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Couples Motivational Interviewing with Mobile Breathalyzers to Reduce Alcohol Use in South Africa: A Pilot Randomized Controlled Trial of Masibambisane

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| | |

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Manuscripts

1 **Couples Motivational Interviewing with Mobile Breathalyzers to Reduce Alcohol**
2 **Use in South Africa: A Pilot Randomized Controlled Trial of Masibambisane**

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7
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2
3 **Abstract**4
5 **Introduction:**

6
7 33 Heavy alcohol use among people living with HIV in sub-Saharan Africa can hinder the
8
9 34 success of HIV treatment programs, impacting progress towards UNAIDS goals. Primary
10
11 35 partners can provide critical forms of social support to reduce heavy drinking and could
12
13 36 be included in motivational interviewing (MI) interventions to address heavy drinking;
14
15 37 however, few studies have evaluated MI interventions for couples living with HIV in sub-
16
17 38 Saharan Africa. We aim to evaluate the feasibility and acceptability of a couple-based MI
18
19 39 intervention with mobile breathalyzer technology to reduce heavy alcohol use and
20
21 40 improve HIV treatment outcomes among HIV-affected couples in South Africa.

22
23 **Methods and analysis:**

24
25 43 We will employ a three-arm randomized controlled trial to assess the efficacy of couple-
26
27 44 based MI (MI-only arm) and in conjunction with mobile breathalyzers (MI-plus arm) to
28
29 45 address alcohol use and HIV outcomes, as compared to enhanced usual care (control
30
31 46 arm). We will enroll heterosexual couples aged 18-49 in a primary relationship for at least
32
33 47 six months who have at least one partner reporting hazardous alcohol use and on
34
35 48 antiretroviral therapy for six months. Participants in both MI arms will attend three
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37 49 manualized counselling sessions and those in the MI-plus arm will receive real-time
38
39 50 feedback on blood alcohol concentration (BAC) levels using a mobile breathalyzer.
40
41 51 Couples randomized in the control arm will receive enhanced usual care based on the
42
43 52 South African ART Clinical Guidelines. Feasibility and acceptability indicators will be
44
45 53 analyzed descriptively, and exploratory hypotheses will be examined through regression
46
47 54 models considering timepoints and treatment arms.

48
49 **Ethics and dissemination:**

50
51 58 The study was approved by the University of California, San Francisco (HRPP; Protocol
52
53 59 Number 21-35034) and HSRC Research Ethics Committee (REC: Protocol Number
54
55 60 1/27/20/21). We will disseminate the results at local community meetings, community-
56
57 61 level health gatherings, and conferences focused on HIV and alcohol use.

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Strengths and limitations of this study

- Intervention was developed and tailored to the cultural context of heterosexual couples in a rural setting of KwaZulu-Natal
- Uses a dyadic approach to intervene to collect and analyse intervention effects on both partners
- Incorporates an alcohol biomarker to mitigate the limitations of self-reported drinking behavior
- Small pilot study not powered to detect changes in behavioral outcomes
- Relatively short follow-up period of six months does not allow for the assessment of long-term health effects

Trial registration: ClinicalTrials.gov Protocol Registration; NCT05756790; registered on March 6, 2023; <https://register.clinicaltrials.gov/>

Protocol Version 1.0: 19 December 2023

Keywords: Motivational interviewing with couples; heavy alcohol use; HIV/AIDS; antiretroviral therapy; South Africa

81 Introduction

82 *Background*

83 In sub-Saharan Africa (SSA), alcohol use is described as “adding fuel to the fire” for
84 people living with HIV (PLWH) (1), threatening the success of HIV treatment programs
85 and progress towards United Nations Programme on HIV/AIDS (UNAIDS) goals (2–5).
86 South Africa is severely impacted by HIV, particularly in KwaZulu-Natal (KZN) where 27%
87 of adults are infected with HIV (6). At 11 liters of pure alcohol per year, South Africa has
88 some of the highest levels of per capita drinking in the world (7). Among PLWH who drink
89 in South Africa, 50-90% report heavy alcohol use (8–10). Notably, South Africa also has
90 some of the highest rates of gender-based violence worldwide (11,12), which is closely
91 linked to heavy alcohol use (13,14). For PLWH, alcohol use contributes to poor adherence
92 to antiretroviral therapy (ART) and retention in HIV care (15–17).

93 Our research in SSA suggests that primary partners are key to the success of alcohol
94 interventions given their critical role in helping people reduce alcohol use and the couple
95 dynamics that intersect with alcohol use (18–21). In South Africa, partners mitigate the
96 harms of alcohol use by helping drinkers manage their alcohol use while maintaining
97 adherence to ART (19); however, communication around reducing alcohol use is not
98 always effective and can be limited by gender-based power imbalances. This suggests
99 the need for interventions to build couples’ communication skills and shared decision-
100 making around alcohol use (20). Harnessing this powerful form of social support is critical
101 in a setting where clinical services for alcohol misuse are inadequate and can be costly
102 for patients.

103 One approach that has been effective at reducing alcohol use among PLWH is
104 motivational interviewing (MI) in conjunction with mobile technology for real-time feedback
105 on drinking levels (22–29). MI is a collaborative, goal-oriented style of communication
106 with particular attention to the language of change (30). It is designed to strengthen
107 personal motivation for and commitment to a specific goal by eliciting and exploring the
108 person’s own reasons for change in an atmosphere of acceptance and compassion (30).
109 Few MI approaches with couples have been developed for alcohol use, particularly in the
110 African context (21,31–33). Although Starks articulated a comprehensive framework for
111 MI practice with couples (34), most of the research on feasibility and acceptability (21,35),

1 112 and preliminary efficacy (32,36) of the approach has come from the study of male couples
2 113 in the US.

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5 114 In studies with individuals, daily monitoring of drinking levels, when paired with MI, has a
6 115 greater effect on drinking than MI alone (27–29) and we hypothesize that monitoring may
7 116 have additional benefits with couples. Although primary partners are generally aware of
8 117 a person's alcohol use, they may have inaccurate knowledge of drinking amounts and
9 118 frequency if not drinking together. Accurate knowledge of drinking levels in real-time is
10 119 critical to trigger couples' communication as well as timely and tailored social support.
11 120 Mobile breathalyzers have been shown to be a feasible and acceptable strategy for self-
12 121 monitoring alcohol use in studies with individuals and new products have been developed
13 122 for dyads that allow for sharing of blood alcohol concentration (BAC) levels with support
14 123 partners via a mobile app (37–39). In sum, mobile breathalyzers can provide real-time
15 124 feedback and support, which can be synergistic with an MI approach with couples that
16 125 fosters couple communication and problem-solving skills to effectively engage with the
17 126 breathalyzers and work together to reduce alcohol use.

27 28 127 **Objectives**

29
30 128 The main aim of this study is to evaluate the feasibility and acceptability (F&A) of a
31 129 couples-based intervention for heavy alcohol consumption among HIV-affected couples
32 130 (*Masibambisane*, “Let's work together” in *isiZulu*). Our primary hypothesis is that
33 131 *Masibambisane* will be feasible and acceptable. As exploratory hypotheses, we expect
34 132 that participants who receive the intervention will report lower number of drinking days
35 133 and heavy alcohol use (a combined measure of self-report and an alcohol biomarker),
36 134 and greater rates of viral suppression and adherence to ART at follow-up visits.

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43 44 136 **Methods and analysis**

45 46 137 ***Trial design***

47 138 We will conduct a three-arm randomized controlled trial (RCT) with couples randomized
48 139 to the following arms: 1) an enhanced usual care (EUC) control condition; 2) couple-
49 140 based MI (MI-only arm); and 3) couple-based MI with mobile breathalyzers (MI-plus arm).
50 141 Couples in arm 2 and 3 will receive three MI sessions over a 60-day period with an
51 142 experienced counselor to help strengthen communication and problem-solving skills
52 143 around alcohol use. Couples in Arm 3 will use a mobile breathalyzer and app for 60 days

1 144 and receive the same MI sessions, which will incorporate feedback on BAC results into
2 145 the sessions. This design will allow us to assess the efficacy of couple-based MI alone
3 146 and the added synergistic effect of the mobile breathalyzers on alcohol use and HIV
4 147 outcomes (e.g., adherence to ART, viral suppression).
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9 149 **Study setting**

11 150 The *Masibambisane* study will be conducted by the Human Sciences Research Council
12 151 (HSRC) in the Sweetwaters community, a rural area west of the capital of KwaZulu-Natal,
13 152 Pietermaritzburg, South Africa.
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18 154 **Eligibility criteria**

19 155 Couples will be included in the study if they are: (1) in a primary relationship for at least
20 156 six months; (2) aged 18-49; (3) have at least one partner (the “index patient”) with a
21 157 positive AUDIT-C screen (score of 3 or more for women and 4 for of more for men;
22 158 modified to cover the prior 3 months) (40) and on ART for at least six months. We expect
23 159 all participants to be on oral ART regimens as long-acting ART was not available at the
24 160 time of this study in South Africa. All participants living with HIV will be required to have
25 161 disclosed their HIV status to their partner in the study. Lastly, both partners will separately
26 162 agree to participate in order for the couple to be enrolled.
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30 163
31 164 We will exclude participants with an AUDIT-C score greater than 12, indicating risk of
32 165 severe alcohol use disorder. Participants with severe drinking issues may not benefit from
33 166 a short-term counseling-based intervention and may need more intensive treatment than
34 167 our study can provide. Our intervention may also not be appropriate for couples
35 168 experiencing severe intimate partner violence (IPV). Thus, we will exclude those who fear
36 169 for their safety by participating in the study and/or report severe IPV in the past 3 months.
37 170 IPV is assessed using the WHO measure for South Africa, which assesses physical,
38 171 sexual, and emotional violence, and determines whether it is mild, moderate, or severe
39 172 (41). This trial does not place restrictions on concomitant receipt of care for alcohol use
40 173 or HIV care and treatment.
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187 **Intervention development**

188 We adapted the *Masibambisane* intervention from the 3-session couples MI intervention
189 protocol originally developed by Starks et al. for use in the *Couples Health Project* (36).
190 The original intervention was intended to reduce drug use and enhance primary HIV
191 prevention among male couples in the US. In contrast, the *Masibambisane* intervention
192 will address heavy alcohol use among heterosexual couples in South Africa in which at
193 least one partner is living with HIV. The adaptation process therefore had to consider: 1)
194 cultural and linguistic context; 2) reformulation of the new target behavior (i.e., to heavy
195 alcohol use); and, 3) integration of the mobile breathalyzer component.

196
197 We followed the ADAPT-ITT framework (42) to arrive at the final version of the
198 *Masibambisane* intervention. Consistent with step 5 in the ADAPT-ITT framework, we
199 conducted focus group discussions (FGDs) with 36 key stakeholders to gain feedback on
200 the intervention content and activities, including perceptions of the mobile breathalyzer
201 technology. This feedback was integrated in the creation of a modified intervention
202 manual (ADAPT-ITT step 6). The revised manual was reviewed by 8 members of the
203 research team during the intervention training process (ADAPT-ITT step 7) – including
204 the counselors who would deliver the intervention. Their feedback was used to refine and
205 finalize the *Masibambisane* manual to maximize usability and enhance cultural relevance.

