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The Impact of Multiple-Behavior HIV Interventions as a Function of Regional Disadvantages: An Analysis of Syndemics

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Abstract

Disadvantaged populations, including inhabitants of developing countries as well as racial/ethnic and sexual minorities in the U.S., are disproportionately burdened by Human Immunodeficiency Virus (HIV) infection, delayed HIV diagnosis, and unfavorable HIV-treatment outcomes. HIV interventions targeting single behaviors (e.g., testing) in these populations have shown to be efficacious at producing behavioral and clinical change but have been unable to eliminate the social health disparities associated with syndemics (i.e., a set of connected risks, interacting synergistically, and contributing to excess burden of disease in a population). This meta-analysis of 331 reports (clusters; Number of Effect Sizes [k] = 1364) assessed whether multiple-behavior interventions that target clusters of syndemic risks are more efficacious for those in disadvantaged regions and social groups. Across the board, multiple-behavior interventions were more efficacious than single-behavior ones as well as passive control groups among samples from countries with lower log Gross Domestic Product (GDP), lower Human Development Index (HDI) and lower Healthcare Access and Quality (HAQ) Index. Within the United States, the efficacy of multiple-behavior interventions was similar across different levels of representation of racial/ethnic and sexual minorities. The analyses used robust variance estimation (RVE) with small-sample corrections to assess the differential effects of multiple-behavior interventions and Egger Sandwich test with the MLMA (multilevel meta-analysis) approach to detect selection biases.

Keywords

HIV intervention; disadvantaged groups; country development; syndemics; meta-analysis

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From its beginning, the Human Immunodeficiency Virus (HIV) epidemic has disproportionately burdened disadvantaged populations with differential access to prevention resources, decision-making ability, and treatment (Bonvicini, 2017; Operario et al., 2022; Zea et al., 2022). Globally, HIV is concentrated in low-income regions (GBD 2019 HIV Collaborators, 2021; WHO, 2022a), and this disparity has remained stable even after decades of HIV prevention and treatment efforts (CDC, 2019; WHO, 2022). Within the United States, HIV prevalence and incidence have remained higher among under-resourced and stigmatized groups such as racial/ethnic and sexual minorities (CDC, 2019), and treatment adherence is lower in under-resourced and stigmatized groups in the U.S. and other countries (Galea et al., 2021). Furthermore, adherence to treatment with antiretroviral medication ranges from 20 – 95 percent in low-income countries or territories (Hudelson & Cluver, 2015) but about 67.7 – 83.5 percent in the U.S. (McComsey et al., 2021).¹ These social health disparities have continued despite efforts to reverse them and are the focus of this paper.

Syndemic theory offers an explanation for disparities in both health and health intervention outcomes: Populations from racial/ethnic minorities, sexual minorities, economically disadvantaged areas, and low- and middle-income countries are burdened by adversity across the lifespan and develop psychosocial health problems with multiplicative negative effects on their health (Garcia & Kushel, 2022; Kerrigan & Barrington, 2022; Operario et al., 2022; P. A. Wilson et al., 2014). For example, systematic marginalization impairs psychological wellbeing via heightened stress, which leads to alcohol and substance use, which are themselves highly correlated as well (Collins, 2016). Alcohol and other substance use can lead to more sexual violence and condomless sex, thus increasing the risk of HIV infection (Decker et al., 2016; Meyer et al., 2011; Parks et al., 2012). Indeed, heavy drinking and nonmedical drug use both correlate with higher HIV seropositivity (des Jarlais et al., 2020; Guerras et al., 2021), higher levels of unsafe sex (Hutton et al., 2019; Ip et al., 2019), decreased psychological wellbeing (Skalski et al., 2015), higher viral load (Ladak et al., 2019), more sexual violence (Wechsberg et al., 2006), and greater HIV-treatment non-adherence (Bauman et al., 2013; Glynn et al., 2019; Kalichman, 2008). Likewise, harmful social conditions such as poverty are often associated with food insecurity, homelessness, and comorbidities that make HIV treatment challenging to maintain (Garcia & Kushel, 2022; Tang et al., 2011). In a nutshell, rather than individual risk factors, these findings suggest the existence of *patterns of correlated risk factors* like the ones proposed in syndemic theory and the literature on multimorbidity (Freedland et al., 2021; Jain et al., 2022; Strathdee et al., 2013). We define *syndemics in HIV* as the synergistic epidemics of substance use, violence, diminished psychological wellbeing, and HIV among impacted populations, particularly those burdened by socioeconomic disadvantages (Sheehan et al., 2020; Tsai, 2018; Tsai & Burns, 2015).

Intervention researchers and policymakers have been acutely aware of syndemics and the needs of disadvantaged groups (Bonevski et al., 2014; Glynn et al., 2019) and have

¹Adherence ranges are both due to natural differences between countries and differences in how adherence is defined (e.g., total doses taken versus total doses taken at the correct time).

identified ways to maximize intervention efficacy for these groups. In particular, multiple-behavior interventions concurrently target multiple risks and are likely to be most efficacious for populations susceptible to syndemics (Rotheram-Borus et al., 2009). For example, nonmedical substance use is associated with lower rates of condom use (Ritchwood et al., 2015). In that case, interventions recommending both condom use and alcohol use should produce more change than interventions recommending condom use solely. This difference between multiple- and single-behavior interventions may hence be larger for groups with syndemic risks, including populations from low-resource regions or racial/ethnic and sexual minorities within the U.S. Nonetheless, prior intervention research has studied program efficacy among disadvantaged populations without comparing these effects with those among more advantaged ones. In this paper, we conducted a meta-analysis to examine whether multiple- versus single-behavior interventions are differentially successful across samples with different levels of disadvantage. First, we gauged differences in efficacy across higher versus lower income/development countries. Second, we examined possible differences in efficacy across racial/ethnic and sexual minorities and majority samples in the U.S. We asked the question of whether, relative to single-behavior interventions, multiple-behavior interventions, which address syndemics, would result in higher intervention efficacy in disadvantaged samples.

Health Disparities and Multiple Risks

Social health disparities in the area of HIV are associated with syndemic differences across countries. In particular, Gross Domestic Product (GDP), Human Development Index (HDI) and Healthcare Access and Quality (HAQ) Index are useful to differentiate the level of resources across countries. Overall, lower scores indicate lower financial resources, lower human development, and poorer healthcare access and quality. Most countries scoring poorly on these indices are in Africa and Central Asia, and their gaps relative to the U.S. and European countries are large. Lower (versus higher) GDP, HDI, and HAQ countries often have higher HIV incidence (Essig et al., 2015; Lou et al., 2014), as well as lower healthcare access, lower HIV testing rates, lower antiretroviral therapy (ART) coverage, and lower uptake of preventive measures (e.g., pre-exposure prophylaxis [PrEP] and protected sex; Levi et al., 2018). Thus, we were interested in assessing whether multiple-behavior interventions are more efficacious in countries with lower GDP, HDI, and HAQ than in countries with higher GDP, HDI, and HAQ.

Both in the U.S. and abroad, MSM are at substantially higher HIV risk than other groups. First, MSM are at greater risk because of the higher level of HIV prevalence in the MSM community (CDC, 2019). Compared to other men, MSM are also more likely to engage in unprotected anal intercourse (Koblin et al., 2003), have multiple sexual partners (Rosenberg et al., 2011), and use substances nonmedically (Stall & Purcell, 2000). These behaviors, which often co-occur (Outlaw et al., 2011), are all associated with a greater risk of contracting HIV (Koblin et al., 2006), and substance use also decreases adherence to ART (Hendershot et al., 2009) and PrEP (Van der Elst et al., 2013).

Within the U.S., racial/ethnic minorities are also at greater risk for HIV and other health problems than other groups. Compared to White individuals, Latinx individuals have a

higher prevalence and incidence of HIV (CDC, 2019), higher rates of substance abuse (SAMHSA, 2013), higher rates of binge drinking (Chartier & Caetano, 2010), worse educational attainment (Woolf & Braveman, 2011), lower rates of condom use among females (Reece et al., 2010), greater stress (Mulia et al., 2008), and worse ART adherence (CDC, 2019). Compared to White people, Black individuals have higher levels of condom use (Reece et al., 2010) but a greater risk of HIV infection because of the higher HIV prevalence in their social networks (CDC, 2019). Black populations are also more likely to be undiagnosed for HIV (Singh et al., 2018), to have low ART adherence rates (Beer & Skarbinski, 2014), to have lower educational attainment and income (Woolf & Braveman, 2011), to experience greater stress (Beckie, 2012), to use substance nonmedically (e.g., crack; SAMHSA, 2019), and to have higher rates of sexually transmitted infections (STIs; De Francesco et al., 2018). Finally, younger adults also have a unique pattern of risk. Specifically, adolescents and young adults have higher rates of unprotected sex (SAMHSA, 2013), alcohol use (Hingson & White, 2014), nonmedical substance use (Baumann et al., 2007), anxiety and suicide (Organization, 2017), as well as greater medication non-adherence (Reisner et al., 2009). The picture is further complicated by varying disparities among younger people in different racial/ethnic minority groups (Valleroy et al., 2000), suggesting that disparities may compound and exacerbate each other.

Multiple-Behavior Interventions

Whether multiple-behavior interventions work better than single ones in HIV is an empirical question. A prior meta-analytic review of 15 randomized controlled trials found that interventions recommending at least two behaviors that related to transmission risk, care management, or medication adherence had lower rates of unprotected sexual intercourse than did other interventions (Crepaz et al., 2015). Although this meta-analysis was small and only included studies targeting people living with HIV, it did suggest that multiple-behavior interventions may be more efficacious than single-behavior ones across the board. A more recent meta-analysis focusing on trials with sexual minority men also led to the conclusion that multiple-behavior interventions were associated with improvements in mental health and substance use (Pantalone et al., 2020).

Multiple-behavior interventions may lead to greater engagement with the intervention and, therefore, more change because the intervention offers several pathways and increases the probability that at least one would be more interesting to a participant. In addition, multiple-behavior interventions may require greater effort to meet multiple goals and promote more change due to higher expectations of success (Förster et al., 2005). Multiple-behavior interventions are also likely to leverage “motivational spill-over,” such that success in changing one behavior increases motivation and self-regulation for other behaviors (Mata et al., 2009; K. Wilson et al., 2015). An example of HIV would be that successfully reducing alcohol and nonmedical substance use may promote positive expectations and, in turn, increase the regulation of sexual risk (Parsons et al., 2014).

