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BMJ Open

Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for a multicentre randomised controlled trial in Indonesia

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3 **1 Title**
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5 2 Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for
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8 3 a multicentre randomised controlled trial in Indonesia
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40 Abstract

41 **Background:** Substance use disorder (SUD) is a leading contributor to the global burden of
42 disease. In Indonesia, treatment availability falls below the expected coverage for people with
43 SUD needing care. An effective therapeutic option for SUD with potential for widespread
44 implementation is urgently needed, yet evidence-based data in the country is scarce. Here, we
45 developed a cognitive behavioural therapy (CBT)-based group telemedicine model and proposed
46 to investigate the effectiveness and implementability for providers, in a multicentre randomised
47 controlled trial (RCT).

48 **Methods:** Participants will be recruited from the communities across Indonesia. Recruitment will
49 be done through the social networks of eight sites: three hospitals, two primary healthcare centres,
50 and three rehabilitation centres. The intervention is a relapse prevention program called Indo-
51 DARPP, a newly-developed 12-week module based on CBT and motivational interviewing
52 constructed in the Indonesian context. The program is delivered in a group therapy via video-
53 conferencing—intervention will be given in addition to treatment as usual. Control comparison is
54 treatment as usual only. A total of 160 participants will be randomly divided by half into the
55 intervention and control group. The primary outcome is the increase of percent days of abstinence
56 from the primarily used substance in the past 30 days. Secondary outcomes include addiction
57 severity, quality of life, motivation to change, psychiatric symptoms, cognitive function, and stress
58 coping mechanisms. Assessments will be done at baseline (week 0), post-treatment (week 13), and
59 follow-up (week 24). Retention, participant satisfaction, and cost-effectiveness will be assessed as
60 implementation outcomes.

61 **Ethics and dissemination:** The study protocol was reviewed and approved by the Ethics
62 Committees in Universitas Indonesia and Kyoto University. Provided positive outcomes, the

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3 63 treatment program will be advocated to the Indonesian government for adoption as a healthcare-
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5 64 based approach to tackle substance use epidemic in the country.
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8 65 **Trial registration number:** UMIN000042186
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11 66 **Keywords:** *substance use disorder, telemedicine, online therapy, cognitive behavioural therapy,*
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13 67 *relapse prevention, motivational interviewing, low- and middle- income country*
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3 **69 Strengths and limitations of this study**
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- 6 70 ● The proposed study will be the first to establish high-quality evidence for a cognitive
7
8 71 behavioural therapy (CBT)-based relapse prevention program for substance use disorder
9
10 72 (SUD) in Indonesia.
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13 73 ● Telemedicine enables far-reaching nationwide participation, connecting participants with
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15 74 providers in major cities, which in this study will include providers from three different
16
17 75 levels of health care: tertiary hospitals, primary healthcare centres, and rehabilitation
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19 76 centres.
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22 77 ● A successful outcome may produce a new SUD treatment module in Indonesia and pave
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24 78 way for adoption into the national guideline.
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27 79 ● Study limitations include risk of recall and social desirability bias, heterogeneous control
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29 80 condition, and possible variability in treatment provision.
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82 Introduction

83 Substance use disorder (SUD) is a condition characterised by the inability to control the
84 use of psychoactive substances, i.e., alcohol and psychotropic drugs, which disrupts daily living.
85 SUD remains a major and growing health problem worldwide. According to the Global Burden of
86 Disease (GBD) survey in 2016, SUD globally contributes to 131 million disability-adjusted life
87 years (DALY), or 5.5% of all DALYs,¹ and this number has been increasing since the 1990s.²
88 While substance use itself is more widespread in high-income countries (HICs), low- and middle-
89 income countries (LMICs) are disproportionately burdened. Absolute mortality rate due to SUD
90 was greatest in LMICs with large populations,³ and people with economic disadvantage are more
91 likely to develop SUD.⁴ Most importantly, substantial treatment gaps exist in limited-resource
92 settings, where the number of people with SUD in need of health care far exceeds the availability
93 of treatment services^{5–7}—merely 1% of people with SUD in LMICs received treatment above the
94 minimal standard.⁸

95 In Indonesia, the world's third most populous LMIC, the national SUD prevalence was
96 estimated at 1.8% or 3.3 million people, with the most used substance being marijuana (68%),
97 followed by amphetamine-type stimulants (ATS, 42%), opioids (38%) and sedatives (35%).^{9,10} Its
98 strategic intercontinental location contributes to the country's infamous reputation as a marijuana
99 exporter and drug trafficking hub.¹¹ While there is an 80% decrease of injecting drug use (IDU)
100 from 2002 to 2016,¹⁰ an increasing use of psychoactive medications out of prescription has been
101 noted, particularly benzodiazepines.¹² Similar to other Muslim majority countries,¹³ alcohol
102 consumption is comparatively low in Indonesia—prevalence estimate of alcohol use disorder was
103 0.8% in 2016, much lower than the overall rate in Southeast Asia (3.9%).¹⁴ New psychoactive
104 substances (NPS) has also entered the country in the last decade.¹⁵ The current COVID-19

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3 105 pandemic may also further complicate the SUD situation in Indonesia, as observed elsewhere.¹⁶ In
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5 106 unpublished data from our co-author (KS), since the start of pandemic in early April 2020, there
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8 107 has been an increase in both drug and alcohol use in Indonesia of up to 2.5%. Higher drug use
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10 108 might be influenced by lockdown isolation, socio-economic issues due to unemployment, and
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12 109 heavier mental burden.

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15 110 The treatment gap for mental health care is evident in Indonesia, where only 0.5% of people
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17 111 with SUD are connected with treatment and rehabilitative care.¹⁷ Health providers and facilities
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19 112 are severely lacking; in a nation of 267 million people, only 773 psychiatrists (0.32 per 100,000
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21 113 people) are employed—second lowest in Southeast Asia¹⁸—across hospitals with psychiatric care,
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23 114 half of which are located within the capital island of Java.¹⁹ In terms of government-run primary
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25 115 healthcare centres (abbreviated as *Puskesmas* in Indonesian), out of all *Puskesmas* (~1,700
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27 116 nationwide), only a fifth actively provide mental health care.^{19,20} Current treatment options for
28
29 117 SUD include one-on-one supportive psychotherapy, symptomatic pharmacotherapy, peer
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31 118 counselling, and opioid substitution. Methadone maintenance therapy (MMT) is available in
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33 119 *Puskesmas* since 2006, but coverage remains low: only 5% in a 2012 study²¹ due to methadone
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35 120 cost, reliance on subsidisation, lack of program sustainability,²² and the tendency to incarcerate
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37 121 patients under the 'war on drugs' policy.^{21,23} Three-months retention rate of MMT was only 60-
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39 122 74%.^{24,25} Psychiatric comorbidities were also common in MMT users and quality of life was
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41 123 evidently lower,²⁶ indicating the need for a more comprehensive mental health care approach.

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45 124 Behavioural therapies in many forms are commonly applied for SUD, most popular of
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47 125 which is cognitive behavioural therapy (CBT). Strong evidence backs the efficacy of CBT for
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49 126 SUD treatment. A meta-analysis gave a moderate overall effect size ($d = 0.45$), with outcomes
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51 127 ranging from the self-report abstinence, drug-free urine at treatment exit, to increased retention in
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3 128 therapy.^{27,28} CBT strategies include: (a) contingency management (CM)²⁹ which introduces reward
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5 129 for abstinence, (b) motivational interviewing (MI) which explores and resolves ambivalence,³⁰ (c)
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7 130 relapse prevention (RP) which helps participants to identify high-risk triggers and prevent craving,
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10 131 or (d) combinations thereof.³¹ Therapy could be delivered individually or in groups; the latter
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12 132 evidently increased adherence and self-disclosure, as well as decreased the time needed by
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14 133 providers to treat a participant by 40%.^{32,33} CBT (particularly MI and RP) is relatively low-cost
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17 134 and can be delivered by non-specialists, making it beneficial in resource-limited settings.^{34,35} In
18
19 135 regard to LMICs, while an ample amount of RCTs have supported CBT efficacy to reduce alcohol
20
21 136 use,^{36,37} evidence for drug use disorders is limited. Only five RCTs have been published so far,^{38–}
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24 137 ⁴² in which three of them were inpatient-based, even though SUD management mandates
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26 138 sustainable outpatient care in community settings.

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29 139 Telemedicine has the potential to elevate SUD treatment coverage in Indonesia. Internet
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31 140 communication overcomes the geographical barriers of the Indonesian archipelago, and saves time
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33 141 as well as transportation cost for both patients and providers, either in remote areas where health
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35 142 services are thinly spread,⁴³ or major cities with heavy traffic such as Jakarta.⁴⁴ Privacy is better
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38 143 ensured; visiting clinics may disclose SUD diagnosis, which is one of the most stigmatised health
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40 144 conditions.⁴⁵ Synchronous telemedicine via live video feed connects participants in real-time,
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43 145 improving rapport and potentially adherence, relative to asynchronous telemedicine (e.g., text
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45 146 message or web application). Video-conferencing has been effectively used in SUD treatment,^{46–}
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47 147 ⁵¹ but recent systematic reviews^{52–57} have revealed three lacking points: (1) previous reports merely
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49 148 focused on alcohol and opioid use,^{46,49–51} (2) group therapy was investigated by only one small-
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51 149 scale pilot RCT,⁵⁰ and (3) no studies were done in LMICs. The use of internet devices has been
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54 150 rapidly expanding in LMICs, including Indonesia. Smartphone users accounted for 74% of the

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3 151 Indonesian population in 2019, possibly reaching 89% by 2025.⁶⁷ Furthermore, the COVID-19
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5 152 pandemic has elevated telemedicine from an accessory to a necessity, including for psychiatric
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8 153 care.⁶⁸ Its accessibility and acceptance among SUD patients, as shown in a recent survey,⁷⁰ may
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10 154 potentially sustain telemedicine as the 'new normal' even in the post-pandemic world.^{69,71}

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13 155 Given the above challenges and opportunities, we propose a clinical trial to evaluate a
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15 156 relapse prevention telemedicine program for SUD in Indonesia. We have developed a new
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17 157 treatment module called *Indonesia Drug Addiction Relapse Prevention Program* (Indo-DARPP),
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20 158 which is a 12-week CBT-based group therapy. The primary objective is to evaluate the
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22 159 effectiveness of Indo-DARPP delivered via video conference (tele-Indo-DARPP), added to
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24 160 treatment as usual (TAU), to increase abstinence from primarily-used substances, compared to
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27 161 TAU only. Secondary objectives are to assess the effectiveness of the program toward changes in
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29 162 quality of life, motivation to change, psychological symptoms, cognitive function, and coping
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31 163 mechanisms. Retention, participant satisfaction, and group cohesion will be assessed as
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34 164 implementation outcomes, and cost-effectiveness analyses will be conducted to inform health
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36 165 policy investment.

37 38 39 166 40 41 167 **METHODS**

42 43 44 168 **Trial design**

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47 169 This trial is a parallel-group, two-arm, assessor-blinded, multicentre superiority
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49 170 randomised controlled trial. The protocol adheres to the Standard Protocol Items:
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51 171 Recommendations for Interventional Trials (SPIRIT) checklist (**Supplementary file 1**). We
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54 172 design the study as a pragmatic type 1 hybrid effectiveness-implementation trial,⁷² which allows
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3 173 concurrent investigation of intervention effectiveness as well as implementation in clinical practice,
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5 174 focusing on the former. After intake screening, participants will undergo baseline assessment (T1)
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8 175 and randomly allocated in a 1:1 ratio either to the intervention arm receiving tele-Indo-DARPP in
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10 176 addition to TAU, or control arm receiving TAU only. Treatment will be done for 12 weeks,
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12 177 followed by post-treatment assessment (T2) in week 13, and follow-up assessment (T3) in week
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14 178 24 (**Figure 1**).

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180 [Figure 1 approximately here.]

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182 **Participants and settings**

183 Participants will be recruited from the community across Indonesia via social networks of
184 eight sites: two primary health centres (Puskesmas), three referral hospitals, and three drug
185 rehabilitation services (**Table 1**). These facility types constitute the community-based treatment
186 model for SUD in Indonesia,⁷³ encompassing patients with various characteristics in motivation
187 for behavioural change, substance use history, comorbidities, and current stage in treatment.
188 Recruitment will be done via online advertisement (i.e., social networking services, group chat,
189 website) and direct approach to current and former clients through outpatient services, in a
190 consecutive sampling.

191 Puskesmas provides general primary care, pharmacotherapy for cases without any
192 complications, and MMT. Referral hospitals provide psychotherapy, pharmacotherapy, opioid
193 substitution therapy using buprenorphine/naloxone, and specialised care for cases with
194 complications, such as severe psychiatric disorder. Rehabilitation services provide long-term

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3 195 psychosocial care, typically in a mutual-aid group form. Selection of sites was based on feasibility,
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5 196 client demographic, recruitment potential, and availability of providers. While recruited
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7 197 participants may not be under treatment in the aforementioned sites at the time, facilitators for tele-
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10 198 Indo-DARPP will be the staffs of respective sites: general practitioners in Puskesmas, psychiatrists
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12 199 in referral hospitals, and counsellors in rehabilitation centres.
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18 201 [Table 1 approximately here.]
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23 203 Inclusion criteria will be those who: 1) aged 18-65 years old; 2) are diagnosed as having
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25 204 substance use disorder based on DSM-5; 3) have used primarily-used substance for at least one
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27 205 day in the past one year; 4) have access to electronic devices (i.e., smartphone, mobile tablet,
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29 206 personal computer) with internet connection; and 5) are proficient in Indonesian. Exclusion criteria
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31 207 will be those who: 1) have severe comorbidity that hinder informed consent or group therapy
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33 208 participation; and 2) currently hospitalised or are using residential care.
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39 210 **Recruitment**

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43 211 Patients eligibility will be assessed by collaborating staff at respective sites. For those who
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45 212 have never been diagnosed as having SUD, addiction psychiatrists will conduct clinical
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47 213 assessments via video call. Oral and written informed consent will be given to those eligible. For
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49 214 urine tests, explanations will be given immediately after post-treatment (T2) assessment, as
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51 215 anticipation for urine tests may influence substance use behaviour. Consent to urine test or absence
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53 216 thereof will not affect study participation.
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218 Randomisation and blinding

219 Participants will be randomly allocated to either an intervention (tele-Indo-DARPP +
220 TAU) or a control (TAU only) arm, with stratification by study site. Each site will conduct two
221 waves of recruitment with 10 participants in each wave. After the first wave at each site, we will
222 randomly allocate 5 participants to either intervention or control group. Recruitment will be
223 continued until another 10 participants (second wave) joined, and random allocation will be done
224 similarly. Allocation will be done using computer-generated random numbers by a researcher who
225 will be blinded to participants' information, except for ID. Data will be collected by researchers
226 who are blinded to the allocation arm of each participant.

227

228 Development of Indo-DARPP

229 Indo-DARPP was based on the Serigaya Methamphetamine Relapse Prevention Program
230 (SMARPP), a face-to-face group CBT-based intervention in Japan developed by a co-author
231 (TM),⁷⁴ which itself is based on the Matrix Model developed in the US.⁷⁵ Efficacy of SMARPP in
232 increasing abstinence duration, motivation to change, and participation in self-help groups have
233 been reported.⁷⁶⁻⁷⁸ SMARPP has been widely implemented as a psychotherapy for SUD not only
234 in psychiatric clinics but also primary healthcare, rehabilitation, and probation offices in Japan,
235 covered by the national insurance scheme. SMARPP has excellent scalability via the use of a
236 workbook, and can be delivered by non-specialists who have received a brief training.

237 Contents of Indo-DARPP are based on the RP model, where participants are guided to
238 learn high-risk situations for substance use and coping strategies. The program also incorporates

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3 239 elements of MI and psychoeducation on substances, SUD, and its common comorbidities. While
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5 240 CM could also be added, it increases cost and may not be effective in the longer term,⁷⁹ and thus,
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8 241 MI and RP approaches will be utilised in this study. Adaptations from SMARPP were done via
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10 242 focus group discussions involving Japanese researchers, Indonesia-based psychiatrists, general
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12 243 practitioners, and peer counsellors, all of whom have extensive experience ranging 4-20 years in
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14 244 the addiction field. Substances discussed in the module are amphetamine-type stimulants,
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16 245 benzodiazepines and other prescribed medicines, opioids, marijuana, NPS, and alcohol. Indo-
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18 246 DARPP is designed to be delivered in a small group format using workbook, and sessions will be
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20 247 provided by one facilitator and one co-facilitator who is a peer counsellor with lived experiences
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22 248 of SUD.
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27 249 A pilot test was held at Site 1, recruiting nine SUD patients into a 12-week tele-Indo-
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29 250 DARPP, to check the content acceptability and feasibility of the online delivery format. Further
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31 251 adjustments were made based on the pilot results and patient feedback.
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35 36 37 253 **Intervention via video conference: tele-Indo-DARPP**

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40 254 Tele-Indo-DARPP will be implemented in group therapy with a maximum of five patients, in
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42 255 a weekly 2-hour session for 12 weeks, delivered using the online video-conferencing application
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44 256 Zoom. URLs for video conferences will be informed weekly by the research team to the private
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46 257 Whatsapp group chat consisting of five Indo-DARPP participants plus two providers, which will
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48 258 be created after randomisation. Each Indo-DARPP session consists of three parts: (1) "check-in",
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50 259 where participants share history of substance use and craving in the past week, and analyse high-
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52 260 risk situations and coping actions taken; (2) "today's topic", where providers guide discussion of
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54 261 specific workbook chapters and participants fill in exercises, and (3) "check-out", where providers
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262 give summary and invite feedback, and participants anticipate triggers and coping strategies for
263 the following week.

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265 **Providers of tele-Indo-DARPP**

266 At least two persons from each site will serve as facilitators, who meet the following criteria:
267 psychiatrist with at least 1-year experience in treating SUD patients, or healthcare provider with
268 at least 2-year experience in providing care for SUD patients, or peer counsellor with at least 2-
269 year involvement in any organisation providing services for people with SUD. The roles of
270 facilitators are to (1) lead and moderate Indo-DARPP sessions, (2) elaborate on chapter contents,
271 (3) manage participants to follow rules, (4) establish safe and warm environment, (5) provide
272 consultation including out-of-session, and (6) contact absent participants to encourage attendance.

273 Similarly, at least two persons from each site will serve as co-facilitators for the tele-Indo-
274 DARPP, described as peer counsellors who have also experienced SUD and recovered, with at
275 least 6-month involvement in any organisations providing services for people with SUD. The role
276 of co-facilitator is to (1) share personal experiences relevant to discussion topics, (2) assist
277 facilitators in ensuring a safe and warm environment, (3) provide general support to the Indo-
278 DARPP process, and (4) provide counsel, including out-of-session.

279

280 **Training and supervision**

281 Prior to recruitment, all providers received a full-day training of trainers (TOT) online
282 session on basic knowledge of SUD treatment, Indo-DARPP contents, video demonstration,
283 hands-on role play, discussion on difficult cases, tele-Indo-DARPP, and study-related quality

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3 284 control. Workbooks and manuals were handed to all providers, and close communication with the
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5 285 research team will be kept via WhatsApp group chat throughout the research period. To maintain
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7 286 treatment fidelity and quality control, during actual tele-Indo-DARPP sessions, addiction
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9 287 psychiatrists from the research team (KS and EH) will randomly select and observe at least one
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11 288 session at each site and review the providers using a structured checklist.
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18 290 **Control condition**

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21 291 Participants who received treatment before the study will continue to receive treatment as
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23 292 usual, regardless of group allocation. TAU was chosen as the control condition because the Indo-
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25 293 DARPP is expected to complement the existing treatment services for SUD in every level of care.
26
27 294 TAU differs according to the service location (**Table 1**). Individual psychotherapy is typically
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29 295 conducted via in-person short consultation (~15 minutes) with clinical psychiatrists.
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31 296 Pharmacotherapy is given to alleviate symptoms, e.g., anxiolytics for anxiety. Patients undergoing
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33 297 MMT visit the site almost every day to receive their daily doses, while patients undergoing
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35 298 substitution therapy with buprenorphine with naloxone visit every week. All participants will be
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37 299 able to continue any outpatient pharmacological treatment (e.g., MMT, antidepressants) and
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39 300 psychotherapy (e.g., twelve-step group sessions).
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47 302 **Primary outcome**

50 303 **Abstinence from primarily used substance**

51
52 304 The primary outcome is the percent days of abstinence from the primarily used substance during
53
54 305 the past 30 days. Percent days of abstinence has been shown to be sensitive to the effects of CBT
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3 306 and are good predictors of SUD treatment follow-up.⁸⁰ Use of primarily used substance each day
4
5 307 (yes/no) for 30 days will be retrospectively interviewed using the timeline followback (TLFB)
6
7 308 method (**Table 2**), which has good validity and high test-retest reliability in measuring substance
8
9 309 consumption.^{81,82} The participants will be asked to recount every week, to reduce the risk of recall
10
11 310 bias. The primarily used substance is defined as the substance causing the most problems for
12
13 311 participants and drives them to seek care, at T1. For validation purposes, urine samples will be
14
15 312 collected at T2 to test the presence of the primarily used substance. Thresholds for a positive result
16
17 313 are >100 ng/ml for ethyl glucuronide (for alcohol use), >300 ng/ml for amphetamine-type
18
19 314 stimulant (i.e., d-methamphetamine and MDMA), >100 ng/ml for diacetyl morphine (heroin),
20
21 315 cocaine, and benzodiazepine, >50 ng/ml for synthetic cannabis (K2), and > 25 ng/ml for
22
23 316 tetrahydrocannabinol (marijuana).
24
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31 [Table 2 approximately here.]
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34 320 **Secondary outcomes**

35 321 *Addiction severity*

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37
38 322 The Addiction Severity Index (ASI) is the most widely used measure in the field of
39
40 323 addiction.⁸³ Internal consistency, test-retest reliability, and scale independence of ASI to measure
41
42 324 substance use have long been established.^{84,85} The Treatnet ASI version 3.0 by the United Nations
43
44 325 Office on Drugs and Crime (UNODC) will be used; the scale is available in Indonesian, and one
45
46 326 addiction treatment centre in Indonesia was included in its development trial.⁸⁶
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51 327 *Health-related quality of life*

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3 328 The five-level version of the five-dimensional EuroQoL (EQ-5D)^{87,88} will be used to assess
4
5 329 health-related quality of life (HRQoL), which has been done before among SUD patients with
6
7
8 330 confirmed construct validity.^{90,91} The total utility score will be obtained using the already
9
10 331 established value set in Indonesia.⁸⁹

11 332 *Motivation to change*

12
13
14 333 Motivation to change will be assessed by the Action subscale the University of Rhode
15
16 334 Island Change Assessment (URICA).⁹² URICA has been shown to have good validity, where
17
18
19 335 higher scores indicate that the person has committed to develop positive behavioural changes
20
21 336 (Diclemente and County, 2000; Diclemente et al., 2004).⁹³

22 337 *Coping strategies*

23
24 338 Types of engaged stress coping will be assessed by the Brief Coping Orientations to
25
26 339 Problems Experienced (Brief COPE),⁹⁴ which is commonly used for SUD patients.⁹⁵ A higher
27
28
29 340 score indicates that the person has adopted the coping type more frequently.

30 341 *Psychiatric symptoms*

31 342 Psychiatric symptoms will be evaluated by the Symptom Checklist 90-R (SCL-90-R).⁹⁶ The
32
33 343 Global Severity Index (GSI) will be used, which is feasible to measure psychiatric symptoms
34
35
36 344 among SUD patients.⁹⁷

37 345 *Cognitive function*

38 346 Cognitive function will be assessed by the Rey Auditory Verbal Learning Test (RAVLT),⁹⁸
39
40 347 which is useful to diagnose cognitive impairment as well as post-treatment improvement in SUD
41
42
43 348 patients.^{99,100}

44 349

45 350 **Implementation outcomes**

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3 351 ***Retention in treatment***
4

5 352 Participants will be coded as ‘retained in treatment’ if they had therapeutic contacts—
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7
8 353 including attending tele-Indo-DARPP and visiting any outpatient clinic for TAU—in at least 75%
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10 354 of the planned contacts during the past 3 months.