206 ***Masibambisane* intervention arms**

207 Participants in the MI-only and MI-plus arms will receive three in-person manualized MI
208 sessions as a couple with a trained counselor in the language of their preference (either
209 *isiZulu* or English). Sessions take place approximately 30 days apart over a period of 2
210 months. In addition, the index participant in the MI-plus arm will make use of the mobile
211 breathalyzer and companion app, which will deliver real-time feedback on the index
212 participant's BAC levels to both partners for two months. The couples randomized to MI-
213 plus will receive brief technology training on how to operate the mobile breathalyzer and
214 app followed by a short trial period to become familiar with the technology before starting
215 intervention activities. All sessions are conducted with both partners together and each
216 lasts 60 to 75 minutes. The manual will provide guidance on sequencing of content. It is
217 executed in a manner consistent with the spirit, processes, and techniques of couples MI
218 outlined by Starks (34,36).

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2
3 211 **Session 1.** The counselor first orients the couple to the structure and nature of the
4 212 intervention and reminds them about the limits of confidentiality. After initial engagement
5 213 and rapport building, the counselor invites the couple to reflect on communication
6 214 strengths and weaknesses before engaging in strengths-based communication skill
7
8 215 building. The topic of alcohol use is introduced through the use of a calendar activity
9 216 developed for Dr. Starks' previous studies (32,36). Partners who report heavy alcohol use
10
11 217 at baseline complete the calendar by indicating days they consumed alcohol in the past
12
13 218 30 days. This serves as an immediate feedback tool that the counselor uses to catalyze
14
15 219 a conversation about alcohol use and evoke relevant change talk. This discussion
16
17 220 culminates in the couple identifying what they would like alcohol use to look like in the
18
19 221 coming month and developing a shared plan to accomplish that goal. The session ends
20
21 222 with the counselor inviting the couple to notice communication successes and challenges
22
23 223 and to schedule a pleasant event together in the coming month (in addition to
24
25 224 summarizing the couple's alcohol related goals and plans).
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27 225

28 226 **Session 2.** The session begins with a check-in on recent communication and goals from
29
30 227 the previous session. The couple then completes a values card-sort exercise highlighting
31
32 228 shared values and joint goals. For *Masibambisane*, the standard values card sort deck
33
34 229 (43) used in previous MI interventions with couples (36) was modified to increase cultural
35
36 230 relevance and translated into *isiZulu*. Following the card-sort exercise, counselors refocus
37
38 231 the conversation on alcohol use by completing another calendar activity. For participants
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40 232 randomized to couples MI, this procedure mirrors that used in Session 1. For couples
41
42 233 randomized to MI-plus, the counselor presents the couple with breathalyzer data for the
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44 234 index partner from the prior month, presented in a calendar format. Data for the non-index
45
46 235 partner (if also reporting heavy alcohol use at baseline) are added to this calendar. In
47
48 236 addition to debriefing the calendar, couples in the MI-plus condition discuss their
49
50 237 experiences using the breathalyzer and receiving the BAC readings of their partner. After
51
52 238 the calendar is created and debriefed, the counselor further evokes change talk with a
53
54 239 series of questions about potential consequences of drinking. Similar to session 1, the
55
56 240 discussion culminates in the couple identifying what might be reasonable drinking limits
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58 241 for the coming month and developing a shared plan to accomplish that goal. The session
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60 242 ends with the counselor inviting the couple to notice communication successes and

243 challenges and to schedule a pleasant event together in the coming month (in addition to
244 summarizing the couple's alcohol related goals and plans).

245
246 **Session 3.** The session begins with a check-in on recent communication and goals from
247 the previous session. Similar to session 2, counselors then refocus the conversation on
248 alcohol use by completing another calendar activity. As in session 2, participants
249 randomized to MI-only complete the calendar following session 1 procedures. Those
250 randomized to MI-plus are presented with a calendar containing prior month breathalyzer
251 data. After the calendar is created and debriefed, the counselor further evokes change
252 talk with a series of questions about potential consequences of drinking specifically for
253 HIV-related health care outcomes and the couple's communication and sexual
254 interactions. Similar to session 1, this discussion culminates in the couple identifying their
255 drinking goals for the coming month and developing a shared plan to accomplish that
256 goal. Finally, counselors engage in a termination discussion. This begins by inviting the
257 couple to reflect on their experiences over the past two months while engaged in the
258 intervention. The couple then looks ahead and considers long-term goals – including
259 specific goals for limits on alcohol use – and constructs a shared plan to accomplish them.

261 **Mobile breathalyzer and app**

262 We will use BACtrack View®, which consists of a handheld commercial-grade
263 breathalyzer and accompanying mobile app. Index patients will receive twice-daily SMS
264 message requests to complete a breathalyzer reading at 11 am and again at 8 pm. Given
265 the frequent power outages in South Africa, which often result in a loss of cellular service,
266 participants will be allowed to complete missed tests as soon as the power returns. To
267 avoid disruptions in cellular service by having to manually purchase data, we will
268 automatically provide cellular data to perform the tests. We will also provide phones to
269 participants who do not have compatible smartphones and power banks to keep phones
270 and breathalyzers charged during power outages.

271
272 To complete a breathalyzer test, the participant will log into the mobile phone app and
273 follow a series of prompts to blow into the breathalyzer in front of the phone camera,
274 which displays the BAC value, and transmits the BAC value and photo of the participant
275 taking the test to the BACtrack View® server for storage. After successfully completing

1 276 the test, the partner will receive an SMS message informing them of the BAC value from
2 277 the index patient. The study coordinator is notified of BAC results and/or missed tests and
3
4 278 can log into the BACtrack View® app to view all tests results completed over a monthly
5
6 279 period. A trained technology navigator will be assigned to each couple, who will reach out
7
8 280 to couples who are missing tests and will be available for support as couples are getting
9
10 281 started with the BAC tests. At the end of each 30-day period, BAC results are mapped
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12 282 onto monthly calendars and used in subsequent MI counseling sessions.

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14 284 **Control arm: Enhanced usual care (EUC)**

15 285 Couples in the control arm will receive EUC, with usual care defined by the South African
16
17 286 national 2019 ART Clinical Guidelines (44). As part of clinical care for HIV, the harms of
18
19 287 alcohol use are briefly discussed during the morning health talks in the waiting rooms of
20
21 288 HIV clinics. HIV clients are advised that alcohol intake should be fewer than 2 standard
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23 289 drinks/day for men and 1 for women, and drinking should not occur daily (at most 5 out
24
25 290 of 7 days per week). After randomization, couples in the control arm will receive additional
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27 291 alcohol counseling modeled on WHO guidelines and Conroy et al.'s intervention in
28
29 292 Malawi, which uses participants' baseline AUDIT scores for messaging around alcohol
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31 293 reduction and lasts 10-15 minutes (45). In selecting the control, we chose to balance our
32
33 294 ethical obligation to provide basic health information on alcohol use (minimal in this
34
35 295 setting), while maximizing the generalizability of our findings to inform a future RCT, which
36
37 296 will employ a EUC control group. Clinical trial experts recommend the usual care condition
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39 297 over other designs such as a time-and-attention control (TAC) when the long-term goal
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41 298 is to inform implementation science and scale-up (46,47). Our long-term goal will be to
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43 299 test the effectiveness of a scalable alcohol intervention. Moreover, because TAC designs
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45 300 have an active but different intervention, there is the risk of positively-biased intervention
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47 301 results because the comparison arm can distract participants from making reductions in
48
49 302 alcohol use they would have otherwise made (46,47).

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304 **Training of staff**

305 305 Given the skills required to deliver MI, we will hire certified HIV testing counselors with 2+
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307 306 years of counselling and/or facilitation and community experience. Facilitators and the
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308 307 HSRC research manager will attend a week-long didactic training workshop (in-person,

1 308 at the HSRC) with Dr. Starks. Dr. Starks is a licensed clinical psychologist and an MI-
2 309 trainer certified by the Motivational Interviewing Network of Trainers.
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5
6 311 The training workshop will begin with a 1-day introduction to individual MI skills (30). This
7 312 workshop will focus on the spirit of MI, engaging skills (open questions, affirmations,
8 313 reflections, and summary statements), and recognizing change talk (expressions of
9 314 desire, ability, reasons, need, commitment, activation, and taking-steps to change). The
10 315 first training day will end with a demonstration of couples MI delivered in *isiZulu* (through
11 316 a translator) by Dr. Starks. Days 2 through 5 will focus on the spirit, processes, and skills
12 317 of MI with couples. Activities will consist of brief didactic presentations of content
13 318 interspersed with worksheets to reinforce knowledge acquisition and a wide variety of
14 319 role-play activities permitting practice. Beginning in day 3, role play activities will be used
15 320 to introduce counselors to key aspects of the intervention protocol and facilitate practice
16 321 with immediate feedback from Dr. Starks.
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26 323 Following the training workshop, all interventionists will complete a series of training mock
27 324 sessions to practice the intervention content. These will be completed in English,
28 325 recorded, and reviewed by Dr. Starks. Counselors will receive written feedback and meet
29 326 biweekly with Dr. Starks to discuss progress in the mock session process and review
30 327 relevant skills. All interventionists will complete a minimum of 2 mock sessions for each
31 328 intervention component before being cleared to deliver the intervention to participants.
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39 330 We will also train a pair of interviewers to recruit couples and conduct assessment visits,
40 331 who will be gender-matched to partners. Drs. Conroy and Butterfield will lead additional
41 332 training with staff, covering topics on couples counseling, the mobile breathalyzer
42 333 technology, how to handle ethical issues with couples, health education around alcohol
43 334 use and HIV, the intervention manuals and procedures, and professional conduct.
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49 336 **Fidelity monitoring and supervision**

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51 338 Once cleared, interventionists will meet monthly (via Zoom) with Dr. Starks for group
52 339 supervision while sessions are ongoing during the trial. These meetings will provide an
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1 340 opportunity to present and discuss cases, review relevant skills, and discuss ongoing
2 341 challenges to protocol delivery.
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5 342 Given the large number of sessions conducted, we will select a sample of sessions
6 343 (around 15%) to perform additional fidelity checks giving equal attention to all counselors
7 344 and all sessions. For these sessions, a peer facilitator (i.e., another counselor) or the
8 345 research manager will complete a checklist using either transcripts or audio-recordings
9 346 to ensure each activity in the manual was covered. Intervention sessions will be audio-
10 347 recorded. Self-assessment forms will contain rating for key MI components (e.g.,
11 348 collaboration, respect, etc.). A separate space on the checklist and self-assessment forms
12 349 will be provided for written comments. After each session, counselors will complete the
13 350 self-assessment form. Completed forms will be discussed in regular Zoom calls with the
14 351 team to discuss areas where further guidance is needed and to help problem-solve
15 352 challenges. Finally, Dr. Starks will listen and provide feedback on any sessions conducted
16 353 with English-speaking couples as an additional check on fidelity to the intervention
17 354 protocol.
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30 356 **Recruitment**

