Drug use disorder module - evidence profile DRU4: Digital or telemedicine interventions for adults with drug use disorders or people using drugs

WHO mhGAP guideline update: Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders

2023

World Health Organization

Contents

Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders, available at: https://www.who.int/publications/i/item/9789240084278

1. Background

Drug use and drug use disorders constitute a public health, developmental and security problem both in developed and developing countries worldwide. According to the latest global estimates, about 5.5 per cent of the population aged between 15 and 64 years have used drugs at least once in the past year, while 36.3 million people, or 13 per cent of the total number of persons who use drugs, suffer from drug use disorders (UNODC, 2021). Approximately 0.5 million deaths annually attributable to drug use (UNODC, 2021).

Strengthening prevention and treatment for people with DUDs is an essential demand reduction strategy of significant public health importance, which is a cornerstone of the 2016 United Nations General Assembly Special Session on the World Drug Problem (UNGASS, 2016) outcome document, and has been specifically set as Target 3.5 of Goal 3, under the 2030 Agenda for Sustainable Development Goals (SDGs).

There is a range of effective interventions for the prevention and treatment of drug use disorders (WHO/UNODC, 2020; UNODC/WHO, 2018). However, the coverage of treatment for people with drug use disorders is extremely low in majority of countries, with only 7.1% of those with past-year substance use disorders received minimally adequate treatment (Degenhardt et al., 2017). Digital interventions have shown promising results for a variety of conditions including drug use disorders (Boumparis et al. 2017, 2019). The benefits of digital interventions include the removal of barriers such as time constrains, distance, and stigmatization and can therefore lower the threshold to access support and treatment options.

Based on preliminary searches, we suggest that an update of an existing systematic review is required before the evidence summaries can be prepared.

2. Methodology

2.1. PICO question

The following main question is applied in the present review:
DRU4: In adults with drug use disorders or people using drugs, are digital or telemedicine interventions effective?
Moreover, the following PICO (population, intervention, comparator, outcome) definition will be applied:
Population (P): Adults with drug use disorders or people using drugs
Intervention (I): Digital interventions
Comparator (C): Treatment as usual, waitlist, no treatment, head to head comparison
Outcomes (O): Drug use reduction

List critical outcomes:
Days of drug use last 30 days as a primary outcome (measuring drug use reduction)

List important outcomes:

- DUDIT,
- CUDIT,
- days of abstinence last 30 days

2.2. Search strategy

We conducted a systematic literature search in the following bibliographic databases: PubMed, Embase, PsycInfo, CENTRAL. We used various combinations of key and index terms covering the concepts of drug use and digital interventions. The full search strings are given in Appendix II. Furthermore, we applied a filter for randomized controlled trials (RCTs) in these databases. Our initial selection was based on titles and abstracts. Subsequently, full texts of studies possibly meeting inclusion criteria were retrieved and evaluated. The identified interventions were delivered through various options (web-based, computerized, telemedicine, smartphone applications). For the sake of clarity, we will refer to the included interventions as “digital interventions”.

2.2.1. Selection criteria

Our systematic review was based on two previous relevant publications (Boumparis et al. 2017, 2019), which have reviewed studies conducted in the field of digital interventions for substance use reduction. However, given that those systematic reviews have slightly different scopes and inclusion criteria we conducted in addition a new systematic search that will comprise all available studies until January 2022. We included RCTs that compare digital interventions with active [e.g. TAU, motivational interviewing (MI), brief intervention (BI), psychoeducation] or non-active (e.g. waiting-list, assessment-only) control conditions. The RCTs had to focus upon adult substance users. Furthermore, studies had to include a measurement of substance use at post treatment measured through self-report, toxicology screening or both.

2.3. Data collection and analysis

Our initial selection was based on titles and abstracts. Subsequently, full texts of studies possibly meeting inclusion criteria were retrieved and evaluated. The search strategy and results were carefully documented. The flow of articles throughout the search and up to the final cohort of included studies are depicted through the PRISMA flow diagram. Outcome measures assessing drug use were extracted at post-treatment.

All analyses were carried out with the program Comprehensive Meta-Analysis (CMA). Effect sizes were calculated by subtracting the mean post-treatment result of the experimental condition from the mean post-treatment result of the control condition and dividing that difference by the pooled standard deviation of the two (Cohen 1988). Effect sizes of about 0.8 are considered large, 0.5

moderate, and 0.2 small (Cohen 1988). Given the expected heterogeneity among the RCTs, we calculated the mean effect sizes using a random-effects model, which implies that the included studies were drawn from populations of studies that systematically differed from one another (Borenstein et al. 2009).

2.4. Selection and coding of identified records

For the purpose of organizing the obtained studies from our systematic searches we used the reference management software Endnote. A copy of the reference library in electronic format is supplied alongside the final report.

2.5. Quality assessment

The validity of all included RCTs was assessed using the Cochrane Risk of bias tool.

2.6. Analysis of subgroups or subsets

We will conduct subgroup analyses based on the intervention type (guided, unguided) and recruitment style (cut-off, clinical diagnosis).

3. Results

3.1. Systematic reviews and/or studies identified by the search process

Riggs, N. R., Conner, B. T., Parnes, J. E., Prince, M. A., Shillington, A. M., & George, M. W. (2018). "Marijuana eCHECKUPTO GO: effects of a personalized feedback plus protective behavioral strategies intervention for heavy marijuana-using college students." Drug and Alcohol Dependence 190(pp 13-19).

Baumgartner, C., et al. (2021). "CANreduce 2.0 Adherence-Focused Guidance for Internet SelfHelp Among Cannabis Users: Three-Arm Randomized Controlled Trial." J Med Internet Res 23(4): e27463.

Becker, J., et al. (2014). "Effectiveness of different Web-based interventions to prepare co-smokers of cigarettes and cannabis for double cessation: a three-arm randomized controlled trial." J Med Internet Res 16(12): e273.

Bickel, W. K., et al. (2008). "Computerized behavior therapy for opioid-dependent outpatients: a randomized controlled trial." Exp Clin Psychopharmacol 16(2): 132-143.