11
12 355 ***Treatment satisfaction***
13

14 356 Client Satisfaction Questionnaire-3 (CSQ-3)¹⁰¹ is commonly used for treatment programs,
15
16
17 357 including for SUD.¹⁰²
18

19 358 ***Group cohesion***
20

21 359 Group Therapy Experience Scale (GTES) will be used to measure the level of group
22
23
24 360 cohesion and self-disclosure in group therapy, as implementation outcomes of tele-Indo-
25
26 361 DARPP.¹⁰³
27

28 362 ***Indo-DARPP attendance***
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30
31 363 Attendance to each session will be recorded by the facilitator.
32

33 364 ***Cost effectiveness***
34

35 365 Cost-effectiveness will be assessed from a patient, provider, and societal perspective. Cost
36
37
38 366 data will be calculated by multiplying the quantity of utilised resources by unit price. Data on
39
40 367 quantity and unit price will be obtained from within the trial, or estimated from relevant data
41
42 368 sources. For effectiveness data, both clinical and economic indexes will be used. The clinical index
43
44
45 369 is abstinence from primarily used substance in the past 30 days, which will be converted into
46
47 370 abstinent year. The economic index is quality-adjusted life year (QALY) calculated from the utility
48
49 371 score of EQ-5D.
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51 372 ***Feedback interviews***
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3 373 Semi-structured interviews will be done with both participants and providers to assess the
4
5 374 following: satisfaction with content quality, comprehensibility, technical experience regarding
6
7 375 video-conferencing, comfortableness, module practicability, and participants' perception on the
8
9 376 credibility of providers. Interviews will be audio-recorded under the interviewees' consent.
10
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12 377

14 378 **Participant characteristics**

16
17 379 The following data will be obtained via a self-administered questionnaire: age, gender,
18
19 380 approximate residential location, marital status, household co-habitants, ethnicity, religion, highest
20
21 381 education level, employment status, individual and household income, type of internet device used,
22
23 382 frequency of video calls in the past year, age of first drug use, primarily used substance, inpatient
24
25 383 history or incarceration in the past month, type of treatments received, treatment locations in the
26
27 384 past three months, status of current outpatient care (voluntary or involuntary, legal or non-legal),
28
29 385 and transportation time and cost from own residence to the outpatient location.
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32 386

34 387 **Data collection procedure**

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38 388 Researchers blinded to the treatment allocation will collect data at three different time
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40 389 points: at baseline (week 0, T1), the week after the completion of treatment (week 13, T2), and
41
42 390 three months after the completion of treatment (week 24, T3) using self-answered questionnaire
43
44 391 and one-on-one interview. As for the primary outcome, the participants will be asked to recall
45
46 392 weekly using the TLFB, and thus, an assessment period of approximately 4 weeks will be added
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48 393 after each assessment time point. Urine specimens will be collected only at T2, at the final 2 weeks
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50 394 within the TLFB assessment period. Assessment schedule is shown in **Table 2** and **Figure 2**.
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3 396 [Figure 2 approximately here.]
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9 398 **Sample size**

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11 399 Sample size was calculated for the primary outcome to detect a medium effect size of $d =$
12
13 400 0.59, which is based on a previous study examining the efficacy of telemedicine for people with
14
15 401 SUD in an LIMC.⁶⁵ Using $\alpha = 0.05$ and power = 0.80, a simple t-test requires $n = 46$ per arm. We
16
17 402 estimated the design effect of clustering within Indo-DARPP group, using the formula, $D = 1 +$
18
19 403 $(m - 1) \rho$,¹⁰⁴ assuming intraclass correlation within Indo-DARPP groups or $\rho = 0.05$, and group
20
21 404 size or $m = 5$, which yielded the design effect or $D = 1.2$. Multiplying the result of simple
22
23 405 calculation by the design effect, the minimal number of participants in data analysis was 56 per
24
25 406 arm. Assuming attrition proportion = 26%,¹⁰⁵ the sample size for enrolment was set as 76 per arm,
26
27 407 or 152 in total. We will recruit 10 participants for each wave at a site, thus the number was rounded
28
29 408 up to 160 participants.
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38 410 **Statistical analysis**

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40 411 A detailed statistical analysis plan will be developed by a statistician who is blinded to
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42 412 patients' allocation, prior to data analysis. Baseline data description and main analyses will be
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44 413 conducted on an intention-to-treat basis, i.e., participants' data will be handled according to their
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46 414 initially assigned arms, regardless of actual received treatment. Analyses will be conducted with a
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48 415 significance level of 5% in the two-sided test, using Stata/SE 16.1.
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53 416 ***Consideration for correlated outcome data***
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3 417 Correlation within sites for a control arm will be ignored, as the TAU within one site varies
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5 418 per patient and some participants may not receive any treatment. For an intervention arm,
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7 419 correlation within each Indo-DARPP group due to the nature of group therapy should be accounted
8
9 420 for. We will define a new variable termed ‘clustering group identification (CID)’, where the control
10
11 421 arm will be coded as a unique CID for each person, while the intervention arm will be coded based
12
13 422 on the tele-Indo-DARPP group they were in, i.e., the same CID for five participants.
14

17 423 *Main analysis*

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20 424 Primary endpoint will be set at T2. The mean of the outcome changes from T1 to T2 will
21
22 425 be compared between the intervention and control arms using a linear model. To investigate the
23
24 426 durability of the treatment effect, outcome changes from T1 to T3 will also be compared between
25
26 427 both arms. We will account for the aforementioned correlations by clustering data, based on CID
27
28 428 in the generalised estimation equations (GEE). To help interpret effect size, Cohen’s *d* between
29
30 429 arms will be calculated.
31
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34 430 *Missing values*

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37 431 A complete case analysis will be done, which will only include participants with no
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39 432 missing values in the variables of interest. Sensitivity analysis for missing values will be conducted
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41 433 by either inverse probability weighted GEE¹⁰⁶ or multiple imputation.
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45 434 *Subgroup analysis*

46
47 435 The effect of intervention will be investigated by subgroups, as the observed effect may
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49 436 vary depending on specific population. The participants will be divided by the types of primarily
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51 437 used substance, gender, previous and current utilisation of other SUD treatment, high and low
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3 438 values in clinical characteristics at T1, e.g., percent days of abstinence, ASI drug use composite
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5 439 score, URICA readiness score, and cognitive function.
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7 440 ***Implementation evaluation***

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10 441 Chi-squared tests and *t*-tests will be done to compare retention in treatment and treatment
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12 442 satisfaction between the arms, exclusively for participants who were already receiving SUD
13
14 443 treatment at T1. Group cohesion and Indo-DARPP attendance will be descriptively reported by
15
16 444 mean and standard deviation. For cost-effectiveness analysis, the incremental cost-effectiveness
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18 445 ratios (ICERs) will be calculated, which will yield costs per QALY and abstinent year. Feedback
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20 446 interviews will be transcribed and thematic analysis will be conducted.
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26 448 **Compensations**

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29 449 Participants in both the control and intervention groups will receive 300,000 IDR (\approx 21.3
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31 450 USD) to compensate for their transportation to treatment sites for TAU throughout the 12 weeks,
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33 451 and also 98,000 IDR (\approx 7.0 USD) for every time they complete an online video assessment as
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35 452 compensation for internet data and 2-hour data collection. Specific to the intervention group,
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37 453 participants will receive internet mobile data equivalent to 50,000 IDR (\approx 3.5 USD) before the first
38
39 454 session of tele-Indo-DARPP, and receive the same amount of mobile data every time they attended
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41 455 four sessions of tele-Indo-DARPP. As all monetary amounts were set at the approximate cost, the
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43 456 amounts are intended purely for compensation and not as reward, as in contingency management.
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45 457 For providers, compensation amounted to 170,000 IDR (\approx 12.1 USD) and 150,000 IDR (\approx 10.7
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47 458 USD) will be given for each tele-Indo-DARPP session to facilitator and co-facilitator, respectively.
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52 459

54 460 **Data monitoring**

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3 461 Data on adverse events including hospitalisation, arrest, and death will be collected from the
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5 462 participants' treating psychiatrist or medical staff. In addition, participants will be interviewed at
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7 463 T2 on whether they experience any subjective harmful effect (e.g., withdrawal syndrome,
8
9 464 increased cravings) after joining Indo-DARPP. An independent data monitoring committee will
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11 465 not be convened, as the study involves short-term non-invasive psychotherapeutic intervention.
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13 466 No interim analysis is planned due to the short duration of intervention. Completeness and
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15 467 accuracy of data collection will be checked by Japanese co-investigators, and there will be no
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17 468 auditing process by independent investigators.
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24 470 **Data publication**

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26 471 Deidentified results of the study will be published in scientific publication, and reported to
27
28 472 relevant government body in Indonesia to advocate adoption of the treatment module.
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33 474 **Ethical consideration**

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35
36 475 This study protocol (version 2.0, May 2020) was approved by the Research Ethical
37
38 476 Committee of Faculty of Medicine, Universitas Indonesia (approval number: KET-1175/2019),
39
40 477 the Ethics Committee of Graduate School and Faculty of Medicine, Kyoto University (approval
41
42 478 number: C1483). The study protocol was registered at the University Hospital Medical Information
43
44 479 Network clinical trial registry (UMIN-CTR) (registry number: UMIN000042186).
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48 480 Consent process will be conducted carefully to ensure that all potential participants fully
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50 481 understand research objectives, procedures, risks, benefits, costs, and alternatives. It will be
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52 482 emphasised that study participation is voluntary and consent can be withdrawn at any time before
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54 483 research publication. We will allocate participants to treatment arms only when written informed
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3 484 consents for participation are obtained. Likewise, urine specimens will only be collected if written
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5 485 informed consents for urine collection are obtained. Participants will not receive any adverse
6
7 486 influence in deciding study participation and/or urine collection. Personal data will be protected
8
9
10 487 by separating study data from participants' identifiable information. To quickly respond to adverse
11
12 488 events arising when outpatient visits are not possible, a dedicated phone number and a WhatsApp
13
14 489 account for the study will be opened to ease communication to the research team. Participants will
15
16
17 490 be instructed to text or call when experiencing any adverse events. Importantly, written agreement
18
19 491 will be obtained from participants to never share others' information to any third party. This
20
21 492 regulation will be enforced in both during and outside tele-Indo-DARPP sessions, in any medium,
22
23 493 including video conference and group chat.
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29 495 **Discussion**

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31
32 496 Up until the time of writing, nine RCTs from LMICs have reported the effectiveness of digital
33
34 497 delivery of interventions for SUD. Utilised formats were telephone calls,⁵⁸⁻⁶¹ webpages,⁶²⁻⁶⁴ and
35
36 498 mobile applications,^{65,66} however, and no study in LMICs has so far investigated the effectiveness
37
38 499 of video-conference-based psychotherapy. The latter may facilitate honest, interactive discussions
39
40 500 on personal substance use and cravings, founded on better rapport between providers and
41
42 501 patients,¹⁰⁷ all of which is integral for CBT for SUD. One meta-analysis concluded that web-based
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44 502 mental health interventions had better retention rate and treatment outcomes when therapists were
45
46 503 synchronously involved.¹⁰⁸
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51 504 The proposed study has several strengths. This is the first RCT to investigate the
52
53 505 effectiveness of video-conference based psychotherapy in any LMIC, as well as the first study to
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55 506 establish quality evidence on psychotherapy for SUD in Indonesia. Recruitment will be done
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3 507 throughout multiple levels of care, i.e., tertiary (referral hospitals), primary (Puskesmas) and
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5 508 community (rehabilitation centres). The latter have extensive reach encompassing all major
6
7 509 Indonesian islands, and advertising will be done via online social media, facilitating recruitment
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9
10 510 from across the nation. While CBT effectiveness is the primary outcome, the study allows
11
12 511 elucidation of real-world implementation and cost-effectiveness in a hybrid effectiveness-
13
14 512 implementation design.⁷² This is particularly true in Puskesmas, where the providers will be
15
16 513 general practitioners, and in rehabilitation centres, where the providers will be peer counsellors.
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18 514 This pragmatic RCT aims to mimic the usual clinical practice, and we hope that the result may be
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20
21 515 used to inform decision-making by patients, providers, and policymakers.¹⁰⁹
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24 516 Several limitations can also be presumed. While urine drug tests will be done for objective
25
26 517 validation, all data from participants will be self-reported and prone to recall and social desirability
27
28 518 bias. As the study will include people who use various substances, in multiple sites where TAU
29
30 519 differs, and possibly people who are not receiving any treatment, the control condition will be
31
32
33 520 heterogeneous. Variability in the providers' background may create inconsistency in CBT delivery,
34
35 521 even though TOT and treatment manuals were introduced as an effort to standardise care.
36
37 522 Treatment delivery via online video-conferencing might have poor generalizability toward people
38
39 523 with low internet literacy, as well as people in low socio-economic strata who could not afford
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41 524 smartphones—although entry-level Android-based smartphones (less than ~80 USD) are available
42
43 525 nationwide in Indonesia.
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48 526 Efforts to establish evidence-based treatment for SUD should be scaled up in Indonesia
49
50 527 and LMICs in general, where effectiveness data is sparse. The proposed study may present high-
51
52 528 quality evidence, and a successful outcome may birth a new SUD treatment module in Indonesia,
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54 529 paving way for the adoption of Indo-DARPP into the national guideline. We hope that our efforts
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3 530 may further promote a comprehensive, healthcare-centric approach—as opposed to repressive
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5 531 anti-drug policies—to tackle the substance use epidemic in the country.
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10 533 **Figure legends**

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12 534 **Figure 1.** Study flowchart for each site. A total of 20 participants will be recruited through the
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14
15 535 social network of each site. After 10 participants have been recruited in the first wave,
16
17 536 randomisation will be done to allocate participants into two groups: intervention (Indo-DARPP +
18
19 537 TAU) and control (TAU only), with 5 participants in each group. Recruitment will be continued
20
21 538 until another 10 participants (second wave) joined before randomisation and allocation, similar as
22
23
24 539 before. Treatment period will be 12 weeks. Assessments will be done 3 times: T1 (Week 0) during
25
26 540 baseline or before randomisation, T2 (Week 13-16) during post-assessment or 1-4 weeks after
27
28 541 treatment period ends, and T3 (Week 24) during 3 months after treatment ends.
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33 543 **Figure 2.** Planned trial schedule across all 8 research sites. Staggered schedules were designed to
34
35 544 spread the workload of providers in regard to Indo-DARPP intervention, as well as research staff
36
37 545 in regard to assessments. After training of providers, all sites were given approximately 1-2 months
38
39 546 to recruit at least 20 participants. Sites with relatively higher potential to recruit faster, i.e., those
40
41 547 with higher rate of patient turnover, were selected ahead in the schedule. Each site will have 2
42
43 548 waves of recruitment and treatment period.
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49 550 **Acknowledgement**

50
51
52 551 We would like to thank Dr. Takashi Kawamura for his valuable comments on the study design.
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553 **Author contributions**

554 CY, KS, and YO conceptualised the study. CY, KS, EH, and YO are the main developers of the
555 Indo-DARPP module, designed study methodology, invited and coordinated site investigators,
556 conducted training of providers, wrote the protocol, reviewed and edited the final manuscript. EB,
557 VR, PA, and AP helped in module development, study design, training of providers, and sites
558 coordination. TS provided biostatistical and epidemiological supervision. TM provided the
559 original SMARPP module and clinical input and perspectives to improve study quality. RS
560 supervised the study and procured grant. CY and RS are the principal investigators of the grants.
561 All authors have read and approved the final manuscript.

562

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567 Grants-in-Aid for Scientific Research (KAKENHI) (Grant number JP19K24256).

568

569 **Competing interests**

570 The authors declare no competing interest.

571

572 **Patient and public involvement**

573 Patients' feedback during the pilot study was incorporated into the Indo-DARPP module design.
574 Apart from that, patients and/or the public were not involved in the conduct, reporting, or
575 dissemination plans of this study.

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3 5764
5 **577 Patient consent for publication**6
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8 578 Not required.9
10 57911
12 **580 Ethics approval and trial registration**

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14 581 This study protocol was approved by the Research Ethical Committee of Faculty of Medicine,
15 582 Universitas Indonesia (approval number: KET-1175/2019), and the Ethics Committee of Graduate
16
17 583 School and Faculty of Medicine, Kyoto University (approval number: C1483). The study protocol
18
19 584 was registered at the University Hospital Medical Information Network clinical trial registry
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23 585 (UMIN-CTR) (registry number: UMIN000042186).

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29 **587 Availability of data and materials**

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31 588 The full protocol and datasets of the planned study will be available from the corresponding author
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33 589 on reasonable request.

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Table 1. Recruitment sites in this study

Name	Location	Type	Treatment as usual	Most reported primarily used substance
Cipto Mangunkusumo Hospital	Jakarta	Tertiary national general hospital	Individual psychotherapy, symptomatic pharmacotherapy	Benzodiazepine
Aceh Mental Hospital	Aceh	Tertiary provincial mental hospital	Individual psychotherapy, symptomatic pharmacotherapy	Methamphetamine
Duren Sawit Regional Hospital	Jakarta	Tertiary regional general hospital	Individual psychotherapy, symptomatic pharmacotherapy, opioid substitution therapy (buprenorphine, naloxone)	Opioid
Karisma Foundation	Jakarta	Rehabilitation center	Individual and group peer counselling	Methamphetamine, opioid
Kapeta Foundation	Banten	Rehabilitation center	Individual and group peer counselling	Methamphetamine, benzodiazepine, synthetic cannabinoids
Kios Atma Jaya	Jakarta	Rehabilitation center and regional HIV clinic	Individual psychotherapy, group peer counselling, outreach program	Opioid
Puskesmas Jatinegara	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin
Puskesmas Gambir	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin

854 Counselling focuses on education and giving advice.

855 Symptomatic pharmacotherapy gives medication for helping patients with specific psychopathologies.

856 Psychotherapy aims to help a person identify and change troubling emotions, thoughts, and behaviour.

857

Table 2. Outcome and measurement

Outcome	Measurement	Data for analysis	Type and score range	Hypothesis for intervention (vs control)	Assessment time point		
					T1	T2	T3
Primary outcome							
Abstinence from primary substance	Timeline followback (TLFB) for the past 30 days	Number of days being abstinent from primary substance divided by 30 (%).	Continuous, 0 (no use) to 100 (used every day).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/> a	✓ <input type="checkbox"/>
Secondary outcomes							
Addiction severity	Addiction Severity Index (ASI)	7 composite scores: medical, employment, alcohol use, drug use, legal, family/social, and psychiatric status. Each composite score calculated using standard formula.	Continuous, 0 (no problems) to 1 (severe problems).	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Health-related quality of life	EuroQoI-5D (EQ-5D-5L)	Health utility score, calculated from 5 items on mobility, self-care, usual activities, pain/discomfort and anxiety/depression, using Indonesian value set.	Continuous, -0.865 (impaired health) to 1 (full health).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Motivation to change	University of Rhode Island Change Assessment (URICA)	Action stage subscale, sum of 8 items.	Continuous, 8 (not active in behavioural change) to 40 (highly active in behavioural change).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Coping strategies	Brief-Coping Orientation to Problems Experienced (Brief COPE)	3 subscales: problem-focused, emotion-focused, and dysfunctional coping. Sum of 6, 10, 12 items, respectively.	Continuous, problem-focused 6 to 24, emotion-focused 10 to 40, dysfunctional 12 to 48.	Lower in dysfunctional, higher in the others	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Psychiatric symptoms	Symptom Checklist-90 Revised (SCL-90-R)	Global Severity Index (GSI), average of 90 items.	Continuous, 0 (no symptoms) to 4 (severe symptoms).	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Cognitive function	Rey Auditory Verbal Learning Test (RAVLT)	3 test results; immediate, learning, and recalling.	Continuous, 0 (low functioning) to 15 (high functioning).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Implementation outcomes							
Retention in treatment	Self-reporting for the past 3 months	Coded as 'retained' if they had therapeutic contacts in at least 75% of the planned number of therapeutic contacts.	Categorical, 'retained' = 1, 'not retained' = 0.	More 'retained'		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Treatment satisfaction	Client Satisfaction Questionnaire-3 (CSQ-3)	Sum of 3 items.	Continuous, 4 (not satisfied) to 12 (satisfied).	Higher		✓ <input type="checkbox"/>	
Group cohesion	Group Therapy Experience Scale (GTES)	Sum of 16 items.	Continuous, 16 (poor cohesion) to 80 (great cohesion).	Not applicable: measured only in intervention arm		✓ <input type="checkbox"/>	

^a Objective validation by urine drug test for 8 substances: alcohol, amphetamine, morphine, cannabinoids, methamphetamine, benzodiazepine, cocaine, synthetic cannabinoids

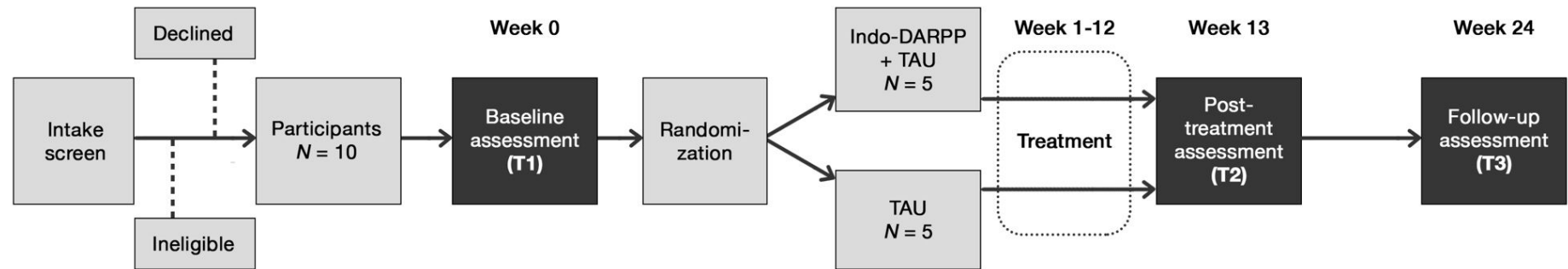


Figure 1. Study flowchart for each site. A total of 20 participants will be recruited through the social network of each site. After 10 participants have been recruited to constitute one wave, randomisation will be done to allocate participants into two groups: intervention (Indo-DARPP + TAU) and control (TAU only), with 5 participants in each group. Recruitment will be continued until another 10 participants (second wave) joined before randomisation and allocation similar as before. Treatment period will be 12 weeks. Assessments will be done 3 times: T1 (Week 0) during baseline or before randomisation, T2 (Week 13-16) during post-assessment or 1-4 weeks after treatment period ends, and T3 (Week 24) during 3 months after treatment ends.

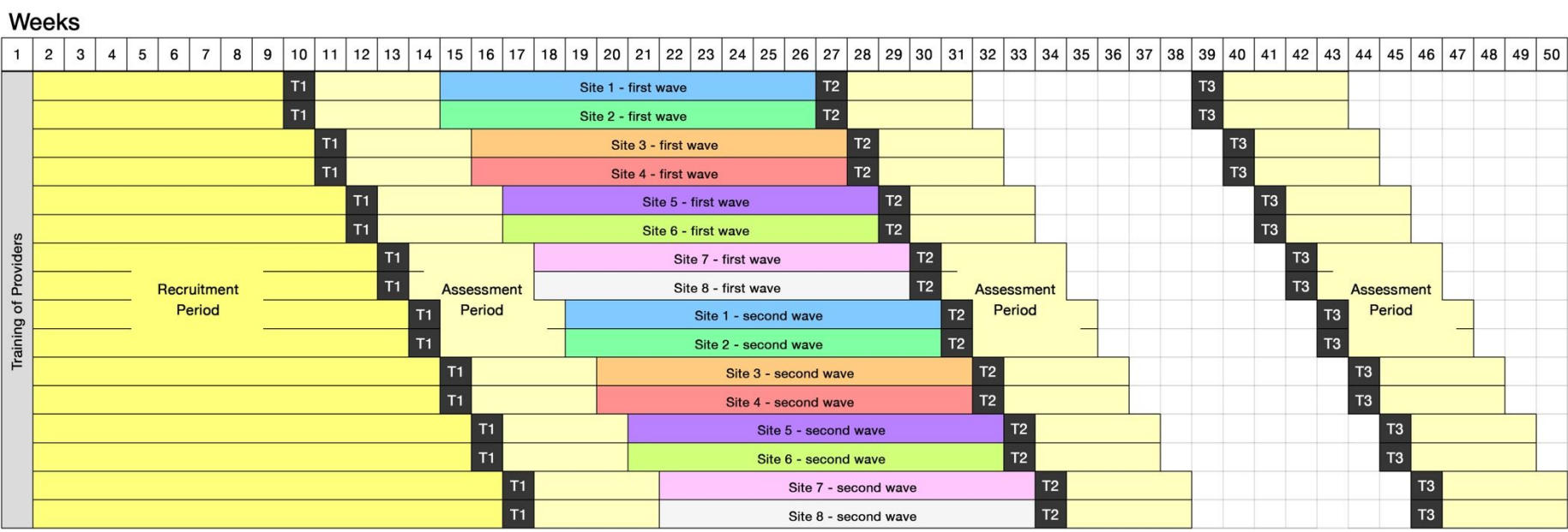


Figure 2. Planned trial schedule across all 8 research sites. Staggered schedules were designed to spread the workload of providers in regard to Indo-DARPP intervention, as well as research staff in regard to assessments. After training of providers, all sites were given approximately 1-2 months to recruit at least 20 participants. Sites with relatively higher potential to recruit faster, i.e., those with higher rate of patient turnover, were selected ahead in the schedule. Each site will have 2 waves of recruitment and treatment period.