31 357 Community-based recruitment will be used to identify index patients at community-based
32 358 organizations or locations in the community where people who drink alcohol can be found.
33 359 Recruiters will use procedures established at HSRC to identify and recruit participants
34 360 using a community mobilization approach. A team of recruiters will target individuals and
35 361 couples in public areas in the community, including alcohol venues (e.g., shebeens, bottle
36 362 shops), markets, sports grounds, taxi ranks, HIV clinics, and community events. Though
37 363 couples will be targeted together if possible, couples may not be together in public (48)
38 364 and this could hinder successful recruitment of couples into research studies in the area.
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47 366 Passive recruitment will also be utilized. This includes distributing community flyers
48 367 describing the study and encouraging interested individuals to contact the project staff by
49 368 calling or sending a free "please call me" SMS text message to the listed cellular phone
50 369 number. Recruiters will respond to these messages as soon as possible, typically no later
51 370 than the next working day. Passive recruitment will further be employed through flyers
52 371 placed at the clinics. Clinic-based outreach teams and care providers will assist in
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1 372 identifying HIV patients who use alcohol use and have been on ART for at least six
2 373 months, referring them to HSRC recruiters. In all recruitment approaches, recruiters will
3 374 ask potential participants if they would like to hear about the study and explain the nature
4 375 of the study using standard recruitment scripts.
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8 377 **Screening for participation**

9 378 Screening will be a two-step process. The initial screener will be delivered either in-person
10 379 or over the phone. If recruited in person, the screener will take place in a private location
11 380 identified by the recruiter. Partners in a couple will be screened separately to ensure
12 381 confidentiality. If the participant cannot complete the initial screener in the field, the
13 382 recruiter will record their contact information for a later phone screening. Once deemed
14 383 eligible to continue, the recruiter will inform the index participant that their partner must
15 384 also be screened. Contact information for the recruited partner will be collected and
16 385 permission to call them will be obtained. Alternatively, the partner can initiate contact via
17 386 a "please call me" SMS text message. The index participant will be provided with study
18 387 information to share with the partner.
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21 389 Couples meeting initial eligibility criteria will be given a secondary screener in person that
22 390 asks a variety of questions not limited to IPV. The members of the couple will be screened
23 391 simultaneously but separately by gender-matched interviewers. The goal is to screen out
24 392 illegitimate couples or those who experienced severe IPV in the past three months or
25 393 have safety concerns. In case a couple is deemed ineligible due to IPV, they will not be
26 394 informed of the reason for ineligibility to minimize any unintended harms. As part of the
27 395 second screener, questions about how the couple met will be asked (with the answer not
28 396 recorded). After completing the second screener, the two recruiters will compare their
29 397 notes and determine if the couple is legitimate. If not, the recruiters will inform the couple
30 398 of their ineligibility without providing a specific reason.
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33 400 During this screening interview, staff will use a rapid HIV test to confirm HIV status for all
34 401 participants who reported living with HIV. If the index patient tests negative for HIV on the
35 402 point-of-care (POC) HIV test, they will be considered ineligible. Both partners must be
36 403 eligible for the couple to be considered eligible for the study.
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1 405 If both members of the couple report heavy alcohol use during screening and are on ART,
2 406 the male partner will be assigned to be the index patient given that drinking among men
3 407 is generally more frequent than women in similar types of couples (18,49). For the MI-
4 408 plus arm, only the index patient will receive the breathalyzer and mobile app as the tester;
5 409 their partner will only receive SMS text notifications of their BAC levels.
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411 **Randomization**

12 412 After informed consent and the baseline assessment, couples will be randomized to the
13 413 control arm, the couple-based MI arm, or the couple-based MI with mobile breathalyzers
14 414 arm (MI-plus). We will use randomly permuted block sizes (e.g., 3, 6, and 9) generated
15 415 using a computerized and secure process. The UCSF project coordinator and the HSRC
16 416 data manager will use the table that the study statistician created to print documents that
17 417 assign participants to one of the three arms. These documents will be placed in sealed
18 418 envelopes ordered sequentially in a box and maintained by the HSRC data manager in a
19 419 locked cabinet. HSRC interviewers will take a small subset of envelopes into the field with
20 420 them and will be trained to administer random assignments following the order of the
21 421 envelopes. At the end of the baseline survey, the index patient will be given the envelope
22 422 that contains the random assignment. Couples will receive an appointment card with a
23 423 date for their next study visit following randomization.
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425 **Blinding**

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35 426 Counselors delivering the intervention cannot be blinded to the intervention condition.
36 427 Assessment staff are different from the staff who delivered the intervention to a given
37 428 couple. However, because the assessment staff work in close collaboration with the
38 429 counselors in tracing couples and assisting with technology navigation for those in the
39 430 MI-plus arm, we cannot fully guarantee that assessment staff will be blinded from the
40 431 intervention condition as well. Participants will also not be blinded to the intervention
41 432 condition and will be informed during randomization of their assigned group.
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50 434 **Data collection**

51 435 Study assessments will occur at baseline, 2-months and 6-months post intervention
52 436 initiation. The two-month visit will occur after completion of the MI sessions. All surveys
53 437 will be delivered in-person using same-sex interviewers who are fluent in both English
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1 438 and *isiZulu* to be able to use the participants' preferred language. Study staff will enter
2 439 data directly into REDCap using a mobile tablet. The REDCap mobile app is designed to
3 440 be used without internet access, so it is suitable for areas with an internet connection.
4 441

5 442

6 442 **Laboratory testing**

7 443 At the 2-month visit, dried blood spot (DBS) samples will be collected from all participants
8 444 who reported heavy alcohol use at baseline to test for Phosphatidylethanol (PEth), an
9 445 alcohol biomarker that is well correlated with total alcohol consumption in the prior 2-4
10 446 weeks (50,51). Additionally, at the 2-month visit, DBS samples will be collected for all
11 447 index patients living with HIV to test for viral load. We will prepare DBS by pipetting whole
12 448 blood onto Whatman 903 cards. DBS cards for PEth will be stored at room temperature
13 449 in locked cabinets and transported to a commercial laboratory in the United States for
14 450 PEth quantification (16:0/18:1 analog), with lower limit of quantification of 8 ng/ml (52).
15 451 PEth is well-correlated with breathalyzer-assessed number of days drinking over 21 days
16 452 (53) and the volume of alcohol consumed in the past 21 days (51). DBS cards for viral
17 453 load will be transported on a daily basis to an accredited laboratory in South Africa and
18 454 processed using the Panther System with a lower limit of detection of 883 copies/ml.
19 455

20 456

21 456 **Data management**

22 457 We will use built-in controls within REDCap to restrict out of range values and prompts
23 458 will be given to alert the user to missing data or unusual entries. The mobile application
24 459 displays questions on the screen and then gives interviewers the ability to enter
25 460 responses directly into the mobile phone or tablet. Once complete, the research
26 461 instrument (i.e., survey, baseline interview) is temporarily stored in a non-readable
27 462 encrypted file on the device/tablet. When in an area with network coverage or back at the
28 463 research office, completed forms are uploaded and removed from the tablets
29 464 approximately every 60 seconds. If no network signal is present, the data is stored on the
30 465 mobile device until such time that it detects a network signal. Checks will be placed to
31 466 ensure correct information has been entered by the HSRC Research Manager.
32 467 Information from the research instruments is then uploaded to a secured server. The data
33 468 undergoes both internal and external quality checks, conducted by the UCSF Research
34 469 Manager and the HSRC Data Science Unit. Additionally, incoming data will be monitored
35 470 daily to identify any unusual or unexpected entries. In cases where such entries are
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1 471 detected, data queries will be generated, and the HSRC team will be contacted to address
2 472 and resolve these queries.
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4 473

6 474 **Retention**

7 475 Upon enrollment, we will obtain contact information (e.g., two cell phone numbers,
8 476 directions to households, and contact information for up to three other individuals) to
9 477 facilitate tracking. Participants will be contacted regularly (e.g., twice a month) to update
10 478 contact information and check on location. Prior to the assessment visits, reminder calls
11 479 and SMS messages will be made to both partners one week before the appointment and
12 480 again 1-2 days prior. For participants who miss appointments, we will limit the number of
13 481 phone call attempts to 3-4 to respect privacy and the right to refuse. There may be special
14 482 circumstances when outreach workers will be dispatched to participants' communities
15 483 (with their prior consent) such as when calls do not go through.

16 484 We anticipate that we will lose a very small percentage of couples due to break-ups,
17 485 deaths, and migration (<5%), which we have accounted for in recruitment and analysis
18 486 plans. One assessment will be conducted with each partner separately following the
19 487 break-up to understand when the couple broke up, whether study participation contributed
20 488 to the break-up, and if not, other reasons for why the couple broke-up.

21 489 The breakup assessment will also allow us to identify any negative effects of participation
22 490 on couples. If the study contributed to the break-up or the break-up was a negative
23 491 experience, we will follow the adverse event logging process. We will continue to follow
24 492 each partner individually and administer study assessments given that our study
25 493 outcomes (e.g., alcohol use) are at the individual level. This will allow us to explore
26 494 whether participation in the study, despite the break-up, had any effect on their alcohol
27 495 use; however, couples who break-up before participation in the intervention will exit the
28 496 study.

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30 498 **Study outcomes**

31 499 ***Primary outcomes***

32 500 The primary goal of this pilot trial is to assess feasibility and acceptability (F&A) of
33 501 *Masibambisane* using the following metrics and *a priori* targets: recruitment rate (number

of couples enrolled over six months; target: 120 couples), randomization rate (proportion of enrolled couples who are randomized; target: 90% of recruited couples), breathalyzer test completion rate (proportion of tests taken after prompted; target: 70%), satisfaction levels (proportion of couples who report being satisfied or very satisfied with *Masibambisane*: target: 75%), session completion rates (proportion of couples who attend 100% of sessions; target: 75%), and retention at 2-month and 6-month follow-up visits (proportion of couples who complete follow-up surveys; target: 85%). We will also assess fidelity to the intervention by having the manager or facilitators complete detailed checklists after each session to document activities conducted. As a second check, we will audio-record all sessions and have an independent research assistant listen to a subset of recordings and complete the same checklists. We set a target of 80% fidelity.

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514 **Secondary outcomes**

515 Although we are not powered to examine treatment effects, we will explore the effect of
516 *Masibambisane* on the alcohol use among the partner reporting hazardous alcohol use
517 at baseline: number of drinking days in the past 30 days (assessed via the timeline follow-
518 back), hazardous alcohol use (i.e., positive AUDIT-C score (40) in the past three months
519 and/or a PEth value ≥ 35 ng/ml, a recommended cutoff value (54)), and raw AUDIT-C
520 score (0-12); and among the partner with HIV: optimal ART adherence (95% or higher on
521 the Visual Analog Scale/VAS (55)), and viral suppression (less than 1000 copies/ml per
522 HIV clinical guidelines) (44).