Blow, F. C., et al. (2017). "A randomized controlled trial of brief interventions to reduce drug use among adults in a low-income urban emergency department: the HealthiER You study." Addiction 112(8): 1395-1405.

Brooks, A. C., et al. (2010). "Feasability and effectiveness of computer-based therapy in a comunity-based program." Proceedings of the 72th annual scientific meeting of the college on problems of drug dependence; 2010 june 12-17; scottsdale, arizona. USA: 18.

Budney, A. J., et al. (2015). "Computer-assisted behavioral therapy and contingency management for cannabis use disorder." Psychol Addict Behav 29(3): 501-511.

Campbell, A. N. C., et al. (2014). "Internet-delivered treatment for substance abuse: A multisite randomized controlled trial." The American Journal of Psychiatry 171(6): 683-690.

Carroll, K. M., et al. (2008). "Computer-assisted delivery of cognitive-behavioral therapy for addiction: a randomized trial of CBT4CBT." American Journal of Psychiatry 165(7): 881-888.

Carroll, K. M., et al. (2014). "Computer-assisted delivery of cognitive-behavioral therapy: efficacy and durability of CBT4CBT among cocaine-dependent individuals maintained on methadone." Am J Psychiatry 171(4): 436-444.

Carroll, K. M., et al. (2018). "Galantamine and Computerized Cognitive Behavioral Therapy for Cocaine Dependence: A Randomized Clinical Trial." J Clin Psychiatry 79(1).

Chopra, M. P., et al. (2009). "Buprenorphine medication versus voucher contingencies in promoting abstinence from opioids and cocaine." Exp Clin Psychopharmacol 17(4): 226-236.

Christensen, D. R., et al. (2014). "Adding an Internet-delivered treatment to an efficacious treatment package for opioid dependence." J Consult Clin Psychol 82(6): 964-972.

Christoff Ade, O. and R. Boerngen-Lacerda (2015). "Reducing substance involvement in college students: a three-arm parallel-group randomized controlled trial of a computer-based intervention." Addict Behav 45: 164-171.

Cunningham, J. A., et al. (2021). "Online personalized feedback intervention to reduce risky cannabis use. Randomized controlled trial." Internet Interventions 26.

Elliott, J. C., et al. (2014). "A preliminary evaluation of a web-based intervention for college marijuana use." Psychol Addict Behav 28(1): 288-293.

Goodness, T. M. (2020). Electronic screening and brief intervention to reduce marijuana use and consequences among graduate students presenting to a student health center: A pilot study, ProQuest Information & Learning. 81.

Gryczynski, J., et al. (2016). "Immediate Versus Delayed Computerized Brief Intervention for Illicit Drug Misuse." J Addict Med 10(5): 344-351.

Jonas, B., et al. (2012). "Efficacy of a single-session online-intervention on problematic substance use." Sucht 58(3): 173-182.

Kay-Lambkin, F. J., et al. (2011). "Clinician-assisted computerised versus therapist-delivered treatment for depressive and addictive disorders: a randomised controlled trial." Medical Journal of Australia 195(3): S44-50.

Kay-Lambkin, F. J., et al. (2009). "Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy." Addiction (Abingdon, England) 104(3): 378-388.

Kelpin, S. S., et al. (2021). "A pilot randomized trial of CBT4CBT for women in residential treatment for substance use disorders." Journal of Substance Abuse Treatment.

Kiluk, B. D., et al. (2018). "Randomized Clinical Trial of Computerized and Clinician-Delivered CBT in Comparison With Standard Outpatient Treatment for Substance Use Disorders: Primary Within-Treatment and Follow-Up Outcomes." Am J Psychiatry 175(9): 853-863.

Lee, C. M., et al. (2010). "A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial." Psychol Addict Behav 24(2): 265-273.

Liang, D., et al. (2018). "A pilot study of a smartphone application supporting recovery from drug addiction." J Subst Abuse Treat 88: 51-58.

Macatee, R. J., et al. (2021). "Impact of a computerized intervention for high distress intolerance on cannabis use outcomes: A randomized controlled trial." Journal of Substance Abuse Treatment 121.

Marsch, L. A., et al. (2014). "Web-based behavioral treatment for substance use disorders as a partial replacement of standard methadone maintenance treatment." Journal of Substance Abuse Treatment 46(1): 43-51.

Moore, B. A., et al. (2019). "A randomized clinical trial of the Recovery Line among methadone treatment patients with ongoing illicit drug use." J Subst Abuse Treat 97: 68-74.

Ondersma, S. J., et al. (2005). "Computer-based brief motivational intervention for perinatal drug use." Journal of Substance Abuse Treatment 28(4): 305-312.

Ondersma, S. J., et al. (2007). "Computer-based brief intervention a randomized trial with postpartum women." American Journal of Preventive Medicine 32(3): 231-238.

Ondersma, S. J., et al. (2018). "Computer-delivered indirect screening and brief intervention for drug use in the perinatal period: A randomized trial." Drug Alcohol Depend 185: 271-277.

Ondersma, S. J., et al. (2014). "Computer-delivered screening and brief intervention (e-SBI) for postpartum drug use: a randomized trial." Journal of Substance Abuse Treatment 46(1): 52-59.

Palfai, T. P., et al. (2014). "Web-based screening and brief intervention for student marijuana use in a university health center: pilot study to examine the implementation of eCHECKUP TO GO in different contexts." Addict Behav 39(9): 1346-1352.

Paris, M., et al. (2018). "Culturally Adapted, Web-Based Cognitive Behavioral Therapy for Spanish-Speaking Individuals With Substance Use Disorders: A Randomized Clinical Trial." Am J Public Health 108(11): 1535-1542.

Prochaska, J. J., et al. (2021). "A randomized controlled trial of a therapeutic relational agent for reducing substance misuse during the COVID-19 pandemic." Drug Alcohol Depend 227: 108986.

Reback, C. J., et al. (2019). "Cost effectiveness of text messages to reduce methamphetamine use and HIV sexual risk behaviors among men who have sex with men." J Subst Abuse Treat 100: 59-63.