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

	Reporting Item	Page Number
Administrative information		
Title	#1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a Trial identifier and registry name. If not yet registered, name of intended registry	4, 23
Trial registration: data set	#2b All items from the World Health Organization Trial Registration Data Set	n/a, trial already registered as described in 2a.
Protocol version	#3 Date and version identifier	23
Funding	#4 Sources and types of financial, material, and other support	26-27
Roles and	#5a Names, affiliations, and roles of protocol	26

1	responsibilities:	contributors	
2	contributorship		
3			
4	Roles and	#5b	Name and contact information for the trial
5	responsibilities:		sponsor
6	sponsor contact		
7	information		
8			
9			
10			
11	Roles and	#5c	Role of study sponsor and funders, if any, in
12	responsibilities:		study design; collection, management,
13	sponsor and funder		analysis, and interpretation of data; writing of
14			the report; and the decision to submit the
15			report for publication, including whether they
16			will have ultimate authority over any of these
17			activities
18			
19			
20			
21			
22			
23	Roles and	#5d	Composition, roles, and responsibilities of the
24	responsibilities:		coordinating centre, steering committee,
25	committees		endpoint adjudication committee, data
26			management team, and other individuals or
27			groups overseeing the trial, if applicable (see
28			Item 21a for data monitoring committee)
29			
30			
31			
32			
33	Introduction		
34			
35	Background and	#6a	Description of research question and
36	rationale		justification for undertaking the trial, including
37			summary of relevant studies (published and
38			unpublished) examining benefits and harms
39			for each intervention
40			
41			
42			
43			
44	Background and	#6b	Explanation for choice of comparators
45	rationale: choice of		
46	comparators		
47			
48			
49	Objectives	#7	Specific objectives or hypotheses
50			
51			
52	Trial design	#8	Description of trial design including type of
53			trial (eg, parallel group, crossover, factorial,
54			single group), allocation ratio, and framework
55			(eg, superiority, equivalence, non-inferiority,
56			exploratory)
57			
58			
59			
60			

1 **Methods:**

2 **Participants,**

3 **interventions, and**

4 **outcomes**

5

6

7

8 Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10-11
15 Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	11
24 Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13
29 Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	22-23
38 Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	22-23
45 Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	15
50 Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome.	15-19

1 Explanation of the clinical relevance of
 2 chosen efficacy and harm outcomes is
 3 strongly recommended
 4

5
 6 Participant timeline [#13](#) Time schedule of enrolment, interventions 10, 19, 26
 7 (including any run-ins and washouts),
 8 assessments, and visits for participants. A
 9 schematic diagram is highly recommended
 10 (see Figure)
 11
 12

13
 14 Sample size [#14](#) Estimated number of participants needed to 20
 15 achieve study objectives and how it was
 16 determined, including clinical and statistical
 17 assumptions supporting any sample size
 18 calculations
 19
 20
 21
 22

23 Recruitment [#15](#) Strategies for achieving adequate participant 11
 24 enrolment to reach target sample size
 25
 26

27 **Methods:**
 28 **Assignment of**
 29 **interventions (for**
 30 **controlled trials)**
 31
 32
 33

34 Allocation: [#16a](#) Method of generating the allocation 12
 35 sequence
 36 generation
 37 (eg, computer-generated random
 38 numbers), and list of any factors for
 39 stratification. To reduce predictability of a
 40 random sequence, details of any planned
 41 restriction (eg, blocking) should be provided
 42 in a separate document that is unavailable to
 43 those who enrol participants or assign
 44 interventions
 45
 46
 47
 48

49 Allocation [#16b](#) Mechanism of implementing the allocation 12
 50 concealment
 51 mechanism
 52 (eg, central telephone; sequentially
 53 numbered, opaque, sealed envelopes),
 54 describing any steps to conceal the
 55 sequence until interventions are assigned
 56
 57

58 Allocation: [#16c](#) Who will generate the allocation sequence, 12
 59
 60

1	implementation		who will enrol participants, and who will	
2			assign participants to interventions	
3				
4	Blinding (masking)	#17a	Who will be blinded after assignment to	12, 19
5			interventions (eg, trial participants, care	
6			providers, outcome assessors, data	
7			analysts), and how	
8				
9				
10				
11	Blinding (masking):	#17b	If blinded, circumstances under which	n/a, only assessors are
12	emergency		unblinding is permissible, and procedure for	blinded
13	unblinding		revealing a participant's allocated	
14			intervention during the trial	
15				
16				
17				
18	Methods: Data			
19	collection,			
20	management, and			
21	analysis			
22				
23				
24				
25	Data collection plan	#18a	Plans for assessment and collection of	15-19
26			outcome, baseline, and other trial data,	
27			including any related processes to promote	
28			data quality (eg, duplicate measurements,	
29			training of assessors) and a description of	
30			study instruments (eg, questionnaires,	
31			laboratory tests) along with their reliability	
32			and validity, if known. Reference to where	
33			data collection forms can be found, if not in	
34			the protocol	
35				
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42	Data collection plan:	#18b	Plans to promote participant retention and	19, 22-23
43	retention		complete follow-up, including list of any	
44			outcome data to be collected for participants	
45			who discontinue or deviate from intervention	
46			protocols	
47				
48				
49				
50				
51	Data management	#19	Plans for data entry, coding, security, and	23
52			storage, including any related processes to	
53			promote data quality (eg, double data entry;	
54			range checks for data values). Reference to	
55			where details of data management	
56			procedures can be found, if not in the	
57				
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60				

1		protocol	
2			
3	Statistics: outcomes	#20a Statistical methods for analysing primary and	20-22
4		secondary outcomes. Reference to where	
5		other details of the statistical analysis plan	
6		can be found, if not in the protocol	
7			
8			
9			
10	Statistics: additional	#20b Methods for any additional analyses (eg,	21-22
11	analyses	subgroup and adjusted analyses)	
12			
13			
14	Statistics: analysis	#20c Definition of analysis population relating to	21
15	population and	protocol non-adherence (eg, as randomised	
16	missing data	analysis), and any statistical methods to	
17		handle missing data (eg, multiple imputation)	
18			
19			
20			
21	Methods:		
22	Monitoring		
23			
24			
25	Data monitoring:	#21a Composition of data monitoring committee	23, DMC will not be
26	formal committee	(DMC); summary of its role and reporting	convened as the
27		structure; statement of whether it is	intervention involves a
28		independent from the sponsor and competing	short-term
29		interests; and reference to where further	psychotherapy with
30		details about its charter can be found, if not in	known minimal risk.
31		the protocol. Alternatively, an explanation of	
32		why a DMC is not needed	
33			
34			
35			
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37			
38	Data monitoring:	#21b Description of any interim analyses and	23, interim analysis is
39	interim analysis	stopping guidelines, including who will have	not planned due to the
40		access to these interim results and make the	short duration of
41		final decision to terminate the trial	intervention.
42			
43			
44			
45	Harms	#22 Plans for collecting, assessing, reporting, and	22-23
46		managing solicited and spontaneously	
47		reported adverse events and other	
48		unintended effects of trial interventions or trial	
49		conduct	
50			
51			
52			
53			
54	Auditing	#23 Frequency and procedures for auditing trial	23, there will be no
55		conduct, if any, and whether the process will	auditing process by
56		be independent from investigators and the	independent
57		sponsor	investigators.
58			
59			
60			

Ethics and dissemination

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	23, 28
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	23
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	23
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	23
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	23
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	15, CBT intervention will be made available for control group after the end of the study.

1	Dissemination	#31a	Plans for investigators and sponsor to	23
2	policy: trial results		communicate trial results to participants,	
3			healthcare professionals, the public, and	
4			other relevant groups (eg, via publication,	
5			reporting in results databases, or other data	
6			sharing arrangements), including any	
7			publication restrictions	
8				
9				
10				
11				
12				
13	Dissemination	#31b	Authorship eligibility guidelines and any	26-27
14	policy: authorship		intended use of professional writers	
15				
16				
17	Dissemination	#31c	Plans, if any, for granting public access to the	28
18	policy: reproducible		full protocol, participant-level dataset, and	
19	research		statistical code	
20				
21				
22	Appendices			
23				
24				
25	Informed consent	#32	Model consent form and other related	11, 23
26	materials		documentation given to participants and	
27			authorised surrogates	
28				
29				
30	Biological	#33	Plans for collection, laboratory evaluation,	16
31	specimens		and storage of biological specimens for	
32			genetic or molecular analysis in the current	
33			trial and for future use in ancillary studies, if	
34			applicable	
35				
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Notes:

- 2b: n/a, trial already registered as described in 2a.
- 5b: n/a, no trial sponsor.
- 5c: n/a, no involvement of funders in the study design.
- 5d: n/a, no direct intervention in the study design by the host universities.
- 17b: n/a, only assessors are blinded
- 21a: 23, DMC will not be convened as the intervention involves a short-term psychotherapy with known minimal risk.
- 21b: 23, interim analysis is not planned due to the short duration of intervention.

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- 23: 23, there will be no auditing process by independent investigators.
 - 30: 15, CBT intervention will be made available for control group after the end of the study. The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 15. February 2021 using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)

BMJ Open

Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for a multicentre randomised controlled trial in Indonesia

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Primary Subject Heading:	Addiction
Secondary Subject Heading:	Addiction, Global health, Mental health, Evidence based practice
Keywords:	Substance misuse < PSYCHIATRY, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, PSYCHIATRY, Clinical trials < THERAPEUTICS

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1
2
3 **1 Title**
4

5 2 Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for
6
7
8 3 a multicentre randomised controlled trial in Indonesia
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10 4
11
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35 38 Abstract: 261 words
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37 39 Main text: 5,598 words
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40 Abstract

41 **Background:** Substance use disorder (SUD) is a leading contributor to the global burden of
42 disease. In Indonesia, formal treatment availability falls below the targeted coverage for people
43 with SUD needing care. A standardised and scalable therapeutic option for SUD with potential for
44 widespread implementation is needed, yet evidence-based data in the country is scarce. Here, we
45 developed a cognitive behavioural therapy (CBT)-based group telemedicine model and proposed
46 to investigate the effectiveness and implementability for providers, in a multicentre randomised
47 controlled trial (RCT).

48 **Methods:** Participants will be recruited from the communities across Indonesia. Recruitment will
49 be done through the social networks of eight sites: three hospitals, two primary healthcare centres,
50 and three rehabilitation centres. The intervention is a relapse prevention program called Indo-
51 DARPP, a newly-developed 12-week module based on CBT and motivational interviewing
52 constructed in the Indonesian context. The program is delivered by healthcare providers and peer
53 counsellors in a group therapy via video-conferencing—intervention will be given in addition to
54 treatment as usual. Control comparison is treatment as usual only. A total of 220 participants will
55 be randomly divided by half into the intervention and control group. The primary outcome is the
56 increase of percent days of abstinence from the primarily used substance in the past 28 days.
57 Secondary outcomes include addiction severity, quality of life, motivation to change, psychiatric
58 symptoms, cognitive function, coping, and internalised stigma. Assessments will be done at
59 baseline (week 0), post-treatment (week 13), three, and twelve months after the treatment
60 completion (week 24 and 60). Retention, participant satisfaction, and cost-effectiveness will be
61 assessed as implementation outcomes.

1
2
3 62 **Ethics and dissemination:** The study protocol was reviewed and approved by the Ethics
4
5 63 Committees in Universitas Indonesia and Kyoto University. Results will be disseminated into
6
7 64 academic journals and international conferences. Provided positive outcomes, the treatment
8
9 65 program will be advocated to the Indonesian government for adoption as a formal healthcare-based
10
11 66 approach for SUD..
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15 67 **Trial registration number:** UMIN000042186
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18 68 **Keywords:** *substance use disorder, telemedicine, cognitive behavioural therapy, relapse*
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20 69 *prevention, motivational interviewing, Indonesia, peer counsellor*
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3 71 **Strengths and limitations of this study**
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- 6 72 ● The proposed study will be the first to establish high-quality evidence for a cognitive
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8 73 behavioural therapy (CBT)-based relapse prevention program for substance use disorder
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10 74 (SUD) in Indonesia.
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13 75 ● Telemedicine enables far-reaching nationwide participation, connecting participants with
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15 76 providers in major cities, which in this study will include providers from three different
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17 77 levels of health care: tertiary hospitals, primary healthcare centres, and rehabilitation
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19 78 centres.
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22 79 ● A successful outcome may produce a new SUD treatment module in Indonesia and pave
23
24 80 the way for adoption into the national guideline.
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27 81 ● Study limitations include risk of recall and social desirability bias, heterogeneous control
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29 82 condition, and possible variability in treatment provision.
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84 Introduction

85 Substance use disorder (SUD) is a condition characterised by the inability to control the
86 use of psychoactive substances, i.e., alcohol and psychotropic drugs, which disrupts daily living.
87 SUD remains a major and growing health problem worldwide. According to the Global Burden of
88 Disease (GBD) survey in 2016, SUD globally contributes to 131 million disability-adjusted life
89 years (DALY), or 5.5% of all DALYs,¹ and this number has been increasing since the 1990s.²
90 While substance use itself is more widespread in high-income countries (HICs), low- and middle-
91 income countries (LMICs) are disproportionately burdened. Absolute mortality rate due to SUD
92 was greatest in LMICs with large populations,³ and people with economic disadvantage are more
93 likely to develop SUD.⁴ The Movement for Global Mental Health and the World Health
94 Organization both have described substantial treatment gaps in LMICs, where the number of
95 people with SUD in need of health care far exceeds the availability of formal treatment services.⁵⁻⁷
96 While this does not take traditional care into account, indeed, merely 1% of people with SUD in
97 LMICs received treatment standardised by the government.⁸

98 In Indonesia, the world's third most populous LMIC, the national SUD prevalence was
99 estimated by the national government at 1.8% or 3.3 million people, with the most used substance
100 being marijuana (68%), followed by amphetamine-type stimulants (ATS, 42%), opioids (38%)
101 and sedatives (35%).^{9,10} Its strategic intercontinental location contributes to the country's infamous
102 reputation as a marijuana exporter and drug trafficking hub.¹¹ While there is an 80% decrease of
103 injecting drug use (IDU) from 2002 to 2016,¹⁰ an increasing use of psychoactive medications out
104 of prescription has been noted, particularly benzodiazepines.¹² Similar to other Muslim majority
105 countries,¹³ alcohol consumption is comparatively low in Indonesia—prevalence estimate of
106 alcohol use disorder was 0.8% in 2016, much lower than the overall rate in Southeast Asia

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3 107 (3.9%).¹⁴ New psychoactive substances (NPS) has also entered the country in the last decade.¹⁵
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5 108 The current COVID-19 pandemic may also further complicate the SUD situation in Indonesia, as
6
7 109 observed elsewhere.¹⁶ In unpublished data from our co-author (KS), since the start of pandemic in
8
9 110 early April 2020, there has been an increase in both drug and alcohol use in Indonesia of up to
10
11 111 2.5%. Higher drug use might be influenced by lockdown isolation, socio-economic issues due to
12
13 112 unemployment, and heavier mental burden.
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16
17 113 In Indonesia, formal mental health providers and facilities are severely lacking; in a nation
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19 114 of 267 million people, only 773 psychiatrists (0.32 per 100,000 people) are employed—second
20
21 115 lowest in Southeast Asia¹⁷—across hospitals with psychiatric care, half of which are located within
22
23 116 the capital island of Java.¹⁸ In terms of government-run primary healthcare centres (abbreviated as
24
25 117 *Puskesmas* in Indonesian), out of all *Puskesmas* (~1,700 nationwide), only a fifth actively provide
26
27 118 mental health care.^{18,19} Current formal treatment options for SUD include one-on-one supportive
28
29 119 psychotherapy, symptomatic pharmacotherapy, peer counselling, and opioid substitution.
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31 120 Methadone maintenance therapy (MMT) is available in *Puskesmas* since 2006, but coverage
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33 121 remains low: only 5% in a 2012 study²⁰ due to methadone cost, reliance on subsidisation, lack of
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35 122 program sustainability,²¹ and the tendency to incarcerate patients under the 'war on drugs'
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37 123 policy.^{20,22} Three-months retention rate of MMT was only 60-74%.^{23,24} Psychiatric comorbidities
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39 124 were also common in MMT users and quality of life was evidently lower.²⁵ Most concerning,
40
41 125 insufficient formal treatment coverage and the lack of standardised care for SUD prompted
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43 126 policymakers to enact punitive criminalization practices—even more evident by the current
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45 127 Indonesian administration—in place of a comprehensive mental health care approach.^{26,27}
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52 128 Behavioural therapies in many forms are commonly applied for SUD, most popular of
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54 129 which is cognitive behavioural therapy (CBT). Strong evidence backs the efficacy of CBT for
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3 130 SUD treatment. A meta-analysis gave a moderate overall effect size ($d = 0.45$), with outcomes
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5 131 ranging from the self-report abstinence, drug-free urine at treatment exit, to increased retention in
6
7 132 therapy.^{28,29} CBT strategies include: (a) contingency management (CM)³⁰ which introduces reward
8
9 133 for abstinence, (b) motivational interviewing (MI) which explores and resolves ambivalence,^{31,32}
10
11 134 (c) relapse prevention (RP) which helps participants to identify high-risk triggers and prevent
12
13 135 craving, or (d) combinations thereof.³³ Therapy could be delivered individually or in groups; the
14
15 136 latter evidently increased adherence and self-disclosure, as well as decreased the time needed by
16
17 137 providers to treat a participant by 40%.^{34,35} CBT (particularly MI and RP) is relatively low-cost
18
19 138 and can be delivered by non-specialists, making it beneficial in resource-limited settings.^{36,37} In
20
21 139 regard to LMICs, while an ample amount of RCTs have supported CBT efficacy to reduce alcohol
22
23 140 use,^{38,39} evidence for drug use disorders is limited. Only five RCTs have been published so far,^{40–}
24
25 141 ⁴⁴ in which three of them were inpatient-based, even though SUD management mandates
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27 142 sustainable outpatient care in community settings.

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33 143 Telemedicine has the potential to elevate SUD treatment coverage in Indonesia. Internet
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35 144 communication overcomes the geographical barriers of the Indonesian archipelago, and saves time
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37 145 as well as transportation cost for both patients and providers, either in remote areas where health
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39 146 services are thinly spread,⁴⁵ or major cities with heavy traffic such as Jakarta.⁴⁶ Privacy is better
40
41 147 ensured; visiting clinics may disclose SUD diagnosis, which is one of the most stigmatised health
42
43 148 conditions.⁴⁷ Synchronous telemedicine via live video feed connects participants in real-time,
44
45 149 improving rapport and potentially adherence, relative to asynchronous telemedicine (e.g., text
46
47 150 message or web application). Video-conferencing has been effectively used in SUD treatment,^{48–}
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49 151 ⁵³ but recent systematic reviews^{54–59} have revealed three lacking points: (1) previous reports merely
50
51 152 focused on alcohol and opioid use,^{48,51–53} (2) group therapy was investigated by only one small-

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3 153 scale pilot RCT,⁵² and (3) no studies were done in LMICs. The use of internet devices has been
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5 154 rapidly expanding in LMICs, including Indonesia. Smartphone users accounted for 74% of the
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8 155 Indonesian population in 2019, possibly reaching 89% by 2025.⁶⁰ Furthermore, the COVID-19
9
10 156 pandemic has elevated telemedicine from an accessory to a necessity, including for psychiatric
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12 157 care.⁶¹ Its accessibility and acceptance among SUD patients, as shown in a recent survey,⁶² may
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14
15 158 potentially sustain telemedicine as the 'new normal' even in the post-pandemic world.^{63,64}
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17 159 Given the above challenges and opportunities, we propose a clinical trial to evaluate a
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20 160 relapse prevention telemedicine program for SUD in Indonesia. We have developed a new
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22 161 treatment module called *Indonesia Drug Addiction Relapse Prevention Program* (Indo-DARPP),
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24 162 which is a 12-week CBT-based group therapy. The primary objective is to evaluate the
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26
27 163 effectiveness of Indo-DARPP delivered via video conference (tele-Indo-DARPP), added to
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29 164 treatment as usual (TAU), to increase abstinence from primarily-used substances, compared to
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31 165 TAU only. Secondary objectives are to assess the effectiveness of the program toward changes in
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34 166 quality of life, motivation to change, psychological symptoms, cognitive function, coping, and
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36 167 internalised stigma. Retention, participant satisfaction, and group cohesion will be assessed as
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38 168 implementation outcomes, and cost-effectiveness analyses will be conducted to inform health
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40 169 policy investment.
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46 171 **METHODS**

49 172 **Trial design**

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52 173 This trial is a parallel-group, two-arm, assessor-blinded, multicentre superiority
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54 174 randomised controlled trial. The protocol adheres to the Standard Protocol Items:
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3 175 Recommendations for Interventional Trials (SPIRIT) checklist (**Supplementary file 1**). We
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5 176 design the study as a pragmatic type 1 hybrid effectiveness-implementation trial,⁶⁵ which allows
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7 177 concurrent investigation of intervention effectiveness as well as implementation in clinical practice,
8
9 178 focusing on the former. After intake screening, participants will undergo baseline assessment (T1)
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11 179 and randomly allocated in a 1:1 ratio either to the intervention arm receiving tele-Indo-DARPP in
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13 180 addition to TAU, or control arm receiving TAU only. Treatment will be done for 12 weeks,
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15 181 followed by post-treatment assessment (T2) in week 13, and follow-up assessment (T3) in week
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17 182 24 (**Figure 1**).