Critical to our research question, multiple-behavior interventions are one response to syndemics because they target change in two or more risky behaviors either simultaneously or sequentially (Prochaska et al., 2008). By doing so, these interventions can take advantage

of the ability of change in one behavior to promote changes in another (Albarracín et al., 2017; Albarracín, Sunderrajan, et al., 2018; Albarracín, Wang, et al., 2018). For example, reducing substance use may lead to reductions in alcohol use, sexual violence, having sex under the influence, and increases in condom use (Pitpitan et al., 2018). Addressing multiple behaviors that correlate with a target behavior in the syndemics cluster may also increase success in implementing the target behavior. For example, one intervention targeted alcohol use and medication adherence together as a way of improving intervention efficacy (Bachanas et al., 2016). Additionally, an intervention combining ART adherence with the introduction of mindfulness meditation practice has been shown to reduce self-management barriers (e.g., panic, lack of focus, and timing problems) to adherence (Creswell et al., 2009).

To summarize, multiple-behavior interventions may address syndemics better than single-behavior interventions. Individual multiple-behavior interventions for HIV prevention, testing, and treatment have shown promising results by addressing correlated risk behaviors (e.g., injection and sexual risk behaviors, Garfein et al., 2007). For example, one study of young MSM utilized motivational interviewing to reduce two high-risk behaviors – the use of recreational drugs and unprotected anal sex (Parsons et al., 2014). This study found that the multiple-behavior approach to change was more successful than a typical single-behavior intervention for MSM. In this meta-analysis, we examined whether multiple-behavior intervention addresses syndemics with a comprehensive dataset of 331 reports (see Supplemental Materials), considering the income and development of countries, and within the US samples, representation by racial/ethnic and sexual minorities and age.

The Present Meta-Analysis

We assessed the associations between the efficacy of multiple-behavior interventions and the disadvantaged population status in two ways. First, we used data from all the included countries to assess whether multiple-behavior interventions are more efficacious in countries with different levels of log GDP, GDP per capita, HDI, and HAQ index, in addition to the proportion of gay/bisexual or MSM in the sample and being young adults. Second, we used US data to assess whether, relative to single-behavior interventions, multiple-behavior interventions are more efficacious for racial/ethnic minorities (i.e., Black and Latinx participants), MSM (Grey et al., 2016), and young adults. The analyses involved meta-regression models using Robust Variance Estimation (RVE) clustered by report with small-sample corrections (Pustejovsky & Tipton, 2022; Tipton & Pustejovsky, 2015) to account for the statistical non-independence between effect sizes from the same study samples (Hedges et al., 2010). These models controlled for methodological and sample characteristics. We also specified the single-behavior intervention as the reference group. The effect sizes represent changes in outcomes from the pretest to the posttest, which is the optimal approach when clinical trials use a variety of control groups (Dai et al., 2020; Sunderrajan et al., 2021a). A review of the literature showed only one meta-analysis about multiple-behavior interventions (Sunderrajan et al., 2021b). However, this work focused on examining whether the number of recommendations included in HIV interventions improved intervention efficacy. It did not answer the question of the differential effects of three conditions (i.e., multiple-behavior, single-behavior, and passive controls) across more and

less advantaged groups. We pre-registered this project as RQ3 (i.e., research question 3) in <https://osf.io/mq5kr>. The full dataset and analysis codes are available at https://osf.io/cg7ea/?view_only=a5a9e84d73e3403ea56d29ecd5b3131a.

Method

Search Strategy

We used the same methods as other recent publications that have used other components of this project (Dai et al., 2020; Sunderrajan et al., 2021a), which spanned various domains. We searched MEDLINE, PsycINFO, and EBSCO through July 27, 2022. Our search terms included: *intervention, health education, persuasion, recommendation, treatment, educational program, rehabilitation, counseling outcomes, treatment outcomes, treatment effectiveness evaluation, treatment compliance, health promotion, behavior change, and randomized trial*. To identify HIV-related recommendations, these keywords were entered in combination with keywords for interventions promoting change in HIV and related behaviors, including *HIV, AIDS, STI/STD, condom use, circumcision, alcohol use, drug use, and adherence*. In addition, we searched conference titles (i.e., conferences of American Public Health Association), emailed the most published authors in our database to request published and unpublished works, sent requests to relevant organizations and listservs, and examined the reference lists of prior reviews to identify other possible reports for inclusion. This search yielded 17,387 total possible articles.

Inclusion Criteria

Once our search was complete, we used the following criteria to determine the inclusion and exclusion of reports from our analysis (see Figure 1):

- 1. Presence of at least two groups.** Reports had to include both a comparison group and a multiple-behavior intervention group. Comparison groups were separated into three categories: (a) passive controls (no recommendations), (b) active control or single-behavior interventions (i.e., interventions making one recommendation), and (c) multiple-behavior interventions (i.e., interventions making two or more recommendations).
- 2. Presence of at least one behavioral or clinical outcome.** Reports had to include at least one behavioral or one clinical outcome. We excluded reports that only included information on behavioral intentions, attitudes, perceived social norms, or other non-behavioral or non-clinical outcomes.
- 3. Presence of appropriate statistics to estimate change over time.** Reports had to include enough statistical information to calculate effect sizes representing change over time. Thus, reports had to include outcome values at both the baseline and at least one follow-up. When information was only reported for the follow-up, reports were excluded. Studies that only included reported analyses with statistical controls or other statistical corrections were excluded as well.

After screening abstracts, we excluded 15599 articles and assessed 1788 full-text reports for eligibility. After applying our inclusion criteria, 331 reports from 153 studies were included in our analyses (see Supplemental Material).

Coding and Data Extraction

The coding and data extraction was comprehensive and included determining the type of condition to which a group was assigned, moderators related to social disadvantages, and other exploratory moderators related to the report, the intervention, and the methods. All coding and data extraction were conducted via an in-house online data entry system using a coding and data entry manual developed by the research team. One researcher extracted the means and standard deviations or proportions for each available study outcome. A second researcher later rechecked the entries of these data entry for each paper.

Coding of Reports about Syndemic Conditions

We combined a text analysis of the study titles and gave a score of 1 (versus 0) to any study that had any of the following keywords: “acute hiv infection”, “aids/hiv patient”, “antiretroviral”, “concordant”, “hiv infection”, “hiv-infectat”, “hiv-infected”, “hiv-positive”, “hiv/aids-infected”, “hiv+”, “living with hiv”, “living with hiv/aid”, “men with aids”, “medication adherence”, “nonadherence”, “seropositive”, “serostatus”, “women with aids”, “addiction”, “binge substance use”, “cocaine”, “crack”, “depress”, “drug use”, “hazardous alcohol”, “hazardous drinker”, “heavy drinker”, “history of drug use”, “homeless”, “incarcerated”, “inject drug”, “injection”, “intravenous”, “jail”, “justice-involved”, “marginalized”, “marijuana”, “methadone”, “methamphetamine”, “migrants”, “narcology”, “offender”, “opioid”, “probationer”, “relapse”, “residential drug abuse”, “sex worker”, “substance abuser”, “substance misuse”, “substance user”, “substance-dependent”, “substance-using”, “trauma”, “unhealthy alcohol use”, “use stimulant”, and/or “violence.” Studies without those keywords were coded 0. In addition, we coded whether studies included participants from a clinical population or other vulnerable populations (a report scored as 1 if participants were at-risk, such as drug dependent or female sex workers and 0 otherwise; see Table 1). We next calculated the sum of these three indicators. Scores equal to one or above indicate the reports were with participants who were at-risk or experienced syndemic conditions.

Determination of Multiple-Behavior Intervention, Single-Behavior Intervention, and Passive Control

Each report condition was coded into one of three categories: (a) multiple-behavior intervention, (b) single-behavior intervention, or (c) passive control group. Multiple-behavior interventions had two or more behavioral recommendations (e.g., use condoms more frequently and reduce alcohol consumption). As an example, (Amaro et al., 2007) recommended that participants both reduce their substance use and reduce their sexual risk through abstinence. This intervention was therefore coded as a multiple-behavior intervention. Similarly, Go et al. (2015) included one intervention group that recommended clients (a) reduce their sexual risk behaviors and (b) reduce their injection drug use, (c) seek social support, (d) disclose their HIV status, and (e) ask about their partners to get tested. As

this group involved changing more than two behaviors, it was coded as a multiple-behavior intervention.

Single-behavior interventions had only one behavioral recommendation. For instance, one study of HIV adherence had a group whose only recommendation was to take their pills as prescribed (Pop-Eleches et al., 2011). Other general examples of single-behavior interventions include intervention arms that only recommended HIV adherence or only HIV testing (e.g., Barnett et al., 2009). Finally, if a group had no direct behavioral recommendations, it was coded as a passive control condition. An example of a no-recommendation condition would be either a waitlist control or a condition providing general information without a recommendation to change a behavior (Santos et al., 2014).

Coding of Moderators Related to Population Disadvantages

Country Code and Country Development Indices.—Each report was coded for the country where the study was conducted. Country indices of development were included by obtaining GDP and GDP per capita from the World Bank, HDI from the United Nations Human Development Report, and the HAQ index from the Institute for Health Metrics and Evaluation (University of Washington School of Medicine, 2023).

For a given report, we estimated the developmental indices using the closest year available. Therefore, studies from the same countries (e.g., the U.S.) but conducted at different time periods were linked to different developmental indices. Four studies included in our dataset provided data with a sample representing multiple countries (Amirkhanian et al., 2005; Bachanas et al., 2016b; Latkin et al., 2009; Nöstlinger et al., 2016). All of these studies, except for Latkin et al. (2009), reported only overall sample sizes (e.g., $n = 488$). We, therefore, assumed even representation from each country and calculated a simple average of the country indices corresponding to the represented countries. For example, the sample included 244 US participants and 244 Thai participants, the calculation of log GDP was $[244*30 + 244*25.6]/(244+244) = 27.8$.

MSM and Race/Ethnicity.—We coded the following sample characteristics: (a) percentage of females in each group, (b) percentages of gay/bisexual or MSM, (c) percentages of participants of European, African, Latin, Asian, and Native American descent, and (d) mean age. Most of the included reports did not include all sample characteristics. In some cases, specific races/ethnicities were missing despite others being reported (e.g., only White and Black representation was reported). In these cases, the unknown portions of the sample were coded as percentages of “Other” racial/ethnic representation.

Coding of Exploratory Moderators

Relevant characteristics of the reports, as well as the methods used in the reports, were coded. Intercoder reliability coefficients (Fleiss' kappa for categorical variables and Pearson correlations for continuous variables) are summarized in Table 1. Disagreements between coders were resolved by discussion, further examination of the reports, and consultation with an additional coder if needed.

Report Characteristics.—We coded (a) publication year, (b) first authors' institution (e.g., college, hospital, research center), (c) first authors' institutional area (e.g., psychology, public health, and medicine), (d) source type (e.g., journal article and dissertation), (e) language of the report, and (f) research quality by calculating a total score of three binary indicators (i.e., 1 = yes versus 0 = no), including whether the study had random assignment of participants into groups, included a 6-month follow-up, and had analyses using intention-to-treat principles.