Rooke, S., et al. (2013). "Effectiveness of a self-guided web-based cannabis treatment program: randomized controlled trial." J Med Internet Res 15(2): e26.

Schaub, M., et al. (2012). "Web-based cognitive behavioral self-help intervention to reduce cocaine consumption in problematic cocaine users: Randomized controlled trial." Journal of Medical Internet Research 14(6): p47-p60.

Schaub, M. P., et al. (2019). "Web-based self-help with and without chat counseling to reduce cocaine use in cocaine misusers: Results of a three-arm randomized controlled trial." Internet Interventions 17.

Schaub, M. P., et al. (2015). "A Web-Based Self-Help Intervention With and Without Chat Counseling to Reduce Cannabis Use in Problematic Cannabis Users: three-Arm Randomized Controlled Trial." Journal of Medical Internet Research 17(10): e232.

Schwartz, R. P., et al. (2014). "Computerized versus in-person brief intervention for drug misuse: a randomized clinical trial." Addiction (Abingdon, England) 109(7): 1091-1098

Sinadinovic, K., et al. (2020). "Guided web-based treatment program for reducing cannabis use: a randomized controlled trial." Addict Sci Clin Pract 15(1): 9.

Sinadinovic, K., et al. (2012). "Targeting problematic users of illicit drugs with Internet-based screening and brief intervention: a randomized controlled trial." Drug Alcohol Depend 126(1-2): 42-50.

Tait, R. J., et al. (2015). "Six-month outcomes of a Web-based intervention for users of amphetamine-type stimulants: Randomized controlled trial." Journal of Medical Internet Research 17(4).

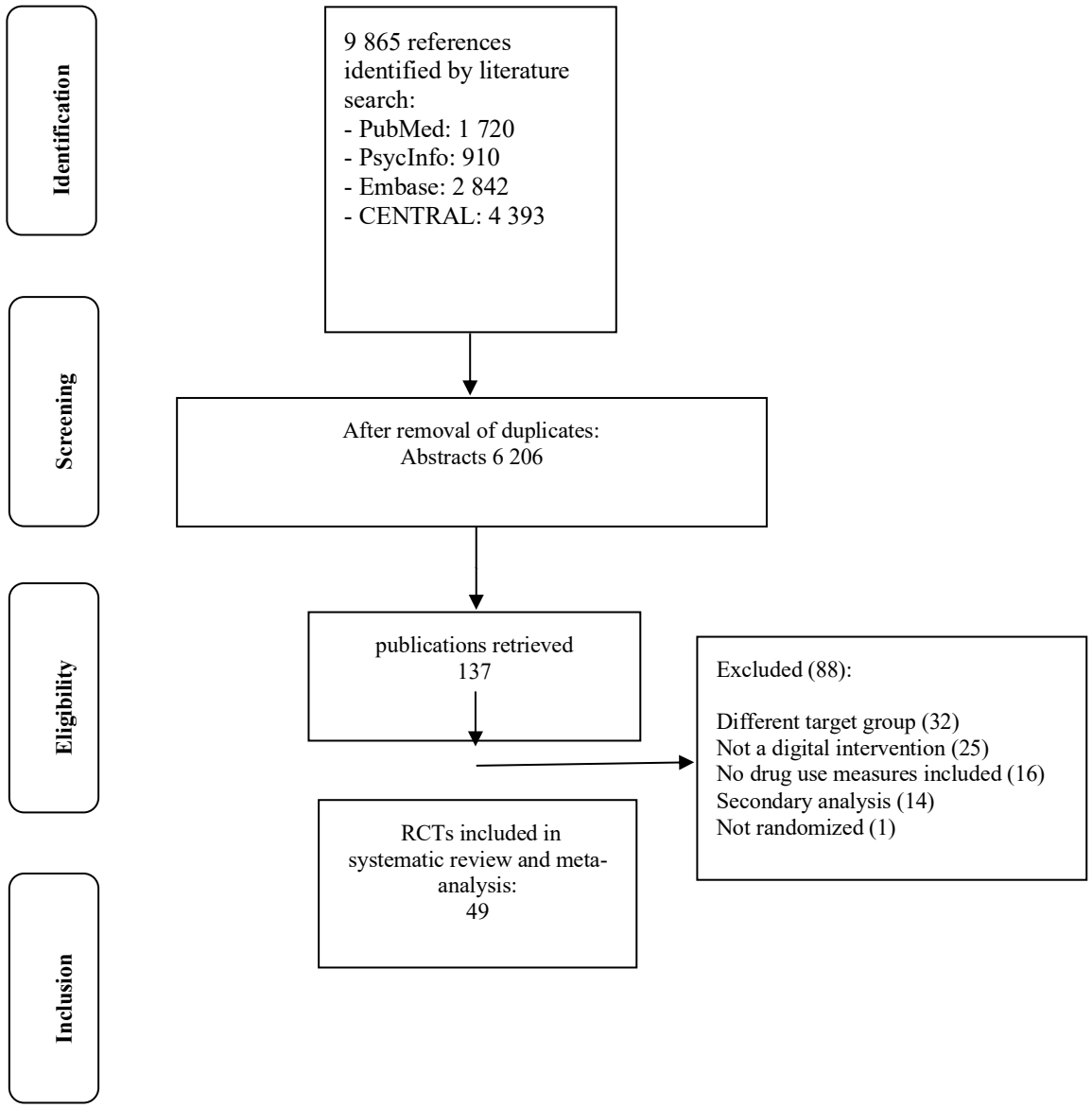
Takano, A., et al. (2020). "Effect of a web-based relapse prevention program on abstinence among Japanese drug users: A pilot randomized controlled trial." J Subst Abuse Treat 111: 37-46.

Tetrault, J. M., et al. (2020). "Computerized Cognitive Behavioral Therapy for Substance Use Disorders in a Specialized Primary Care Practice: A Randomized Feasibility Trial to Address the RT Component of SBIRT." J Addict Med 14(6): e303-e309.

Thompson, R. G., et al. (2020). "Smartphone application plus brief motivational intervention reduces substance use and sexual risk behaviors among homeless young adults: Results from a randomized controlled trial." Psychol Addict Behav 34(6): 641-649.