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25 184 [Figure 1 approximately here.]
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29 30 186 **Participants and settings**

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33 187 Participants will be recruited from the community across Indonesia via social networks of
34
35 188 eight sites: two primary health centres (Puskesmas), three referral hospitals, and three drug
36
37 189 rehabilitation services (**Table 1**). These facility types constitute the community-based treatment
38
39 190 model for SUD in Indonesia,⁶⁶ encompassing patients with various characteristics in motivation
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41 191 for behavioural change, substance use history, comorbidities, and current stage in treatment.
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43 192 Recruitment will be done via online advertisement (i.e., social networking services, group chat,
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45 193 website) and direct approach to current and former clients through outpatient services, in a
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47 194 consecutive sampling. Although all facilities are located in urban settings, the recruitment process
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49 195 will include online social media of each site, whose coverage is nationwide particularly for the
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3 196 rehabilitation centers, and we expect recruitment of participants from anywhere in Indonesia and
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5 197 not limited to the physical scope of each site.
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8 198 Puskesmas provides general primary care, pharmacotherapy for cases without any
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10 199 complications, and MMT. Referral hospitals provide psychotherapy, pharmacotherapy, opioid
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12 200 substitution therapy using buprenorphine/naloxone, and specialised care for cases with
13
14 201 complications, such as severe psychiatric disorder. Rehabilitation services provide long-term
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16 202 psychosocial care, typically in a mutual-aid group form. Selection of sites was based on feasibility,
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18 203 client demographic, recruitment potential, and availability of providers. While recruited
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20 204 participants may not be under treatment in the aforementioned sites at the time, facilitators for tele-
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22 205 Indo-DARPP will be the staff of respective sites: general practitioners in Puskesmas, psychiatrists
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24 206 in referral hospitals, and counsellors in rehabilitation centres.
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32 208 [Table 1 approximately here.]
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38 210 Inclusion criteria will be those who: 1) aged 18-65 years old; 2) are diagnosed as having
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40 211 substance use disorder based on DSM-5; 3) have used primarily-used substance for at least one
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42 212 day in the past one year; 4) have access to electronic devices (i.e., smartphone, mobile tablet,
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44 213 personal computer) with internet connection; and 5) are proficient in Indonesian. Exclusion criteria
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46 214 will be those who: 1) have severe comorbidity that hinder informed consent or group therapy
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48 215 participation; and 2) currently hospitalised or are using residential care.
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52 216 We set a broad inclusion criteria, i.e. substance use in the past one year, for two reasons.
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54 217 First, proportional hazard models showed that the probability of relapse remains high before
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3 218 achieving one year of abstinence, and only declined substantially after 16 months^{67,68}. Thus, it is
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5 219 clinically important to examine treatment efficacy on people who have not achieved one-year
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8 220 abstinence.⁶⁸ Second, in this pragmatic effectiveness study,⁶⁹ we design eligibility criteria to more
9
10 221 closely represent a population seen in real-world Indonesian clinical practice. Indeed, patients
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12 222 treated at the collaborating clinical sites include people who have been abstinent for more than one
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14
15 223 month, but still experience cravings and tendency to relapse.
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20 225 **Recruitment**

21
22 226 Patients eligibility will be assessed by collaborating staff at respective sites. For those who
23
24 227 have never been diagnosed as having SUD, addiction psychiatrists will conduct clinical
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26 228 assessments via video call. Oral and written informed consent will be given to those eligible. The
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28 229 consent form in English is provided in **Supplementary file 2**. For urine tests, explanations will be
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30 230 given immediately after post-treatment (T2) assessment, as anticipation for urine tests may
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32 231 influence substance use behaviour. Consent to urine test or absence thereof will not affect study
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35 232 participation.
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40 234 **Randomisation and blinding**

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42 235 Participants will be randomly allocated to either an intervention (tele-Indo-DARPP +
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44 236 TAU) or a control (TAU only) arm, with stratification by study site. Each site will conduct two
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46 237 waves of recruitment with 10 participants in each wave. After the first wave at each site, we will
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48 238 randomly allocate 5 participants to either intervention or control group. All participants in a given
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50 239 tele-Indo-DARPP group will be from the same recruitment site. Recruitment will be continued
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3 240 until another 10 participants (second wave) joined, and random allocation will be done similarly.
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5 241 Allocation will be done using computer-generated random numbers by a researcher who will be
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7 242 blinded to participants' information, except for ID. Data will be collected by researchers who are
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9 243 blinded to the allocation arm of each participant. Participants and treatment providers are not
10
11 244 blinded as the intervention is a psychotherapy.
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18 246 **Development of Indo-DARPP**

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21 247 Indo-DARPP was based on the Serigaya Methamphetamine Relapse Prevention Program
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23 248 (SMARPP), a face-to-face group CBT-based intervention in Japan developed by a co-author
24
25 249 (TM),⁷⁰ which itself is based on the Matrix Model developed in the US.⁷¹ Efficacy of SMARPP in
26
27 250 increasing abstinence duration, motivation to change, and participation in self-help groups have
28
29 251 been reported.⁷²⁻⁷⁴ SMARPP has been widely implemented as a psychotherapy for SUD not only
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31 252 in psychiatric clinics but also primary healthcare, rehabilitation, and probation offices in Japan,
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33 253 covered by the national insurance scheme. SMARPP has excellent scalability via the use of a
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35 254 workbook, and can be delivered by non-specialists who have received a brief training.
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40 255 Contents of Indo-DARPP are based on the RP model, where participants are guided to
41
42 256 learn high-risk situations for substance use and coping strategies. The program also incorporates
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44 257 elements of MI and psychoeducation on substances, SUD, and its common comorbidities. While
45
46 258 CM could also be added, it increases cost and may not be effective in the longer term,⁷⁵ and thus,
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48 259 MI and RP approaches will be utilised in this study. Adaptations from SMARPP were done via
49
50 260 focus group discussions involving Japanese researchers, Indonesia-based psychiatrists, general
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52 261 practitioners, and peer counsellors, all of whom have extensive experience ranging 4-20 years in
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54 262 the addiction field. Substances discussed in the module are amphetamine-type stimulants,
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3 263 benzodiazepines and other prescribed medicines, opioids, marijuana, NPS, and alcohol. Indo-
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5 264 DARPP is designed to be delivered in a small group format using a workbook (see **Supplementary**
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8 265 **file 3** for table of contents of the workbook), and sessions will be provided by one facilitator and
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10 266 one co-facilitator who is a peer counsellor with lived experiences of SUD.

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12
13 267 A pilot test was held at Site 1, recruiting nine SUD patients into a 12-week tele-Indo-
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15 268 DARPP, to check the content acceptability and feasibility of the online delivery format. Further
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17 269 adjustments were made based on the pilot results and patient feedback.

20 270

23 271 **Intervention via video conference: tele-Indo-DARPP**

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26 272 Tele-Indo-DARPP will be implemented in group therapy with a maximum of five patients, in
27
28 273 a weekly 2-hour session for 12 weeks, delivered using the online video-conferencing application
29
30 274 Zoom. URLs for video conferences will be informed weekly by the research team to five Indo-
31
32 275 DARPP participants and two providers via online group chat for participants who agreed to share
33
34 276 their contacts. Those who declined to share will be notified via personal messages. Each Indo-
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36 277 DARPP session consists of three parts: (1) "check-in", where participants share history of
37
38 278 substance use and craving in the past week, and analyse high-risk situations and coping actions
39
40 279 taken; (2) "today's topic", where providers guide discussion of specific workbook chapters and
41
42 280 participants fill in exercises, and (3) "check-out", where providers give summary and invite
43
44 281 feedback, and participants anticipate triggers and coping strategies for the following week.

49 282

52 283 **Providers of tele-Indo-DARPP**

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3 284 At least two persons from each site will serve as facilitators, who meet the following criteria:
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5 285 psychiatrist with at least 1-year experience in treating SUD patients, or healthcare provider with
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7 286 at least 2-year experience in providing care for SUD patients, or peer counsellor with at least 2-
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9 287 year involvement in any organisation providing services for people with SUD. The roles of
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11 288 facilitators are to (1) lead and moderate Indo-DARPP sessions, (2) elaborate on chapter contents,
12
13 289 (3) manage participants to follow rules, (4) establish safe and warm environment, (5) provide
14
15 290 consultation including out-of-session, and (6) contact absent participants to encourage attendance.
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20 291 Similarly, at least two persons from each site will serve as co-facilitators for the tele-Indo-
21
22 292 DARPP, described as peer counsellors who have also experienced SUD and recovered, with at
23
24 293 least 6-month involvement in any organisations providing services for people with SUD. The role
25
26 294 of co-facilitator is to (1) share personal experiences relevant to discussion topics, (2) assist
27
28 295 facilitators in ensuring a safe and warm environment, (3) provide general support to the Indo-
29
30 296 DARPP process, and (4) provide counsel, including out-of-session.
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37 298 **Training and supervision**

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39 299 Prior to recruitment, all providers will receive two full-day training online sessions on basic
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41 300 knowledge of SUD treatment, Indo-DARPP contents, video demonstration, hands-on role play,
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43 301 discussion on difficult cases, tele-Indo-DARPP, and study-related quality control. Workbooks and
44
45 302 manuals were handed to all providers, and close communication with the research team will be
46
47 303 kept via WhatsApp group chat throughout the research period. To maintain treatment fidelity and
48
49 304 quality control, during actual tele-Indo-DARPP sessions, addiction psychiatrists from the research
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51 305 team (KS and EH) will randomly select and observe at least two sessions per Indo-DARPP group,
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3 306 meaning at each wave at each site thus constituting 16.7% of the all sessions, and review the
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5 307 providers using a structured checklist.
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10 309 **Control condition**

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14 310 Participants who received treatment before the study will continue to receive treatment as
15
16 311 usual, regardless of group allocation. TAU was chosen as the control condition because the Indo-
17
18 312 DARPP is expected to complement the existing treatment services for SUD in every level of care.
19
20 313 TAU differs according to the service location (**Table 1**). Individual psychotherapy is typically
21
22 314 conducted via in-person short consultation (~15 minutes) with clinical psychiatrists.
23
24 315 Pharmacotherapy is given to alleviate symptoms, e.g., anxiolytics for anxiety. Patients undergoing
25
26 316 MMT visit the site almost every day to receive their daily doses, while patients undergoing
27
28 317 substitution therapy with buprenorphine with naloxone visit every week. All participants will be
29
30 318 able to continue any outpatient pharmacological treatment (e.g., MMT, antidepressants) and
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32 319 psychotherapy (e.g., twelve-step group sessions).
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40 321 **Primary outcome**

41 42 322 **Abstinence from primarily used substance**

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45 323 The primary outcome is the percent days of abstinence from the primarily used substance
46
47 324 during the past 28 days. Percent days of abstinence has been shown to be sensitive to the effects
48
49 325 of CBT and are good predictors of SUD treatment follow-up.⁷⁶ Use of primarily used substance
50
51 326 each day (yes/no) for 28 days will be retrospectively interviewed on a weekly-basis using the
52
53 327 timeline followback (TLFB) method (**Table 2**), which has good validity and high test-retest
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3 328 reliability in measuring substance consumption.^{77,78} The participants will be asked to recount every
4
5 329 week, to reduce the risk of recall bias. The primarily used substance is defined as the substance
6
7 330 causing the most problems for participants and drives them to seek care, at T1.

8
9
10 331 We will collect urine samples to test the presence of the primarily used substance once at
11
12 332 T2. Thresholds for a positive result are >100 ng/ml for ethyl glucuronide (for alcohol use), >300
13
14 333 ng/ml for amphetamine-type stimulant (i.e., d-methamphetamine and MDMA), >100 ng/ml for
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16 334 diacetyl morphine (heroin), cocaine, and benzodiazepine, >50 ng/ml for synthetic cannabis (K2),
17
18 335 and > 25 ng/ml for tetrahydrocannabinol (marijuana). Urine tests in this study will only serve to
19
20 336 corroborate the data of self-reported substance use at the primary endpoint (T2), and not as an
21
22 337 objective surrogate of all self-reported substance use data at every time point. This was planned to
23
24 338 improve feasibility for participants and minimise drop-out due to the burden of data collection
25
26 339 (urine test needs in-person assessment, unlike all other measurements in this study), especially
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28 340 among participants who reside in remote areas deemed most benefited from online therapy.
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35 342 [Table 2 approximately here.]
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39 344 **Secondary outcomes**

40 345 *Addiction severity*

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42 346 The Addiction Severity Index (ASI) is the most widely used measure in the field of
43
44 347 addiction.⁷⁹ Internal consistency, test-retest reliability, and scale independence of ASI to measure
45
46 348 substance use have long been established.^{80,81} The Treatnet ASI version 3.0 by the United Nations
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48 349 Office on Drugs and Crime (UNODC) will be used; the scale is available in Indonesian, and one
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50 350 addiction treatment centre in Indonesia was included in its development trial.⁸²
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3 351 ***Health-related quality of life***
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5 352 The five-level version of the five-dimensional EuroQoL (EQ-5D)^{83,84} will be used to assess
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7
8 353 health-related quality of life (HRQoL), which has been done before among SUD patients with
9
10 354 confirmed construct validity.^{85,86} The total utility score will be obtained using the already
11
12 355 established value set in Indonesia.⁸⁷
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15 356 ***Motivation to change***
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17 357 Motivation to change will be assessed by the Action subscale the University of Rhode
18
19 358 Island Change Assessment (URICA).⁸⁸ URICA has been shown to have good validity, where
20
21 359 higher scores indicate that the person has committed to develop positive behavioural changes
22
23 360 (Diclemente and County, 2000; Diclemente et al., 2004).⁸⁹
24
25

26 361 ***Coping***
27

28 362 Types of engaged stress coping will be assessed by the Brief Coping Orientations to
29
30 363 Problems Experienced (Brief COPE),⁹⁰ which is commonly used for SUD patients.⁹¹ A higher
31
32 364 score indicates that the person has adopted the coping type more frequently.
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34

35 365 ***Psychiatric symptoms***
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37 366 Psychiatric symptoms will be evaluated by the Symptom Checklist 90-R (SCL-90-R).⁹² The
38
39 367 Global Severity Index (GSI) will be used, which is feasible to measure psychiatric symptoms
40
41 368 among SUD patients.⁹³
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44 369 ***Cognitive function***
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46 370 Cognitive function will be assessed by the Rey Auditory Verbal Learning Test (RAVLT),⁹⁴
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48 371 which is useful to diagnose cognitive impairment as well as post-treatment improvement in SUD
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50 372 patients.^{95,96}
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54 373 ***Internalised stigma***
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3 374 Internalised stigma will be assessed by the Internalized Stigma of Mental Illness (ISMI)
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5 375 scale.⁹⁷ The term ‘mental illness’ in the statements will be replaced with ‘substance addiction.’
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9
10 377 **Implementation outcomes**

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12 378 ***Retention in treatment***

13
14 379 Participants will be coded as ‘retained in treatment’ if they had therapeutic contacts—
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16 380 including attending tele-Indo-DARPP and visiting any outpatient clinic for TAU—in at least 75%
17
18 381 of the planned contacts during the past 3 months.

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21 382 ***Treatment satisfaction***

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23 383 Client Satisfaction Questionnaire-3 (CSQ-3)⁹⁸ is commonly used for treatment programs,
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25 384 including for SUD.⁹⁹

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28 385 ***Group cohesion***

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30 386 Group Therapy Experience Scale (GTES) will be used to measure the level of group
31
32 387 cohesion and self-disclosure in group therapy, as implementation outcomes of tele-Indo-
33
34 388 DARPP.¹⁰⁰

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37 389 ***Indo-DARPP attendance***

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39 390 Attendance to each session will be recorded by the facilitator.

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42 391 ***Cost effectiveness***

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44 392 Cost-effectiveness will be assessed from a patient, provider, and societal perspective. Cost
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46 393 data will be calculated by multiplying the quantity of utilised resources by unit price. Data on
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48 394 quantity and unit price will be obtained from within the trial, or estimated from relevant data
49
50 395 sources. For effectiveness data, both clinical and economic indexes will be used. The clinical index
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52 396 is abstinence from primarily used substance in the past 28 days, which will be converted into
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3 397 abstinent year. The economic index is quality-adjusted life year (QALY) calculated from the utility
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5 398 score of EQ-5D.
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8 399 ***Feedback interviews***
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10 400 Semi-structured interviews will be done with both participants and providers to assess the
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12 401 following: satisfaction with content quality, comprehensibility, technical experience regarding
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14 402 video-conferencing, comfortableness, module practicability, and participants' perception on the
15
16 403 credibility of providers. Interviews will be audio-recorded under the interviewees' consent.
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21 405 **Participant characteristics**
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23
24 406 The following data will be obtained via a self-administered questionnaire: age, gender,
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26 407 approximate residential location, marital status, household co-habitants, ethnicity, religion, highest
27
28 408 education level, employment status, individual and household income, type of internet device used,
29
30 409 frequency of video calls in the past year, age of first drug use, primarily used substance, inpatient
31
32 410 history or incarceration in the past month, type of treatments received, treatment locations in the
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34 411 past three months, status of current outpatient care (voluntary or involuntary, legal or non-legal),
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36 412 and transportation time and cost from own residence to the outpatient location.
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43 414 **Data collection procedure**
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45 415 Researchers blinded to the treatment allocation will collect data at three different time
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47 416 points: at baseline (week 0, T1), the week after the completion of treatment (week 13, T2), three
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49 417 months after the completion of treatment (week 24, T3), and twelve months after the completion
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51 418 of treatment (week 60, T4), using self-answered questionnaire and online one-on-one interview.
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55 419 As for the primary outcome, the participants will be asked to recall weekly using the TLFB, and
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3 420 thus, an assessment period of approximately 4 weeks will be added after each assessment time
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5 421 point. Urine specimens will be collected only at T2, at the final 2 weeks within the TLFB
6
7 422 assessment period. Assessment schedule is shown in **Table 2** and **Figure 2**. To facilitate honest
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9 423 disclosure from participants, we will not record any Indo-DARPP video-conferencing sessions
10
11 424 throughout the study.
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18 426 [Figure 2 approximately here.]
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21 428 **Sample size**

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26 429 Sample size was calculated for the primary outcome to detect a medium effect size of $d =$
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28 430 0.50, which is slightly more modest than a previous study examining the efficacy of telemedicine
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30 431 for people with SUD in an LIMC ($d = 0.59$).¹⁰¹ Using $\alpha = 0.05$ and power = 0.80, a simple t-test
31
32 432 requires $n = 64$ per arm. We estimated the design effect of clustering within Indo-DARPP group,
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34 433 using the formula, $D = 1 + (m - 1) \rho$,¹⁰² assuming intraclass correlation within Indo-DARPP
35
36 434 groups or $\rho = 0.05$, and group size or $m = 5$, which yielded the design effect or $D = 1.2$. Multiplying
37
38 435 the result of simple calculation by the design effect, the minimal number of participants in data
39
40 436 analysis was 77 per arm. Assuming attrition proportion = 30% which is more conservative than a
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42 437 previous similar study (26%),¹⁰³ the sample size for enrolment was set as 110 per arm, or 220 in
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44 438 total.
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51 440 **Statistical analysis**

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3 441 A detailed statistical analysis plan will be developed by a statistician who is blinded to
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5 442 patients' allocation, prior to data analysis. Baseline data description and main analyses will be
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7
8 443 conducted on an intention-to-treat basis, i.e., participants' data will be handled according to their
9
10 444 initially assigned arms, regardless of actual received treatment. Analyses will be conducted with a
11
12 445 significance level of 5% in the two-sided test, using Stata/SE 16.1.
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14

15 446 ***Consideration for correlated outcome data***

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18 447 Correlation within sites for a control arm will be ignored, as the TAU within one site varies
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20 448 per patient and some participants may not receive any treatment. For an intervention arm,
21
22 449 correlation within each Indo-DARPP group due to the nature of group therapy should be accounted
23
24 450 for. We will define a new variable termed 'clustering group identification (CID)', where the control
25
26 451 arm will be coded as a unique CID for each person, while the intervention arm will be coded based
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28 452 on the tele-Indo-DARPP group they were in, i.e., the same CID for five participants.
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32 453 ***Main analysis***

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35 454 Primary endpoint will be set at T2. The mean of the outcome changes from T1 to T2 will
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37 455 be compared between the intervention and control arms using a linear model. To investigate the
38
39 456 durability of the treatment effect, outcome changes from T1 to T3 and T4 will also be compared
40
41 457 between both arms. We will account for the aforementioned correlations by clustering data, based
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43 458 on CID in the generalised estimation equations (GEE). To help interpret effect size, Cohen's *d*
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45 459 between arms will be calculated.
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49 460 ***Missing values***

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3 461 A complete case analysis will be done, which will only include participants with no
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5 462 missing values in the variables of interest. Sensitivity analysis for missing values will be conducted
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7
8 463 by either inverse probability weighted GEE¹⁰⁴ or multiple imputation.
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10 464 ***Subgroup analysis***

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13 465 The effect of intervention will be investigated by subgroups, as the observed effect may
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15 466 vary depending on specific population. The participants will be divided by the types of primarily
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18 467 used substance, gender, previous and current utilisation of other SUD treatment, high and low
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20 468 values in clinical characteristics at T1, e.g., percent days of abstinence, ASI drug use composite
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22 469 score, URICA readiness score, and cognitive function. Specifically, based on previous studies
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25 470 which showed that treatment effectiveness varied depending on baseline severity levels^{105,106}, we
26
27 471 hypothesised that participants assigned to tele-Indo-DARPP with more severe level of substance
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29 472 use at T1 would report more increased abstinent days at T2, T3, and T4.
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31 473 ***Implementation evaluation***

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34 474 Chi-squared tests and *t*-tests will be done to compare retention in treatment and treatment
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36 475 satisfaction between the arms, exclusively for participants who were already receiving SUD
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38 476 treatment at T1. Group cohesion and Indo-DARPP attendance will be descriptively reported by
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40 477 mean and standard deviation. For cost-effectiveness analysis, the incremental cost-effectiveness
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42 478 ratios (ICERs) will be calculated, which will yield costs per QALY and abstinent year. Feedback
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44 479 interviews will be transcribed and thematic analysis will be conducted.
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49 50 481 **Compensations**

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53 482 Participants in both the control and intervention groups will receive 300,000 IDR (\approx 21.3
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55 483 USD) to compensate for their transportation to treatment sites for TAU throughout the 12 weeks,
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3 484 and also 98,000 IDR (\approx 7.0 USD) for every time they complete an online video assessment as
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5 485 compensation for internet data and 2-hour data collection. Specific to the intervention group,
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7 486 participants will receive internet mobile data equivalent to 50,000 IDR (\approx 3.5 USD) before the first
8
9 487 session of tele-Indo-DARPP, and receive the same amount of mobile data every time they attended
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11 488 four sessions of tele-Indo-DARPP. As all monetary amounts were set at the approximate cost, the
12
13 489 amounts are intended purely for compensation and not as reward, as in contingency management.
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15 490 For providers, compensation of 170,000 IDR (\approx 12.1 USD) and 150,000 IDR (\approx 10.7 USD) will
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17 491 be given for each tele-Indo-DARPP session to facilitator and co-facilitator, respectively.
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24 493 **Data monitoring**

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26 494 Data on adverse events including hospitalisation, arrest, and death will be collected from the
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28 495 participants' treating psychiatrist or medical staff. In addition, participants will be interviewed at
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30 496 T2 on whether they experience any subjective harmful effects (e.g., withdrawal syndrome,
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32 497 increased cravings) after joining Indo-DARPP. An independent data monitoring committee will
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34 498 not be convened, as the study involves short-term non-invasive psychotherapeutic intervention.
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36 499 No interim analysis is planned due to the short duration of intervention. Completeness and
37
38 500 accuracy of data collection will be checked by Japanese co-investigators, and there will be no
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40 501 auditing process by independent investigators.
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47 503 **Data publication**

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49 504 Deidentified results of the study will be published in scientific publication, and reported to
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51 505 relevant government bodies in Indonesia to advocate adoption of the treatment module.
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507 **Ethical consideration and dissemination**

508 This study protocol (version 2.0, May 2020) was approved by the Research Ethical
509 Committee of Faculty of Medicine, Universitas Indonesia (approval number: KET-1175/2019),
510 the Ethics Committee of Graduate School and Faculty of Medicine, Kyoto University (approval
511 number: C1483). The study protocol was registered at the University Hospital Medical Information
512 Network clinical trial registry (UMIN-CTR) (registry number: UMIN000042186).

513 Consent process will be conducted carefully to ensure that all potential participants fully
514 understand research objectives, procedures, risks, benefits, costs, and alternatives. It will be
515 emphasised that study participation is voluntary and consent can be withdrawn at any time before
516 research publication. We will allocate participants to treatment arms only when written informed
517 consents for participation are obtained. Likewise, urine specimens will only be collected if written
518 informed consents for urine collection are obtained. Participants will not receive any adverse
519 influence in deciding study participation and/or urine collection. Personal data will be protected
520 by separating study data from participants' identifiable information. To quickly respond to adverse
521 events arising when outpatient visits are not possible, a dedicated phone number and a WhatsApp
522 account for the study will be opened to ease communication to the research team. Participants will
523 be instructed to text or call when experiencing any adverse events. Importantly, written agreement
524 will be obtained from participants to never share others' information to any third party. This
525 regulation will be enforced in both during and outside tele-Indo-DARPP sessions, in any medium,
526 including video conference and group chat.

527 Results of this study will be disseminated into peer-reviewed journals and international
528 academic conferences. Provided positive outcomes, Indo-DARPP will be advocated to the
529 Indonesian government for adoption as a nationwide formal treatment program.

530

531 Patient and public involvement

532 Patients' feedback during the pilot study was incorporated into the Indo-DARPP module design.

533 Apart from that, patients and/or the public were not involved in the conduct, reporting, or
534 dissemination plans of this study.