523 Additional exploratory outcomes include relationship dynamics such as constructive
524 communication (communication patterns questionnaire (56); $\alpha=0.69-0.72$); alcohol-
525 specific partner social support (adapted based on the social provision scale (57);
526 $\alpha=0.84$), trust (dyadic trust scale (58); $\alpha=0.82$), intimacy (emotional intimacy subscale
527 of Sternberg love scale(59); $\alpha=0.90$), unity (inclusion of self-in-other measure (60)),
528 relationship satisfaction (couple satisfaction index (61), single item), and sexual
529 satisfaction (couple sexual satisfaction scale (62); $\alpha=0.89$). Because we expect that
530 reductions in alcohol use and improvements in relationship dynamics may reduce IPV,
531 we will also explore effects on physical, sexual, and emotional violence as measured by
532 the WHO domestic violence module (63,64). All relationship dynamics and IPV types will
533 be modelled as continuous variables.

534 **Sample size**

535 Formal tests of health outcomes or attempts to obtain valid estimates of effect sizes are
536 not statistically justified for the proposed study (65–69). Pilot studies, by design, cannot
537 definitively test hypotheses due to their smaller sample sizes and the frequent design
538 adjustments necessary to maximize recruitment, retention and quality assessment of
539 outcomes (65–69). Effect size estimates are not sufficiently reliable given the breadth of
540 the confidence intervals; however, to supply additional information, we conducted several
541 power analyses using NCSS PASS. In sum, our study is powered to detect small to
542 medium distances to confidence limits for descriptive statistics and medium to large
543 longitudinal analysis effects, though, as noted above, formal hypothesis testing will not
544 be the focus of this pilot study.

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546 **Data analysis plan**

547 ***Feasibility and acceptability data analysis***

548 The primary analyses will include descriptive statistics of F&A indicators, comparing each
549 statistic (e.g., percent retained) to the threshold described above. Above-threshold
550 findings will suggest a reasonable level of F&A while below-threshold findings would
551 suggest that remedial modifications to study procedures and/or design would be required
552 prior to moving forward with a full-scale trial. We will stratify the statistics by gender to
553 consider sex as a biological variable.

554

555 ***Exploratory hypotheses and analyses***

556 Although the primary objective is to assess F&A rather than to conduct formal hypothesis
557 tests, we will evaluate exploratory hypotheses as part of the assessment process. For
558 example, we expect that: 1) participants in the MI-only arm will report a greater reduction
559 in the number of drinking days and in lower odds of engaging in hazardous alcohol use
560 than participants in the EUC control arm; 2) participants in the MI-plus arm will report a
561 greater reduction in the number of drinking days and lower odds of engaging in hazardous
562 alcohol use than participants in the MI-only arm. Secondly, we anticipate that
563 intervention participants will report higher odds of adherence to ART and viral
564 suppression than those in the EUC arm. We also anticipate the intervention participants
565 in both arms will report higher (indicating more positive) scores on relationship dynamics
566 and lower scores on IPV than those in the EUC arm.

1 567
2 568 We will compute descriptive statistics to capture measures of central tendency for
3 569 continuous variables and proportions for binary variables, by visit and by treatment arm.
4 570 To explore the effect of *Masibambisane* on the secondary outcome of number of drinking
5 571 days, we will use mixed-effects negative binomial regression models including all three
6 572 timepoints. Negative binomial models are recommended for count-based outcomes like
7 573 drinking days (70). For the AUDIT-C score, we will use linear mixed-effects models
8 574 including all three timepoints. For optimal adherence to ART, we will use mixed-effects
9 575 logistic regression models including all three timepoints. Models will include random
10 576 effects for participants and couples, and fixed effects for timepoint and study arm,
11 577 interaction of time and arm, and sex of the index patient. We will also explore the whether
12 578 the effects are moderated by respondent type (i.e., index patient versus partner).

13 579 To explore effects on biomarker-based outcomes captured only at 2-months (e.g., heavy
14 580 alcohol use, viral suppression) and only on index participants, we will use logistic
15 581 regression models with treatment arm as the main predictor. For heavy alcohol use, which
16 582 will be collected on both members of the couple, we will cluster based on couple ID to
17 583 account for non-independent drinking levels within dual-drinking couples. All analyses will
18 584 use an intent-to-treat approach to include every participant within the analysis based on
19 585 their original randomization group. Statistical analyses will be conducted in Stata 18. If
20 586 missing data exceeds 5%, we will use multiple imputation via chained equations following
21 587 methods in our prior studies (71).

22 588 **Ethical considerations and dissemination**

23 589 ***Informed consent***

24 590 Participants will provide written informed consent for the following activities: 1) to
25 591 participate in the second screening interview, which asks personal questions about IPV;
26 592 2) to participate in the RCT and all procedures, including providing blood samples for
27 593 PEth and viral load testing; and 3) to export alcohol biomarker DBS samples to the US
28 594 laboratory for testing. Partners will be consented individually in a private interview room
29 595 by a gender-matched interviewer in the isiZulu or English, depending on the participant's
30 596 preference. The consent process will cover topics on the purpose of the study, study
31 597 procedures, potential risks and benefits, how confidentiality will be ensured, voluntary
32 598 participation, the funding agency and study investigators, and contact information for the

1 599 study PIs. The interviewer will go over all aspects of consent verbally and address any
2 600 questions that the participant has about participation. We will capture signed consent
3 601 using the REDCap mobile app. Participants will be given a paper copy of the consent
4 602 forms. If participants are unable to read and write (as assessed by a brief reading
5 603 comprehension tool), the interviewer will have a witness monitor the informed consent
6 604 process and sign the consent form.
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12 606 ***Confidentiality and privacy***

13 607 Participants may face a loss of confidentiality, which could lead to social stigma,
14 608 discrimination, or physical and psychological harm due to their HIV status and alcohol
15 609 use. To protect confidentiality, various measures will be taken, including staff training,
16 610 using research identification numbers instead of names, and secure data storage. There
17 611 is also a risk of loss of privacy, especially when discussing sensitive topics like HIV and
18 612 alcohol use. Privacy will be maintained by using coded language and providing
19 613 participants with strategies to protect their privacy, such as using discreet covers for
20 614 breathalyzer devices and phones. Participants will be assured that their responses will
21 615 not be shared with their partners, and steps will be taken to address coercion or violence,
22 616 including referrals to appropriate services.
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33 618 ***Data safety and monitoring***

34 619 This study protocol was approved by the HSRC Research Ethics Committee (REC:
35 620 Protocol Number 1/27/20/21), the UCSF Human Research Protection Program (HRPP;
36 621 Protocol Number 21-35034) and is registered with Clinicaltrials.gov (NCT#05756790). A
37 622 Data Safety and Monitoring Board (DSMB), composed of three independent experts in
38 623 the field of HIV and alcohol abuse, has been convened in accordance with NIH policy.
39 624 They reviewed and approved the study procedures for trial monitoring on November 15,
40 625 2022. The DSMB will convene every six months and also in response to the occurrence
41 626 of any serious adverse events. Data on anticipated adverse events, including couple
42 627 dissolution and IPV, will be gathered throughout the study and reported to the DSMB at
43 628 biannual meetings. Unanticipated events and events reported spontaneously will also be
44 629 summarized and reported at the meetings.
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55 631 ***Trial modification and discontinuation***

1 632 Trial modifications will be allowed given that this is a pilot study designed to maximize
2 633 feasibility and acceptability; however, major changes such as to eligibility criteria or key
3 634 aspects of the trial design will require approval from the study sponsor and DSMB. In the
4 635 case of major changes, amendments would be filed with the UCSF and HSRC institutional
5 636 review boards and the clinicaltrials.gov record would be updated. Adverse events will be
6 637 monitored by the DSMB, who could recommend pausing or halting of the study if needed.
7 638 We have no plans to conduct any interim analyses for this small pilot study other than
8 639 preliminary analyses of baseline data.

14 640

16 641 ***Ancillary and post-trial care***

18 642 Participants will be provided with a list of resources for community-based services for
19 643 HIV, couples, and behavioral health at the start of the study. Participants who are flagged
20 644 for suicidality, IPV, or serious mental health concerns will be referred by the research staff
21 645 to *Lifeline* (i.e., a local organization that handles psychosocial or mental health issues and
22 646 has expertise in couples counseling) or other mental health services. The research team
23 647 will contact the service provider to set up an appointment and then inform the participant
24 648 of their appointment schedule. The team will follow up with the participant later to ensure
25 649 they were linked into services if they expressed an interest in obtaining help.

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33 651 ***Dissemination***

35 652 Sharing of data and results generated by this project will be carried out in several ways.
36 653 The study findings will be made available on clinicaltrials.gov. We will also deposit de-
37 654 identified data in the US National Institute of Mental Health (NIMH) data archive (NDA)
38 655 as required by the terms of the award. In collaboration with the HSRC community
39 656 outreach team, results will be presented at local community meetings attended by
40 657 participants and key stakeholders such as alcohol vendors. Results will also be presented
41 658 at community-level meetings held by district and local health officials in collaboration with
42 659 local HIV care clinics to ensure findings are disseminated to HIV policy makers. Finally,
43 660 results will be presented at HIV and alcohol use conferences and published in peer-review
44 661 journals with authorship based upon intellectual contribution and guided by American
45 662 Psychological Association guidelines.

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664 **Abbreviations**

665 SSA - Sub-Saharan Africa; PLWH - People Living with HIV; MI - Motivational Interviewing;
666 BAC - Blood Alcohol Concentration; ART - Antiretroviral Therapy; HIV - Human
667 Immunodeficiency Virus; F& A -Feasibility & Acceptability; IPV - Intimate Partner
668 Violence; POC - Point-of-Care. EUC – Enhanced Usual Care; NIMH-National Institute of
669 Mental Health. DSMB - Data Safety and Monitoring Board; HSRC- Human Sciences
670 Research Council; USCF- University of California San Francisco; KZN - KwaZulu-Natal;
671 TAC- Time-and-Attention Control; FGD – Focus Group Discussion; UNAIDS- The Joint
672 United Nations Programmes on HIV/AIDS.

673

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676 and the study staff at the Human Sciences Research Council.

677

678 **Authors' contributions**

679 AC serves as the principal investigator for the Masibambisane study and oversaw the
680 completion of this manuscript. RB, LM, BC, and HH were contributing authors and served
681 as project managers overseeing the implementation of the study protocol. TS, AvH, JH,
682 and TN are study co-investigators. All authors have read and approved the final
683 manuscript.

684

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688 K24AA022586 (PI Hahn). The funder had no role in study design and will not have any
689 role during its execution, data analysis and interpretation, or dissemination of results.

690 **Availability of data and materials**

691 Please contact corresponding author for details. The data will be deposited in the National
692 Institute of Mental Health (NIMH) Data Archive repository at regular intervals throughout
693 the study.

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2 697 **Declarations**

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4 699 **Ethics approval and consent to participate**

7 700 All procedures were reviewed by the University of California San Francisco (UCSF)
8 701 Human Research Protections Program and the Human Sciences Research Council
9 702 (HSRC) Research Ethics Program.

12 703

14 704 **Consent for publication**

16 705 Not applicable.

18 706

19 707 **Competing interests**

21 708 The authors have no competing interests to disclose.