Methodological and Other Sample Characteristics.—We coded for factors related to the design of the intervention, including (a) whether the intervention involved samples with limited refusal freedom (e.g., prisoners) or samples without such limitations, (b) what the exposure setting (e.g., school, community) was, which was recoded to represent a clinical versus non-clinical setting, (c) what the exposure format (e.g., radio, brochure) was, which was recoded to indicate face-to-face versus other formats, (d) whether the intervention was delivered to a group, to individuals, or to a combination of the two, (e) whether the intervention was described as culturally appropriate, (f) the number of days between the intervention and posttest, (g) the duration of intervention (in hours), (h) whether the intervention facilitator was a professional (e.g., physician, nurse, social worker, and professional counselor) or lay community member (e.g., community leaders and peers), (i) whether the measured outcome was targeted in the intervention (e.g., HIV testing for a testing intervention versus depression for an HIV treatment intervention that did not target depression), (j) whether the intervention targeted specific populations (e.g., race and gender), (k) where participants were recruited (e.g., drug treatment facility, social service agency), which was recoded to describe a medical versus non-medical setting, (l) whether the intervention was ensured to have high fidelity, for example, the intervention implemented any best practices and recommendations from the NIH Behavior Change Consortium (Bellg et al., 2004), and whether the intervention relied on (m) attitudinal elements (e.g., attitudinal arguments, threat arguments), (n) passive strategies, e.g., informational arguments (Albarracín et al., 2005), (o) motivational elements (e.g., feedback, encouragement), or (p) skills training elements (e.g., role playing, goal setting; Michie et al., 2014).

Effect Sizes

Our effect size of interest was within-group change over time (d) for all intervention-relevant behaviors and clinical outcomes and for all available follow-ups. The decision to use change as our effect size was based on careful consideration of the characteristics of our data. First, a substantive problem with between-group effect sizes is that a control group may be a passive or active control (Karlsson & Bergmark, 2015). Comparing a treatment group to a passive control group is an absolute comparison (i.e., the maximum amount of change relative to no treatment) that tends to produce larger effect sizes, whereas comparing a treatment group to an active control group is a relative comparison (i.e., the amount of change relative to another treatment) that produces smaller effects (Brookmeyer et al., 2016). In addition, many control groups in this literature are themselves multiple-behavior interventions. Therefore, the impact of these conditions is best verified over time. Another advantage of analyzing changes over time is that this approach allows for individual slope

models to assess if moderators have differential effects on multiple-and single-behavior intervention groups, allowing for more informative conclusions. Ascertaining intervention efficacy over time, with everyone serving as their own control, was therefore optimal.

To calculate d for continuous outcomes, the mean of the pre-test measure was subtracted from the mean of the post-test measure, and this difference was then divided by the pooled standard deviation of the means (Borenstein et al., 2009). To calculate d for proportional outcomes, an odds ratio was calculated by dividing the odds of the behavior at the post-test by the odds of the behavior at the pre-test and then converting it into a d by taking the natural log and dividing it by 1.81 (Borenstein et al., 2009). In cases where the reported proportions were 0 or 1, a correction of 0.005 was added to 0's and subtracted from 1's to reduce the skew produced by extreme odds ratio calculations (Sweeting et al., 2004). All effect sizes were corrected for small sample sizes (Freeman et al., 1986) and coded such that positive effect sizes reflect health improvement (e.g., increased testing rates and decreases in unprotected sex). As the correlation between pre-test and post-test observations was unknown, we assumed that $r = .5$ in our analyses (Morris et al., 2000). We used corrected estimates and standard errors for studies reporting results from three reports of cluster-randomized trials (Hedges, 2007). Previous analyses from other domains of the larger dataset have found that models are robust to changes in the assumed correlation (K. Wilson et al., 2015). Due to potential limitations of this approach, we also repeated all analyses with difference-in-differences scores (see Supplemental Material).

Our dataset included 39 different outcome types, which are shown in Table 2. These measures are related to HIV/sexual risk, substance use, psychological wellbeing, and other syndemic outcomes. Examples of HIV/sexual risk outcomes are measures like the numbers of unprotected sexual encounters in a specific time period, proportions of the sample that received an HIV test since the last measurement, HIV viral load measures, or proportions of the sample meeting treatment adherence standards. Examples of substance use outcomes include self-reports of the amount of alcohol or substance use in a given period, as well as clinical measures such as chemical representation in urine samples. Psychological wellbeing measures include reports of depression and quality of life. Other syndemic outcomes includes quality of life, body mass index, and unwanted pregnancy.

Main Analyses

We first examined selection bias by conducting the Egger Sandwich test (Sterne et al., 2006) with the use of a multilevel meta-analysis (MLMA) approach and a modified covariate (Pustejovsky & Rodgers, 2019). We did not use PET-PEESE (precision-effect test and precision-effect estimate with standard errors), trim-and-fill, or selection models because these detection methods are biased when the data contain statistically dependent effect sizes (Rodgers & Pustejovsky, 2021). Second, we estimated the average effect in each of the three types of conditions and estimated the impact of exploratory moderators to be included in our main analyses using robust variance estimation (RVE) models with small-sample corrections (Tipton & Pustejovsky, 2015). Third, we conducted a confirmatory factor analysis among changes in HIV/sexual risk, substance use, psychological wellbeing, and other syndemic

measures. The presence of a satisfactory model fit would support the notion that these outcomes are, in fact, intercorrelated as proposed by syndemics.

The key analyses were to test the differential effects of multiple-behavior intervention as a function of country development indices, proportion of gay/bisexual or MSM, different races/ethnicities, and different ages. Using log GDP as an example, we fit a meta-regression model clustered by report with small-sample corrections that include the main effects for intervention groups (with single-behavior intervention as a reference group) and log GDP, the interaction between these two moderators, also controlling for covariates suggested by our exploratory moderators. A significant interaction between multiple-behavior intervention and log GDP implies differential effects of multiple-behavior intervention programs related to log GDP, relative to the effects of single-behavior intervention programs. The analyses for country development indices, gay/bisexual or MSM, and different ages were conducted with the entire dataset from all countries.

We next analyzed the US data to examine the differential effects of multiple-behavior intervention for racial/ethnic minority (e.g., non-White Americans) versus majority representation, specific racial/ethnic minorities (e.g., African Americans, Latinx people, and Other²), gay/bisexual or MSM, different ages, and the intersection of racial/ethnic minority (see CDC, 2019). These meta-regression models were specified in a similar way to the international ones, except that the country development indices were replaced with the gay/bisexual or MSM, race/ethnicity, and age variables. For the meta-regression model testing the interaction between racial/ethnic minorities and gay/bisexual or MSM, we only analyzed multiple-behavior intervention groups due to insufficient data in other conditions.

In addition to coefficients from the random-effects models, we calculated \hat{P}^2 , which indicates the proportion of total variance due to random-effects variance (Higgins et al., 2003; Huedo-Medina et al., 2006). We used R packages *metafor* (Viechtbauer, 2019) to perform the bias test and combined the *metafor* object with the package *clubSandwich* (Pustejovsky, 2022) to conduct the main analyses, including the mean effect size estimation and meta-regression analyses clustered by report with small-sample corrections. Following the significant interactions between multiple behavior intervention and country development indices identified in the meta-regression models, we computed the predicted *ds* and included them in the analyses of pair-wise comparisons to interpret the interaction. The interpretation of effect sizes was based on Cohen (1988).

Results

The meta-analysis included 331 reports, which provided 205 intervention groups recommending multiple behaviors (MBI), 76 intervention groups recommending a single behavior (SBI), and 50 passive control (PC) groups. About 96 percent of the included reports (i.e., 317; 98% of the records) were with samples that were at-risk or experienced syndemic conditions (e.g., HIV infection and substance use disorder). The average study

²Reporting of Asian and Native American representation was too low to appropriately assess model convergence problems in both groups due to a lack of degrees of freedom.

group had 4.11 effect sizes, and a total of 32 countries were represented in the dataset. About fifty-nine percent of the reports were conducted in the U.S. ($n = 810$), and of the non-US studies, the more represented countries outside the U.S. were South Africa ($n = 105$), Thailand ($n = 74$), China ($n = 66$), Kenya ($n = 50$), and. Overall, the data had adequate variability to assess differences across countries.

Within the U.S., 59 percent of the samples reported being gay/bisexual or MSM, 27 percent of participants were of European descent, 49 percent of participants were of African descent, 19 percent of Latinx descent, and 1 percent of participants were of Asian descent. The average age was 29.60 years ($SD = 11.34$), and the samples were 48 percent female. As with countries, there was considerable demographic variability in assessing demographic differences within the U.S.

Selection Bias

Figure 2 shows a contoured-enhanced funnel plot of effect sizes, which plots d s on the x -axis and the standard error of each effect on the y -axis. Although the funnel plot must be viewed with caution due to the inclusion of non-independent effect sizes, asymmetry is often considered as possibly associated with bias. We followed Rodgers and Pustejovsky (2020)'s proposed analytical procedures to conduct Egger Sandwich tests with the MLMA approach for all effect sizes and then separately for the effects from multiple-behavior interventions, single-behavior interventions, and passive controls. The Egger Sandwich test is essentially a modified regression test using a modified covariate proposed in Pustejovsky and Rodgers (2019) to test the significance of a regression slope as an indicator of asymmetry in the funnel plot. The overall analysis showed a significant slope, $p = .026$, suggesting potential selection bias in the overall dataset. When dividing the dataset according to intervention types, we also detected selection bias in the effect sizes from multiple-behavior interventions, $p = .044$ and marginally significant for passive controls, $p = .069$, but not from single-behavior interventions, $p = .182$. Given the possible presence of selection bias from results of the Egger Sandwich test, we included the modified covariate in the following analyses to mitigate bias in our results.

Average Intervention Efficacy

In the preliminary analyses, we first assessed possible differences in efficacy across interventions by testing whether the effect sizes were associated with three dummy indicators for multiple-behavior intervention, single-behavior intervention, and passive control group. Results showed no difference in intervention efficacy between multiple-behavior intervention, $d = 0.29$, 95% CI [0.12, 0.45], and single-behavior intervention, $d = 0.25$, 95% CI [0.02, 0.48], $b = 0.03$, $SE = 0.09$, $p = .697$. In contrast, passive controls had lower efficacy than both multiple-behavior and single-behavior interventions (see Table 3). The estimated mean effect size of passive controls was nonsignificant, $d = 0.04$, 95% CI [-0.14, 0.23]. There was also substantial heterogeneity among effect sizes, $I^2 = 94.63\%$.