535

536 Discussion

537 Up until the time of writing, nine RCTs from LMICs have reported the effectiveness of digital
538 delivery of interventions for SUD. Utilised formats were telephone calls,^{107–110} webpages,^{111–113}
539 and mobile applications,^{101,114} however, no study in LMICs has so far investigated the
540 effectiveness of video-conference-based psychotherapy. The latter may facilitate honest,
541 interactive discussions on personal substance use and cravings, founded on better rapport between
542 providers and patients,¹¹⁵ all of which is integral for CBT for SUD. One meta-analysis concluded
543 that web-based mental health interventions had better retention rate and treatment outcomes when
544 therapists were synchronously involved.¹¹⁶

545 The proposed study has several strengths. This is the first RCT to investigate the
546 effectiveness of video-conference based psychotherapy in any LMIC, as well as the first study to
547 establish quality evidence on psychotherapy for SUD in Indonesia. Recruitment will be done
548 throughout multiple levels of care, i.e., tertiary (referral hospitals), primary (Puskesmas) and
549 community (rehabilitation centres). The latter have extensive reach encompassing all major
550 Indonesian islands, and advertising will be done via online social media, facilitating recruitment
551 from across the nation. While CBT effectiveness is the primary outcome, the study allows
552 elucidation of real-world implementation and cost-effectiveness in a hybrid effectiveness-

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3 553 implementation design.⁶⁵ This is particularly true in Puskesmas, where the providers will be
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5 554 general practitioners, and in rehabilitation centres, where the providers will be peer counsellors.
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8 555 This pragmatic RCT aims to mimic the usual clinical practice, and we hope that the result may be
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10 556 used to inform decision-making by patients, providers, and policymakers.¹¹⁷
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13 557 Several limitations can also be presumed. All data from participants will be self-reported
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15 558 and prone to recall and social desirability bias. Urine tests will be done to corroborate subjective
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17 559 data, but this is not a full validation as it is only done once to represent substance-detectable period
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19 560 within a 28-days period, and only at T2, which in turn was planned to improve feasibility for
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21 561 participants and reduce drop-out risk. Control conditions will be heterogeneous, as the study will
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23 562 include people who use various substances, in multiple sites where TAU differs, and possibly
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25 563 people who are not receiving any treatment. Variability in the providers' background may create
26
27 564 inconsistency in CBT delivery, even though training and treatment manuals were introduced as an
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29 565 effort to standardise care. Treatment delivery via online video-conferencing might have poor
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31 566 generalisability toward people with low internet literacy, as well as people in low socio-economic
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33 567 strata who could not afford smartphones—although entry-level Android-based smartphones (less
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35 568 than 100 USD) are available nationwide in Indonesia. Group psychotherapy provided in the
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37 569 Indonesian language would induce low external validity to people with limited proficiency in the
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39 570 language.
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45 571 Efforts to establish evidence-based treatment for SUD should be scaled up in Indonesia
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47 572 and LMICs in general, where effectiveness data is sparse. The proposed study may present high-
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49 573 quality evidence, and a successful outcome may birth a new SUD treatment module in Indonesia,
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51 574 paving way for the adoption of Indo-DARPP into the national guideline. We hope that our efforts
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3 575 may further promote a comprehensive, healthcare approach—as opposed to repressive anti-drug
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5 576 policies for the SUD population.
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10 578 **Acknowledgement**

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13 579 We would like to thank Dr Takashi Kawamura for his valuable comments on the study design.
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19 581 **Author contributions**

20
21 582 CY, KS, and YO conceptualised the study. CY, KS, EH, and YO are the main developers of the
22
23 583 Indo-DARPP module, designed study methodology, invited and coordinated site investigators,
24
25 584 conducted training of providers, wrote the protocol, reviewed and edited the final manuscript. EB,
26
27 585 VR, PA, and AP helped in module development, study design, training of providers, and site
28
29 586 coordination. TS provided biostatistical and epidemiological supervision. TM provided the
30
31 587 original SMARPP module and clinical input and perspectives to improve study quality. RS
32
33 588 supervised the whole study and procured grants. CY and RS are the principal investigators of the
34
35 589 grants. All authors have read and approved the final manuscript.
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43 590

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3 **597 Competing interests**
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5 598 The authors declare no competing interest.
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10 **600 Patient consent for publication**
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12 601 Not required.
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16
17 **603 Ethics approval and trial registration**
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19 604 This study protocol was approved by the Research Ethical Committee of Faculty of Medicine,
20
21 605 Universitas Indonesia (approval number: KET-1175/2019), and the Ethics Committee of Graduate
22
23 606 School and Faculty of Medicine, Kyoto University (approval number: C1483). The study protocol
24
25 607 was registered at the University Hospital Medical Information Network clinical trial registry
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27
28 608 (UMIN-CTR) (registry number: UMIN000042186).
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33 **610 Availability of data and materials**
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36 611 The full protocol and datasets of the planned study will be available from the corresponding author
37
38 612 on reasonable request.
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43 **615 Figure legends**
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46 616 **Figure 1.** Study flowchart for each site. A total of 20 or 30 participants will be recruited through
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48 617 the social network of each site. After 10 participants have been recruited to constitute one wave,
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50 618 randomisation will be done to allocate participants into two groups: intervention (Indo-DARPP +
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52 619 TAU) and control (TAU only), with 5 participants in each group. Recruitment will be continued
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55 620 until another 10 or 20 participants (second or third wave) joined before randomisation and
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3 621 allocation similar as before. Treatment period will be 12 weeks. Assessments will be done four
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5 622 times: T1 (Week 0) during baseline or before randomisation, T2 (Week 13-16) during post-
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7 623 assessment or 1-4 weeks after treatment period ends, T3 (Week 24) at 3 months after treatment
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9 624 ends, and T4 (Week 60) at 12 months after treatment ends.

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14 626 **Figure 2.** Planned trial schedule across all 8 research sites. Staggered schedules were designed to
15
16 627 spread the workload of providers in regard to Indo-DARPP intervention, as well as research staff
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18 628 in regard to assessments. After training of providers, all sites were given approximately 1-2
19
20 629 months to recruit participants. Sites with relatively higher potential to recruit faster, i.e., those
21
22 630 with higher rate of patient turnover, were selected ahead in the schedule. Each site will have 2 or
23
24 631 3 waves of recruitment and treatment periods.

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Table 1. Recruitment sites in this study

Name	Location	Type	Treatment as usual	Most reported primarily used substance
Cipto Mangunkusumo Hospital	Jakarta	Tertiary national general hospital	Individual psychotherapy, symptomatic pharmacotherapy	Benzodiazepine
Aceh Mental Hospital	Aceh	Tertiary provincial mental hospital	Individual psychotherapy, symptomatic pharmacotherapy	Methamphetamine
Duren Sawit Regional Hospital	Jakarta	Tertiary regional general hospital	Individual psychotherapy, symptomatic pharmacotherapy, opioid substitution therapy (buprenorphine, naloxone)	Opioid
Karisma Foundation	Jakarta	Rehabilitation center	Individual and group peer counselling	Methamphetamine, opioid
Kapeta Foundation	Banten	Rehabilitation center	Individual and group peer counselling	Methamphetamine, benzodiazepine, synthetic cannabinoids
Kios Atma Jaya	Jakarta	Rehabilitation center and regional HIV clinic	Individual psychotherapy, group peer counselling, outreach program	Opioid
Puskesmas Jatinegara	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin
Puskesmas Gambir	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin

Counselling focuses on education and giving advice.

Symptomatic pharmacotherapy gives medication for helping patients with specific psychopathologies.

Psychotherapy aims to help a person identify and change troubling emotions, thoughts, and behaviour.

Table 2. Outcome and measurement

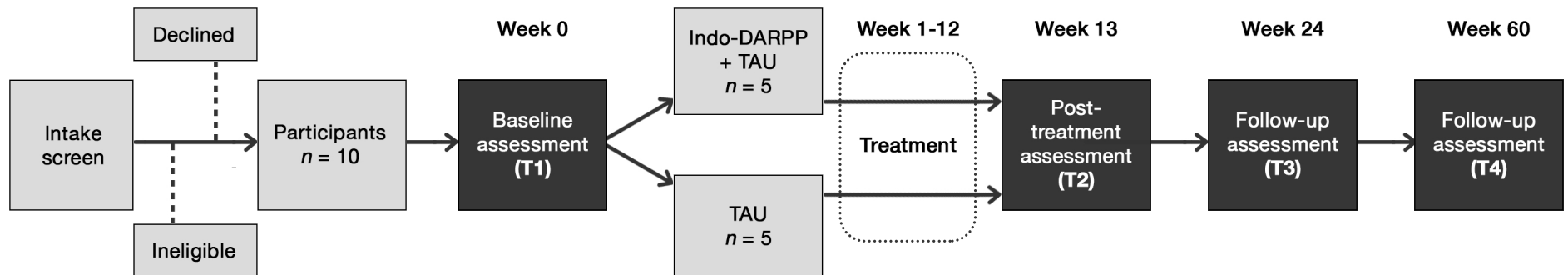
Outcome	Measurement	Data for analysis	Type and score range	Hypothesis for intervention (vs control)	Assessment time point			
					T1	T2	T3	T4
Primary outcome								
Abstinence from primary substance	Timeline followback (TLFB) for the past 28 days	Number of days being abstinent from primary substance divided by 28 (%).	Continuous, 0 (no use) to 100 (used every day).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/> ^a	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Secondary outcomes								
Addiction severity	Addiction Severity Index (ASI)	7 composite scores: medical, employment, alcohol use, drug use, legal, family/social, and psychiatric status. Each composite score calculated using standard formula.	Continuous, 0 (no problems) to 1 (severe problems).	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Health-related quality of life	EuroQol-5D (EQ-5D-5L)	Health utility score, calculated from 5 items on mobility, self-care, usual activities, pain/discomfort and anxiety/depression, using Indonesian value set.	Continuous, -0.865 (impaired health) to 1 (full health).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Motivation to change	University of Rhode Island Change Assessment (URICA)	Action stage subscale, sum of 8 items.	Continuous, 8 (not active in behavioural change) to 40 (highly active in behavioural change).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Coping	Brief-Coping Orientation to Problems Experienced (Brief COPE)	Sum of substance use coping (2 items)	Continuous, 2 (low substance use coping) to 8 (high substance use coping)	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Psychiatric symptoms	Symptom Checklist-90 Revised (SCL-90-R)	Global Severity Index (GSI), average of 90 items.	Continuous, 0 (no symptoms) to 4 (severe symptoms).	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Cognitive function	Rey Auditory Verbal Learning Test (RAVLT)	3 test results; immediate, learning, and recalling.	Continuous, 0 (low functioning) to 15 (high functioning).	Higher	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Internalised stigma	Internalized Stigma of Mental Illness (ISMI)	Sum of 4 subscales: alienation, stereotype endorsement, social withdrawal, and stigma resistances.	Continuous, 24 (low internalised stigma) to 96 (high internalised stigma)	Lower	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Implementation outcomes								
Retention in treatment	Self-reporting for the past 3 months	Coded as 'retained' if they had therapeutic contacts in at least 75% of the planned number of therapeutic contacts.	Categorical, 'retained' = 1, 'not retained' = 0.	More 'retained'	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
Treatment satisfaction	Client Satisfaction Questionnaire-3 (CSQ-3)	Sum of 3 items.	Continuous, 4 (not satisfied) to 12 (satisfied).	Higher	✓ <input type="checkbox"/>			
Group cohesion	Group Therapy Experience Scale (GTES)	Sum of 16 items.	Continuous, 16 (poor cohesion) to 80 (great cohesion).	Not applicable: measured only in intervention arm	✓ <input type="checkbox"/>			

^a Objective validation by urine drug test for 8 substances: alcohol, amphetamine, morphine, cannabinoids, methamphetamine, benzodiazepine, cocaine, synthetic cannabinoids

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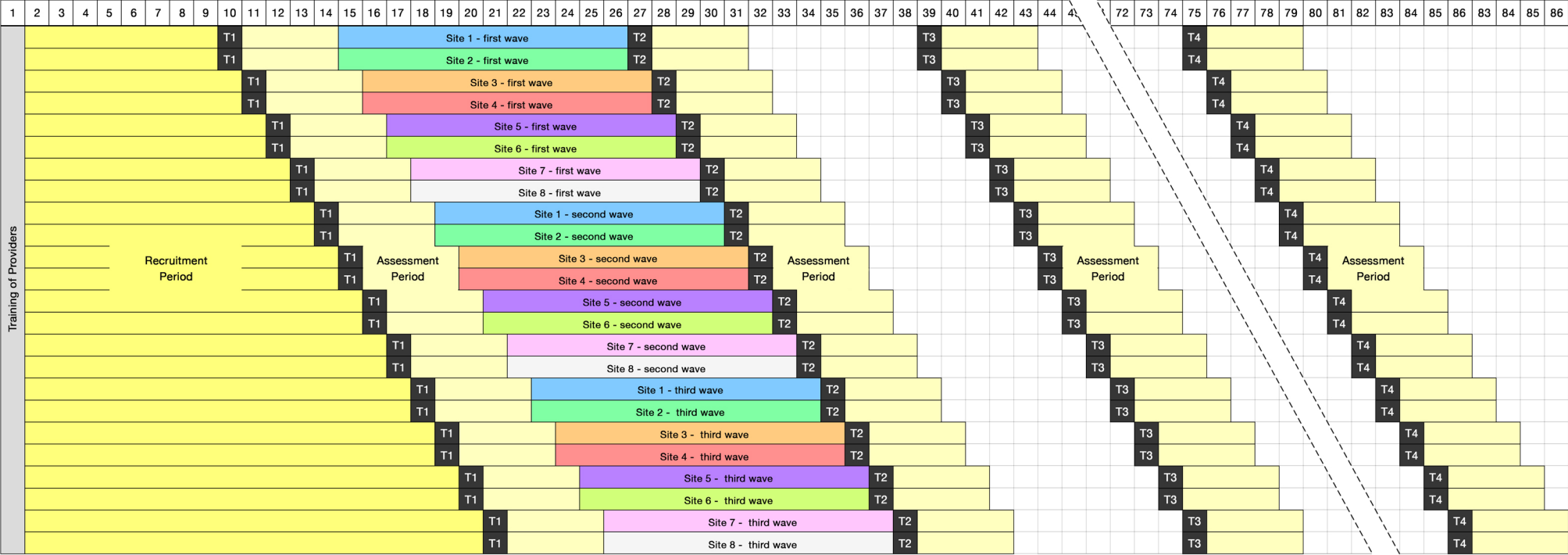
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Weeks



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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	Reporting Item	Page Number
Administrative information		
Title	#1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a Trial identifier and registry name. If not yet registered, name of intended registry	4, 23
Trial registration: data set	#2b All items from the World Health Organization Trial Registration Data Set	n/a, trial already registered as described in 2a.
Protocol version	#3 Date and version identifier	23
Funding	#4 Sources and types of financial, material, and other support	26-27
Roles and	#5a Names, affiliations, and roles of protocol	26

1	responsibilities:		contributors	
2	contributorship			
3				
4	Roles and	#5b	Name and contact information for the trial	n/a, no trial sponsor.
5	responsibilities:		sponsor	
6	sponsor contact			
7	information			
8				
9				
10				
11	Roles and	#5c	Role of study sponsor and funders, if any, in	n/a, no involvement of
12	responsibilities:		study design; collection, management,	funders in the study
13	sponsor and funder		analysis, and interpretation of data; writing of	design.
14			the report; and the decision to submit the	
15			report for publication, including whether they	
16			will have ultimate authority over any of these	
17			activities	
18				
19	Roles and	#5d	Composition, roles, and responsibilities of the	n/a, no direct
20	responsibilities:		coordinating centre, steering committee,	intervention in the study
21	committees		endpoint adjudication committee, data	design by the host
22			management team, and other individuals or	universities.
23			groups overseeing the trial, if applicable (see	
24			Item 21a for data monitoring committee)	
25				
26				
27				
28				
29				
30				
31				
32				
33	Introduction			
34				
35	Background and	#6a	Description of research question and	6-9
36	rationale		justification for undertaking the trial, including	
37			summary of relevant studies (published and	
38			unpublished) examining benefits and harms	
39			for each intervention	
40				
41				
42				
43				
44	Background and	#6b	Explanation for choice of comparators	15
45	rationale: choice of			
46	comparators			
47				
48				
49	Objectives	#7	Specific objectives or hypotheses	9
50				
51				
52	Trial design	#8	Description of trial design including type of	9-10
53			trial (eg, parallel group, crossover, factorial,	
54			single group), allocation ratio, and framework	
55			(eg, superiority, equivalence, non-inferiority,	
56			exploratory)	
57				
58				
59				
60				

1 **Methods:**

2 **Participants,**

3 **interventions, and**

4 **outcomes**

5			
6			
7			
8	Study setting	#9	Description of study settings (eg, community
9			clinic, academic hospital) and list of countries
10			where data will be collected. Reference to
11			where list of study sites can be obtained
12			
13			
14			
15	Eligibility criteria	#10	Inclusion and exclusion criteria for
16			participants. If applicable, eligibility criteria for
17			study centres and individuals who will
18			perform the interventions (eg, surgeons,
19			psychotherapists)
20			
21			
22			
23			
24	Interventions:	#11a	Interventions for each group with sufficient
25	description		detail to allow replication, including how and
26			when they will be administered
27			
28			
29	Interventions:	#11b	Criteria for discontinuing or modifying
30	modifications		allocated interventions for a given trial
31			participant (eg, drug dose change in
32			response to harms, participant request, or
33			improving / worsening disease)
34			
35			
36			
37			
38	Interventions:	#11c	Strategies to improve adherence to
39	adherence		intervention protocols, and any procedures
40			for monitoring adherence (eg, drug tablet
41			return; laboratory tests)
42			
43			
44			
45	Interventions:	#11d	Relevant concomitant care and interventions
46	concomitant care		that are permitted or prohibited during the
47			trial
48			
49			
50			
51	Outcomes	#12	Primary, secondary, and other outcomes,
52			including the specific measurement variable
53			(eg, systolic blood pressure), analysis metric
54			(eg, change from baseline, final value, time to
55			event), method of aggregation (eg, median,
56			proportion), and time point for each outcome.
57			
58			
59			
60			

1 Explanation of the clinical relevance of
 2 chosen efficacy and harm outcomes is
 3 strongly recommended
 4

5
 6 Participant timeline [#13](#) Time schedule of enrolment, interventions 10, 19, 26
 7 (including any run-ins and washouts),
 8 assessments, and visits for participants. A
 9 schematic diagram is highly recommended
 10 (see Figure)
 11
 12

13
 14 Sample size [#14](#) Estimated number of participants needed to 20
 15 achieve study objectives and how it was
 16 determined, including clinical and statistical
 17 assumptions supporting any sample size
 18 calculations
 19
 20
 21
 22

23 Recruitment [#15](#) Strategies for achieving adequate participant 11
 24 enrolment to reach target sample size
 25
 26

27 **Methods:**
 28 **Assignment of**
 29 **interventions (for**
 30 **controlled trials)**
 31
 32
 33

34 Allocation: [#16a](#) Method of generating the allocation 12
 35 sequence
 36 generation
 37 (eg, computer-generated random
 38 numbers), and list of any factors for
 39 stratification. To reduce predictability of a
 40 random sequence, details of any planned
 41 restriction (eg, blocking) should be provided
 42 in a separate document that is unavailable to
 43 those who enrol participants or assign
 44 interventions
 45
 46
 47
 48

49 Allocation [#16b](#) Mechanism of implementing the allocation 12
 50 concealment
 51 mechanism
 52 (eg, central telephone; sequentially
 53 numbered, opaque, sealed envelopes),
 54 describing any steps to conceal the
 55 sequence until interventions are assigned
 56
 57

58 Allocation: [#16c](#) Who will generate the allocation sequence, 12
 59
 60

1	implementation		who will enrol participants, and who will	
2			assign participants to interventions	
3				
4	Blinding (masking)	#17a	Who will be blinded after assignment to	12, 19
5			interventions (eg, trial participants, care	
6			providers, outcome assessors, data	
7			analysts), and how	
8				
9				
10				
11	Blinding (masking):	#17b	If blinded, circumstances under which	n/a, only assessors are
12	emergency		unblinding is permissible, and procedure for	blinded
13	unblinding		revealing a participant's allocated	
14			intervention during the trial	
15				
16				
17				
18	Methods: Data			
19	collection,			
20	management, and			
21	analysis			
22				
23				
24				
25	Data collection plan	#18a	Plans for assessment and collection of	15-19
26			outcome, baseline, and other trial data,	
27			including any related processes to promote	
28			data quality (eg, duplicate measurements,	
29			training of assessors) and a description of	
30			study instruments (eg, questionnaires,	
31			laboratory tests) along with their reliability	
32			and validity, if known. Reference to where	
33			data collection forms can be found, if not in	
34			the protocol	
35				
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42	Data collection plan:	#18b	Plans to promote participant retention and	19, 22-23
43	retention		complete follow-up, including list of any	
44			outcome data to be collected for participants	
45			who discontinue or deviate from intervention	
46			protocols	
47				
48				
49				
50				
51	Data management	#19	Plans for data entry, coding, security, and	23
52			storage, including any related processes to	
53			promote data quality (eg, double data entry;	
54			range checks for data values). Reference to	
55			where details of data management	
56			procedures can be found, if not in the	
57				
58				
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60				

1		protocol	
2			
3	Statistics: outcomes	#20a Statistical methods for analysing primary and	20-22
4		secondary outcomes. Reference to where	
5		other details of the statistical analysis plan	
6		can be found, if not in the protocol	
7			
8			
9			
10	Statistics: additional	#20b Methods for any additional analyses (eg,	21-22
11	analyses	subgroup and adjusted analyses)	
12			
13			
14	Statistics: analysis	#20c Definition of analysis population relating to	21
15	population and	protocol non-adherence (eg, as randomised	
16	missing data	analysis), and any statistical methods to	
17		handle missing data (eg, multiple imputation)	
18			
19			
20			
21	Methods:		
22	Monitoring		
23			
24			
25	Data monitoring:	#21a Composition of data monitoring committee	23, DMC will not be
26	formal committee	(DMC); summary of its role and reporting	convened as the
27		structure; statement of whether it is	intervention involves a
28		independent from the sponsor and competing	short-term
29		interests; and reference to where further	psychotherapy with
30		details about its charter can be found, if not in	known minimal risk.
31		the protocol. Alternatively, an explanation of	
32		why a DMC is not needed	
33			
34			
35			
36			
37			
38	Data monitoring:	#21b Description of any interim analyses and	23, interim analysis is
39	interim analysis	stopping guidelines, including who will have	not planned due to the
40		access to these interim results and make the	short duration of
41		final decision to terminate the trial	intervention.
42			
43			
44			
45	Harms	#22 Plans for collecting, assessing, reporting, and	22-23
46		managing solicited and spontaneously	
47		reported adverse events and other	
48		unintended effects of trial interventions or trial	
49		conduct	
50			
51			
52			
53			
54	Auditing	#23 Frequency and procedures for auditing trial	23, there will be no
55		conduct, if any, and whether the process will	auditing process by
56		be independent from investigators and the	independent
57		sponsor	investigators.
58			
59			
60			

Ethics and dissemination

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	23, 28
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	23
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	23
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	23
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	23
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	15, CBT intervention will be made available for control group after the end of the study.

1	Dissemination	#31a	Plans for investigators and sponsor to	23
2	policy: trial results		communicate trial results to participants,	
3			healthcare professionals, the public, and	
4			other relevant groups (eg, via publication,	
5			reporting in results databases, or other data	
6			sharing arrangements), including any	
7			publication restrictions	
8				
9				
10				
11				
12				
13	Dissemination	#31b	Authorship eligibility guidelines and any	26-27
14	policy: authorship		intended use of professional writers	
15				
16				
17	Dissemination	#31c	Plans, if any, for granting public access to the	28
18	policy: reproducible		full protocol, participant-level dataset, and	
19	research		statistical code	
20				
21				
22	Appendices			
23				
24				
25	Informed consent	#32	Model consent form and other related	11, 23
26	materials		documentation given to participants and	
27			authorised surrogates	
28				
29				
30	Biological	#33	Plans for collection, laboratory evaluation,	16
31	specimens		and storage of biological specimens for	
32			genetic or molecular analysis in the current	
33			trial and for future use in ancillary studies, if	
34			applicable	
35				
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38				

Notes:

- 2b: n/a, trial already registered as described in 2a.
- 5b: n/a, no trial sponsor.
- 5c: n/a, no involvement of funders in the study design.
- 5d: n/a, no direct intervention in the study design by the host universities.
- 17b: n/a, only assessors are blinded
- 21a: 23, DMC will not be convened as the intervention involves a short-term psychotherapy with known minimal risk.
- 21b: 23, interim analysis is not planned due to the short duration of intervention.

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- 23: 23, there will be no auditing process by independent investigators.
 - 30: 15, CBT intervention will be made available for control group after the end of the study. The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 15. February 2021 using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)

For peer review only

Supplementary file 2

Research Participation Consent Form

Title of the Research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

An explanation has been given which includes the following discussion :

- | | |
|---|--|
| 1. Research Title | 18. General management of drug addiction patients outside of research interventions |
| 2. Research Clearance | 19. Follow up management after the research ends |
| 3. Research institutes and researchers | 20. Report of the participant's genetic information |
| 4. Research purposes | 21. Compensation for illness related to research and invasive procedures |
| 5. Research procedure | 22. Secondary research data for other institutions |
| 6. Research period | 23. Samples and participant information related to invasive procedures |
| 7. Inclusion Criteria | 24. Name, position, and affiliation of the person in charge of managing data and information related to research |
| 8. Risks, benefits, and side effects | 25. CBT group participant commitments and drop out possibility of research participation |
| 9. Right to refuse and drop out | |
| 10. Voluntary participation and risk of involvement | |
| 11. Research data publication | |
| 12. How to access research-related materials for participants | |
| 13. Privacy of personal data | |
| 14. Research data storage | |
| 15. Research funds and conflicts of interest | |
| 16. Researcher contact list | |
| 17. Remuneration for participants | |

Explanations have been given according to the explanation sheet, and consent has been obtained voluntarily.

