adjusted for 10 or more baseline covariates and two-way interactions between geographical site and covariate. Age at baseline, age at IDU initiation, years since HIV diagnosis, and CD4 count were fully observed and modeled as continuous using a restricted cubic spline with 4 equally spaced knots.[9] Categorical covariates were site, randomization arm, relationship status, employment, baseline ART and MAT, as well as gender and education in Ukraine-specific analyses. To control for chance imbalance between treatment arms, adjusted analyses of the effect of intervention by baseline depression subgroup used the above covariates, and included the arm by depression subgroup interaction; employment was excluded due to small sample sizes. As a sensitivity analysis, participants with a PHQ-9 score of 5 or above were classified as having depression (mild, moderate, or severe) and compared with the participants without depressive symptoms.

Baseline data were over 99% observed. Missing outcome data were accounted for using

multiple imputation. The imputation model used a fully conditional specification discriminant function, and included the exposure, covariates, interactions, and splines described above.[10] Data from baseline through week 78, including the outcome variables and CD4 counts, were used in the imputations. Thirty imputed datasets were created and results were combined using Rubin's method.[11] Analyses were conducted in Windows SAS version 9.4 (Cary, NC) with no adjustment for multiplicity; 95% confidence intervals are presented throughout.

References

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