23 709

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Couples Motivational Interviewing with Mobile Breathalyzers to Reduce Alcohol Use in South Africa: A Pilot Randomized Controlled Trial of Masibambisane

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SCHOLARONE™
Manuscripts

1 **Couples Motivational Interviewing with Mobile Breathalyzers to Reduce Alcohol**
2 **Use in South Africa: A Pilot Randomized Controlled Trial of Masibambisane**

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2
3 **Abstract**4
5 **Introduction:**

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7 33 Heavy alcohol use among people living with HIV in sub-Saharan Africa can hinder the
8
9 34 success of HIV treatment programs, impacting progress towards UNAIDS goals. Primary
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11 35 partners can provide critical forms of social support to reduce heavy drinking and could
12
13 36 be included in motivational interviewing (MI) interventions to address heavy drinking;
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15 37 however, few studies have evaluated MI interventions for couples living with HIV in sub-
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17 38 Saharan Africa. We aim to evaluate the feasibility and acceptability of a couple-based MI
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19 39 intervention with mobile breathalyzer technology to reduce heavy alcohol use and
20
21 40 improve HIV treatment outcomes among HIV-affected couples in South Africa.

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23 **Methods and analysis:**

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25 43 We will employ a three-arm randomized controlled trial to assess the efficacy of couple-
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27 44 based MI (MI-only arm) and in conjunction with mobile breathalyzers (MI-plus arm) to
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29 45 address alcohol use and HIV outcomes, as compared to enhanced usual care (control
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31 46 arm). We will enroll heterosexual couples aged 18-49 in a primary relationship for at least
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33 47 six months who have at least one partner reporting hazardous alcohol use and on
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35 48 antiretroviral therapy for six months. Participants in both MI arms will attend three
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37 49 manualized counselling sessions and those in the MI-plus arm will receive real-time
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39 50 feedback on blood alcohol concentration (BAC) levels using a mobile breathalyzer.
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41 51 Couples randomized in the control arm will receive enhanced usual care based on the
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43 52 South African ART Clinical Guidelines. Feasibility and acceptability indicators will be
44
45 53 analyzed descriptively, and exploratory hypotheses will be examined through regression
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47 54 models considering timepoints and treatment arms.

48
49 **Ethics and dissemination:**

50
51 58 The study was approved by the University of California, San Francisco (HRPP; Protocol
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53 59 Number 21-35034) and HSRC Research Ethics Committee (REC: Protocol Number
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55 60 1/27/20/21). We will disseminate the results at local community meetings, community-
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57 61 level health gatherings, and conferences focused on HIV and alcohol use.

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Strengths and limitations of this study

- Intervention was developed and tailored to the cultural context of heterosexual couples in a rural setting of KwaZulu-Natal
- Uses a dyadic approach to intervene to collect and analyse intervention effects on both partners
- Incorporates an alcohol biomarker to mitigate the limitations of self-reported drinking behavior
- Small pilot study not powered to detect changes in behavioral outcomes
- Relatively short follow-up period of six months does not allow for the assessment of long-term health effects

Trial registration: ClinicalTrials.gov Protocol Registration; NCT05756790; registered on March 6, 2023; <https://register.clinicaltrials.gov/>

Protocol Version 1.0: 19 December 2023

Keywords: Motivational interviewing with couples; heavy alcohol use; HIV/AIDS; antiretroviral therapy; South Africa

81 Introduction

82 *Background*

83 In sub-Saharan Africa (SSA), alcohol use is described as “adding fuel to the fire” for
84 people living with HIV (PLWH) (1), threatening the success of HIV treatment programs
85 and progress towards United Nations Programme on HIV/AIDS (UNAIDS) goals (2–5).
86 South Africa is severely impacted by HIV, particularly in KwaZulu-Natal (KZN) where 27%
87 of adults are infected with HIV (6). At 11 liters of pure alcohol per year, South Africa has
88 some of the highest levels of per capita drinking in the world (7). Among PLWH who drink
89 in South Africa, 50-90% report heavy alcohol use (8–10). Notably, South Africa also has
90 some of the highest rates of gender-based violence worldwide (11,12), which is closely
91 linked to heavy alcohol use (13,14). For PLWH, alcohol use contributes to poor adherence
92 to antiretroviral therapy (ART) and retention in HIV care (15–17).

93 Our research in SSA suggests that primary partners are key to the success of alcohol
94 interventions given their critical role in helping people reduce alcohol use and the couple
95 dynamics that intersect with alcohol use (18–21). In South Africa, partners mitigate the
96 harms of alcohol use by helping drinkers manage their alcohol use while maintaining
97 adherence to ART (19); however, communication around reducing alcohol use is not
98 always effective and can be limited by gender-based power imbalances. This suggests
99 the need for interventions to build couples’ communication skills and shared decision-
100 making around alcohol use (20). Harnessing this powerful form of social support is critical
101 in a setting where clinical services for alcohol misuse are inadequate and can be costly
102 for patients.

103 One approach that has been effective at reducing alcohol use among PLWH is
104 motivational interviewing (MI) in conjunction with mobile technology for real-time feedback
105 on drinking levels (22–29). MI is a collaborative, goal-oriented style of communication
106 with particular attention to the language of change (30). It is designed to strengthen
107 personal motivation for and commitment to a specific goal by eliciting and exploring the
108 person’s own reasons for change in an atmosphere of acceptance and compassion (30).
109 Few MI approaches with couples have been developed for alcohol use, particularly in the
110 African context (21,31–33). Although Starks articulated a comprehensive framework for
111 MI practice with couples (34), most of the research on feasibility and acceptability (21,35),

1 112 and preliminary efficacy (32,36) of the approach has come from the study of male couples
2 113 in the US.

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5 114 In studies with individuals, daily monitoring of drinking levels, when paired with MI, has a
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7 115 greater effect on drinking than MI alone (27–29) and we hypothesize that monitoring may
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9 116 have additional benefits with couples. Although primary partners are generally aware of
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11 117 a person's alcohol use, they may have inaccurate knowledge of drinking amounts and
12
13 118 frequency if not drinking together. Accurate knowledge of drinking levels in real-time is
14
15 119 critical to trigger couples' communication as well as timely and tailored social support.
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17 120 Mobile breathalyzers have been shown to be a feasible and acceptable strategy for self-
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19 121 monitoring alcohol use in studies with individuals and new products have been developed
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21 122 for dyads that allow for sharing of blood alcohol concentration (BAC) levels with support
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23 123 partners via a mobile app (37–39). In sum, mobile breathalyzers can provide real-time
24
25 124 feedback and support, which can be synergistic with an MI approach with couples that
26
27 125 fosters couple communication and problem-solving skills to effectively engage with the
28
29 126 breathalyzers and work together to reduce alcohol use.

30 127 **Objectives**

31 128 The main aim of this study is to evaluate the feasibility and acceptability (F&A) of a
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33 129 couples-based intervention for heavy alcohol consumption among HIV-affected couples
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35 130 (*Masibambisane*, “Let's work together” in *isiZulu*). Our primary hypothesis is that
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37 131 *Masibambisane* will be feasible and acceptable. As exploratory hypotheses, we expect
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39 132 that participants who receive the intervention will report lower number of drinking days
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41 133 and heavy alcohol use (a combined measure of self-report and an alcohol biomarker),
42
43 134 and greater rates of viral suppression and adherence to ART at follow-up visits.

44 135 **Methods and analysis**

45 136 **Trial design**

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47 137 We will conduct a three-arm randomized controlled trial (RCT) with couples randomized
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49 138 to the following arms: 1) an enhanced usual care (EUC) control condition; 2) couple-
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51 139 based MI (MI-only arm); and 3) couple-based MI with mobile breathalyzers (MI-plus arm).
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53 140 Couples in arm 2 and 3 will receive three MI sessions over a 60-day period with an
54
55 141 experienced counselor to help strengthen communication and problem-solving skills
56
57 142 around alcohol use. Couples in Arm 3 will use a mobile breathalyzer and app for 60 days

1 144 and receive the same MI sessions, which will incorporate feedback on BAC results into
2 145 the sessions. This design will allow us to assess the efficacy of couple-based MI alone
3 146 and the added synergistic effect of the mobile breathalyzers on alcohol use and HIV
4 147 outcomes (e.g., adherence to ART, viral suppression).
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9 149 **Study setting**

11 150 The *Masibambisane* study will be conducted by the Human Sciences Research Council
12 151 (HSRC) in the Sweetwaters community, a rural area west of the capital of KwaZulu-Natal,
13 152 Pietermaritzburg, South Africa.
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18 154 **Eligibility criteria**

19 155 Couples will be included in the study if they are: (1) in a primary relationship for at least
20 156 six months; (2) aged 18-49; (3) have at least one partner (the “index patient”) with a
21 157 positive AUDIT-C screen (score of 3 or more for women and 4 for of more for men;
22 158 modified to cover the prior 3 months) (40) and on ART for at least six months. We expect
23 159 all participants to be on oral ART regimens as long-acting ART was not available at the
24 160 time of this study in South Africa. All participants living with HIV will be required to have
25 161 disclosed their HIV status to their partner in the study. Lastly, both partners will separately
26 162 agree to participate in order for the couple to be enrolled.
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31 164 We will exclude participants with an AUDIT-C score greater than 12, indicating risk of
32 165 severe alcohol use disorder. Participants with severe drinking issues may not benefit from
33 166 a short-term counseling-based intervention and may need more intensive treatment than
34 167 our study can provide. Our intervention may also not be appropriate for couples
35 168 experiencing severe intimate partner violence (IPV). Thus, we will exclude those who fear
36 169 for their safety by participating in the study and/or report severe IPV in the past 3 months.
37 170 IPV is assessed using the WHO measure for South Africa, which assesses physical,
38 171 sexual, and emotional violence, and determines whether it is mild, moderate, or severe
39 172 (41). This trial does not place restrictions on concomitant receipt of care for alcohol use
40 173 or HIV care and treatment.
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187 **Patient and public involvement**

188 We adapted the *Masibambisane* intervention from the 3-session couples MI intervention
189 protocol originally developed by Starks et al. for use in the *Couples Health Project* (36).
190 The original intervention was intended to reduce drug use and enhance primary HIV
191 prevention among male couples in the US. In contrast, the *Masibambisane* intervention
192 will address heavy alcohol use among heterosexual couples in South Africa in which at
193 least one partner is living with HIV. The adaptation process therefore had to consider: 1)
194 cultural and linguistic context; 2) reformulation of the new target behavior (i.e., to heavy
195 alcohol use); and, 3) integration of the mobile breathalyzer component.

196 We followed the ADAPT-ITT framework (42) to arrive at the final version of the
197 *Masibambisane* intervention. Consistent with step 5 in the ADAPT-ITT framework, we
198 conducted focus group discussions (FGDs) with 36 key stakeholders to gain feedback on
199 the intervention content and activities, including perceptions of the mobile breathalyzer
200 technology. Key stakeholders included HIV care providers, alcohol vendors, community
201 leaders, and couples who drink alcohol. This feedback was integrated in the creation of
202 a modified intervention manual (ADAPT-ITT step 6). The revised manual was reviewed
203 by 8 members of the research team during the intervention training process (ADAPT-ITT
204 step 7) – including the counselors who would deliver the intervention. Their feedback was
205 used to refine and finalize the *Masibambisane* manual to maximize usability and enhance
206 cultural relevance.