Date of consent : ____ / ____ / 20 ____

Researcher's affiliation : _____

Researcher's Name :

Researcher's Signature :

Acknowledged by:

1. Dean of the Faculty Medicine, University Indonesia
2. Director of the *Center for South East Asian Studies, Kyoto University*

Supplementary file 2

CBT-Group Participation Consent Form

I, the undersigned, hereby acknowledge, consent and agree to fulfill the following matters during my participation in CBT group therapy, in order to ensure the safe and secure continuation of the program:

1. I will not divulge information about other participants in the group to external parties without the consent of the parties concerned.
2. I will not record audio, video, or take camera pictures without the permission of the parties concerned and the research team.
3. I will not use drugs during the CBT session.
4. I will not divulge links (URL), ID, and passwords for online meetings in the Zoom application to external parties, without the approval of the research team.
5. I will not harass, say offensive words related to ethnicity, religion and race, or commit acts of violence for any reason to any party related to the research, whether other participants or the research team.

If I infringe the points of the agreement above, I will be given 1 (one) warning. If I do not show any improvement after being warned, or infringe it for the second time, or it is deemed that my participation will interfere with the continuation of CBT therapy in the future, I have no objection to my participation being unilaterally terminated.

I, the undersigned, hereby declare that I have understood the explanation given and agree to my participation in the research mentioned above. In my behavior after being warned, or infringe it for the second time, or it is deemed that my participation will interfere with the continuation of CBT therapy in the future, I have no objection to my participation being unilaterally terminated.

Date of Consent : ____ / _____ / 20 ____

Name : _____

Signature : _____

Supplementary file 2

Urine Test Informed Consent

Title of Research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

An explanation has been given which includes the following discussion:

1. Purpose of the urine sampling
2. Urine test procedure
3. Analysis of urine test results data and maintaining data confidentiality

Explanations have been given according to the explanation sheet, and consent has been obtained voluntarily.

I, the undersigned, declare that I

Agree / do not agree

*please circle one of these options above

...to provide the urine sample to be tested for the research team, and I have acknowledged and understood the purposes, procedures and data analysis as described previously.

Date of consent : ____ / _____ / 20 ____

Name : _____

Signature : _____

Supplementary file 2

Withdrawal of Informed Consent for Urine Test

Title of the research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

I, the undersigned, hereby wish to withdraw my prior consent to participate in the urinary test for this research by signing this form.

Withdrawal Date : ____ / _____ / 20 ____

Participant's Name : _____

Participant's Signature : _____

Supplementary file 3

Table of contents of Indo-DARPP (English translation)

Chapter no.	Chapter title	Page no.
Preface	The beginning of Indo-DARPP The purpose of SMARPP	x xii
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2	Why should we stop using drugs? Why drug use is a problem Drugs and behavior disorder Advantages and disadvantages of using drugs and stop using drugs Stages of change The urge to continue or to stop using drugs	11 11 13 16 17 19
3	Recovery stage of drug addiction - First year Stage (1) Stress phase (0-14 days) Stage (2) 'Honeymoon' phase (15-90 days) Stage (3) The 'wall' phase (91-180 days) Stage (4) Adjustment phase (181-270 days) Stage (5) Resolution phase (271-365 days) Understanding our "wall" symptoms	21 21 22 23 24 24 25
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6	Trigger inside us Internal trigger High risk conditions: hungry, angry, lonely, tired (HALT)	42 42 44
7	Prevention of harmful behavior Distant and self-isolating behavior Drug dreams	48 48 51
8	Let's make schedule of our daily activities Why is scheduling so important? Make your schedule and practice! Calendars and marks of achievement	54 54 57 60
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12	Opioid: Heroin, morphine and maintenance therapy Types of opioids & how do they work Symptoms and side effects of opioid usage Effects on opioid use Treatments & therapy for opioid addiction Opioid addiction prognosis	84 84 85 86 88 90
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21	Reasons a person experiencing relapse What causes relapse? Due to chance or influences of others? Because of some extraordinary events, misfortunes or disasters Because of the desire to achieve something	153 153 154 154 155

	Because of emotions: depression, anger, lonely, fright	155
	Because of perception that the addiction problems was already solved	156
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	Celebrating something	157
22	Characters towards recovery: trust, honesty, friendships	160
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	Honesty	162
	Creating new friendships	164
23	Negative relationships with other people	166
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	Relationship that hurts you and the drugs recovery phase	170
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BMJ Open

Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for a multicentre randomised controlled trial in Indonesia

Journal:	<i>BMJ Open</i>
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Article Type:	Protocol
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Primary Subject Heading:	Addiction
Secondary Subject Heading:	Addiction, Global health, Mental health, Evidence based practice
Keywords:	Substance misuse < PSYCHIATRY, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, PSYCHIATRY, Clinical trials < THERAPEUTICS

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1
2
3 **1 Title**
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5 2 Relapse prevention group therapy via video-conferencing for substance use disorder: protocol for
6
7 3 a multicentre randomised controlled trial in Indonesia
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10 4
11
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40 Abstract

41 **Background:** Substance use disorder (SUD) is a leading contributor to the global burden of
42 disease. In Indonesia, the availability of formal treatment for SUD falls short of the targeted
43 coverage. A standardised therapeutic option for SUD with potential for widespread
44 implementation is required, yet evidence-based data in the country are scarce. In this study, we
45 developed a cognitive behavioural therapy (CBT)-based group telemedicine model, and will
46 investigate effectiveness and implementability in a multicentre randomised controlled trial (RCT).

47 **Methods:** A total of 220 participants will be recruited from the social networks of eight sites in
48 Indonesia: three hospitals, two primary healthcare centres, and three rehabilitation centres. The
49 intervention arm will participate in a relapse prevention programme called the Indonesia Drug
50 Addiction Relapse Prevention Programme, a newly developed 12-week module based on CBT and
51 motivational interviewing constructed in the Indonesian context. The programme will be delivered
52 by a healthcare provider and a peer counsellor in a group therapy setting via video-conferencing,
53 as a supplement to participants' usual treatments. The control arm will continue treatment as usual.
54 The primary outcome will be the percentage increase in days of abstinence from the primarily used
55 substance in the past 28 days. Secondary outcomes will include addiction severity, quality of life,
56 motivation to change, psychiatric symptoms, cognitive function, coping, and internalised stigma.
57 Assessments will be performed at baseline (week 0); post-treatment (week 13); and three and 12
58 months post-treatment completion (weeks 24 and 60). Retention, participant satisfaction, and cost-
59 effectiveness will be assessed as the implementation outcomes.

60 **Ethics and dissemination:** The study protocol was reviewed and approved by the Ethics
61 Committees of Universitas Indonesia and Kyoto University. The results will be disseminated via

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3 62 academic journals and international conferences. Depending on trial outcomes, the treatment
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5 63 programme will be advocated for adoption as a formal healthcare-based approach for SUD.
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8 64 **Trial registration number:** UMIN000042186
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11 65 **Keywords:** *substance use disorder, telemedicine, cognitive behavioural therapy, relapse*
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13 66 *prevention, motivational interviewing, Indonesia, peer counsellor*
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3 **68 Strengths and limitations of this study**
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- 6 **69** ● The proposed study will be the first to establish high-quality evidence for a cognitive
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8 **70** behavioural therapy (CBT)-based relapse prevention programme for substance use
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10 **71** disorder (SUD) in Indonesia.
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13 **72** ● Telemedicine enables far-reaching, nationwide participation, connecting participants from
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15 **73** across the nation with providers in major cities.
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17 **74** ● A successful outcome may produce a new SUD treatment module in Indonesia and pave
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19 the way for its adoption by national guidelines.
20 **75**
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22 **76** ● Study limitations include risk of recall and social desirability bias, heterogeneous control
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24 **77** conditions, and possible variability in treatment provision.
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27 **78**

79 Introduction

80 Substance use disorder (SUD) is characterised by the inability to control the use of
81 psychoactive substances, such as alcohol and psychotropic drugs, which disrupt daily living. SUD
82 remains a significant and growing health problem worldwide. According to the 2016 Global
83 Burden of Disease (GBD) survey, SUD contributed to 131 million disability-adjusted life years
84 (DALYs), or 5.5% of all DALYs,¹ and its prevalence has been increasing since the 1990s.² While
85 substance use itself is more widespread in high-income countries (HICs), low- and middle-income
86 countries (LMICs) had disproportionately high SUD mortality rates. The absolute mortality rate
87 due to SUD was greatest in LMICs with large populations,³ and people with economic
88 disadvantages were more likely to develop SUD.⁴ The Movement for Global Mental Health and
89 the World Health Organization have found substantial treatment gaps in LMICs. For instance, the
90 number of individuals with SUD far exceed the availability of formal treatment services.⁵⁻⁷ While
91 these numbers do not take traditional care into account, it is still concerning that only 1% of
92 individuals with SUD in LMICs have reported receiving government-standardised treatment.⁸

93 In Indonesia, the world's third most populous LMIC, government statistics have estimated
94 the prevalence of drug use to be 1.8% (3.3 million residents), with the most used substance being
95 marijuana (68%), followed by amphetamine-type stimulants (ATS, 42%), opioids (38%) and
96 sedatives (35%).^{9,10} While injecting drug use (IDU) decreased by 80% between 2002 to 2016,¹⁰
97 unprescribed use of psychoactive medications like benzodiazepines has become significant.¹¹
98 Similar to other Muslim majority countries,¹² alcohol consumption is comparatively low in
99 Indonesia, with alcohol use disorder being prevalent only among 0.8% residents in 2016, much
100 lower than the overall rate in Southeast Asia (3.9%).¹³ However, new psychoactive substances
101 (NPS) have entered the country in the last decade.¹⁴ Moreover, the COVID-19 pandemic may

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3 102 further complicate the SUD situation in Indonesia, as has been observed in other countries.¹⁵ For
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5 103 instance, unpublished data from our co-author (KS) revealed that since the pandemic began in
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7 104 early April 2020, both drug and alcohol use have increased in Indonesia by up to 2.5%. Increased
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9 105 drug use might have been influenced by lockdown isolation, socio-economic issues due to
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11 106 unemployment, and severe psychological burden.

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15 107 In Indonesia, formal mental health providers and facilities are severely lacking; in a nation
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17 108 of 267 million people, only 773 psychiatrists (0.32/100,000 people) are employed—the second
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19 109 lowest proportion in Southeast Asia¹⁶—across hospitals with psychiatric care, half of which are
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21 110 located in the capital island of Java.¹⁷ Among the ~1700 government-run primary healthcare
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23 111 centres (abbreviated as *Puskesmas* in Indonesian), only a fifth actively provide mental health
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25 112 care.^{17,18} Current formal treatment options for SUD include one-on-one supportive psychotherapy,
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27 113 symptomatic pharmacotherapy, peer counselling, and opioid substitution. Methadone maintenance
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29 114 therapy (MMT) has been available in Puskesmas since 2006, but as of 2012, its coverage was only
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31 115 5%,¹⁹ due to methadone cost, reliance on subsidisation, lack of programme sustainability,²⁰ and
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33 116 the tendency to incarcerate patients under the 'war on drugs' policy.^{19,21} The three-month retention
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35 117 rate of MMT was only 60-74%.^{22,23} Psychiatric comorbidities, and lower quality of life, are
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37 118 common among MMT recipients.²⁴ Most concerning, insufficient formal treatment coverage and
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39 119 the lack of standardised care for SUD have prompted policymakers to enact punitive
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41 120 criminalisation practices, which are even more stringent under the current administration, instead
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43 121 of a comprehensive mental health care approach.^{25,26}

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45 122 Behavioural therapies in many forms are commonly administered for SUD, the most
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47 123 popular method being cognitive behavioural therapy (CBT). There is strong evidence supporting
48
49 124 the efficacy of CBT in treating SUD. A meta-analysis reported a moderate overall effect size ($d =$

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3 125 0.45) of CBT treatments, with outcomes such as self-reported abstinence, drug-free urine at
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5 126 treatment exit, and increased retention in therapy.^{27,28} CBT strategies include: (a) contingency
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7 127 management (CM),²⁹ which introduces rewards for abstinence, (b) motivational interviewing (MI),
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9 128 which explores and resolves ambivalence,^{30,31} (c) relapse prevention (RP), which helps participants
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11 129 to identify high-risk triggers and prevent cravings, or (d) combinations thereof.³² Therapy can be
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14 130 delivered individually or in groups; the latter has reportedly increased adherence and self-
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16 131 disclosure, and decreased the treatment duration by 40%.^{33,34} CBT (particularly MI and RP) is
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18 132 relatively low-cost and can be delivered by non-specialists, making it adaptable to and beneficial
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20 133 in settings with limited formal mental health professionals.^{35,36} In LMICs, while ample RCTs have
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22 134 supported CBT's efficacy in reducing alcohol use,^{37,38} evidence for treating drug use disorders is
23
24 135 limited, with only five RCTs published so far.³⁹⁻⁴³ Among these, three were inpatient-based, even
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26 136 though SUD management mandates sustainable outpatient care in community settings.

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31 137 Telemedicine has the potential to improve SUD treatment coverage in Indonesia. Internet
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33 138 communication overcomes the geographical barriers of the Indonesian archipelago, and saves time
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35 139 as well as transportation costs for both patients and providers, both in remote areas where health
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37 140 services are sparse,⁴⁴ and in major cities with heavy traffic, such as Jakarta.⁴⁵ Privacy is also better
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39 141 ensured online as opposed to in visiting clinics, where there is a greater risk of inappropriate
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41 142 disclosure of SUD diagnoses, which is one of the most stigmatised health conditions.⁴⁶
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43 143 Synchronous telemedicine via live video feed connects participants in real-time, improving rapport
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45 144 and potentially adherence, as compared to asynchronous telemedicine (e.g. through text messages
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47 145 or web application). Video-conferencing has been effectively used in SUD treatment⁴⁷⁻⁵²; however,
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49 146 recent systematic reviews⁵³⁻⁵⁸ have revealed three gaps in research: (1) previous reports have only
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51 147 focused on alcohol and opioid use,^{47,50-52} (2) group therapy was investigated by only one small-

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3 148 scale pilot RCT,⁵¹ and (3) no studies have been conducted in LMICs. This latter gap is particularly
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5 149 relevant because the use of internet devices has been rapidly expanding in LMICs, including
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8 150 Indonesia. Smartphone users accounted for 74% of the Indonesian population in 2019, possibly
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10 151 reaching 89% by 2025.⁵⁹ The COVID-19 pandemic has further elevated telemedicine from an
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12 152 accessory to a necessity, including for psychiatric care.⁶⁰ Its accessibility and acceptance among
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15 153 SUD patients, as shown in a recent survey,⁶¹ may potentially sustain telemedicine as the 'new
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17 154 normal' even in the post-pandemic world.^{62,63}

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20 155 Given the above challenges and opportunities, we propose a clinical trial to evaluate a
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22 156 relapse prevention telemedicine programme for SUD in Indonesia. We have developed a new 12-
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24 157 week CBT-based group therapy called *the Indonesia Drug Addiction Relapse Prevention*
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26 158 *Programme* (Indo-DARPP), which will be delivered via video conference (tele-Indo-DARPP).
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29 159 The primary objective will be to evaluate the effectiveness of tele-Indo-DARPP in addition to
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31 160 treatment as usual (TAU) towards increasing abstinence from primarily used substances, as
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33 161 compared to the effectiveness of TAU only. The secondary objectives will be to assess impacts on
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36 162 quality of life, motivation to change, psychological symptoms, cognitive function, coping, and
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38 163 internalised stigma. Retention, participant satisfaction, and group cohesion will be assessed as
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40 164 implementation outcomes, and cost-effectiveness analyses will be conducted to inform health
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43 165 policy investments.

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48 167 **METHODS**

51 168 **Trial design**

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3 169 This trial is a parallel-group, two-arm, assessor-blinded, multicentre randomised controlled
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5 170 trial. The protocol adheres to the Standard Protocol Items: Recommendations for Interventional
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7 171 Trials (SPIRIT) checklist (**Supplementary file 1**). We designed the study as a pragmatic type 1
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10 172 hybrid effectiveness-implementation trial,⁶⁴ which allows concurrent investigation of intervention
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12 173 effectiveness as well as implementation in clinical practice, focusing on the former. After intake
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14 174 screening, participants will undergo baseline assessment (T1) and be randomly allocated in a 1:1
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16 175 ratio either to the intervention arm receiving tele-Indo-DARPP in addition to TAU, or the control
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18 176 arm receiving TAU only. Treatment will be administered for 12 weeks, followed by a post-
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20 177 treatment assessment (T2) at week 13, and follow-up assessments (T3) at week 24 and (T4) at
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22 178 week 60 (**Figure 1**).

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35 182 **Participants and settings**

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38 183 Participants will be recruited across Indonesia via social networks of eight sites: two
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40 184 primary health centres (Puskesmas), three referral hospitals, and three drug rehabilitation services
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42 185 (**Table 1**). These facility types constitute the community-based treatment model for SUD in
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44 186 Indonesia,⁶⁵ encompassing patients with diverse motivations for behavioural change, substance
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46 187 use histories, comorbidities, and stages of treatment. Recruitment will be conducted via online
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48 188 advertisements (i.e. on social networking services, group chat, website), and through consecutive
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50 189 sampling by directly approaching current and former clients through outpatient services. Although
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52 190 all targeted facilities are located in urban settings, the recruitment process will include social media
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3 191 services of each site, particularly rehabilitation centres, which have nationwide coverage. Hence,
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5 192 we expect that participants will be recruited from anywhere in Indonesia, and will not be limited
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8 193 to the physical scope of each site.
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10 194 The services offered by each type of site vary. Puskesmas provide general primary care,
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12 195 pharmacotherapy for cases without complications, and MMT. Referral hospitals provide
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14 196 psychotherapy, pharmacotherapy, opioid substitution therapy using buprenorphine/naloxone, and
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16 197 specialised care for cases with complications, such as severe psychiatric disorders. Rehabilitation
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18 198 services provide long-term psychosocial care, typically in a mutual-aid group. Sites were selected
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20 199 based on feasibility, client demographics, recruitment potential, and availability of providers.
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22 200 While recruited participants may not be undergoing treatment at these sites at the time, facilitators
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24 201 for tele-Indo-DARPP will be staff members of the respective sites: general practitioners in
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26 202 Puskesmas, psychiatrists in referral hospitals, and counsellors in rehabilitation centres.
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34 204 **[Insert Table 1 here]**
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40 206 Inclusion criteria will be those who: 1) be aged 18-65 years old; 2) be diagnosed with
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42 207 substance use disorder based on DSM-5; 3) have used primarily used substances for at least one
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44 208 day in the past year; 4) have access to electronic devices (i.e. smartphone, mobile tablet, personal
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46 209 computer) with internet connection; and 5) be proficient in Indonesian. Individuals who 1) have
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48 210 severe comorbidities that hinders informed consent or group therapy participation, and 2) are
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50 211 hospitalised or using residential care, will be excluded.
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3 212 We set a broad inclusion criterion, i.e., substance use in the past one year, for two reasons.
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5 213 First, proportional hazard models have showed that the probability of relapse remains high before
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7 214 achieving one year of abstinence, and declines substantially only after 16 months.^{66,67} Thus, it is
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9 215 clinically important to examine treatment efficacy for people who have not achieved one-year
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11 216 abstinence.⁶⁷ Second, in this pragmatic effectiveness study,⁶⁸ we designed eligibility criteria to
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13 217 accurately represent the population encountered in real-world Indonesian clinical practice. Indeed,
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15 218 patients treated at the collaborating clinical sites include those who have been abstinent for more
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17 219 than one month but still experience cravings and a tendency to relapse.
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24 221 **Recruitment**

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27 222 Patient eligibility will be assessed by collaborating staff at the respective sites. Addiction
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29 223 psychiatrists will conduct clinical assessments via video calls for those who have never been
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31 224 diagnosed with SUD. The consent form in English is provided in **Supplementary File 2**. For urine
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33 225 tests, explanations will be given immediately after post-treatment (T2) assessment, as anticipation
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35 226 for urine tests may influence substance use behaviour. Consent to urine tests or absence thereof
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37 227 will not affect study participation.
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44 229 **Randomisation and blinding**

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47 230 Depending on the study site, participants will be randomly allocated to either the
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49 231 intervention (tele-Indo-DARPP + TAU) or the control (TAU only) arm. Each site will conduct two
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51 232 or three waves of recruitment, with 10 participants in each wave. For each wave at a site, we will
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53 233 randomly allocate five participants to either the intervention or control arm. All participants in
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3 234 each tele-Indo-DARPP group will belong to the same recruitment site. Allocation will be
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5 235 performed using computer-generated random numbers by a researcher who will be blinded to the
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7 236 participants' information, except for ID. Data will be collected by researchers who are blinded to
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10 237 participants' study conditions. Participants and treatment providers will not be blinded, as it would
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12 238 not be possible given the psychotherapeutic nature of the intervention.
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18 240 **Development of the Indo-DARPP**

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20 241 The Indo-DARPP is based on the Serigaya Methamphetamine Relapse Prevention Programme
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22 242 (SMARPP), a face-to-face CBT-based group intervention developed by a co-author (TM) in
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24 243 Japan,⁶⁹ which itself is based on the Matrix Model developed in the US.⁷⁰ It has demonstrated
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26 244 efficacy in increasing abstinence duration, motivation to change, and participation in self-help
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28 245 groups.⁷¹⁻⁷³ SMARPP is covered by the national insurance scheme and has been widely
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30 246 implemented as a psychotherapy for SUD not only in psychiatric clinics, but also in primary
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32 247 healthcare centres, rehabilitation centres, and probation offices in Japan. SMARPP has excellent
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34 248 scalability as it is delivered through workbooks, and can be facilitated by non-specialists who have
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36 249 received brief training.
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42 250 The contents of Indo-DARPP are based on the RP model, wherein participants are guided
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44 251 to learn about high-risk situations for substance use, and coping strategies. Elements of MI are
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46 252 incorporated in the earlier parts of the workbook in a form of open questions to assess participants'
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48 253 ambivalence and motivation to change. The programme also includes psychoeducation on
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50 254 substances, SUD, and common comorbidities. While CM could also be added, it increases cost
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52 255 and may not be effective in the longer term;⁷⁴ thus, only MI and RP approaches will be utilised in
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55 256 this study. Adaptations from SMARPP were determined via focus group discussions involving
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3 257 Japanese researchers, and psychiatrists, general practitioners, and peer counsellors based in
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5 258 Indonesia, all of whom have extensive experience ranging from 4 to 20 years in the addiction field.
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8 259 The substances discussed in the module are amphetamine-type stimulants, benzodiazepines, and
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10 260 other prescribed medicines, opioids, marijuana, NPS, and alcohol. Indo-DARPP is designed to be
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12 261 delivered in a small group format using a workbook (see **Supplementary File 3** for the table of
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14 262 contents of the workbook). Sessions will be delivered by one facilitator, and one peer counsellor
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17 263 with lived experiences of SUD as co-facilitator.
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20 264 A pilot test was conducted at Site 1, with nine SUD patients recruited for a 12-week tele-
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22 265 Indo-DARPP to check content acceptability and feasibility of the online delivery format. Further
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24 266 adjustments were made based on pilot results and patient feedback.
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30 268 **Intervention via video conference: tele-Indo-DARPP**

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33 269 Tele-Indo-DARPP will be delivered as group therapy for 12 weeks in weekly 2-hour sessions
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35 270 over the online video-conferencing application Zoom, with a maximum of five participants. The
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37 271 research team will provide video conference links to participants and two providers. Participants
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39 272 who agree to share their contact information will receive the links on an online group chat, while
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42 273 others will be notified via personal messages. Each Indo-DARPP session consists of three parts:
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44 274 (1) ‘check-in’, where participants share history of substance use and craving in the past week, and
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46 275 analyse high-risk situations and coping actions taken; (2) ‘today’s topic’, where providers guide
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48 276 discussions of specific workbook chapters and participants complete exercises, and (3) ‘check-
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51 277 out’, where providers give summary and invite feedback, and participants anticipate triggers and
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53 278 coping strategies for the following week.
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6 **280 Providers of tele-Indo-DARPP**

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9 281 At least two persons from each site will serve as facilitators, who meet either of the following
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11 282 criteria: psychiatrists with at least a year of experience in treating patients with SUD; healthcare
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13 283 providers with at least two years of experience in providing care for patients with SUD; or peer
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15 284 counsellors with at least 2 years of involvement with any organisations providing services for
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17 285 patients with SUD. The roles of facilitators are to: (1) lead and moderate Indo-DARPP sessions;
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19 286 (2) elaborate on chapter contents; (3) manage participants to follow rules; (4) establish a safe and
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21 287 warm environment; (5) provide consultation, including out-of-session; and (6) contact absent
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23 288 participants to encourage attendance.

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27 289 Similarly, at least two persons from each site will serve as co-facilitators for the tele-Indo-
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29 290 DARPP. Co-facilitators will be peer counsellors who have also experienced SUD and recovered,
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31 291 with at least 6 months of involvement with any organisations providing services for patients with
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33 292 SUD. The role of co-facilitators is to: (1) share personal experiences relevant to discussion topics,
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35 293 (2) assist facilitators in ensuring a safe and warm environment, (3) provide general support to the
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37 294 Indo-DARPP process, and (4) provide counsel, both in and out of sessions.