Tossmann, H.-P., et al. (2011). "A controlled trial of an internet-based intervention program for cannabis users." Cyberpsychology, Behavior, and Social Networking 14(11): 673-679.

Fig. 1. Flow diagram for new systematic reviews which included searches of databases and registers only



3.2.1. Included in GRADE tables/footnotes

Boumparis, N., Khazaal, Y., Krupchanka, D., & Schaub, M. P., (2022). Digital interventions for adult drug users: a systematic review and meta-analysis [Unpublished manuscript].

3.2.2. Excluded from GRADE tables/footnotes

N/A

Table 1. PICO Table

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
1	Digital interventions compared to nonactive and active comparators for illicit substance use reduction	Reduction in illicit substance use	Boumparis et al., 2022	We conducted an updated systematic review and meta-analysis based on our previous publications (Boumparis et al. 2017, 2019) in which we had previously reviewed studies conducted in the field of digital interventions for substance use reduction. The updated systematic review and meta-analysis comprises all available studies until January 2022.

3.3. Narrative description of studies that contributed to GRADE analysis

Boumparis et al., 2022

Background: We assessed the effects of digital interventions on drug use reduction in comparison with non-active and active comparators. **Methods:** Systematic review with separate meta-analyses for every primary substance based on the suitable comparator. Forty-nine randomized controlled trials met the inclusion criteria for the systematic review and meta-analyses. Primary outcome was drug use at post-treatment. Hedges's g was calculated for all comparisons. Risk of bias was examined with the Cochrane risk-of-bias tool 2. **Results:** The risk of bias varied across the included studies. The meta-analyses showed significantly reduced cannabis use at post-treatment (17 comparisons, N = 1 629, g = 0.24; 95% CI: 0.18- 0.29, P < 0.001) as compared with non-active comparisons and active comparisons (5 comparisons, N = 946, g = 0.25; 95% CI: 0.12- 0.38, P < 0.001). For the reduction of any drug use, we did not find a significant reduction (6 comparisons, N = 1 325, g = 0.19, P = 0.106) for non-active comparisons, whereas we did find a significant reduction for active comparators (6 comparisons, N = 1760, g = 0.30; 95% CI: 0.20- 0.41, P < 0.001). For opioid use reduction, we found a significant effect (5 comparisons, N = 668, g = 0.40; 95% CI: 0.25- 0.56, P < 0.001) compared to active comparisons. For stimulant use reduction, we did not find a significant effect (4 comparisons, N = 875, g = 0.32, P = 0.190) for non-active comparisons, while we did find a significant effect compared to active comparators (3 comparisons, N = 247, g = 0.34; 95% CI: 0.09- 0.59, P = 0.007). **Conclusions:** Digital interventions showed small, significant reduction effects on diverse target populations based on different comparators at post-treatment. However, given the small number of available studies for certain substances, the findings should be interpreted with caution.

3.4. Grading the Evidence

Table 2. Effects of digital interventions for adult illicit substance users compared to non-active comparators

Author(s): Boumparis, N., Khazaal, Y., Krupchanka, D., & Schaub, M. P.
Question: Digital interventions compared to nonactive comparators for illicit substance use reduction
Population: Adults illicit substance users
Reference List: Boumparis et al., 2022

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in cannabis use compared to non-active comparators										
17	RCT	very serious[a]	serious[b]	not serious[c]	not serious[d]	none[e]	1629	g = 24 CI = 0.18- 0.29	⊕◯◯◯ VERY LOW	CRITICAL
Reduction in any drug use compared to non-active comparators										
6	RCT	very serious[a]	serious[b]	not serious[c]	serious[f]	none[e]	1325	g = 0.19 CI = -0.04 to 0.41	⊕◯◯◯ VERY LOW	CRITICAL
Reduction in stimulant use compared to non-active comparators										
4	RCT	very serious[a]	serious[b]	not serious[c]	serious[f]	none[e]	875	g = 0.32 CI = -0.16 to 0.79	⊕◯◯◯ VERY LOW	CRITICAL

a. The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results. Downgraded by two.
b. Some inconsistency exists. Heterogeneity seems substantial. Downgraded by one
c. Indirectness does not appear to be an issue. Populations, interventions, comparators and outcomes are highly relevant and comparable.
d. imprecision does not appear to be an issue. Large enough sample size to calculate a precise effect estimate.
e. Publication bias unlikely.
f. Some imprecision exists. The number of available studies is small and the confidence intervals of the effect estimate are large. Downgraded by one.

Table 3: Effects of digital interventions for adult illicit substance users compared to active comparators

Author(s): Boumparis, N., Khazaal, Y., Krupchanka, D., & Schaub, M. P.

Question: Digital interventions compared to active comparators for illicit substance use reduction

Population: Adults illicit substance users

Reference List: Boumparis et al., 2022

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in cannabis use compared to active comparators										
5	RCT	very serious[a]	serious[b]	not serious[c]	serious[d]	none[e]	946	g = 0.25 CI = CI 0.12-0.38	⊕◯◯◯ VERY LOW	CRITICAL
Reduction in any drug use compared to active comparators										
6	RCT	very serious[a]	serious[b]	not serious[c]	serious[d]	none[e]	1760	g = 0.30 CI = 0.20- 0.41	⊕◯◯◯ VERY LOW	CRITICAL
Reduction in opioid use compared to active comparators										
5	RCT	very serious[a]	not serious	not serious[c]	serious[d]	none[e]	668	g = 0.40 CI = 0.25- 0.56	⊕◯◯◯ VERY LOW	CRITICAL
Reduction in stimulant use compared to active comparators										
3	RCT	very serious[a]	not serious	not serious[c]	serious[d]	none[e]	247	g = 0.34 CI = 0.09 to 0.59	⊕◯◯◯ VERY LOW	CRITICAL

a. The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results. Downgraded by two.