207 ***Masibambisane* intervention arms**

208 Participants in the MI-only and MI-plus arms will receive three in-person manualized MI
209 sessions as a couple with a trained counselor in the language of their preference (either
210 *isiZulu* or English). Sessions take place approximately 30 days apart over a period of 2
211 months. In addition, the index participant in the MI-plus arm will make use of the mobile
212 breathalyzer and companion app, which will deliver real-time feedback on the index
213 participant's BAC levels to both partners for two months. The couples randomized to MI-
214 plus will receive brief technology training on how to operate the mobile breathalyzer and
215 app followed by a short trial period to become familiar with the technology before starting
216 intervention activities. All sessions are conducted with both partners together and each
217 lasts 60 to 75 minutes. The manual will provide guidance on sequencing of content. It is

1 210 executed in a manner consistent with the spirit, processes, and techniques of couples MI
2 211 outlined by Starks (34,36).
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5
6 213 **Session 1.** The counselor first orients the couple to the structure and nature of the
7 214 intervention and reminds them about the limits of confidentiality. After initial engagement
8 215 and rapport building, the counselor invites the couple to reflect on communication
9 216 strengths and weaknesses before engaging in strengths-based communication skill
10 217 building. The topic of alcohol use is introduced through the use of a calendar activity
11 218 developed for Dr. Starks' previous studies (32,36). Partners who report heavy alcohol use
12 219 at baseline complete the calendar by indicating days they consumed alcohol in the past
13 220 30 days. This serves as an immediate feedback tool that the counselor uses to catalyze
14 221 a conversation about alcohol use and evoke relevant change talk. This discussion
15 222 culminates in the couple identifying what they would like alcohol use to look like in the
16 223 coming month and developing a shared plan to accomplish that goal. The session ends
17 224 with the counselor inviting the couple to notice communication successes and challenges
18 225 and to schedule a pleasant event together in the coming month (in addition to
19 226 summarizing the couple's alcohol related goals and plans).
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32 228 **Session 2.** The session begins with a check-in on recent communication and goals from
33 229 the previous session. The couple then completes a values card-sort exercise highlighting
34 230 shared values and joint goals. For *Masibambisane*, the standard values card sort deck
35 231 (43) used in previous MI interventions with couples (36) was modified to increase cultural
36 232 relevance and translated into *isiZulu*. Following the card-sort exercise, counselors refocus
37 233 the conversation on alcohol use by completing another calendar activity. For participants
38 234 randomized to couples MI, this procedure mirrors that used in Session 1. For couples
39 235 randomized to MI-plus, the counselor presents the couple with breathalyzer data for the
40 236 index partner from the prior month, presented in a calendar format. Data for the non-index
41 237 partner (if also reporting heavy alcohol use at baseline) are added to this calendar. In
42 238 addition to debriefing the calendar, couples in the MI-plus condition discuss their
43 239 experiences using the breathalyzer and receiving the BAC readings of their partner. After
44 240 the calendar is created and debriefed, the counselor further evokes change talk with a
45 241 series of questions about potential consequences of drinking. Similar to session 1, the
46 242 discussion culminates in the couple identifying what might be reasonable drinking limits
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1 243 for the coming month and developing a shared plan to accomplish that goal. The session
2 244 ends with the counselor inviting the couple to notice communication successes and
3 245 challenges and to schedule a pleasant event together in the coming month (in addition to
4 246 summarizing the couple's alcohol related goals and plans).

5 247
6 248 **Session 3.** The session begins with a check-in on recent communication and goals from
7 249 the previous session. Similar to session 2, counselors then refocus the conversation on
8 250 alcohol use by completing another calendar activity. As in session 2, participants
9 251 randomized to MI-only complete the calendar following session 1 procedures. Those
10 252 randomized to MI-plus are presented with a calendar containing prior month breathalyzer
11 253 data. After the calendar is created and debriefed, the counselor further evokes change
12 254 talk with a series of questions about potential consequences of drinking specifically for
13 255 HIV-related health care outcomes and the couple's communication and sexual
14 256 interactions. Similar to session 1, this discussion culminates in the couple identifying their
15 257 drinking goals for the coming month and developing a shared plan to accomplish that
16 258 goal. Finally, counselors engage in a termination discussion. This begins by inviting the
17 259 couple to reflect on their experiences over the past two months while engaged in the
18 260 intervention. The couple then looks ahead and considers long-term goals – including
19 261 specific goals for limits on alcohol use – and constructs a shared plan to accomplish them.

20 262
21 263 **Mobile breathalyzer and app**
22 264 We will use BACtrack View®, which consists of a handheld commercial-grade
23 265 breathalyzer and accompanying mobile app. Index patients will receive twice-daily SMS
24 266 message requests to complete a breathalyzer reading at 11 am and again at 8 pm. Given
25 267 the frequent power outages in South Africa, which often result in a loss of cellular service,
26 268 participants will be allowed to complete missed tests as soon as the power returns. To
27 269 avoid disruptions in cellular service by having to manually purchase data, we will
28 270 automatically provide cellular data to perform the tests. We will also provide phones to
29 271 participants who do not have compatible smartphones and power banks to keep phones
30 272 and breathalyzers charged during power outages.

31 273
32 274 To complete a breathalyzer test, the participant will log into the mobile phone app and
33 275 follow a series of prompts to blow into the breathalyzer in front of the phone camera,

1 276 which displays the BAC value, and transmits the BAC value and photo of the participant
2 277 taking the test to the BACtrack View® server for storage. After successfully completing
3 278 the test, the partner will receive an SMS message informing them of the BAC value from
4 279 the index patient. The study coordinator is notified of BAC results and/or missed tests and
5 280 can log into the BACtrack View® app to view all tests results completed over a monthly
6 281 period. A trained technology navigator will be assigned to each couple, who will reach out
7 282 to couples who are missing tests and will be available for support as couples are getting
8 283 started with the BAC tests. At the end of each 30-day period, BAC results are mapped
9 284 onto monthly calendars and used in subsequent MI counseling sessions.
10 285

11 286 **Control arm: Enhanced usual care (EUC)**
12 287 Couples in the control arm will receive EUC, with usual care defined by the South African
13 288 national 2019 ART Clinical Guidelines (44). As part of clinical care for HIV, the harms of
14 289 alcohol use are briefly discussed during the morning health talks in the waiting rooms of
15 290 HIV clinics. HIV clients are advised that alcohol intake should be fewer than 2 standard
16 291 drinks/day for men and 1 for women, and drinking should not occur daily (at most 5 out
17 292 of 7 days per week). After randomization, couples in the control arm will receive additional
18 293 alcohol counseling modeled on WHO guidelines and Conroy et al.'s intervention in
19 294 Malawi, which uses participants' baseline AUDIT scores for messaging around alcohol
20 295 reduction and lasts 10-15 minutes (45). In selecting the control, we chose to balance our
21 296 ethical obligation to provide basic health information on alcohol use (minimal in this
22 297 setting), while maximizing the generalizability of our findings to inform a future RCT, which
23 298 will employ a EUC control group. Clinical trial experts recommend the usual care condition
24 299 over other designs such as a time-and-attention control (TAC) when the long-term goal
25 300 is to inform implementation science and scale-up (46,47). Our long-term goal will be to
26 301 test the effectiveness of a scalable alcohol intervention. Moreover, because TAC designs
27 302 have an active but different intervention, there is the risk of positively-biased intervention
28 303 results because the comparison arm can distract participants from making reductions in
29 304 alcohol use they would have otherwise made (46,47).
30 305

31 306 **Training of staff**
32 307 Given the skills required to deliver MI, we will hire certified HIV testing counselors with 2+
33 308 years of counselling and/or facilitation and community experience. Facilitators and the

309 HSRC research manager will attend a week-long didactic training workshop (in-person,
310 at the HSRC) with Dr. Starks. Dr. Starks is a licensed clinical psychologist and an MI-
311 trainer certified by the Motivational Interviewing Network of Trainers.

312
313 The training workshop will begin with a 1-day introduction to individual MI skills (30). This
314 workshop will focus on the spirit of MI, engaging skills (open questions, affirmations,
315 reflections, and summary statements), and recognizing change talk (expressions of
316 desire, ability, reasons, need, commitment, activation, and taking-steps to change). The
317 first training day will end with a demonstration of couples MI delivered in *isiZulu* (through
318 a translator) by Dr. Starks. Days 2 through 5 will focus on the spirit, processes, and skills
319 of MI with couples. Activities will consist of brief didactic presentations of content
320 interspersed with worksheets to reinforce knowledge acquisition and a wide variety of
321 role-play activities permitting practice. Beginning in day 3, role play activities will be used
322 to introduce counselors to key aspects of the intervention protocol and facilitate practice
323 with immediate feedback from Dr. Starks.

324
325 Following the training workshop, all interventionists will complete a series of training mock
326 sessions to practice the intervention content. These will be completed in English,
327 recorded, and reviewed by Dr. Starks. Counselors will receive written feedback and meet
328 biweekly with Dr. Starks to discuss progress in the mock session process and review
329 relevant skills. All interventionists will complete a minimum of 2 mock sessions for each
330 intervention component before being cleared to deliver the intervention to participants.

331
332 We will also train a pair of interviewers to recruit couples and conduct assessment visits,
333 who will be gender-matched to partners. Drs. Conroy and Butterfield will lead additional
334 training with staff, covering topics on couples counseling, the mobile breathalyzer
335 technology, how to handle ethical issues with couples, health education around alcohol
336 use and HIV, the intervention manuals and procedures, and professional conduct.

337
338 **Fidelity monitoring and supervision**
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340 Once cleared, interventionists will meet monthly (via Zoom) with Dr. Starks for group
341 supervision while sessions are ongoing during the trial. These meetings will provide an

342 opportunity to present and discuss cases, review relevant skills, and discuss ongoing
343 challenges to protocol delivery.

344 Given the large number of sessions conducted, we will select a sample of sessions
345 (around 15%) to perform additional fidelity checks giving equal attention to all counselors
346 and all sessions. For these sessions, a peer facilitator (i.e., another counselor) or the
347 research manager will complete a checklist using either transcripts or audio-recordings
348 to ensure each activity in the manual was covered. Intervention sessions will be audio-
349 recorded. Self-assessment forms will contain rating for key MI components (e.g.,
350 collaboration, respect, etc.). A separate space on the checklist and self-assessment forms
351 will be provided for written comments. After each session, counselors will complete the
352 self-assessment form. Completed forms will be discussed in regular Zoom calls with the
353 team to discuss areas where further guidance is needed and to help problem-solve
354 challenges. Finally, Dr. Starks will listen and provide feedback on any sessions conducted
355 with English-speaking couples as an additional check on fidelity to the intervention
356 protocol.

357

358 **Recruitment**

359 Community-based recruitment will be used to identify index patients at community-based
360 organizations or locations in the community where people who drink alcohol can be found.
361 Recruiters will use procedures established at HSRC to identify and recruit participants
362 using a community mobilization approach. A team of recruiters will target individuals and
363 couples in public areas in the community, including alcohol venues (e.g., shebeens, bottle
364 shops), markets, sports grounds, taxi ranks, HIV clinics, and community events. Though
365 couples will be targeted together if possible, couples may not be together in public (48)
366 and this could hinder successful recruitment of couples into research studies in the area.