Identifying Covariates among Exploratory Moderators

We next assessed whether the report, methodological, and sample characteristics moderated effect sizes beyond intervention type and needed to be controlled for in subsequent analyses.

We evaluated each covariate by adding it as a predictor to the model reported in Table 3 if the moderators were had fewer than 10 percent missing data (i.e., NA) in the dataset. For report characteristics, we tested (a) whether the report's institutional area explained the intervention efficacy, $ps = .106 - .769$, as well as (b) whether the research quality explained the intervention efficacy, $p = .572$. For methodological characteristics, we assessed (c) whether the report indicated that the intervention was culturally appropriate, $b = -0.11$, $SE = 0.06$, $p = .070$, (d) whether the intervention involved samples with limited refusal freedom (e.g., prisoners) or samples without such limitations, $ps = .104 - .920$, (e) whether exposure to the interventions took place in clinical or non-clinical (e.g., community) settings, $p = .129$, (f) whether exposure was face-to-face or not, $p = .795$, (g) whether the intervention was delivered as solely individual or non-individual sessions (e.g., group or both individual and group sessions), $p = .401$, (h) the number of days between the intervention and the posttest, $p = .951$, (i) whether the intervention involved expert facilitators or lay community members, $b = 0.22$, $SE = 0.07$, $p = .001$, (j) whether the measured outcome was targeted in the intervention, $p = .141$, (k) whether the intervention targeted specific race, $p = .321$, (l) whether the intervention targeted specific gender, $p = .696$, (m) whether participants were recruited from medical settings, $b = 0.15$, $SE = 0.06$, $p = .011$, and (n) whether the intervention was ensured to have high fidelity, $p = .575$. For sample characteristics, we examined (o) participants' average age, $b = 0.01$, $SE = 0.00$, $p < .001$, and (p) the percentage of females in the samples, $b = -0.00$, $SE = 0.00$, $p = .081$. In summary, results showed larger intervention effects for (a) older participants, (b) female participants, (c) interventions delivered by expert facilitators (e.g., physicians or professionally trained counselors), (d) participants recruited from medical settings, and (e) interventions not described as culturally appropriate. Therefore, we included these five covariates in the main analyses.

Confirmatory Factor Analysis (CFA) among Different Syndemic Outcomes

We next conducted a CFA to examine if HIV/sexual risk, substance use, psychological wellbeing, other syndemic outcomes are interrelated as proposed by the notion of syndemics. We first calculated two latent factors of HIV/sexual risk and substance use, each with many outcomes. These two latent factors were subsumed under a single factor representing syndemic outcomes, which also included psychological well-being and other syndemic outcomes.

Table 4 shows the significant factor loadings of all first order factors on the overall syndemic factor, $p < .001$. As for the goodness of fit, Comparative Fit Index (CFI), Relative Fit Index (RFI), and Incremental Fit Index (IFI), which adjust for and thus are less sensitive to small sample size, showed satisfactory goodness of fit. However, Chi-squared and Root Mean Square Error of Approximation (RMSEA), which are more sensitive to sample size, showed poorer fit. Taken together, the CFA results showed substantial support for HIV/sexual risk, substance use, psychological wellbeing, and other syndemic outcomes as interrelated. Therefore, improvements in one syndemic outcome may be tied to improvements in other syndemic outcomes.

Differential Effects of Multiple-Behavior Interventions Related to Country Development, Gay/bisexual or MSM Representation, and Being Young Adults

Table 5 shows the results of the meta-regression models clustered by report and with small-sample corrections. Log GDP, GDP per capita, HDI, and HAQ all revealed the same pattern of interactions with multiple-behavior intervention across the multi-level meta-regression models, $bs = -1.90 - -0.00$, $ps < .003 - .072$. Specifically, participants from less developed countries, where syndemics are presumably more pronounced, improved more in response to multiple-behavior interventions than in response to single-behavior interventions. Figure 3 illustrates the interactions involving the log GDP, GDP per capita, HDI, and HAQ in the multi-level meta-regression models. As shown, intervention efficacy increases in multiple-behavior interventions as log GDP, GDP per capita, HDI, and HAQ decreases. Next, we included the syndemic categories (i.e., HIV/sexual risk, substance use, psychological wellbeing, and other syndemic) as additional moderators to assess whether the interaction effects were robust to these controls. The direction, strength, and significance of the interaction effects remained the same after controlling for the syndemic categories.³ Overall, the results indicated that multiple-behavior interventions, rather than single-behavior interventions, were associated with larger improvements in samples from less developed countries.

Next, we conducted planned contrasts to decompose the significant interactions between multiple-behavior interventions and development indices at three levels using the current data set (i.e., higher = $M + 1 SD$, medium = M , and lower = $M - 1 SD$). The bottom panel of Table 6 shows the planned contrasts for countries with lower development indices. As hypothesized, in countries with lower development indices, multiple-behavior interventions had greater efficacy than single-behavior interventions in all four development indices, $ts = 3330.36 - 5624.39$, $ps < .001$. The same pattern of results also revealed in the contrasts between multiple-behavior interventions and passive controls, $ts = 3736.16 - 5427.65$, $ps < .001$.

The top panel in Table 6 reports the results for countries with higher development indices. Single-behavior interventions appeared to have greater intervention efficacy than multiple-behavior interventions and passive controls in the models that included each development index, $ts = 3771.92 - 4556.62$, $ps < .001$. However, this pattern of results should not be understood alone. As shown in Figure 3, there is substantial overlap of effect sizes among multiple- and single-behavior interventions and passive controls as development indices increase (i.e., the right side of the x-axis), suggesting no differences in intervention efficacy.

We next assessed whether the efficacy of multiple-behavior interventions varied with gay/bisexual or MSM representation and age, again using the total sample of all countries. These results, which appear in Table 7, showed statistically significant interactions between the proportion of gay/bisexual or MSM representation in the samples and multiple-behavior

³Four syndemic categories were included in the model with the category “other syndemic” set as the reference group. Two factors (i.e., HIV/sexual risk and substance use), except psychological wellbeing, showed main effects on intervention efficacy for all development indices. Specifically, HIV/sexual risk outcomes, $b = 0.41$, $SE = 0.22$, $p = .075$, and substance use outcomes were associated with higher intervention efficacy than other syndemic outcomes, $b = 0.52$, $SE = 0.22$, $p = .032$.

interventions, $b = -0.01$, $SE = 0.00$, $p = .010$, and the proportion of gay/bisexual or MSM representation and passive controls, $b = -0.01$, $SE = 0.00$, $p = .023$. As the interaction effect between the proportion of gay/bisexual or MSM and multiple-behavior interventions was weak and unexpected, we were skeptical to interpret the result (see Table S10 for an additional analysis with other methodological characteristics). Lastly, no significant interaction was found between multiple-behavior interventions and age, $p = .484$.

Differential Effects of Multiple-Behavior Interventions Related to Racial/Ethnic Minority Representation in the U.S.

We last considered disadvantaged status associated with being a racial/ethnic minority or a sexual minority in the U.S. (62% of all the included reports). Specifically, we analyzed the proportion of the sample that was non-White, Black/African-American, Latinx, or “Other”, and the proportion of gay/bisexual or MSM in the sample. We also analyzed age, as young age is a risk factor for HIV infection. These results, which appear in Table 8, showed largely no evidence of differential effects of multiple-behavior interventions across groups in the US sample. Only a weak marginally significant interaction between multiple-behavior intervention and gay/bisexual or MSM representation was found, $b = -0.01$, $SE = 0.00$, $p = .097$. That is, multiple-behavior interventions appeared to benefit all the groups in a similar way.

Differential Effects of Multiple-Behavior Interventions Related to Intersectionality of Racial/Ethnic Minority and MSM Representation in the US

Finally, a distinct possibility for US samples is the differential effects of multiple-behavior intervention due to the intersection between state-level MSM and race/ethnicity. We thus examined whether MSM of different racial/ethnic minority backgrounds responded differently to multiple-behavior interventions. For each minority group, we regressed the effect size on MSM representation (i.e., the state-level estimated MSM percentages), racial/ethnic minority group representation, and their interaction. As shown in Table 9, the interaction between MSM and racial/ethnic minority groups were statistically nonsignificant, $ps = .504 - .949$, suggesting no differential effects among US MSM of different races/ethnicities in multiple-behavior interventions.

Discussion

Overview of Main Findings

We combined a dataset consisting of 331 reports and 1364 effect sizes with open-source data about country development indices obtained from the World Bank, the United Nations Development Program, and the Institute for Health Metrics and Evaluation (University of Washington School of Medicine, 2023), together with the estimated percentages of MSM in the U.S. (Grey et al., 2016), to carry out a comprehensive meta-analysis of the efficacy of multiple behavioral program used in the area of HIV. The confirmatory factor analysis results provided meta-analytic evidence that outcomes about HIV/sexual risk, substance use, psychological wellbeing, and other syndemic group are interrelated, as suggested by the conceptualization of syndemics. Furthermore, even though multiple-behavior interventions and single-behavior interventions were more efficacious than passive controls, across the

board, multiple-behavior interventions were not more efficacious than single-behavior interventions. Multiple-behavior interventions were more efficacious than single-behavior ones in countries that are more likely to experience syndemics.

To understand whether multiple-behavior interventions could be a response to syndemics in HIV, we assessed whether multiple-behavior interventions had the same or differential intervention efficacy across countries with different levels of economic development, and whether multiple-behavior interventions had greater efficacy for disadvantaged groups in the U.S. Results of the interactions showed that, in countries with lower development indices, multiple-behavior interventions had greater efficacy than single-behavior ones, whereas single-behavior interventions did not differ from controls. These effects were consistent for our four development indices, though the interaction with GDP per capita was marginally significant. These findings provide empirical evidence that multiple-behavior interventions could be an appropriate response to syndemics in HIV.

Within the U.S., results suggested largely no differential effects of multiple-behavior interventions related to the representation of disadvantaged groups, including racial/ethnic minorities, gay/bisexual MSM, and young adults, compared to single-behavior interventions. Similarly, results showed no differential effects of multiple-behavior interventions related to the intersection of MSM and racial/ethnic minority groups in the U.S.

Implications

Multiple-behavior interventions show great promise and are well poised to mitigate health disparities in countries with lower development indices compared to single-behavior interventions. For instance, Sub-Saharan African countries have the majority of both new HIV infections and people living with HIV (UNAIDS, 2014) in the world. One successful intervention to reduce HIV transmission targeted serostatus disclosure, alcohol use, condom use, antiretroviral adherence, and counseling all at the same time (Bachanas et al., 2016b). Less developed countries tend to have limited resources for health care and possibly co-occurring diseases and unhealthy conditions. Therefore, addressing multiple problems such as partner relationships, substance use, and HIV prevention is more practical (Tsai & Venkataramani, 2016).