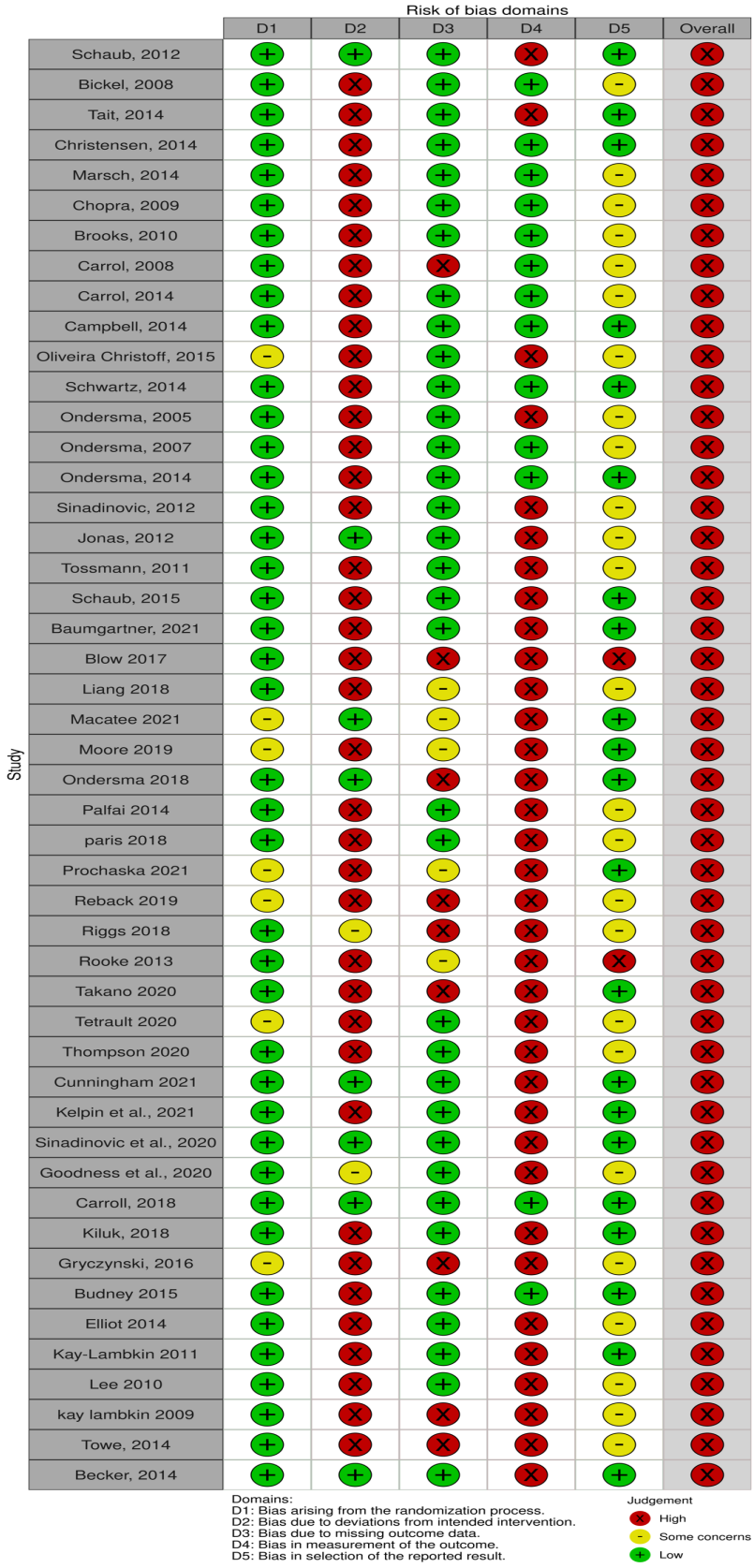
b. Some inconsistency exists. Heterogeneity seems substantial. Downgraded by one

c. Indirectness does not appear to be an issue. Populations, interventions, comparators and outcomes are highly relevant and comparable.

d. Some imprecision exists. The number of available studies is small. Downgraded by one.

e. Publication bias unlikely.

Fig. 2. Risk of Bias assessments of the included studies.