367

368 Passive recruitment will also be utilized. This includes distributing community flyers
369 describing the study and encouraging interested individuals to contact the project staff by
370 calling or sending a free "please call me" SMS text message to the listed cellular phone
371 number. Recruiters will respond to these messages as soon as possible, typically no later
372 than the next working day. Passive recruitment will further be employed through flyers
373 placed at the clinics. Clinic-based outreach teams and care providers will assist in

1 374 identifying HIV patients who use alcohol use and have been on ART for at least six
2 375 months, referring them to HSRC recruiters. In all recruitment approaches, recruiters will
3 376 ask potential participants if they would like to hear about the study and explain the nature
4 377 of the study using standard recruitment scripts.
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9 379 **Screening for participation**

11 380 Screening will be a two-step process. The initial screener will be delivered either in-person
12 381 or over the phone. If recruited in person, the screener will take place in a private location
13 382 identified by the recruiter. Partners in a couple will be screened separately to ensure
14 383 confidentiality. If the participant cannot complete the initial screener in the field, the
15 384 recruiter will record their contact information for a later phone screening. Once deemed
16 385 eligible to continue, the recruiter will inform the index participant that their partner must
17 386 also be screened. Contact information for the recruited partner will be collected and
18 387 permission to call them will be obtained. Alternatively, the partner can initiate contact via
19 388 a "please call me" SMS text message. The index participant will be provided with study
20 389 information to share with the partner.
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30 391 Couples meeting initial eligibility criteria will be given a secondary screener in person that
31 392 asks a variety of questions not limited to IPV. The members of the couple will be screened
32 393 simultaneously but separately by gender-matched interviewers. The goal is to screen out
33 394 illegitimate couples or those who experienced severe IPV in the past three months or
34 395 have safety concerns. In case a couple is deemed ineligible due to IPV, they will not be
35 396 informed of the reason for ineligibility to minimize any unintended harms. As part of the
36 397 second screener, questions about how the couple met will be asked (with the answer not
37 398 recorded). After completing the second screener, the two recruiters will compare their
38 399 notes and determine if the couple is legitimate. If not, the recruiters will inform the couple
39 400 of their ineligibility without providing a specific reason.
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49 402 During this screening interview, staff will use a rapid HIV test to confirm HIV status for all
50 403 participants who reported living with HIV. If the index patient tests negative for HIV on the
51 404 point-of-care (POC) HIV test, they will be considered ineligible. Both partners must be
52 405 eligible for the couple to be considered eligible for the study.
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1 407 If both members of the couple report heavy alcohol use during screening and are on ART,
2 408 the male partner will be assigned to be the index patient given that drinking among men
3 409 is generally more frequent than women in similar types of couples (18,49). For the MI-
4 410 plus arm, only the index patient will receive the breathalyzer and mobile app as the tester;
5 411 their partner will only receive SMS text notifications of their BAC levels.
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413 **Randomization**

12 414 After informed consent and the baseline assessment, couples will be randomized to the
13 415 control arm, the couple-based MI arm, or the couple-based MI with mobile breathalyzers
14 416 arm (MI-plus). We will use randomly permuted block sizes (e.g., 3, 6, and 9) generated
15 417 using a computerized and secure process. The UCSF project coordinator and the HSRC
16 418 data manager will use the table that the study statistician created to print documents that
17 419 assign participants to one of the three arms. These documents will be placed in sealed
18 420 envelopes ordered sequentially in a box and maintained by the HSRC data manager in a
19 421 locked cabinet. HSRC interviewers will take a small subset of envelopes into the field with
20 422 them and will be trained to administer random assignments following the order of the
21 423 envelopes. At the end of the baseline survey, the index patient will be given the envelope
22 424 that contains the random assignment. Couples will receive an appointment card with a
23 425 date for their next study visit following randomization.
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427 **Blinding**

35 428 Counselors delivering the intervention cannot be blinded to the intervention condition.
36 429 Assessment staff are different from the staff who delivered the intervention to a given
37 430 couple. However, because the assessment staff work in close collaboration with the
38 431 counselors in tracing couples and assisting with technology navigation for those in the
39 432 MI-plus arm, we cannot fully guarantee that assessment staff will be blinded from the
40 433 intervention condition as well. Participants will also not be blinded to the intervention
41 434 condition and will be informed during randomization of their assigned group.
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50 436 **Data collection**

51 437 Study assessments will occur at baseline, 2-months and 6-months post intervention
52 438 initiation. The two-month visit will occur after completion of the MI sessions. All surveys
53 439 will be delivered in-person using same-sex interviewers who are fluent in both English
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1 440 and isiZulu to be able to use the participants' preferred language. Study staff will enter
2 441 data directly into REDCap using a mobile tablet. The REDCap mobile app is designed to
3 442 be used without internet access, so it is suitable for areas with an internet connection.
4 443

5 443

6 444 **Laboratory testing**

7 445 At the 2-month visit, dried blood spot (DBS) samples will be collected from all participants
8 446 who reported heavy alcohol use at baseline to test for Phosphatidylethanol (PEth), an
9 447 alcohol biomarker that is well correlated with total alcohol consumption in the prior 2-4
10 448 weeks (50,51). Additionally, at the 2-month visit, DBS samples will be collected for all
11 449 index patients living with HIV to test for viral load. We will prepare DBS by pipetting whole
12 450 blood onto Whatman 903 cards. DBS cards for PEth will be stored at room temperature
13 451 in locked cabinets and transported to a commercial laboratory in the United States for
14 452 PEth quantification (16:0/18:1 analog), with lower limit of quantification of 8 ng/ml (52).
15 453 PEth is well-correlated with breathalyzer-assessed number of days drinking over 21 days
16 454 (53) and the volume of alcohol consumed in the past 21 days (51). DBS cards for viral
17 455 load will be transported on a daily basis to an accredited laboratory in South Africa and
18 456 processed using the Panther System with a lower limit of detection of 883 copies/ml.
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20 457

21 458 **Data management**

22 459 We will use built-in controls within REDCap to restrict out of range values and prompts
23 460 will be given to alert the user to missing data or unusual entries. The mobile application
24 461 displays questions on the screen and then gives interviewers the ability to enter
25 462 responses directly into the mobile phone or tablet. Once complete, the research
26 463 instrument (i.e., survey, baseline interview) is temporarily stored in a non-readable
27 464 encrypted file on the device/tablet. When in an area with network coverage or back at the
28 465 research office, completed forms are uploaded and removed from the tablets
29 466 approximately every 60 seconds. If no network signal is present, the data is stored on the
30 467 mobile device until such time that it detects a network signal. Checks will be placed to
31 468 ensure correct information has been entered by the HSRC Research Manager.
32 469 Information from the research instruments is then uploaded to a secured server. The data
33 470 undergoes both internal and external quality checks, conducted by the UCSF Research
34 471 Manager and the HSRC Data Science Unit. Additionally, incoming data will be monitored
35 472 daily to identify any unusual or unexpected entries. In cases where such entries are
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1 473 detected, data queries will be generated, and the HSRC team will be contacted to address
2 474 and resolve these queries.
3

4 475

6 476 **Retention**

7 477 Upon enrollment, we will obtain contact information (e.g., two cell phone numbers,
8 478 directions to households, and contact information for up to three other individuals) to
9 479 facilitate tracking. Participants will be contacted regularly (e.g., twice a month) to update
10 480 contact information and check on location. Prior to the assessment visits, reminder calls
11 481 and SMS messages will be made to both partners one week before the appointment and
12 482 again 1-2 days prior. For participants who miss appointments, we will limit the number of
13 483 phone call attempts to 3-4 to respect privacy and the right to refuse. There may be special
14 484 circumstances when outreach workers will be dispatched to participants' communities
15 485 (with their prior consent) such as when calls do not go through.

16 486 We anticipate that we will lose a very small percentage of couples due to break-ups,
17 487 deaths, and migration (<5%), which we have accounted for in recruitment and analysis
18 488 plans. One assessment will be conducted with each partner separately following the
19 489 break-up to understand when the couple broke up, whether study participation contributed
20 490 to the break-up, and if not, other reasons for why the couple broke-up.

21 491 The breakup assessment will also allow us to identify any negative effects of participation
22 492 on couples. If the study contributed to the break-up or the break-up was a negative
23 493 experience, we will follow the adverse event logging process. We will continue to follow
24 494 each partner individually and administer study assessments given that our study
25 495 outcomes (e.g., alcohol use) are at the individual level. This will allow us to explore
26 496 whether participation in the study, despite the break-up, had any effect on their alcohol
27 497 use; however, couples who break-up before participation in the intervention will exit the
28 498 study.

29 499

30 500 **Study outcomes**

31 501 ***Primary feasibility and acceptability outcomes***

32 502 The primary goal of this pilot trial is to assess feasibility and acceptability (F&A) of
33 503 *Masibambisane*. The primary F&A outcomes and corresponding targets are: enrollment
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1 504 rate (proportion of eligible couples who enroll in the study; target: 80%) and retention rate
2 505 (proportion of couples who complete the 6-month follow-up survey; target: 85%).
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5 506 **Secondary feasibility and acceptability outcomes**

6 507 Secondary F&A outcomes are: satisfaction rate (proportion of couples who report being
7 508 satisfied or very satisfied with *Masibambisane* at the two-month follow-up: target: 75%),
8 509 mid-point survey completion rate (proportion of couples who complete the 2-month follow-
9 510 up survey; target: 85%), session completion rates (proportion of couples who attend
10 511 100% of sessions; target: 75%), and breathalyzer test completion rate (proportion of tests
11 512 taken after prompted; target: 70%).
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18 513 We will also assess fidelity to the intervention by having the manager or facilitators
19 514 complete detailed checklists after each session to document activities conducted. As a
20 515 second check, we will audio-record all sessions and have an independent research
21 516 assistant listen to a subset of recordings and complete the same checklists. We set a
22 517 target of 80% fidelity.
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29 519 **Secondary health outcomes**

30 520 Although we are not powered to examine treatment effects, we will explore the effect of
31 521 *Masibambisane* on the alcohol use among the partner reporting hazardous alcohol use
32 522 at baseline: number of drinking days in the past 30 days (assessed via the timeline follow-
33 523 back, assessed at 2-months and 6-months), non-heavy alcohol use (i.e., a composite
34 524 measure consisting of a negative AUDIT-C score (40) in the past three months and PEth
35 525 value < 35 ng/ml, a recommended cutoff value (54), both assessed at 2-months), and raw
36 526 AUDIT-C score (0-12); and among the partner with HIV: optimal ART adherence (95% or
37 527 higher on the Visual Analog Scale/VAS (55)), and viral suppression (less than 1000
38 528 copies/ml per HIV clinical guidelines) (44).
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47 529 Additional exploratory outcomes include relationship dynamics such as constructive
48 530 communication (communication patterns questionnaire (56); $\alpha=0.69-0.72$); alcohol-
49 531 specific partner social support (adapted based on the social provision scale (57);
50 532 $\alpha=0.84$), trust (dyadic trust scale (58); $\alpha=0.82$), intimacy (emotional intimacy subscale
51 533 of Sternberg love scale(59); $\alpha=0.90$), unity (inclusion of self-in-other measure (60)),
52 534 relationship satisfaction (couple satisfaction index (61), single item), and sexual
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1 535 satisfaction (couple sexual satisfaction scale (62); $\alpha=0.89$). Because we expect that
2 536 reductions in alcohol use and improvements in relationship dynamics may reduce IPV,
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4 537 we will also explore effects on physical, sexual, and emotional violence as measured by
5
6 538 the WHO domestic violence module (63,64). All relationship dynamics and IPV types will
7
8 539 be modelled as continuous variables.