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45 **296 Training and supervision**

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47 297 Prior to recruitment, all providers will receive two full-day online training sessions on basic
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49 298 knowledge of SUD treatment, Indo-DARPP content, principles of MI (e.g., empathy, reflective
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51 299 listening, empowering affirmations), video demonstrations, hands-on role play, discussion of
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53 300 difficult cases, and study-related quality control. Workbooks and manuals will be handed to all
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3 301 providers, and close communication with the research team will be maintained via a WhatsApp
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5 302 group chat throughout the research period. To maintain treatment fidelity and quality control,
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7 303 during actual tele-Indo-DARPP sessions, addiction psychiatrists from the research team (KS and
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9 304 EH) will randomly select and observe at least two sessions per Indo-DARPP group. Observations
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11 305 will be conducted at each wave at each site, constituting 16.7% of all sessions, and will be reviewed
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13 306 using a structured checklist.
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308 **Control condition**

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23 309 Participants who received treatment before the study will continue to receive treatment as
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25 310 usual, regardless of group allocation. TAU was chosen as the control condition because it is
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27 311 expected to complement the existing treatment services for SUD at every level of care. The TAU
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29 312 differs according to service location (**Table 1**). Individual psychotherapy is typically conducted
30
31 313 via in-person short consultations (~15 minutes) with clinical psychiatrists. Pharmacotherapy is
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33 314 used to alleviate symptoms, by prescribing medications such as anxiolytics for conditions such as
34
35 315 anxiety. Patients undergoing MMT visit their sites almost every day to receive their daily doses,
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37 316 while patients undergoing substitution therapy with buprenorphine with naloxone visit every week.
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39 317 All participants will be able to continue any outpatient pharmacological treatment (e.g. MMT,
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41 318 antidepressants) and psychotherapy (e.g. twelve-step group sessions).
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320 **Primary outcome**

321 **Abstinence from primarily used substance**

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3 322 The primary outcome is the percentage of days of abstinence from the primarily used
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5 323 substance, in the past 28 days. Percent days of abstinence have been shown to be sensitive to the
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7 324 effects of CBT and are good predictors of SUD treatment follow-up.⁷⁵ Data on the use of primarily
8
9 325 used substances each day (measured in a yes/no format) for 28 days will be retrospectively
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11 326 collected on a weekly basis using the timeline follow-up (TLFB) method (**Table 2**), which has
12
13 327 good validity and high test-retest reliability in measuring substance consumption.^{76,77} The
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15 328 participants will be asked to recount every week to reduce the risk of recall bias. The primarily
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17 329 used substance refers to the most problematic substance for participants, which has driven them to
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19 330 seek care at T1.

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24 331 Urine samples will be collected to test for the presence of the primarily used substance
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26 332 once at T2. Thresholds for a positive result are >100 ng/ml for ethyl glucuronide (alcohol), >300
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28 333 ng/ml for amphetamine-type stimulants (i.e. d-methamphetamine and MDMA), >100 ng/ml for
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30 334 diacetyl morphine (heroin), cocaine, and benzodiazepine, >50 ng/ml for synthetic cannabis (K2),
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32 335 and > 25 ng/ml for tetrahydrocannabinol (marijuana). Urine tests in this study will only serve to
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34 336 corroborate the data of self-reported substance use at the primary endpoint (T2), not as an objective
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36 337 substitute of all self-reported substance use data at every time point. This was planned to improve
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38 338 feasibility for participants and minimise drop-out due to the burden of data collection (urine test
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40 339 needs in-person assessment, unlike all other measurements in this study), especially among
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42 340 participants who reside in remote areas who are deemed to benefit the most from online therapy.

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49 342 [Table 2 here]

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54 344 **Secondary outcomes**

345 *Addiction severity*

346 The Addiction Severity Index (ASI) is the most widely used measure in the field of
347 addiction.⁷⁸ Internal consistency, test-retest reliability, and scale independence of ASI to measure
348 substance use have long been established.^{79,80} The Treatnet ASI version 3.0 by the United Nations
349 Office on Drugs and Crime (UNODC) will be used; the scale is available in Indonesian, and one
350 addiction treatment centre in Indonesia was included in its development trial.⁸¹

351 *Health-related quality of life*

352 The five-level version of the five-dimensional EuroQoL (EQ-5D)^{82,83} will be used to assess
353 health-related quality of life (HRQoL), which has been used before for SUD patients with
354 confirmed construct validity.^{84,85} The total utility score will be obtained using the already
355 established value set in Indonesia.⁸⁶

356 *Motivation to change*

357 Motivation to change will be assessed by the Action subscale of the University of Rhode
358 Island Change Assessment (URICA)⁸⁷ which has been shown to have good validity. Higher scores
359 indicate that the person has committed to develop positive behavioural changes.⁸⁸

360 *Coping*

361 Types of engaged stress coping will be assessed by the Brief Coping Orientations to
362 Problems Experienced (Brief COPE),⁸⁹ which is commonly used for SUD patients.⁹⁰ Higher scores
363 for specific types indicate that patients have adopted them more frequently.

364 *Psychiatric symptoms*

365 Psychiatric symptoms will be evaluated by the Symptom Checklist 90-R (SCL-90-R).⁹¹ The
366 Global Severity Index (GSI) will be used, which is widely used for measuring psychiatric
367 symptoms among SUD patients.⁹²

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3 368 ***Cognitive function***
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5 369 Cognitive function will be assessed by the Rey Auditory Verbal Learning Test (RAVLT),⁹³
6
7
8 370 which is useful for diagnosing cognitive impairment as well as post-treatment improvement in
9
10 371 SUD patients.^{94,95}
11

12 372 ***Internalised stigma***
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14 373 Internalised stigma will be assessed using the Internalised Stigma of Mental Illness (ISMI)
15
16 374 scale.⁹⁶ The term ‘mental illness’ in the statements will be replaced with ‘substance addiction.’
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21 376 **Implementation outcomes**
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24 377 ***Retention in treatment***
25

26 378 Participants will be coded as ‘retained in treatment’ if they have had therapeutic contact,
27
28 379 including attending tele-Indo-DARPP and visiting any outpatient clinic for TAU, in at least 75%
29
30 380 of planned contacts in the previous 3 months.
31
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33 381 ***Treatment satisfaction***
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35 382 The Client Satisfaction Questionnaire-3 (CSQ-3)⁹⁷ will be used, as it is commonly used for
36
37 383 treatment programs, including for SUD.⁹⁸
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40 384 ***Group cohesion***
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42 385 The Group Therapy Experience Scale (GTES) will be used to measure the level of group
43
44 386 cohesion and self-disclosure in group therapy, as implementation outcomes of tele-Indo-DARPP.⁹⁹
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47 387 ***Indo-DARPP attendance***
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49 388 Attendance of each session will be recorded by the facilitator.
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51 389 ***Cost effectiveness***
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3 390 Cost-effectiveness will be assessed from patient, provider, and societal perspectives. Cost
4
5 391 data will be calculated by multiplying the quantity of utilised resources by the unit price. Data on
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7
8 392 quantity and unit price will be obtained from within the trial or estimated from relevant data
9
10 393 sources. For effectiveness data, both clinical and economic indices will be used. The clinical index
11
12 394 will be based on days of abstinence from the primarily used substance in the previous 28 days,
13
14 395 which will be converted into years of abstinence. The economic index will be based on the quality-
15
16 396 adjusted life year (QALY) calculated from the utility score of the EQ-5D.

19 397 *Feedback interviews*

21 398 Semi-structured interviews will be conducted with both participants and providers to assess
22
23 399 the following: satisfaction with content quality, comprehensibility, technical experience regarding
24
25 400 video-conferencing, comfort, module practicability, language barriers, and participants'
26
27 401 perception of the credibility of providers. Interviews will be audio-recorded with the interviewees'
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29 402 consent.
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35 404 **Participant characteristics**

37 405 The following data will be obtained via a self-administered questionnaire: age, gender,
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39 406 approximate residential location, marital status, household cohabitants, ethnicity, religion, highest
40
41 407 education level, employment status, individual and household income, type of Internet device used,
42
43 408 frequency of video calls in the past year, age during first instance of drug use, primarily used
44
45 409 substance, inpatient history or incarceration in the past month, types of treatments received,
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47 410 treatment locations in the past three months, status of current outpatient care (voluntary or
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49 411 involuntary, legal or non-legal), and transportation time and cost from residence to outpatient
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52 412 locations.
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6 414 **Data collection procedure**

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9 415 Researchers blinded to the treatment allocation will collect data at three different time
10
11 416 points: at baseline (week 0, T1), the week after the completion of treatment (week 13, T2), three
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13 417 months after the completion of treatment (week 24, T3), and 12 months after the completion of
14
15 418 treatment (week 60, T4), using self-answered questionnaires and online one-on-one interviews.
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17 419 For the primary outcome, participants will be asked to recall weekly drug use using the TLFB;
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19 420 with a period of approximately 4 weeks between each assessment. Urine specimens will be
20
21 421 collected only at T2 and at the final 2 weeks within the TLFB assessment period. The assessment
22
23 422 schedule is presented in **Table 2** and **Figure 2**. To facilitate honest disclosure from participants,
24
25 423 we will not record any Indo-DARPP video-conferencing sessions throughout the study.
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33 425 [Figure 2 here]34
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38 427 **Sample size**

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41 428 The sample size was calculated for the primary outcome to detect a medium effect size of $d =$
42
43 429 0.50 , which is slightly more modest than that of a previous study examining the efficacy of
44
45 430 telemedicine for people with SUD in an LIMC ($d = 0.59$).¹⁰⁰ Using $\alpha = 0.05$, power = 0.80, a
46
47 431 simple t-test requires $n = 64$ per arm. We estimated the design effect of clustering within the
48
49 432 Indo-DARPP group using the formula $D = 1 + (m - 1)\rho$,¹⁰¹ assuming intraclass correlation
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51 433 within Indo-DARPP groups or $\rho = 0.05$, and group size or $m = 5$, which yielded a design effect
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53 434 of $D = 1.2$. We then multiplied $n = 64$ by $D = 1.2$, which yielded the minimal number of
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3 435 participants in the data analysis: $n = 77$ per arm. Assuming an attrition proportion of 30% which
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5 436 is more conservative than a previous similar study (26%),¹⁰² the sample size for enrolment was
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8 437 set as 110 per arm, or 220 in total.
9

10 438

11 12 13 439 **Statistical analysis**

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16 440 A detailed statistical analysis plan will be developed by a statistician who is blinded to the
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18 441 patient allocation prior to data analysis. Baseline data description and main analyses will be
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20
21 442 conducted on an intention-to-treat basis; that is, participants' data will be handled according to
22
23 443 their initially assigned arms, regardless of the actual received treatment. Analyses will be
24
25 444 conducted with a significance level of 5% in the two-sided test, using Stata/SE 16.1.
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28 445 ***Consideration for correlated outcome data***

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31 446 The correlation within sites for the control arm will be ignored, as the TAU within one site
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33 447 varies per patient and some participants may not receive any treatment. For the intervention arm,
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35 448 the correlation within each Indo-DARPP group due to the nature of group therapy needs to be
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37
38 449 considered. We define a new variable termed 'clustering group identification' (CID), in which the
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40 450 control arm will be coded as a unique CID for each person, while the intervention arm will be
41
42 451 coded based on the tele-Indo-DARPP group, hence assigning the same CID for all five participants.
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45 452 ***Main analysis***

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48 453 The primary endpoint has been set at T2. The mean of the outcome changes from T1 to T2
49
50 454 will be compared between the intervention and control arms using a linear model. To investigate
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52
53 455 the durability of the treatment effect, outcome changes from T1 to T3 and T4 will also be compared
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55 456 between the two arms. We will account for the aforementioned correlations by clustering data
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3 457 based on CID in the generalised estimation equations (GEE). To help interpret the effect size,
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5 458 Cohen's *d* between the arms will be calculated.
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8 459 ***Missing values***

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11 460 A complete case analysis will be performed, which will only include participants with no
12
13 461 missing values in the variables of interest. Sensitivity analysis for missing values will be conducted
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15 462 by either inverse probability-weighted GEE¹⁰³ or multiple imputation.
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18 463 ***Subgroup analysis***

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21 464 Effects of the intervention will be investigated by subgroups, as the observed effect may
22
23 465 vary depending on the specific population. Participants will be divided by the types of primarily
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25 466 used substance, gender, previous and current utilisation of other SUD treatment, high and low
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27 467 values in clinical characteristics at T1 (for example, percent days of abstinence, ASI drug use
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29 468 composite score, URICA readiness score, and cognitive function. Specifically, based on previous
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31 469 studies which showed that treatment effectiveness varied depending on baseline severity levels
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33 470 ^{104,105}, we hypothesised that participants assigned to tele-Indo-DARPP with more severe levels of
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35 471 substance use at T1 would report more increase in days of abstinence at T2, T3, and T4.
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40 472 ***Implementation evaluation***

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42 473 Chi-squared tests and *t*-tests will be performed to compare retention in treatment and
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44 474 treatment satisfaction between the arms, exclusively for participants who are already receiving
45
46 475 SUD treatment at T1. Group cohesion and Indo-DARPP attendance will be descriptively reported
47
48 476 by means and standard deviations. For cost-effectiveness analysis, the incremental cost-
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50 477 effectiveness ratios (ICERs) will be calculated, which will yield costs per QALY and abstinent
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52 478 year. Feedback interviews will be transcribed, and thematic analysis will be conducted.
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5 480 **Compensations**

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8 481 Participants in both the control and intervention groups will receive 300,000 IDR (~ 21.3
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10 482 USD) to compensate for their transportation to treatment sites for TAU throughout the 12 weeks,
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12 483 and 98,000 IDR (~ 7.0 USD) every time they completed an online video assessment as
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14 484 compensation for internet data and 2-hour data collection. Participants from the intervention group
15
16 485 will further receive internet mobile data equivalent to 50,000 IDR (~ 3.5 USD) before the first
17
18 486 session of tele-Indo-DARPP, and subsequently every time they attend four sessions of tele-Indo-
19
20 487 DARPP. For providers, compensation of 170,000 IDR (~ 12.1 USD) and 150,000 IDR (~ 10.7
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22 488 USD) will be provided for each tele-Indo-DARPP session to the facilitator and co-facilitator,
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24 489 respectively.
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31 491 **Data monitoring**

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33 492 Data on adverse events, including hospitalisation, arrest, and death, will be collected from
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35 493 the participants' treating psychiatrists or medical staff. In addition, participants will be interviewed
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37 494 at T2 to determine whether they have experienced any subjective harmful effects (e.g. withdrawal
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39 495 syndrome, increased cravings) after joining Indo-DARPP. An independent data monitoring
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41 496 committee will not be convened, as the study involves short-term, non-invasive psychotherapeutic
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43 497 intervention. No interim analysis was planned due to the short duration of the intervention.
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45 498 Completeness and accuracy of data collection will be checked by Japanese co-investigators, and
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47 499 there will be no auditing process by independent investigators.
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53 501 **Data publication**
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3 502 The results of the study will be published in scientific publications and reported to relevant
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5 503 government bodies in Indonesia to advocate adopting the treatment module.
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10 505 **Ethical consideration and dissemination**
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12
13 506 The study protocol was approved by the Research Ethical Committee of Faculty of Medicine,
14
15 507 Universitas Indonesia (approval number: KET-1175/2019) and the Ethics Committee of the
16
17 508 Graduate School and Faculty of Medicine, Kyoto University (approval number: C1483). The study
18
19 509 protocol was registered at the University Hospital Medical Information Network Clinical Trial
20
21 510 Registry (UMIN-CTR) (registry number: UMIN000042186).
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24

25 511 The consent process will be conducted carefully to ensure that all potential participants
26
27 512 fully understand the research objectives, procedures, risks, benefits, costs, and alternatives. It will
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29 513 be emphasised that study participation is voluntary, and consent can be withdrawn at any time
30
31 514 before publication. We will allocate participants to treatment arms only when written informed
32
33 515 consent for participation is obtained. Likewise, urine specimens will only be collected if written
34
35 516 informed consent for urine collection is obtained. Participants will not be influenced when
36
37 517 deciding on study participation and/or urine collection. Personal data will be protected by
38
39 518 separating the study data from the participants' identifiable information. To quickly respond to
40
41 519 adverse events arising when outpatient visits are not possible, a dedicated phone number and
42
43 520 WhatsApp account for the study will be opened to ease communication with the research team.
44
45 521 Participants will be instructed to text or call when experiencing adverse events. Importantly,
46
47 522 written agreement will be obtained from participants to never share others' information with any
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49 523 third party. This regulation will be enforced both during and outside tele-Indo-DARPP sessions,
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51 524 in any medium, including video conference and group chat.
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3 525 The results of this study will be disseminated via peer-reviewed journals and international
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5 526 academic conferences. Depending on trial outcomes, Indo-DARPP will be advocated to the
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8 527 Indonesian government for adoption as a nationwide formal treatment program.
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10 528

13 529 **Patient and public involvement**

15 530 Patient feedback during the pilot study was incorporated into the Indo-DARPP module design. In
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17
18 531 addition, patients and/or the public will not be involved in conducting, reporting, or disseminating
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20 532 this study.
21

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25 534 **Discussion**

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28 535 Till the time of writing, nine RCTs from LMICs had reported the effectiveness of digital
29
30 536 delivery of interventions for SUD. The utilised formats were telephone calls,^{106–109} webpages,^{110–}
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32 537 ¹¹² and mobile applications.^{100,113} However, no study in LMICs has so far investigated the
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35 538 effectiveness of video conference-based psychotherapy. The latter may facilitate honest,
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37 539 interactive discussions on personal substance use and cravings, founded on better rapport between
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39
40 540 providers and patients,¹¹⁴ all of which are integral to CBT for SUD. One meta-analysis concluded
41
42 541 that web-based mental health interventions had better retention rates and treatment outcomes when
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44 542 therapists were synchronously involved.¹¹⁵
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47 543 This study has several strengths. This will be the first RCT to investigate the effectiveness
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49 544 of video conference-based psychotherapy in any LMIC, as well as the first study to establish
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52 545 quality evidence on psychotherapy for SUD in Indonesia. Recruitment will be done throughout
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54 546 multiple levels of care, that is, tertiary (referral hospitals), primary (Puskesmas), and community
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3 547 (rehabilitation centres). The latter have extensive reach encompassing all major Indonesian islands,
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5 548 and social media advertising will facilitate recruitment across the nation. While effectiveness of
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7 549 CBT is the primary outcome, the study allows examinations of real-world implementation and
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9
10 550 cost-effectiveness in a hybrid effectiveness-implementation design.⁶⁴ This is particularly true in
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12 551 Puskesmas, where the providers will be general practitioners, and in rehabilitation centres, where
13
14 552 the providers will be peer counsellors. This pragmatic RCT aims to mimic usual clinical practice,
15
16 553 and we hope that the results may be used to inform decision-making by patients, providers, and
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19 554 policymakers.¹¹⁶
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21

22 555 This study has several limitations. All data from participants will be self-reported and prone
23
24 556 to recall and social desirability bias. Urine tests will be performed to corroborate subjective data,
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26 557 but will not constitute a full validation as they will only be performed once to represent substance-
27
28 558 detectable period. This was planned only at T2 to improve feasibility for participants and reduce
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30
31 559 the risk of drop-outs. Control conditions will be heterogeneous, as the study will include
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33 560 participants who use various substances at multiple sites, where TAU differs or may not even be
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35 561 provided. Variability in the providers' background may create inconsistency in CBT delivery, even
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38 562 though training and treatment manuals will be introduced to standardise care. Treatment delivery
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40 563 via online video-conferencing might have poor generalisability towards people with low Internet
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42 564 literacy, as well as people in low socio-economic strata who cannot afford smartphones, although
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44 565 entry-level Android-based smartphones (less than 100 USD) are available nationwide in Indonesia.
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47 566 Psychotherapy will be provided in Bahasa Indonesia; hence its effectiveness would not be
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49 567 generalisable to people with limited proficiency in the language.
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52 568 Efforts to establish evidence-based treatment for SUD should be scaled up in Indonesia
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55 569 and LMICs in general, where effectiveness data are sparse. The proposed study may present high-
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3 570 quality evidence, and a successful outcome may result in a new SUD treatment module in
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5 571 Indonesia, paving the way for the adoption of Indo-DARPP into the national guidelines. We hope
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7 572 that our efforts may further promote a comprehensive healthcare approach, as opposed to
8
9 573 repressive anti-drug policies, for the SUD population.
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13 574

15 575 **Acknowledgements**

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17
18 576 We would like to thank Dr Takashi Kawamura for his valuable comments on the study design.
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20

21 577

23 578 **Author contributions**

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25
26 579 CY, KS, and YO conceptualised the study. CY, KS, EH, and YO are the main developers of the
27
28 580 Indo-DARPP module, designed study methodology, liaised with site investigators, trained the
29
30 581 providers, wrote the protocol, and reviewed and edited the final manuscript. EB, VR, PA, and AP
31
32 582 helped in module development, study design, training of providers, and site coordination. TS
33
34 583 provided statistical and epidemiological supervision. TM provided the original SMARPP module,
35
36 584 clinical input, and perspectives to improve study quality. RS supervised the study and provided
37
38 585 grant support. CY and RS were the principal investigators of the grant. All authors have read and
39
40 586 approved the final manuscript.
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45 587

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9

10 594 **Competing interests**

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13 595 The authors declare no competing interest.
14

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17 597 **Patient consent for publication**

18
19 598 Not required.
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21

22 599

24 600 **Ethics approval and trial registration**

25
26 601 This study protocol was approved by the Research Ethical Committee of the Faculty of Medicine,
27
28 602 Universitas Indonesia (approval number: KET-1175/2019) and the Ethics Committee of the
29
30 603 Graduate School and Faculty of Medicine, Kyoto University (approval number: C1483). The study
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32 604 protocol was registered at the University Hospital Medical Information Network Clinical Trial
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34 605 Registry (UMIN-CTR) (registry number: UMIN000042186).
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41 607 **Availability of data and materials**

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43 608 The full protocol and datasets of the planned study will be available from the corresponding author
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45 609 upon reasonable request.
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51 612 **Figure legends**

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53 613 **Figure 1.** Study flowchart for each site. A total of 20 or 30 participants will be recruited through
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55 614 the social network of each site. After 10 participants have been recruited to constitute one wave,
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3 615 they will be randomly allocated into two arms: intervention (Indo-DARPP + TAU) and control
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5 616 (TAU only), with 5 participants in each arm. Recruitment will be continued until another 10 or 20
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7 617 participants (second or third wave) join, in a similar procedure. Treatment period will be 12 weeks.
8
9 618 Assessments will be conducted four times: T1 (Week 0) during baseline or before randomisation,
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11 619 T2 (Week 13-16) during post-assessment or 1-4 weeks after treatment period ends, T3 (Week 24)
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13 620 at 3 months after treatment ends, and T4 (Week 60) at 12 months after treatment ends.
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19 622 **Figure 2.** Planned trial schedule across all 8 research sites. Staggered schedules were designed to
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21 623 spread the assessment workload of providers and research staff. After training the providers, all
22
23 624 sites will be given approximately 1-2 months to recruit participants. Sites with relatively higher
24
25 625 potential to recruit faster, i.e., those with higher rates of patient turnover, have been selected first
26
27 626 in the schedule. Each site will have two or three waves of recruitment and treatment periods.
28
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32 628 **References**

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16 654 [10/Survei%20Penyalahgunaan%20Dan%20Peredaran%20Gelap%20Narkoba%20Tahun%202018%20%28%20BNN%20-%20LIPI%29.pdf](https://perpustakaan.bnn.go.id/sites/default/files/Buku_Digital_2020-10/Survei%20Penyalahgunaan%20Dan%20Peredaran%20Gelap%20Narkoba%20Tahun%202018%20%28%20BNN%20-%20LIPI%29.pdf) (May 1, 2019, accessed December 4, 2020).
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Table 1. Recruitment sites in this study

Name	Location	Type	Treatment as usual	Most reported
Cipto Mangunkusumo Hospital	Jakarta	Tertiary national general hospital	Individual psychotherapy, symptomatic pharmacotherapy	Benzodiazep
Aceh Mental Hospital	Aceh	Tertiary provincial mental hospital	Individual psychotherapy, symptomatic pharmacotherapy	Methamphet
Duren Sawit Regional Hospital	Jakarta	Tertiary regional general hospital	Individual psychotherapy, symptomatic pharmacotherapy, opioid substitution therapy (buprenorphine, naloxone)	Opioid
Karisma Foundation	Jakarta	Rehabilitation centre	Individual and group peer counselling	Methamphet
Kapeta Foundation	Banten	Rehabilitation centre	Individual and group peer counselling	Methamphet cannabinoids
Kios Atma Jaya	Jakarta	Rehabilitation centre and regional HIV clinic	Individual psychotherapy, group peer counselling, outreach program	Opioid
Puskesmas Jatinegara	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin
Puskesmas Gambir	Jakarta	Primary health care	Counselling, symptomatic pharmacotherapy, methadone maintenance therapy	Heroin

Counselling focuses on education and giving advice.