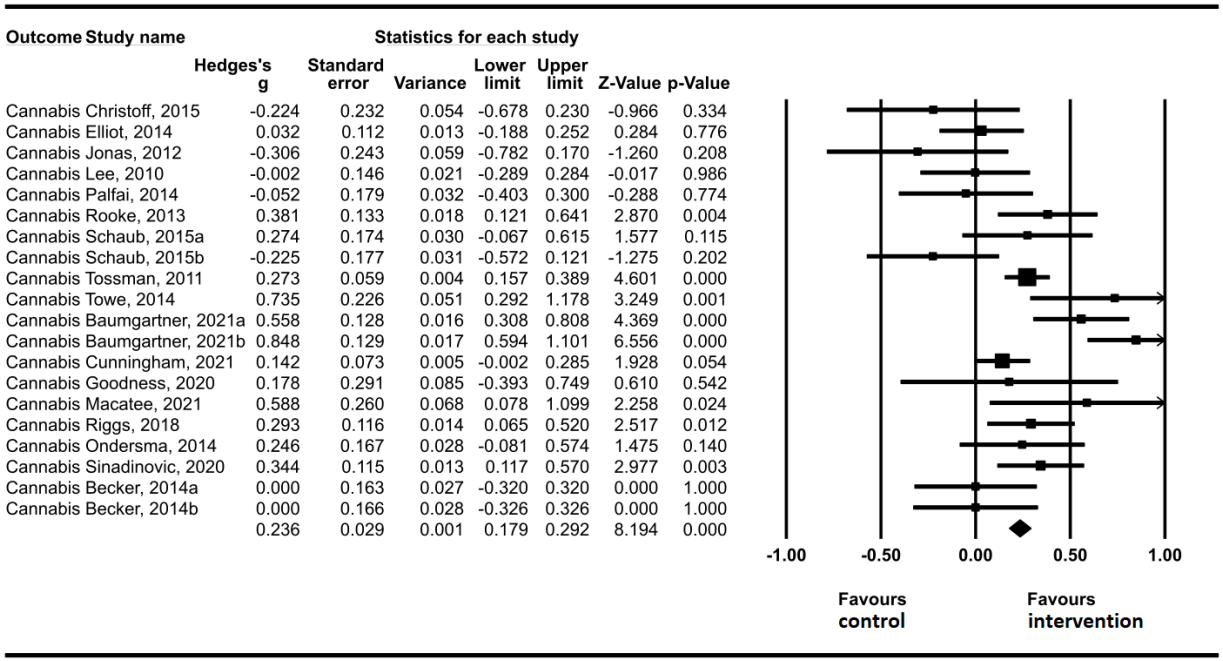
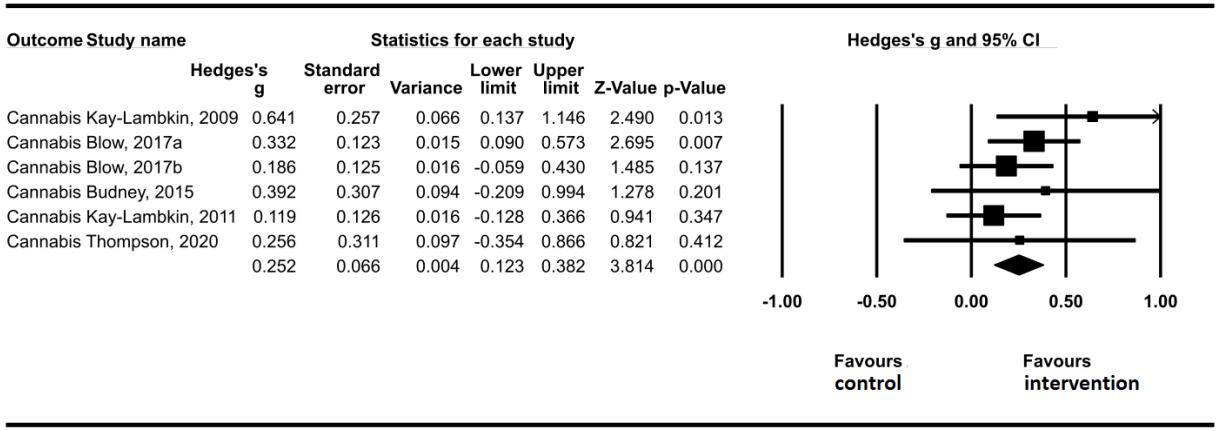


Fig. 4. Forest plot for cannabis use reduction compared to active control conditions at post-treatment.



		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Any	Christoff, 2015	0.390	0.247	0.061	-0.095	0.874	1.577	0.115
Any	Gryczynski, 2016	-0.369	0.223	0.050	-0.806	0.069	-1.650	0.099
Any	Ondersma, 2005	0.227	0.356	0.127	-0.472	0.926	0.637	0.524
Any	Sinadinovic, 2012	0.180	0.140	0.020	-0.096	0.455	1.278	0.201
Any	Prochaska, 2021	0.337	0.163	0.027	0.018	0.656	2.068	0.039
Any	Takano, 2020	0.412	0.302	0.091	-0.180	1.004	1.364	0.173
		0.185	0.115	0.013	-0.039	0.410	1.618	0.106

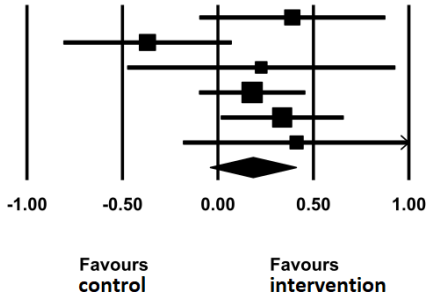


Fig. 6. Forest plot for substance use reduction of any substance users compared to active control conditions at post-treatment.

Outcome	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Any	Blow, 2017a	0.285	0.123	0.015	0.044	0.526	2.318	0.020
Any	Blow, 2017b	0.137	0.125	0.016	-0.107	0.382	1.100	0.271
Any	Campbell, 2014	0.404	0.090	0.008	0.228	0.579	4.504	0.000
Any	Carrol, 2008	0.573	0.230	0.053	0.122	1.024	2.488	0.013
Any	Kelpin, 2021	0.003	0.250	0.062	-0.487	0.492	0.011	0.991
Any	Kiluk, 2018	0.238	0.214	0.046	-0.181	0.658	1.112	0.266
Any	Paris, 2018	0.452	0.210	0.044	0.041	0.864	2.155	0.031
Any	Tetrault, 2020	0.099	0.281	0.079	-0.452	0.651	0.353	0.724
		0.304	0.054	0.003	0.199	0.409	5.664	0.000

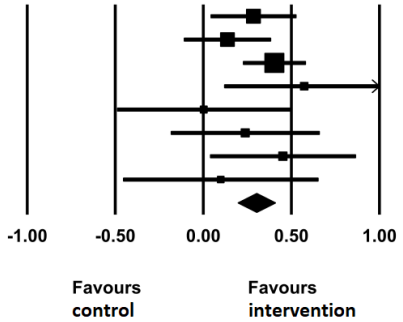
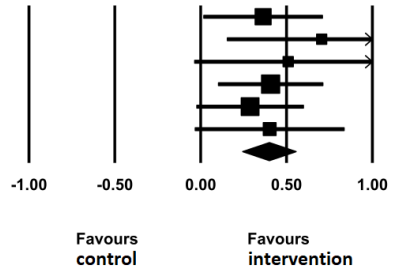


Fig. 7. Forest plot for opioid use reduction compared to active control conditions at post-treatment.