10 540 **Sample size**

11
12 541 Formal tests of health outcomes or attempts to obtain valid estimates of effect sizes are
13
14 542 not statistically justified for the proposed study (65–69). Pilot studies, by design, cannot
15
16 543 definitively test hypotheses due to their smaller sample sizes and the frequent design
17
18 544 adjustments necessary to maximize recruitment, retention and quality assessment of
19
20 545 outcomes (65–69). Effect size estimates are not sufficiently reliable given the breadth of
21
22 546 the confidence intervals; however, to supply additional information, we conducted several
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24 547 power analyses using NCSS PASS. In sum, our study is powered to detect small to
25
26 548 medium distances to confidence limits for descriptive statistics and medium to large
27
28 549 longitudinal analysis effects, though, as noted above, formal hypothesis testing will not
29
30 550 be the focus of this pilot study.

31 551 **Data analysis plan**

32 552 ***Feasibility and acceptability data analysis***

33
34 553 The primary analyses will include descriptive statistics of F&A indicators, comparing each
35
36 554 statistic (e.g., percent retained) to the threshold described above. Above-threshold
37
38 555 findings will suggest a reasonable level of F&A while below-threshold findings would
39
40 556 suggest that remedial modifications to study procedures and/or design would be required
41
42 557 prior to moving forward with a full-scale trial. We will stratify the statistics by gender to
43
44 558 consider sex as a biological variable.

45 559 ***Exploratory hypotheses and analyses***

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48 561 Although the primary objective is to assess F&A rather than to conduct formal hypothesis
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50 562 tests, we will evaluate exploratory hypotheses as part of the assessment process. For
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52 563 example, we expect that: 1) participants in the MI-only arm will report a greater reduction
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54 564 in the number of drinking days and in lower odds of engaging in hazardous alcohol use
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56 565 than participants in the EUC control arm; 2) participants in the MI-plus arm will report a
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1 567 greater reduction in the number of drinking days and lower odds of engaging in hazardous
2 568 alcohol use than participants in the MI-only arm. Secondly, we anticipate that
3 569 intervention participants will report higher odds of adherence to ART and viral
4 570 suppression than those in the EUC arm. We also anticipate the intervention participants
5 571 in both arms will report higher (indicating more positive) scores on relationship dynamics
6 572 and lower scores on IPV than those in the EUC arm.

7 573
8 574 We will compute descriptive statistics to capture measures of central tendency for
9 575 continuous variables and proportions for binary variables, by visit and by treatment arm.
10 576 To explore the effect of *Masibambisane* on the secondary outcome of number of drinking
11 577 days, we will use mixed-effects negative binomial regression models including all three
12 578 timepoints. Negative binomial models are recommended for count-based outcomes like
13 579 drinking days (70). For the AUDIT-C score, we will use linear mixed-effects models
14 580 including all three timepoints. For optimal adherence to ART, we will use mixed-effects
15 581 logistic regression models including all three timepoints. Models will include random
16 582 effects for participants and couples, and fixed effects for timepoint and study arm,
17 583 interaction of time and arm, and sex of the index patient. We will also explore the whether
18 584 the effects are moderated by respondent type (i.e., index patient versus partner).

19 585 To explore effects on biomarker-based outcomes captured only at 2-months (e.g., heavy
20 586 alcohol use, viral suppression) and only on index participants, we will use logistic
21 587 regression models with treatment arm as the main predictor. For heavy alcohol use, which
22 588 will be collected on both members of the couple, we will cluster based on couple ID to
23 589 account for non-independent drinking levels within dual-drinking couples. All analyses will
24 590 use an intent-to-treat approach to include every participant within the analysis based on
25 591 their original randomization group. Statistical analyses will be conducted in Stata 18. If
26 592 missing data exceeds 5%, we will use multiple imputation via chained equations following
27 593 methods in our prior studies (71).

28 594

29 595 **Ethical considerations and dissemination**

30 596 ***Informed consent***

1 597 Participants will provide written informed consent for the following activities: 1) to
2 598 participate in the second screening interview, which asks personal questions about IPV;
3
4 599 2) to participate in the RCT and all procedures, including providing blood samples for
5
6 600 PEth and viral load testing; and 3) to export alcohol biomarker DBS samples to the US
7
8 601 laboratory for testing. Partners will be consented individually in a private interview room
9
10 602 by a gender-matched interviewer in the isiZulu or English, depending on the participant's
11
12 603 preference. The consent process will cover topics on the purpose of the study, study
13
14 604 procedures, potential risks and benefits, how confidentiality will be ensured, voluntary
15
16 605 participation, the funding agency and study investigators, and contact information for the
17
18 606 study PIs. The interviewer will go over all aspects of consent verbally and address any
19
20 607 questions that the participant has about participation. We will capture signed consent
21
22 608 using the REDCap mobile app. Participants will be given a paper copy of the consent
23
24 609 forms. If participants are unable to read and write (as assessed by a brief reading
25
26 610 comprehension tool), the interviewer will have a witness monitor the informed consent
27
28 611 process and sign the consent form.
29

612

613 ***Confidentiality and privacy***

30 614 Participants may face a loss of confidentiality, which could lead to social stigma,
31
32 615 discrimination, or physical and psychological harm due to their HIV status and alcohol
33
34 616 use. To protect confidentiality, various measures will be taken, including staff training,
35
36 617 using research identification numbers instead of names, and secure data storage. There
37
38 618 is also a risk of loss of privacy, especially when discussing sensitive topics like HIV and
39
40 619 alcohol use. Privacy will be maintained by using coded language and providing
41
42 620 participants with strategies to protect their privacy, such as using discreet covers for
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44 621 breathalyzer devices and phones. Participants will be assured that their responses will
45
46 622 not be shared with their partners, and steps will be taken to address coercion or violence,
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48 623 including referrals to appropriate services.

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49 625 ***Data safety and monitoring***

50 626 This study protocol was approved by the HSRC Research Ethics Committee (REC:
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52 627 Protocol Number 1/27/20/21), the UCSF Human Research Protection Program (HRPP;
53
54 628 Protocol Number 21-35034) and is registered with Clinicaltrials.gov (NCT#05756790). A
55
56 629 Data Safety and Monitoring Board (DSMB), composed of three independent experts in

1 630 the field of HIV and alcohol abuse, has been convened in accordance with NIH policy.
2 631 They reviewed and approved the study procedures for trial monitoring on November 15,
3 632 2022. The DSMB will convene every six months and also in response to the occurrence
4 633 of any serious adverse events. Data on anticipated adverse events, including couple
5 634 dissolution and IPV, will be gathered throughout the study and reported to the DSMB at
6 635 biannual meetings. Unanticipated events and events reported spontaneously will also be
7 636 summarized and reported at the meetings.

8 637

9 638 ***Trial modification and discontinuation***

10 639 Trial modifications will be allowed given that this is a pilot study designed to maximize
11 640 feasibility and acceptability; however, major changes such as to eligibility criteria or key
12 641 aspects of the trial design will require approval from the study sponsor and DSMB. In the
13 642 case of major changes, amendments would be filed with the UCSF and HSRC institutional
14 643 review boards and the clinicaltrials.gov record would be updated. Adverse events will be
15 644 monitored by the DSMB, who could recommend pausing or halting of the study if needed.
16 645 We have no plans to conduct any interim analyses for this small pilot study other than
17 646 preliminary analyses of baseline data.

18 647

19 648 ***Ancillary and post-trial care***

20 649 Participants will be provided with a list of resources for community-based services for
21 650 HIV, couples, and behavioral health at the start of the study. Participants who are flagged
22 651 for suicidality, IPV, or serious mental health concerns will be referred by the research staff
23 652 to *Lifeline* (i.e., a local organization that handles psychosocial or mental health issues and
24 653 has expertise in couples counseling) or other mental health services. The research team
25 654 will contact the service provider to set up an appointment and then inform the participant
26 655 of their appointment schedule. The team will follow up with the participant later to ensure
27 656 they were linked into services if they expressed an interest in obtaining help.

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29 658 ***Dissemination***

30 659 Sharing of data and results generated by this project will be carried out in several ways.
31 660 The study findings will be made available on clinicaltrials.gov. We will also deposit de-
32 661 identified data in the US National Institute of Mental Health (NIMH) data archive (NDA)
33 662 as required by the terms of the award. In collaboration with the HSRC community

1 663 outreach team, results will be presented at local community meetings attended by
2 664 participants and key stakeholders such as alcohol vendors. Results will also be presented
3 665 at community-level meetings held by district and local health officials in collaboration with
4 666 local HIV care clinics to ensure findings are disseminated to HIV policy makers. Finally,
5 667 results will be presented at HIV and alcohol use conferences and published in peer-review
6 668 journals with authorship based upon intellectual contribution and guided by American
7 669 Psychological Association guidelines.
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For peer review only

670 **Abbreviations**

671 SSA - Sub-Saharan Africa; PLWH - People Living with HIV; MI - Motivational Interviewing;
672 BAC - Blood Alcohol Concentration; ART - Antiretroviral Therapy; HIV - Human
673 Immunodeficiency Virus; F& A -Feasibility & Acceptability; IPV - Intimate Partner
674 Violence; POC - Point-of-Care. EUC – Enhanced Usual Care; NIMH-National Institute of
675 Mental Health. DSMB - Data Safety and Monitoring Board; HSRC- Human Sciences
676 Research Council; USCF- University of California San Francisco; KZN - KwaZulu-Natal;
677 TAC- Time-and-Attention Control; FGD – Focus Group Discussion; UNAIDS- The Joint
678 United Nations Programmes on HIV/AIDS.

679

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683

684 **Authors' contributions**

685 AC serves as the principal investigator for the Masibambisane study and oversaw the
686 completion of this manuscript. RB, LM, BC, and HH were contributing authors and served
687 as project managers overseeing the implementation of the study protocol. TS, AvH, JH,
688 and TN are study co-investigators. All authors have read and approved the final
689 manuscript.

690

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695 role during its execution, data analysis and interpretation, or dissemination of results.

696 **Availability of data and materials**

697 Please contact corresponding author for details. The data will be deposited in the National
698 Institute of Mental Health (NIMH) Data Archive repository at regular intervals throughout
699 the study.

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1 702

2 703 **Declarations**

3 704

4 705 **Ethics approval and consent to participate**

5 706 All procedures were reviewed by the University of California San Francisco (UCSF)
6 707 Human Research Protections Program and the Human Sciences Research Council
7 708 (HSRC) Research Ethics Program.

8 709

9 710 **Consent for publication**

10 711 Not applicable.

11 712

12 713 **Competing interests**

13 714 The authors have no competing interests to disclose.

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