Symptomatic pharmacotherapy gives medication for helping patients with specific psychopathologies.

Psychotherapy aims to help a person identify and change their emotions, thoughts, and behaviour.

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Table 2. Outcome and measurement

Outcome	Measurement	Data for analysis	Type and score range	Hypothesis for intervention (vs control)	Assessment time point			
					T1	T2	T3	T4
Primary outcome								
Abstinence from primary substance	Timeline followback (TLFB) for the past 28 days	Number of days being abstinent from primary substance divided by 28 (%).	Continuous, 0 (no use) to 100 (used every day).	Higher	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Secondary outcomes								
Addiction severity	Addiction Severity Index (ASI)	7 composite scores: medical, employment, alcohol use, drug use, legal, family/social, and psychiatric status. Each composite score calculated using standard formula.	Continuous, 0 (no problems) to 1 (severe problems).	Lower	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Health-related quality of life	EuroQol-5D (EQ-5D-5L)	Health utility score, calculated from 5 items on mobility, self-care, usual activities, pain/discomfort and anxiety/depression, using Indonesian value set.	Continuous, -0.865 (impaired health) to 1 (full health).	Higher	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Motivation to change	University of Rhode Island Change Assessment (URICA)	Action stage subscale, sum of 8 items.	Continuous, 8 (not active in behavioural change) to 40 (highly active in behavioural change).	Higher	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Coping	Brief-Coping Orientation to Problems Experienced (Brief COPE)	Sum of substance use coping (2 items)	Continuous, 2 (low substance use coping) to 8 (high substance use coping)	Lower	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Psychiatric symptoms	Symptom Checklist-90 Revised (SCL-90-R)	Global Severity Index (GSI), average of 90 items.	Continuous, 0 (no symptoms) to 4 (severe symptoms).	Lower	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Cognitive function	Rey Auditory Verbal Learning Test (RAVLT)	3 test results; immediate, learning, and recalling.	Continuous, 0 (low functioning) to 15 (high functioning).	Higher	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Internalised stigma	Internalized Stigma of Mental Illness (ISMI)	Sum of 4 subscales: alienation, stereotype endorsement, social withdrawal, and stigma resistances.	Continuous, 24 (low internalised stigma) to 96 (high internalised stigma)	Lower	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Implementation outcomes								
Retention in treatment	Self-reporting for the past 3 months	Coded as 'retained' if they had therapeutic contacts in at least 75% of the planned number of therapeutic contacts.	Categorical, 'retained' = 1, 'not retained' = 0.	More 'retained'	✓ ^a	✓ ^a	✓ ^a	✓ ^a
Treatment satisfaction	Client Satisfaction Questionnaire-3 (CSQ-3)	Sum of 3 items.	Continuous, 4 (not satisfied) to 12 (satisfied).	Higher	✓ ^a			
Group cohesion	Group Therapy Experience Scale (GTES)	Sum of 16 items.	Continuous, 16 (poor cohesion) to 80 (great cohesion).	Not applicable: measured only in intervention arm	✓ ^a			

^a Objective validation by urine drug test for 8 substances: alcohol, amphetamine, morphine, cannabinoids, methamphetamine, benzodiazepine, cocaine, synthetic cannabinoids

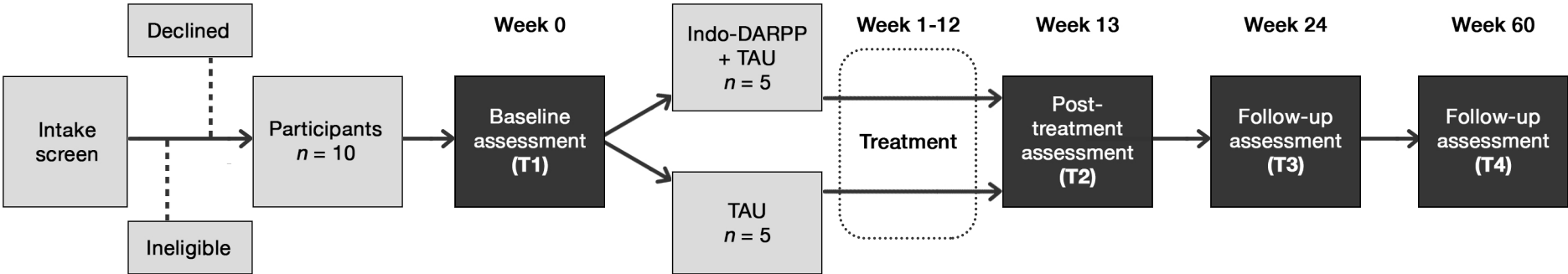
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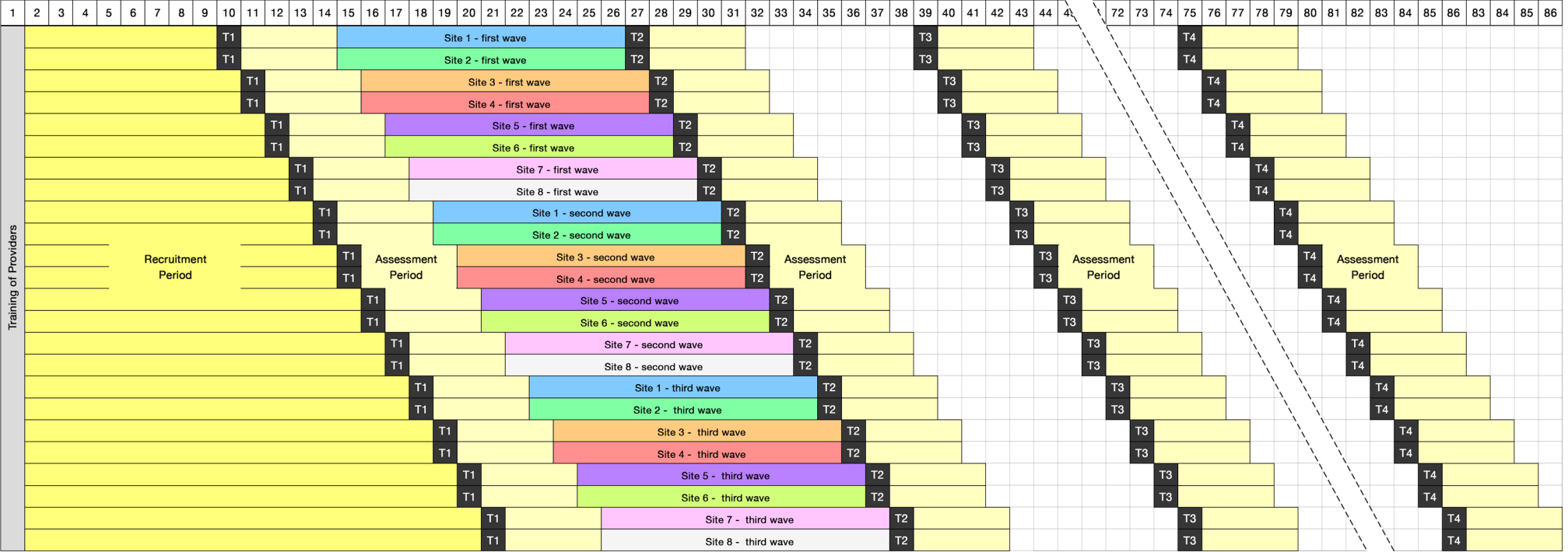
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Weeks



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	4, 23
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a, trial already registered as described in 2a.
Protocol version	#3	Date and version identifier	23
Funding	#4	Sources and types of financial, material, and other support	26-27
Roles and	#5a	Names, affiliations, and roles of protocol	26

1	responsibilities:	contributors	
2	contributorship		
3			
4	Roles and	#5b	Name and contact information for the trial
5	responsibilities:		sponsor
6	sponsor contact		
7	information		
8			
9			
10			
11	Roles and	#5c	Role of study sponsor and funders, if any, in
12	responsibilities:		study design; collection, management,
13	sponsor and funder		analysis, and interpretation of data; writing of
14			the report; and the decision to submit the
15			report for publication, including whether they
16			will have ultimate authority over any of these
17			activities
18			
19			
20			
21			
22			
23	Roles and	#5d	Composition, roles, and responsibilities of the
24	responsibilities:		coordinating centre, steering committee,
25	committees		endpoint adjudication committee, data
26			management team, and other individuals or
27			groups overseeing the trial, if applicable (see
28			Item 21a for data monitoring committee)
29			
30			
31			
32			
33	Introduction		
34			
35	Background and	#6a	Description of research question and
36	rationale		justification for undertaking the trial, including
37			summary of relevant studies (published and
38			unpublished) examining benefits and harms
39			for each intervention
40			
41			
42			
43			
44	Background and	#6b	Explanation for choice of comparators
45	rationale: choice of		
46	comparators		
47			
48			
49	Objectives	#7	Specific objectives or hypotheses
50			
51			
52	Trial design	#8	Description of trial design including type of
53			trial (eg, parallel group, crossover, factorial,
54			single group), allocation ratio, and framework
55			(eg, superiority, equivalence, non-inferiority,
56			exploratory)
57			
58			
59			
60			

1 **Methods:**

2 **Participants,**

3 **interventions, and**

4 **outcomes**

5			
6			
7			
8	Study setting	#9	Description of study settings (eg, community
9			clinic, academic hospital) and list of countries
10			where data will be collected. Reference to
11			where list of study sites can be obtained
12			
13			
14			
15	Eligibility criteria	#10	Inclusion and exclusion criteria for
16			participants. If applicable, eligibility criteria for
17			study centres and individuals who will
18			perform the interventions (eg, surgeons,
19			psychotherapists)
20			
21			
22			
23			
24	Interventions:	#11a	Interventions for each group with sufficient
25	description		detail to allow replication, including how and
26			when they will be administered
27			
28			
29	Interventions:	#11b	Criteria for discontinuing or modifying
30	modifications		allocated interventions for a given trial
31			participant (eg, drug dose change in
32			response to harms, participant request, or
33			improving / worsening disease)
34			
35			
36			
37			
38	Interventions:	#11c	Strategies to improve adherence to
39	adherence		intervention protocols, and any procedures
40			for monitoring adherence (eg, drug tablet
41			return; laboratory tests)
42			
43			
44			
45	Interventions:	#11d	Relevant concomitant care and interventions
46	concomitant care		that are permitted or prohibited during the
47			trial
48			
49			
50			
51	Outcomes	#12	Primary, secondary, and other outcomes,
52			including the specific measurement variable
53			(eg, systolic blood pressure), analysis metric
54			(eg, change from baseline, final value, time to
55			event), method of aggregation (eg, median,
56			proportion), and time point for each outcome.
57			
58			
59			
60			

1		Explanation of the clinical relevance of	
2		chosen efficacy and harm outcomes is	
3		strongly recommended	
4			
5			
6	Participant timeline	#13 Time schedule of enrolment, interventions	10, 19, 26
7		(including any run-ins and washouts),	
8		assessments, and visits for participants. A	
9		schematic diagram is highly recommended	
10		(see Figure)	
11			
12			
13			
14	Sample size	#14 Estimated number of participants needed to	20
15		achieve study objectives and how it was	
16		determined, including clinical and statistical	
17		assumptions supporting any sample size	
18		calculations	
19			
20			
21			
22			
23	Recruitment	#15 Strategies for achieving adequate participant	11
24		enrolment to reach target sample size	
25			
26			
27	Methods:		
28	Assignment of		
29	interventions (for		
30	controlled trials)		
31			
32			
33			
34	Allocation:	#16a Method of generating the allocation	12
35	sequence	sequence (eg, computer-generated random	
36	generation	numbers), and list of any factors for	
37		stratification. To reduce predictability of a	
38		random sequence, details of any planned	
39		restriction (eg, blocking) should be provided	
40		in a separate document that is unavailable to	
41		those who enrol participants or assign	
42		interventions	
43			
44			
45			
46			
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48			
49	Allocation	#16b Mechanism of implementing the allocation	12
50	concealment	sequence (eg, central telephone; sequentially	
51	mechanism	numbered, opaque, sealed envelopes),	
52		describing any steps to conceal the	
53		sequence until interventions are assigned	
54			
55			
56			
57	Allocation:	#16c Who will generate the allocation sequence,	12
58			
59			
60			

1	implementation		who will enrol participants, and who will	
2			assign participants to interventions	
3				
4	Blinding (masking)	#17a	Who will be blinded after assignment to	12, 19
5			interventions (eg, trial participants, care	
6			providers, outcome assessors, data	
7			analysts), and how	
8				
9				
10				
11	Blinding (masking):	#17b	If blinded, circumstances under which	n/a, only assessors are
12	emergency		unblinding is permissible, and procedure for	blinded
13	unblinding		revealing a participant's allocated	
14			intervention during the trial	
15				
16				
17				
18	Methods: Data			
19	collection,			
20	management, and			
21	analysis			
22				
23				
24				
25	Data collection plan	#18a	Plans for assessment and collection of	15-19
26			outcome, baseline, and other trial data,	
27			including any related processes to promote	
28			data quality (eg, duplicate measurements,	
29			training of assessors) and a description of	
30			study instruments (eg, questionnaires,	
31			laboratory tests) along with their reliability	
32			and validity, if known. Reference to where	
33			data collection forms can be found, if not in	
34			the protocol	
35				
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42	Data collection plan:	#18b	Plans to promote participant retention and	19, 22-23
43	retention		complete follow-up, including list of any	
44			outcome data to be collected for participants	
45			who discontinue or deviate from intervention	
46			protocols	
47				
48				
49				
50				
51	Data management	#19	Plans for data entry, coding, security, and	23
52			storage, including any related processes to	
53			promote data quality (eg, double data entry;	
54			range checks for data values). Reference to	
55			where details of data management	
56			procedures can be found, if not in the	
57				
58				
59				
60				

1		protocol	
2			
3	Statistics: outcomes	#20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	20-22
4			
5			
6			
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9			
10	Statistics: additional analyses	#20b Methods for any additional analyses (eg, subgroup and adjusted analyses)	21-22
11			
12			
13			
14	Statistics: analysis population and missing data	#20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	21
15			
16			
17			
18			
19			
20			
21	Methods:		
22	Monitoring		
23			
24			
25	Data monitoring: formal committee	#21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	23, DMC will not be convened as the intervention involves a short-term psychotherapy with known minimal risk.
26			
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38	Data monitoring: interim analysis	#21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	23, interim analysis is not planned due to the short duration of intervention.
39			
40			
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45	Harms	#22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	22-23
46			
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48			
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53			
54	Auditing	#23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	23, there will be no auditing process by independent investigators.
55			
56			
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Ethics and dissemination

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	23, 28
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	23
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	23
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	23
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	23
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	15, CBT intervention will be made available for control group after the end of the study.

1	Dissemination	#31a	Plans for investigators and sponsor to	23
2	policy: trial results		communicate trial results to participants,	
3			healthcare professionals, the public, and	
4			other relevant groups (eg, via publication,	
5			reporting in results databases, or other data	
6			sharing arrangements), including any	
7			publication restrictions	
8				
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10				
11				
12				
13	Dissemination	#31b	Authorship eligibility guidelines and any	26-27
14	policy: authorship		intended use of professional writers	
15				
16				
17	Dissemination	#31c	Plans, if any, for granting public access to the	28
18	policy: reproducible		full protocol, participant-level dataset, and	
19	research		statistical code	
20				
21				
22	Appendices			
23				
24				
25	Informed consent	#32	Model consent form and other related	11, 23
26	materials		documentation given to participants and	
27			authorised surrogates	
28				
29				
30	Biological	#33	Plans for collection, laboratory evaluation,	16
31	specimens		and storage of biological specimens for	
32			genetic or molecular analysis in the current	
33			trial and for future use in ancillary studies, if	
34			applicable	
35				
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Notes:

- 2b: n/a, trial already registered as described in 2a.
- 5b: n/a, no trial sponsor.
- 5c: n/a, no involvement of funders in the study design.
- 5d: n/a, no direct intervention in the study design by the host universities.
- 17b: n/a, only assessors are blinded
- 21a: 23, DMC will not be convened as the intervention involves a short-term psychotherapy with known minimal risk.
- 21b: 23, interim analysis is not planned due to the short duration of intervention.

- 23: 23, there will be no auditing process by independent investigators.
- 30: 15, CBT intervention will be made available for control group after the end of the study. The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 15. February 2021 using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)

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Supplementary file 2

Research Participation Consent Form

Title of the Research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

An explanation has been given which includes the following discussion :

- | | |
|---|--|
| 1. Research Title | 18. General management of drug addiction patients outside of research interventions |
| 2. Research Clearance | 19. Follow up management after the research ends |
| 3. Research institutes and researchers | 20. Report of the participant's genetic information |
| 4. Research purposes | 21. Compensation for illness related to research and invasive procedures |
| 5. Research procedure | 22. Secondary research data for other institutions |
| 6. Research period | 23. Samples and participant information related to invasive procedures |
| 7. Inclusion Criteria | 24. Name, position, and affiliation of the person in charge of managing data and information related to research |
| 8. Risks, benefits, and side effects | 25. CBT group participant commitments and drop out possibility of research participation |
| 9. Right to refuse and drop out | |
| 10. Voluntary participation and risk of involvement | |
| 11. Research data publication | |
| 12. How to access research-related materials for participants | |
| 13. Privacy of personal data | |
| 14. Research data storage | |
| 15. Research funds and conflicts of interest | |
| 16. Researcher contact list | |
| 17. Remuneration for participants | |

Explanations have been given according to the explanation sheet, and consent has been obtained voluntarily.

Date of consent : ____ / ____ / 20 ____

Researcher's affiliation : _____

Researcher's Name :

Researcher's Signature :

Acknowledged by:

1. Dean of the Faculty Medicine, University Indonesia
2. Director of the *Center for South East Asian Studies, Kyoto University*

Supplementary file 2

CBT-Group Participation Consent Form

I, the undersigned, hereby acknowledge, consent and agree to fulfill the following matters during my participation in CBT group therapy, in order to ensure the safe and secure continuation of the program:

1. I will not divulge information about other participants in the group to external parties without the consent of the parties concerned.
2. I will not record audio, video, or take camera pictures without the permission of the parties concerned and the research team.
3. I will not use drugs during the CBT session.
4. I will not divulge links (URL), ID, and passwords for online meetings in the Zoom application to external parties, without the approval of the research team.
5. I will not harass, say offensive words related to ethnicity, religion and race, or commit acts of violence for any reason to any party related to the research, whether other participants or the research team.

If I infringe the points of the agreement above, I will be given 1 (one) warning. If I do not show any improvement after being warned, or infringe it for the second time, or it is deemed that my participation will interfere with the continuation of CBT therapy in the future, I have no objection to my participation being unilaterally terminated.

I, the undersigned, hereby declare that I have understood the explanation given and agree to my participation in the research mentioned above. In my behavior after being warned, or infringe it for the second time, or it is deemed that my participation will interfere with the continuation of CBT therapy in the future, I have no objection to my participation being unilaterally terminated.

Date of Consent : ____ / _____ / 20 ____

Name : _____

Signature : _____

Supplementary file 2

Urine Test Informed Consent

Title of Research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

An explanation has been given which includes the following discussion:

1. Purpose of the urine sampling
2. Urine test procedure
3. Analysis of urine test results data and maintaining data confidentiality

Explanations have been given according to the explanation sheet, and consent has been obtained voluntarily.

I, the undersigned, declare that I

Agree / do not agree

*please circle one of these options above

...to provide the urine sample to be tested for the research team, and I have acknowledged and understood the purposes, procedures and data analysis as described previously.

Date of consent : ____ / _____ / 20 ____

Name : _____

Signature : _____

Supplementary file 2

Withdrawal of Informed Consent for Urine Test

Title of the research:

Effectiveness of a cognitive behavioral therapy for drug use disorders in Indonesia: A randomized controlled trial

(Collaboration research between the Faculty of Medicine, University of Indonesia and Kyoto University)

I, the undersigned, hereby wish to withdraw my prior consent to participate in the urinary test for this research by signing this form.

Withdrawal Date : ____ / _____ / 20 ____

Participant's Name : _____

Participant's Signature : _____

Supplementary file 3

Table of contents of Indo-DARPP (English translation)

Chapter no.	Chapter title	Page no.
Preface	The beginning of Indo-DARPP The purpose of SMARPP	x xii
1	What is addiction? Seven characteristics of addiction	5 5
2	Why should we stop using drugs? Why drug use is a problem Drugs and behavior disorder Advantages and disadvantages of using drugs and stop using drugs Stages of change The urge to continue or to stop using drugs	11 11 13 16 17 19
3	Recovery stage of drug addiction - First year Stage (1) Stress phase (0-14 days) Stage (2) 'Honeymoon' phase (15-90 days) Stage (3) The 'wall' phase (91-180 days) Stage (4) Adjustment phase (181-270 days) Stage (5) Resolution phase (271-365 days) Understanding our "wall" symptoms	21 21 22 23 24 24 25
4	"Triggers" and "cravings" The urge to use drugs Let's take action! Stopping the urge to use drugs	28 28 31 32
5	Triggers around you External triggers Let's take action!	36 36 37
6	Trigger inside us Internal trigger High risk conditions: hungry, angry, lonely, tired (HALT)	42 42 44
7	Prevention of harmful behavior Distant and self-isolating behavior Drug dreams	48 48 51
8	Let's make schedule of our daily activities Why is scheduling so important? Make your schedule and practice! Calendars and marks of achievement	54 54 57 60
9	Adverse effects of drugs on the brain and body Effects of drugs on the brain Effects of drugs on the body Dangerous viral infections: Hepatitis C and HIV	62 62 65 67
10	Drug-induced psychiatric and behavioral disorders What are psychiatric disorders? If a person with psychiatric disorder addicted to drugs Drug-induced psychiatric and behavioral disorders Testimonials of people with comorbidities	72 72 73 73 74

11	Amphetamine-type stimulants Effects of amphetamine on the brain and its symptoms The dangers of using amphetamine Prognosis of amphetamine addiction	78 79 81 83
12	Opioid: Heroin, morphine and maintenance therapy Types of opioids & how do they work Symptoms and side effects of opioid usage Effects on opioid use Treatments & therapy for opioid addiction Opioid addiction prognosis	84 84 85 86 88 90
13	Benzodiazepine and other legal drugs Medical use of benzodiazepines The dangers of benzodiazepines Other legal drugs use Particular problems in benzodiazepine addiction Responsible use of benzodiazepines	92 92 93 94 96 99
14	Alcohol use Alcohol use in Indonesia Triggers on alcohol drinking	100 100 102
15	The dangers of alcohol on brain and body Effects of alcohol on the brain Effects of alcohol on the body Liver disease Heart and vascular disease	107 107 111 112 115
16	Three pillars to stop drinking alcohol Three pillars on stop drinking alcohol What are anti-alcohol drugs? Types of anti-alcohol drugs	118 118 119 121
17	Does marijuana not cause addiction? Getting to know about marijuana Marijuana use in Indonesia Effects of marijuana on the body	127 127 128 129
18	New psychoactive substances (NPS) Types and characteristics of NPS Effects of NPS on the brain and body	132 132 135
19	Abstinence or relapse risk in the future The chance of alcohol-free after treatment The chance & duration of getting relapse after treatment Effects of participation in self help groups on prognosis Prognosis of people with substance addiction	139 139 140 142 143
20	Preventing relapse What is relapse? What is addictive behavior? What is addictive thought? The accumulation of negative emotions	147 147 148 150 150
21	Reasons a person experiencing relapse What causes relapse? Due to chance or influences of others? Because of some extraordinary events, misfortunes or disasters Because of the desire to achieve something	153 153 154 154 155

	Because of emotions: depression, anger, lonely, fright	155
	Because of perception that the addiction problems was already solved	156
	Testing own selves	157
	Celebrating something	157
22	Characters towards recovery: trust, honesty, friendships	160
	Trust	160
	Honesty	162
	Creating new friendships	164
23	Negative relationships with other people	166
	Relationship without appreciation	166
	Controlling relationship (1)	168
	Controlling relationship (2)	169
	Relationship that hurts you and the drugs recovery phase	170
	Value yourself	171
24	Sexual behavior, eating disorders and holidays	173
	Sexual behavior during the recovery phase	173
	Eating disorders	175
	Getting through long holidays	177
25	Preventing relapse: becoming wiser	181
	Recognizing triggers and creating schedule	183
26	How is your relapse cycle?	189