Outcome	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Opioids	Bickel, 2008	0.364	0.176	0.031	0.019	0.709	2.068	0.039
Opioids	Chopra, 2009a	0.705	0.280	0.079	0.156	1.255	2.516	0.012
Opioids	Chopra, 2009b	0.510	0.278	0.077	-0.034	1.055	1.836	0.066
Opioids	Christensen, 2014	0.408	0.155	0.024	0.104	0.711	2.633	0.008
Opioids	Marsch, 2014	0.288	0.158	0.025	-0.022	0.598	1.821	0.069
Opioids	Moore, 2019	0.402	0.221	0.049	-0.031	0.835	1.818	0.069
		0.400	0.079	0.006	0.245	0.555	5.064	0.000



	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
StimulantsReback, 2019a guided	0.015	0.178	0.032	-0.334	0.363	0.082	0.935
StimulantsReback, 2019a unguided	-0.300	0.177	0.031	-0.647	0.047	-1.694	0.090
StimulantsSchaub, 2019a guided	1.045	0.185	0.034	0.683	1.407	5.656	0.000
StimulantsSchaub, 2019b unguided	0.594	0.180	0.032	0.242	0.947	3.306	0.001
StimulantsTait, 2014	0.227	0.224	0.050	-0.212	0.666	1.014	0.310
	0.316	0.241	0.058	-0.157	0.788	1.310	0.190

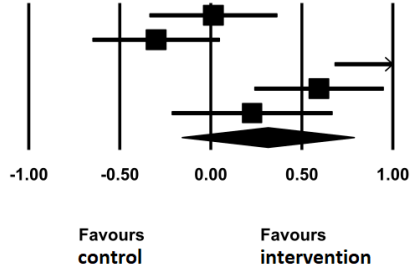
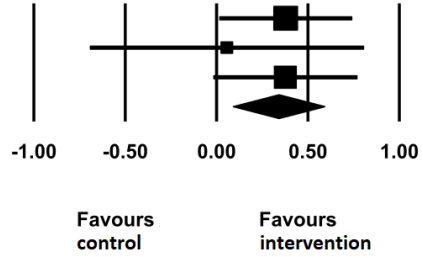


Fig. 9. Forest plot for stimulant use reduction compared to active control conditions at post-treatment.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
StimulantsCarroll, 2018	0.379	0.184	0.034	0.018	0.739	2.058	0.040
StimulantsBrooks, 2010	0.057	0.381	0.145	-0.690	0.804	0.149	0.882
StimulantsCarrol, 2014	0.377	0.200	0.040	-0.015	0.768	1.886	0.059
	0.342	0.128	0.016	0.092	0.592	2.680	0.007



detailed description of the performed subgroup analyses can be seen below.

Table 4. Subgroup analyses

Any substance use - active comparators						
		N comparisons	Hedge's g	95% CI	P	P[a]
Recruitment criteria	DSM-IV diagnosis	5	0.30	0.095 – 0.504	0.004	0.241
	Cut-off criterion	5	0.084	-0.212 – 0.38	0.578	
Guidance	Unguided	2	0.074	-0.338 – 0.487	0.724	0.597
	Guided	8	0.201	-0.020 – 0.421	0.075	
Any substance use – non-active comparators						
Guidance	Unguided	5	0.157	-0.096 – 0.409	0.224	0.436
	Guided	1	0.412	-0.18 – 1.004	0.173	
Cannabis use – non-active comparators						
Guidance	Unguided	17	0.224	0.095 – 0.354	0.001	0.714
	Guided	3	0.157	-0.176 – 0.491	0.355	

[a]The P-values in this column indicate if the difference between the effect sizes in the subgroups are significant.

3.5. Additional evidence not mentioned in GRADE tables

N/A

4. From Evidence to Recommendations

4.1. Summary of findings

Table 5. Summary of findings table

GRADE Table	Source	Outcome	Number of Studies	Effects	Certainty of Evidence
GRADE Table 1 Digital interventions compared to nonactive comparators for illicit substance use reduction	Boumparis et al., 2022	Reduction in cannabis use	17 N = 1 629	g = 24 CI = 0.18- 0.29 Compared to non-active comparators, digital interventions probably reduce cannabis use.	⊕◯◯◯ VERY LOW
		Reduction in any drug use	6 N = 1 325	g = 0.19 CI = -0.04 to 0.41 Compared to non-active comparators, it is uncertain whether digital interventions reduce any drug use.	⊕◯◯◯ VERY LOW
		Reduction in stimulant use	4 N = 875	g = 0.32 CI = -0.16 to 0.79 Compared to non-active comparators, it is uncertain whether digital interventions reduce stimulant use.	⊕◯◯◯ VERY LOW

GRADE Table	Source	Outcome	Number of Studies	Effects	Certainty of Evidence
GRADE Table 2 Digital interventions compared to active comparators for illicit substance use reduction	Boumparis et al., 2022	Reduction in cannabis use	5 N = 946	g = 0.25 CI = CI 0.12- 0.38 Compared to active comparators, digital interventions probably reduce cannabis use.	⊕◯◯◯ VERY LOW
		Reduction in any drug use	6 N = 1 760	g = 0.30 CI = 0.20- 0.41 Compared to active comparators, digital interventions probably reduce any drug use.	⊕◯◯◯ VERY LOW
		Reduction in opioid use	5 N = 668	g = 0.40 CI = 0.25- 0.56 Compared to active comparators, digital interventions probably reduce opioid use.	⊕◯◯◯ VERY LOW
		Reduction in stimulant use	3 N = 247	g = 0.34 CI = 0.09- 0.59 Compared to active comparators, digital interventions probably reduce stimulant use.	⊕◯◯◯ VERY LOW

4.2. Evidence to decision

Table 6. Evidence to decision table

Please note * indicates evidence from overarching qualitative review by Gronholm et al, 2023