The finding that multiple-behavior interventions were more efficacious in countries with lower development indices could provide insights for the design of context-sensitive multiple-behavior interventions. For example, facilitators could assess the syndemic conditions of different contexts or individuals and thus address unique needs (Mendenhall & Singer, 2020). As proposed by Gilbert et al. (2015), a screening protocol may inform the components that can be implemented to target specific syndemic conditions or regional vulnerabilities.

We also found that HIV/sexual risk, substance use, psychological wellbeing, and other syndemic factors are part of an overall syndemic factor (i.e., a second-order factor). However, as highlighted by Bhardwaja and Kohrt's (2020), syndemic research has failed to characterize the relation between syndemic conditions or the strength of these relations.

Future research should refine the syndemic framework to clarify processes and intervention priorities.

MSM, young adults, and Black and Latinx individuals in the U.S. were more likely to be diagnosed with HIV (CDC, 2019b), and Black and Latinx individuals and young adults of color were more likely to have a later HIV diagnosis and worse viral suppression than White adults of the same age (Chen et al., 2012; Schwarcz et al., 2006; Crepaz et al., 2018). Although 98 percent of the included records (i.e., 1342) had participants at risk or who experienced syndemic conditions, we found no differential effects of multiple-behavior interventions related to sexual or ethnic minority groups either internationally or in the U.S. However, the research reports have considerable amounts of missing data (e.g., percentages of Black individuals), which might prevent identifying effects. In addition, syndemic conditions interact with each other (Batchelder et al., 2019) but this meta-analysis did not have the power to estimate the effects of intersectionality. Future attempts at studying the impact of intersectionality will be well served by a greater accumulation of literature in the future (Earnshaw et al., 2015; Rice et al., 2018).

A final point regarding this meta-analysis is that it included all possible behavioral and clinical outcomes targeted in these studies – a total of 39 different outcomes across the studies in our dataset (see Table 2). Due to sample size, coverage limitations, and diversity in reported outcomes, we could not examine if specific mixtures of recommendations are more effective than others due to few exactly comparable studies for specific combinations of behaviors. As discussed before, a more granular approach that compares combinations of behaviors within specific samples could be important to the development of these interventions for under-resourced groups.

Limitations

Our work has several limitations due to the information availability and analyses we chose to conduct. We used general measures of income and development and relied on them to conclude about the resources of specific samples within those countries. Although the general pattern of resources available based on countries is likely correct, further studies could use more precise estimates for each sample. We could not use more precise measures in our analyses due to a lack of reporting of income and a lack of measures of socioeconomic resources of other types.

Likewise, our findings could depend on the fidelity with which interventions are applied. Although we estimated the impact of the intervention fidelity and found no significant moderation, only 20% of the included reports implemented the NIH Behavior Change Consortium's (Ory et al., 2002) recommendations for intervention fidelity recommendations. As intervention fidelity checks become the norm (Bellg et al., 2004; Borrelli et al., 2005), we encourage researchers to thoroughly report on their measures to maximize it (Borrelli, 2011; Borrelli et al., 2005) and report fidelity checks in a standardized way. In this way, future meta-analyses will be able to include more detailed analyses of the impact of processes to maximize fidelity.

For the US analyses, demographic reporting had considerable missing data, in part because certain demographics are not recorded unless a sample was focused on a specific group (e.g., interventions only for Latinx youth). Probably for that reason, approximately 10 to 15 percent of the samples had missing values regarding Latinx percentages. Most likely, the missing information comes from low-percentage studies (i.e., those conducted with a 10-20 percent representation of a group). Future inclusion of more studies may therefore shed light on the role of race and ethnicity.

Finally, an inherent problem in all meta-analyses is aggregation across individuals and often across groups. Group membership is inherently an individual factor, and there is a distinct possibility that the individual patterns are different from the group patterns (e.g., Simpson's Paradox; Simpson, 1951). These problems are difficult to solve other than conducting large randomized controlled trials that are powerful enough to examine the effects of conditions across multiple populations, such as those living in multiple counties. Unfortunately, this limitation could not be overcome in our synthesis because the overwhelming majority of included studies considered samples from single countries, and less than five percent of the included studies had a multinational sample. We highlight these concerns as an area for improvement in future intervention design. Of note, other characteristics such as identification as MSM and race/ethnicity, should be disaggregated whenever possible.

Conclusion

We examined whether multiple-behavior interventions were more efficacious in samples with lower access to resources and thus more likely to be affected by syndemics. We found that relative to single-behavior interventions, multiple-behavior interventions showed greater efficacy in countries with lower development indices, but not in countries with higher development indices. We also examined whether disadvantaged groups across all countries and within the U.S. had differential results from multiple-behavior interventions versus single-behavior interventions. Unlike an earlier analysis of single-recommendation interventions (Albarracín & Durantini, 2010), we found largely no differential effects of multiple-behavior interventions related to the representation of these groups and their intersections, compared to single-behavior interventions. Future research in this area may be well positioned to answer intersectionality questions, but as a whole, multiple-behavior interventions, in general, appear to be meeting the demands of the complex situations for which they were designed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Public Health Impact Statement

This study examines *syndemics in HIV*, defined as the synergistic epidemics of substance use, violence, diminished psychological wellbeing, and HIV among impacted populations, particularly those burdened by socioeconomic disadvantages. The meta-analytic results showed multiple- versus single-behavior interventions are differentially successful across samples with different levels of disadvantage. Specifically, multiple-behavior interventions, rather than single-behavior interventions, were more efficacious for samples from countries with lower log Gross Domestic Product (GDP), lower Human Development Index (HDI), and lower Healthcare Access and Quality (HAQ) Index. Similar but marginal significant results were also found for GDP per capita.

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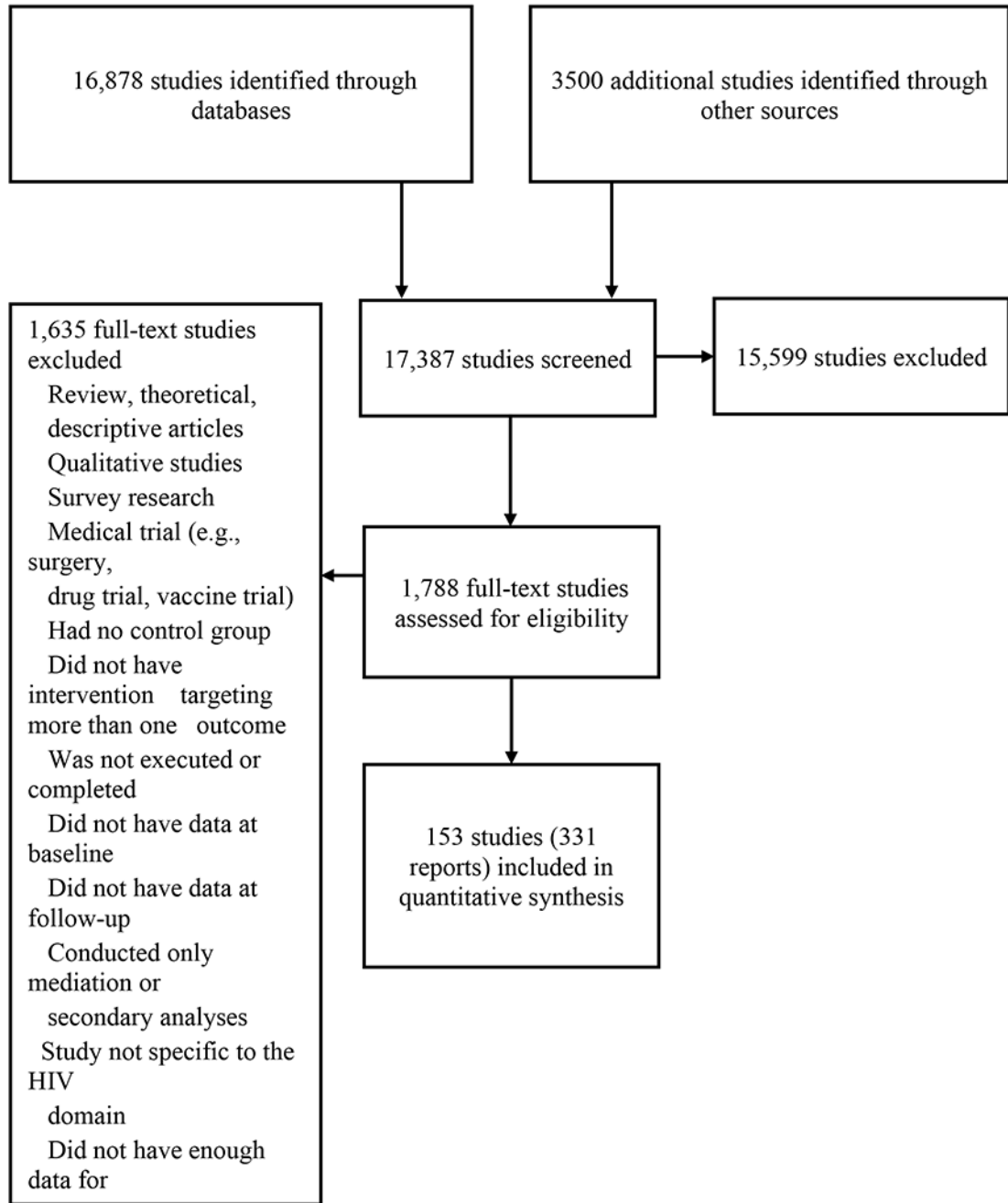


Figure 1.
PRISMA Diagram

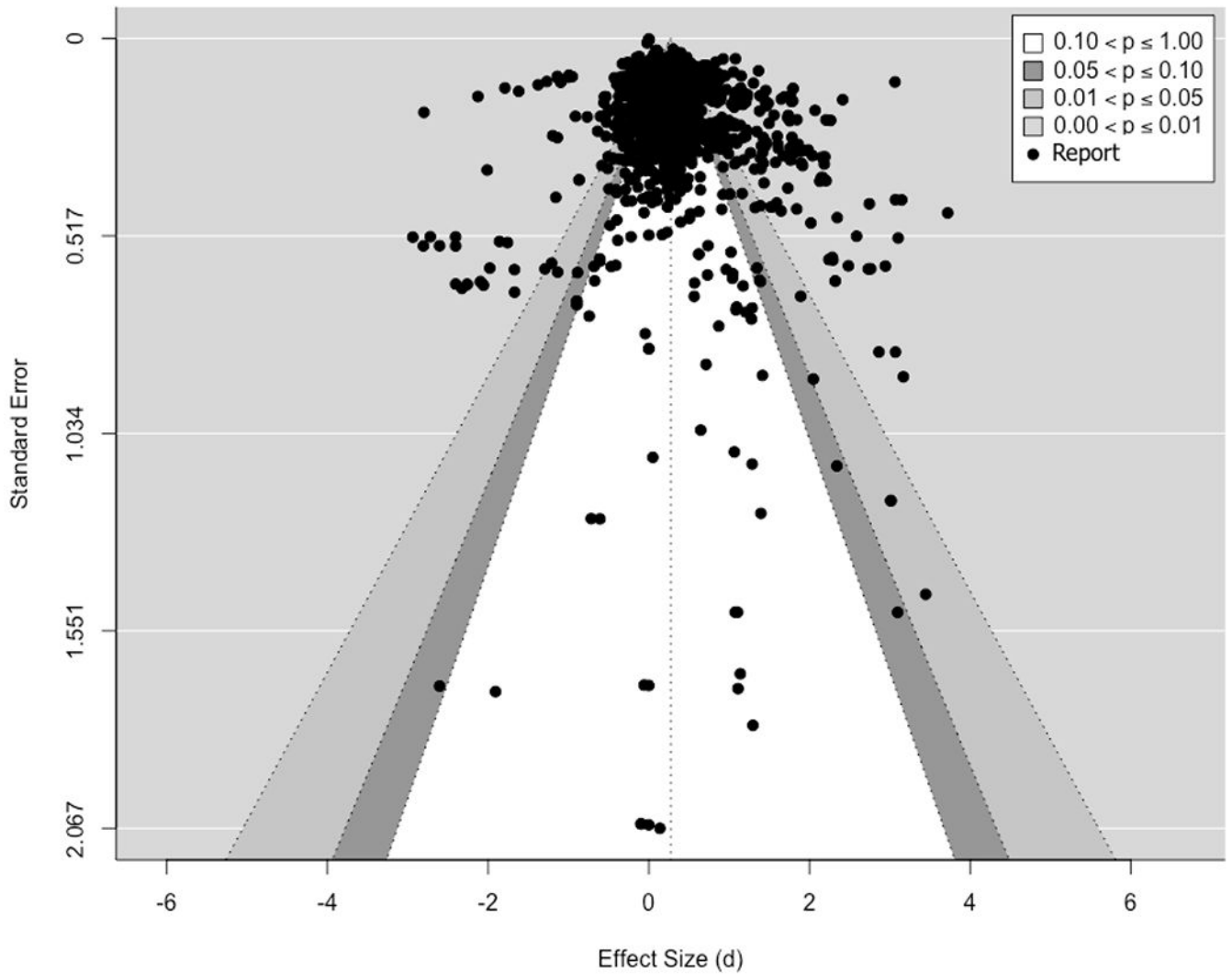


Figure 2.
Contour-Enhanced Funnel Plot

Note. The dotted vertical line corresponds to the random-effects model estimate of average effect (0.273), and the funnel shape corresponds to the 90%, 95%, and 99% pseudo confidence intervals.

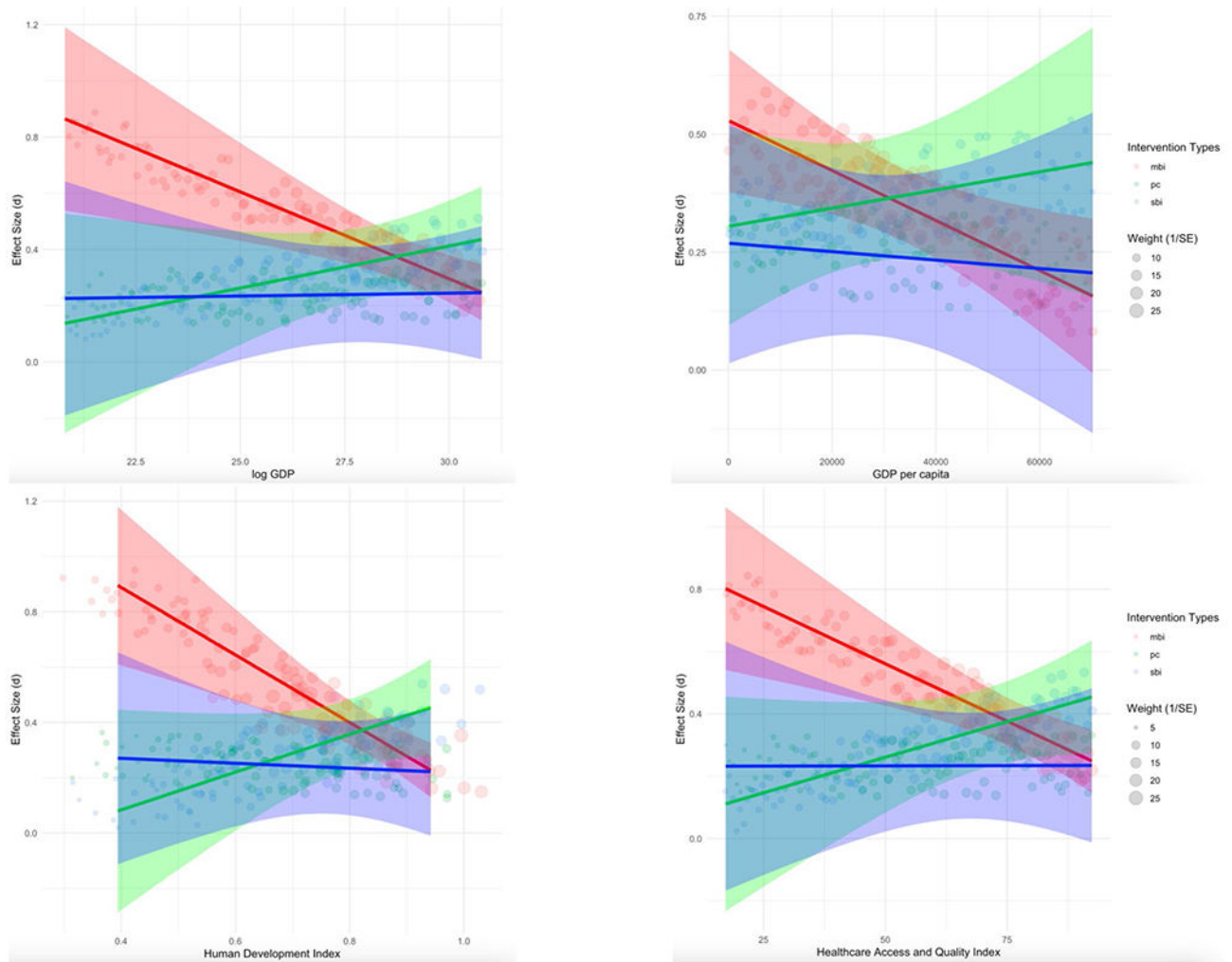


Figure 3.
Modeled Condition Impact

Note. Lines depict the interaction effects between intervention types and development indices, including log GDP (top left), GDP per capita (top right), HDI (bottom left), and HAQ (bottom right). They were computed from the meta-regression model clustered by report with small-sample corrections as reported in Table 4 using a sequence of 100 development indices (i.e., from min to max at an increment interval of max minus min divided by 100). The shading corresponds to 95% *CI*, while keeping the covariates of average age (28.79), percentages of females (43.65), expert facilitator (0.33), medical recruitment setting (0.49), culturally appropriate (0.23), and modified covariate for potential biases (0.23) at their grand means.

Table 1

Descriptive Statistics of Three Hundred and Thirty-One Included Reports (k = 1,364)

Variable	Inter-rater reliability	Count	M (SD) or percentages
<i>Report characteristics:</i>			
Publication year [^]	1.00	311	2011 (6.7)
Source type	1.00		
Journal article		325	98.19%
Other		2	0.60%
Institutional area	1.00		
Psychology		31	9.37%
Community/public health		97	29.31%
Medicine		110	33.23%
Epidemiology		18	5.44%
Social work		9	2.72%
Other		54	16.31%
Language of the report	1.00		
English		329	99.4%
Six-month follow up	1.00		
Yes		250	75.53%
No		79	23.87%
Number of participants [^]	1.00	327	254.80 (691.18)
Age in years [^]	1.00	329	29.49 (9.98)
Gender			
% men [^]	1.00	313	54.53 (36.01)
% women [^]	1.00	314	45.97 (35.91)
Racial/ethnic descent ²			
% White American [^]	1.00	254	21.94 (28.60)
% African American [^]	1.00	264	33.44 (35.75)
% Latin American [^]	1.00	245	15.32 (25.51)
% Asian American [^]	1.00	209	5.61 (21.19)
% Native American Indian [^]	1.00	210	2.3 (13.72)
% High school graduates [^]	1.00	180	44.24 (33.98)
Self-identified sexual orientation			
% heterosexual [^]	1.00	102	47.95 (42.7)
% Gay/bisexual or MSM [^]	1.00	94	53.68 (42.98)
Intention to treat	0.42		
Yes		91	27.49%
No		179	54.08%
<i>Intervention characteristics:</i>			
Sample targeted by race/ethnicity	1.00		
Yes		67	20.24%
No		249	75.23%

Variable	Inter-rater reliability	Count	<i>M (SD) or percentages</i>
Sample targeted by gender	1.00		
Yes		127	38.37%
No		189	57.10%
Targeted sample	1.00		
HIV positive*		55	16.52%
Intravenous drug user*		18	5.44%
Drug dependent*		21	6.34%
Men who have sex with men*		25	7.55%
Female sex workers*		2	0.60%
Prison inmates*		5	1.51%
Minority women*		3	0.91%
African American women*		8	2.42%
College students		8	2.42%
Middle school students		5	1.51%
Combination*		42	12.69%
Self-selected sample	1.00		
Yes		278	83.99%
No ^b		42	12.69%
Both		2	0.60%
Recruitment context	1.00		
Hospital/health clinic		141	42.60%
Drug treatment		26	7.85%
Social service		10	3.02%
Bar		8	2.42%
Street		13	3.93%
Classroom		23	6.95%
Multiple		40	12.08%
Exposure setting	1.00		
Health clinic		132	39.88%
Community		35	10.57%
Schools		19	5.74%
Mass media		2	0.60%
Multiple contexts		13	3.93%
Delivery medium	0.97		
Face-to-face		239	72.21%
Software		10	3.02%
Internet		9	2.72%
Television		9	2.72%
Radio		3	0.91%
Multiple context		11	3.32%
Delivery format	1.00		
Groups		107	32.33%

Variable	Inter-rater reliability	Count	<i>M (SD) or percentages</i>
Individuals		136	41.09%
Both		42	12.69%
Facilitator	0.93		
Doctor/nurse		43	12.99%
Public health educator		47	14.20%
Clinical psychologist		17	5.14%
Community leader		1	0.30%
Multiple		19	5.71%
Culturally appropriate	0.89		
Yes		77	23.26%
No		241	72.81%
Days between intervention and post-test^	0.88	317	164.79 (185.04)
Duration of the intervention (in hours)	0.88	217	9.07 (15.79)
Ensuring high intervention fidelity	0.97		
Yes		65	19.64%
No		266	80.36%
Attitudinal elements:			
Attitude arguments	0.63		
Yes		118	35.65%
No		114	34.44%
Threat arguments	0.45		
Yes		40	12.08%
No		145	43.81%
Norm arguments	0.64		
Yes		60	18.13%
No		139	41.99%
Informational arguments	0.55		
Yes		243	73.41%
No		32	9.67%
Motivational elements:			
Feedback	0.51		
Yes		64	19.34%
No		153	46.22%
Skill training elements:			
Skill training	0.69		
Yes		146	44.11%
No		89	26.89%
Goal setting	0.64		
Yes		66	19.94%
No		145	43.81%
Role playing	0.54		
Yes		57	17.22%

Variable	Inter-rater reliability	Count	<i>M</i> (<i>SD</i>) or percentages
No		160	48.34%

Note. *M* = mean, *SD* = standard deviation. A caret indicates variables used *r* = intercoder reliability for continuous variables; other variables used *κ* = intercoder reliability for categorical variables. An asterisk indicates the at-risk populations.

^a reported for interventions conducted in North America, as these categories are not applicable to most other continents.

^b includes captive audiences (e.g., participants recruited from a prison setting).

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Table 2**Outcome Type and Syndemic Categorization**

Outcome	Syndemic category
Abstinence	HIV/Sexual risk
Adolescent marriage	Other syndemic
Alcohol use	Substance use
Body mass index	Other syndemic
CD4	HIV/Sexual risk
Condom use/unprotected sex	HIV/Sexual risk
Condom-protected intercourse	HIV/Sexual risk
Contraception (other than condoms)	HIV/Sexual risk
Lower depression	Psychological wellbeing
Drug use	Substance use
HIV adherence	HIV/Sexual risk
HIV disclosure	HIV/Sexual risk
HIV prevalence	HIV/Sexual risk
HIV testing	HIV/Sexual risk
HIV treatment	HIV/Sexual risk
Intervention attendance	Other syndemic
Medication adherence	Substance use
Mental health	Psychological wellbeing
Past year physical and/or sexual IPV	HIV/Sexual risk
Physical health	Other syndemic
Quality of life	Other syndemic
Quality of life environmental	Other syndemic
Quality of life physical	Other syndemic
Quality of life psychological	Psychological wellbeing
Quality of life social	Psychological wellbeing
Risk sexual behavior	HIV/Sexual risk
Safe sex strategies	HIV/Sexual risk
School dropout	Other syndemic
Sex	HIV/Sexual risk
Sex and drinking	HIV/Sexual risk
Sex for money	HIV/Sexual risk
Sex partner selection	HIV/Sexual risk
STI rates	HIV/Sexual risk
STI testing	HIV/Sexual risk
Substance use	Substance use
Talk about HIV	HIV/Sexual risk
Tobacco treatment	Substance use
Unwanted pregnancy	Other syndemic
Viral load	HIV/Sexual risk

Table 3

Mean Estimated Effect Sizes of Different Intervention Types (Cluster = 324, k = 1348)

Variable	<i>b</i> (<i>SE</i>)	<i>df</i>
Single-behavior intervention	0.25* (0.12)	76.77
Multiple-behavior intervention	0.29** (0.08)	90.98
Passive control	0.04 (0.09)	56.85
I^2	94.63	

Note. Report of the robust variance estimation meta-regression using single-behavior intervention as the reference (i.e., intercept). *b* = unstandardized coefficient; *SE* = standard error; *df* = degrees of freedom; *p* = *p* value; *k* = number of effect sizes; I^2 = proportion of variance due to between-group heterogeneity.

[†]
p < .10,

*
p < .05,

**
p < .01,

p < .001

Table 4

Confirmatory Factor Analyses of HIV/Sexual Risk, Substance Use, Psychological Wellbeing and Other Syndemic Outcomes

Variable	<i>b</i> *
Factor loading	
HIV/sexual risk	
HIV/sexual risk latent variable 1	0.31***
HIV/sexual risk latent variable 2	1.49***
Substance use	
Substance use latent variable 1	1.00***
Substance use latent variable 2	1.00***
Overall syndemic	
HIV/sexual risk	0.56**
Substance use	0.76***
Psychological wellbeing	0.89***
Other syndemic	1.06***
Fit Indices	
χ^2 (df)	50.90*** (7)
RMSEA	0.1
CFI	0.94
TLI	0.87
SRMR	0.15
RFI	0.85
IFI	0.94

Note. *b** = Parameter estimates when all variables are standardized; RMSEA = Root Mean Square Error of Approximation; CFI = Comparative Fit Index; TLI = Tucker Lewis index; SRMR = (Standardized) Root Mean Square Residual; RFI = Relative Fit Index; IFI = Incremental Fit Index. Bold style indicates a good fit (i.e., CFI and IFI > .90 and RFI ~ 1).

 $p < .001$

Table 5
 Differential Effects of Multiple-Behavior Interventions Related to Country Log GDP, GDP Per Capita, HDI, and HAQ

Variable	Development indices							
	Log GDP		GDP per capita		HDI		HAQ	
	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>
Intercept	(Cluster = 278, <i>k</i> = 1180)		(Cluster = 278, <i>k</i> = 1180)		(Cluster = 276, <i>k</i> = 1172)		(Cluster = 282, <i>k</i> = 1192)	
	-0.96 (0.72)	29.00	-0.16 (0.18)	64.95	-0.68 [†] (0.36)	19.94	-0.41 (0.26)	28.28
Intervention type: MBI	2.63* (1.00)	50.99	0.22 (0.14)	55.28	1.57 ^{**} (0.49)	32.25	0.9 ^{**} (0.31)	39.26
Intervention type: PC	0.67 (0.90)	33.96	-0.04 (0.16)	39.67	0.5 (0.44)	20.55	0.2 (0.31)	22.18
Development index	0.03 (0.03)	32.07	0.00 (0.00)	36.78	0.68 (0.46)	20.40	0.00 (0.00)	28.19
Development index × Intervention type: MBI	-0.09* (0.04)	55.89	-0.00 [†] (0.00)	67.07	-1.9 ^{**} (0.6)	38.75	-0.01 ^{**} (0.00)	52.84
Development index × Intervention type: PC	-0.03 (0.03)	38.82	-0.00 (0.00)	57.83	-0.77 (0.56)	26.73	-0.00 (0.00)	31.82
<i>Covariates:</i>								
Average age	0.01 ^{**} (0.00)	94.75	0.01 ^{**} (0.00)	99.36	0.01 ^{**} (0.00)	94.71	0.01 ^{**} (0.00)	100.51
Percentages of females	0.00 (0.00)	117.30	0.00 (0.00)	117.90	0.00 (0.00)	116.52	0.00 (0.00)	119.32
Expert facilitator	0.13* (0.07)	145.25	0.15* (0.07)	151.71	0.13 [†] (0.07)	145.14	0.12 [†] (0.07)	147.31
Medical recruitment setting	0.02 (0.06)	154.86	0.01 (0.06)	152.54	0.01 (0.06)	152.80	0.04 (0.06)	157.98
Culturally appropriate	-0.05 (0.06)	100.37	-0.07 (0.07)	100.52	-0.06 (0.07)	99.58	-0.07 (0.07)	98.70
Modified covariate for potential biases	0.44 (0.38)	26.41	0.48 (0.4)	26.33	0.48 (0.39)	25.98	0.38 (0.37)	27.21
<i>F</i>	94.30		94.36		94.42		94.57	

Note. Log GDP = the log form of a country's overall gross domestic product; GDP per capita = overall gross domestic product of a country divided by its total population; HDI = human development index; HAQ = healthcare access and quality index; *b* = unstandardized coefficient; *SE* = standard error; *df* = degrees of freedom; *p* = *p* value; *k* = total number of effect sizes; average age = average age of the sample; percentages of females = percentages of female participants; expert facilitator = the intervention program was facilitated by experts (e.g., clinical psychologists); medical recruitment setting = participant recruited from medical settings; culturally appropriate = the intervention was culturally appropriate; clinical delivery setting = the intervention was delivered in clinical settings. *F* = proportion of variance due to between-group heterogeneity.

[†] *p* < .10,
 * *p* < .05,
 ** *p* < .01,
 *** *p* < .001

Table 6
Results of Planned Contrasts of Intervention Type across Levels of Development Index

Intervention type contrast	Log GDP		GDP per capita		HDI		HAQ	
	<i>M_{diff}</i> (SE)	<i>df</i>	<i>M_{diff}</i> (SE)	<i>df</i>	<i>M_{diff}</i> (SE)	<i>df</i>	<i>M_{diff}</i> (SE)	<i>df</i>
	Higher = 31.1		Higher = 53680		Higher = 0.956		Higher = 93.4	
SBI vs. MBI	0.21*** (0.00)	55.89	0.16*** (0.00)	67.07	0.25*** (0.00)	38.75	0.22*** (0.00)	52.84
SBI vs. PC	0.2 (0.24)	38.82	0.19 (0.20)	57.83	0.24 (0.28)	26.73	0.22 (0.26)	31.82
MBI vs . PC	-0.02*** (0.00)	30.01	0.02*** (0.00)	43.16	-0.01*** (0.00)	21.15	0.01*** (0.00)	24.32
	Medium = 28.7		Medium = 31598		Medium = 0.816		Medium = 73.6	
SBI vs. MBI	0.00*** (0.00)	55.89	0.00*** (0.00)	67.07	-0.01*** (0.00)	38.75	-0.02*** (0.00)	52.84
SBI vs. PC	0.13 (0.24)	38.82	0.12 (0.20)	57.83	0.13 (0.28)	26.73	0.13 (0.26)	31.82
MBI vs . PC	0.14*** (0.00)	30.01	0.12*** (0.00)	43.16	0.15*** (0.00)	21.15	0.15*** (0.00)	24.32
	Lower = 26.3		Lower = 9516		Lower = 0.677		Lower = 54.0	
SBI vs. MBI	-0.22*** (0.00)	55.89	-0.16*** (0.00)	67.07	-0.28*** (0.00)	38.75	-0.25*** (0.00)	52.84
SBI vs. PC	0.06 (0.24)	38.82	0.06 (0.20)	57.83	0.03 (.28)	26.73	0.05 (0.26)	31.82
MBI vs . PC	0.29*** (0.00)	30.01	0.22*** (0.00)	43.16	0.3*** (0.00)	21.15	0.3*** (0.00)	24.32

Note. MBI = multiple-behavior intervention; SBI = single-behavior intervention; PC = passive control. SBI vs. MBI = comparing difference from SBI to MBI; SBI vs. PC = comparing difference from SBI to PC; MBI vs. PC = comparing difference from MBI to PC. Mean differences between contrast groups and standard errors in parentheses were derived using all the data (i.e., regressing predicted ϕ on intervention types and development indices clustered by report). Degrees-of-freedom (*df*) method: Derived from the RVE meta-regression models with small-sample corrections.

† $p < .10$,

* $p < .05$,

** $p < .01$,

*** $p < .001$

Table 7

Differential Effects of Multiple-Behavior Interventions Related to Gay/bisexual or MSM Representation and Being Young Adults Across Countries

Variable	Disadvantaged group status			
	Gay/bisexual or MSM representation		Young adult	
	<i>b</i> (<i>SE</i>)	<i>df</i>	<i>b</i> (<i>SE</i>)	<i>df</i>
	(Cluster = 89, <i>k</i> = 415)		(Cluster = 300, <i>k</i> = 1261)	
Intercept	-0.24 (0.25)	9.48	-0.16 (0.33)	30.86
Intervention type: MBI	0.63 ** (0.19)	8.73	0.25 (0.31)	41.74
Intervention type: PC	0.5 (0.35)	9.51	0.07 (0.34)	36.40
Disadvantaged group status	-0.00 (0.00)	11.63	-0.01 (0.01)	31.47
Disadvantaged group status × Intervention type: MBI	-0.01 * (0.00)	16.77	-0.01 (0.01)	51.51
Disadvantaged group status × Intervention type: PC	-0.01 * (0.00)	13.44	-0.01 (0.01)	29.53
<i>Covariates:</i>				
Average age	0.00 (0.00)	29.11	-	-
Percentages of females	-0.01 * (0.00)	25.71	0.00 (0.00)	127.03
Expert facilitator	0.05 (0.12)	40.71	0.15* (0.07)	161.79
Medical recruitment setting	0.12 (0.15)	32.50	0.08 (0.06)	168.61
Culturally appropriate	0.06 (0.09)	17.83	-0.06 (0.06)	105.75
Modified covariate for potential biases	1.13 * (0.4)	22.11	0.25 (0.33)	29.78
\mathcal{I}^2	87.12		94.56	

Note. Report of the robust variance estimation meta-regression using single-behavior intervention as the reference (i.e., intercept). *b* = unstandardized coefficient; *SE* = standard error; *p* = *p* value; *k* = the number of effect sizes; gay/bisexual or MSM representation = percentage of gay/bisexual or MSM in the sample; average age = average age of the sample; percentages of females = percentages of female participants; expert facilitator = the intervention program was facilitated by experts (e.g., clinical psychologists); medical recruitment setting = participant recruited from medical settings; culturally appropriate = the intervention was culturally appropriate; clinical delivery setting = the intervention was delivered in clinical settings; \mathcal{I}^2 = proportion of variance due to between-group heterogeneity.

[†] *p* < .10,

* *p* < .05,

** *p* < .01,

*** *p* < .001

Table 8

Differential Effects of Multiple-Behavior Interventions Related to Minority Group Status and Being Young Adults in the US

Variable	Minority group status					
	Non-White representation		Black representation		Latinx representation	
	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>
	(Cluster = 174, <i>k</i> = 737)		(Cluster = 151, <i>k</i> = 604)		(Cluster = 139, <i>k</i> = 584)	
Intercept	0.16 (0.19)	24.03	-0.11 (0.27)	30.57	0.03 (0.33)	36.29
Intervention type: MBI	-0.36 [†] (0.18)	19.33	-0.21 (0.22)	27.49	-0.37 [†] (0.21)	31.63
Intervention type: PC	-0.3 (0.25)	10.22	-0.51 (0.29)	14.79	-0.26 (0.27)	18.91
Disadvantaged group status	0.00 (0.00)	17.29	0.00 (0.00)	15.00	-0.01 (0.01)	3.51
Disadvantaged group status × Intervention type: MBI	0.00 (0.00)	25.31	0.00 (0.00)	23.19	0.01 (0.01)	6.00
Disadvantaged group status × Intervention type: PC	0.00 (0.00)	17.12	0.01 (0.01)	22.64	0.00 (0.01)	2.78
<i>Covariates:</i>						
Average age	0.01 ^{**} (0.00)	58.94	0.01 ^{**} (0.00)	70.94	0.01 [*] (0.00)	61.70
Percentages of females	0.00 (0.00)	59.56	0.00 (0.00)	51.83	0.00 (0.00)	51.80
Expert facilitator	0.11 (0.07)	88.47	0.08 (0.09)	74.72	0.16 [†] (0.09)	68.62
Medical recruitment setting	0.03 (0.07)	81.90	0.01 (0.08)	73.10	-0.01 (0.08)	66.56
Culturally appropriate	0.00 (0.00)	47.87	0.01 (0.08)	43.14	-0.01 (0.09)	42.03
Modified covariate for potential biases	0.4 (0.45)	18.49	0.6 (0.64)	14.36	0.66 (0.66)	14.14
<i>F</i> ²	93.13		94.16		94.22	
	Other representation		Gay/bisexual MSM representation		Young adult	
	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>	<i>b</i> (SE)	<i>df</i>
	(Cluster = 138, <i>k</i> = 573)		(Cluster = 59, <i>k</i> = 252)		(Cluster = 174, <i>k</i> = 737)	
Intercept	-0.09 (0.33)	42.67	-0.02 (0.21)	4.43	-0.46 (0.51)	16.99
Intervention type: MBI	-0.10 (0.20)	28.82	0.28 [†] (0.14)	7.37	0.36 (0.45)	20.17
Intervention type: PC	-0.04 (0.26)	17.72	0.05 (0.56)	4.09	0.39 (0.47)	21.45
Disadvantaged group status	0.00 (0.00)	2.43	-0.00 [†] (0.00)	5.71	0.02 (0.01)	18.59
Disadvantaged group status × Intervention type: MBI	-0.00 (0.01)	4.95	-0.00 [†] (0.00)	11.92	-0.01 (0.01)	29.20
Disadvantaged group status × Intervention type: PC	-0.01 (0.01)	3.75	-0.00 (0.00)	5.60	-0.02 (0.01)	21.41
<i>Covariates:</i>						
Average age	0.01 [*] (0.00)	52.90	-0.01 (0.00)	16.29	-	-
Percentages of females	0.00 (0.00)	53.41	0.00 (0.00)	11.39	0.00 (0.00)	60.13
Expert facilitator	0.13 (0.10)	74.80	0.15 [†] (0.08)	20.72	0.1 (0.07)	89.51
Medical recruitment setting	0.04 (0.09)	68.14	-0.05 (0.07)	15.65	0.04 (0.07)	73.95
Culturally appropriate	-0.04 (0.10)	44.13	-0.01 (0.11)	6.04	0.00 (0.00)	43.52
Modified covariate for potential biases	0.51 (0.70)	12.78	0.8 [*] (0.36)	17.88	0.35 (0.43)	20.01

Variable	Minority group status					
	Non-White representation		Black representation		Latinx representation	
	<i>b (SE)</i>	<i>df</i>	<i>b (SE)</i>	<i>df</i>	<i>b (SE)</i>	<i>df</i>
I^2	95.01		79.01		93.09	

Note. Report of the robust variance estimation meta-regression using single-behavior intervention as the reference (i.e., intercept). *b* = unstandardized coefficient; *SE* = standard error; *df* = degrees of freedom; *p* = *p* value; *k* = the number of effect sizes; average age = average age of the sample; percentages of females = percentages of female participants; expert facilitator = the intervention program was facilitated by experts (e.g., clinical psychologists); medical recruitment setting = participant recruited from medical settings; culturally appropriate = the intervention was culturally appropriate; clinical delivery setting = the intervention was delivered in clinical settings; I^2 = proportion of variance due to between-group heterogeneity.

[†]*p* < .10,

**p* < .05,

***p* < .01,

****p* < .001

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Table 9 Differential Effects of Multiple-Behavior Interventions Related to Intersectionality of Racial/Ethnic Minority and MSM Representation in the US

Variable	Minority group status					
	Non-White representation		Black representation		Latinx representation	
	<i>b</i> (<i>SE</i>)	<i>df</i>	<i>b</i> (<i>SE</i>)	<i>df</i>	<i>b</i> (<i>SE</i>)	<i>df</i>
Intercept	(Cluster = 98, <i>k</i> = 448) (Cluster = 85, <i>k</i> = 364) (Cluster = 80, <i>k</i> = 365)					
	0.35 (0.54)	11.37	-0.4 (0.56)	16.82	-0.56 (0.38)	20.17
MSM representation	-9.99 (9.83)	10.96	-0.64 (9.5)	15.29	3.15 (5.66)	19.76
Minority group status	-0.00 (0.01)	11.36	0 (0.01)	13.22	-0.00 (0.01)	9.02
MSM representation × Minority group status	0.08 (0.12)	14.77	0.01 (0.15)	14.27	0.02 (0.23)	7.63
<i>Covariates:</i>						
Average age	0.01* (0.00)	25.96	0.01* (0.00)	29.38	0.01* (0.00)	39.24
Percentages of females	0.00 (0.00)	35.50	0.00 (0.00)	32.44	0.00 (0.00)	34.33
Expert facilitator	0.04 (0.07)	48.20	-0.01 (0.09)	41.91	0.09 (0.09)	38.61
Medical recruitment setting	0 (0.08)	46.38	-0.07 (0.1)	43.04	-0.09 (0.09)	38.68
Culturally appropriate	-0.02 (0.08)	28.74	0.04 (0.09)	28.54	0.09 (0.09)	26.86
Modified covariate for potential biases	0.82 [†] (0.44)	20.78	1.22* (0.5)	14.89	1.3* (0.53)	15.40
<i>F</i>	89.42		90.77		89.39	

Note. Report of the robust variance estimation meta-regression using single-behavior intervention as the reference (i.e., intercept). *b* = unstandardized coefficient; *SE* = standard error; *df* = degrees of freedom; *p* = *p* value; *k* = the number of effect sizes; average age = average age of the sample; percentages of females = percentages of female participants; expert facilitator = the intervention program was facilitated by experts (e.g., clinical psychologists); medical recruitment setting = participant recruited from medical settings; culturally appropriate = the intervention was culturally appropriate; clinical delivery setting = the intervention was delivered in clinical settings; *F* = proportion of variance due to between-group heterogeneity.

[†] *p* < .10,

* *p* < .05,

** *p* < .01,

*** *p* < .001