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Priority of the problem	Is the problem a priority? The more serious a problem is, the more likely it is that an option that addresses the problem should be a priority (e.g. diseases that are fatal or disabling are likely to be a higher priority than diseases that only cause minor distress). The more people who are affected, the more likely it is that an option that addresses the problem should be a priority.			
	• Are the consequences of the problem serious (that is, severe or important in terms of the potential benefits or savings)? • Is the problem urgent? • Is it a recognized priority (such as based on a political or policy decision)? [Not relevant when an individual patient perspective is taken]	☐ No ☐ Probably no ☐ Probably yes ☒ **Yes** ☐ Varies ☐ Don't know	Drug use and drug use disorders constitute a public health, developmental and security problem both in developed and developing countries worldwide. According to the latest global estimates, about 5.5 per cent of the population aged between 15 and 64 years have used drugs at least once in the past year, while 36.3 million people, or 13 per cent of the total number of persons who use drugs, suffer from drug use disorders (UNODC, 2021). Approximately 0.5 million deaths annually attributable to drug use (UNODC, 2021).	
Desirable Effects	How substantial are the desirable anticipated effects? The larger the benefit, the more likely it is that an option should be recommended.			
	• Judgements for each outcome for which there is a desirable effect • How substantial (large) are the desirable anticipated effects (including health and other benefits) of the option (taking into account the severity or importance of the desirable consequences and the number of people affected)?	☐ Trivial ☒ **Small** ☐ Moderate ☐ Large ☐ Varies ☐ Don't know	• In adults with cannabis use disorders or those using cannabis, digital interventions when compared to non-active (waitlist, assessment-only) and active (treatment as usual, brief interventions) comparator, show effect for reducing cannabis use (very low certainty) • In adults with any drug use	• The included digital interventions to which we refer throughout our work encompasses unguided digital interventions, in which psychoeducation and psychotherapeutic techniques are provided for the individual to self-manage their symptoms

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
			disorders or those using drugs, it is uncertain if digital interventions when compared to non-active (waitlist, assessment-only) have effect for reducing drug use (very low certainty) • In adults with stimulant use disorders or those using psychostimulants, it is uncertain if digital interventions when compared to non-active (waitlist, assessment-only) have effect for reducing psychostimulants use (very low certainty) • There were no studies examining effect of digital interventions among people with opioid use disorders or using opioids in comparison to non-active comparator. • In adults with any drug use disorder or those using drugs, digital interventions, when compared to active (treatment as usual, brief interventions) comparator, show effect for reducing any drug use (very low certainty) • In adults with any stimulant use disorders or those using psychostimulants, digital interventions, when compared to active (treatment as usual, brief interventions) comparator, show effect for reducing psychostimulants use (very low certainty) • In adults with opioid use disorders or those using opioids, digital interventions, when compared to active	without the help of a health professional. Guided digital interventions, in which additional guidance is provided from health professionals that can assist participants with technical or health-related questions via chat, email, or telephone. • Studies that assess the reduction of any drug use via digital interventions compared to non-active comparators are usually recruiting individuals from settings in which brief interventions are conducted. These settings commonly include hospitals, GP practices, and community health centres. The majority of those interventions consist of very brief screenings and brief interventions lasting up to 30 minutes. • The studies assessing the reduction of drug use via digital interventions compared to active comparators are usually recruiting individuals from specialized treatment facilities. The majority of those interventions combine the digital component with face-to-face treatments, such as treatment as usual or CBT and last 8 to 12 weeks. • Differences in findings

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
			(treatment as usual, brief interventions) comparator, show effect for reducing opioid use (very low certainty)	between active/non-active comparator should be interpreted with caution. For the comparisons involving non-active comparators, the majority of individuals were recruited based on self-reported use patterns and not assessed for a substance use disorder. This is contrary to the studies involving active comparators that recruited participants after the diagnosis of a substance use disorder. For this reason, it is important to stress that different findings for active/non-active comparators are likely due to the different characteristics (such as severity) of the target group and intensity of the provided treatment. • While the evidence is limited it is possible that individuals with a substance use disorder that receive treatment as usual in addition to a digital intervention benefit more from the digital component. This is particularly relevant for individuals with drug use disorders.

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Undesirable Effects	How substantial are the undesirable anticipated effects? The greater the harm, the less likely it is that an option should be recommended.			
	• Judgements for each outcome for which there is an undesirable effect • How substantial (large) are the undesirable anticipated effects (including harms to health and other harms) of the option (taking into account the severity or importance of the adverse effects and the number of people affected)?	☐ Large ☐ Moderate ☐ Small ☒ **Trivial** ☐ Varies ☐ Don't know	Not identified in the current review	
Certainty of evidence	What is the overall certainty of the evidence of effects? The less certain the evidence is for critical outcomes (those that are driving a recommendation), the less likely that an option should be recommended (or the more important it is likely to be to conduct a pilot study or impact evaluation, if it is recommended).			
	• What is the overall certainty of this evidence of effects, across all of the outcomes that are critical to making a decision? • See GRADE guidance regarding detailed judgements about the quality of evidence or certainty in estimates of effects	☒ **Very low** ☐ Low ☐ Moderate ☐ High ☐ No included studies		
Values	Is there important uncertainty about or variability in how much people value the main outcomes? The more likely it is that differences in values would lead to different decisions, the less likely it is that there will be a consensus that an option is a priority (or the more important it is likely to be to obtain evidence of the values of those affected by the option). Values in this context refer to the relative importance of the outcomes of interest (how much people value each of those outcomes). These values are sometimes called “utility values”.			
	• Is there important uncertainty about how much people value each of the main outcomes? • Is there important variability in how much people value each of the main outcomes?	☐ Important uncertainty or variability ☒ **Possibly important uncertainty or variability** ☐ Probably no important uncertainty or variability ☐ No important		

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		uncertainty or variability		
Balance of effects	Does the balance between desirable and undesirable effects favour the intervention or the comparison? The larger the desirable effects in relation to the undesirable effects, taking into account the values of those affected (i.e. the relative value they attach to the desirable and undesirable outcomes) the more likely it is that an option should be recommended.			
	• Judgements regarding each of the four preceding criteria • To what extent do the following considerations influence the balance between the desirable and undesirable effects: - How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)? - People's attitudes towards undesirable effects (how risk averse they are)? - People's attitudes towards desirable effects (how risk seeking they are)?	☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the comparison ☒ **Probably favours the intervention** ☐ Favours the intervention ☐ Varies ☐ Don't know	.	
Resources required	How large are the resource requirements (costs)? The greater the cost, the less likely it is that an option should be a priority. Conversely, the greater the savings, the more likely it is that an option should be a priority.			
	• How large is the difference in each item of resource use for which fewer resources are required? • How large is the difference in each item of resource use for which more resources are required? • How large an investment of resources would the option require or save?	☐ Large costs ☐ Moderate costs ☐ Negligible costs and savings ☐ Moderate savings ☐ Large savings ☒ **Varies** ☐ Don't know		

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Certainty of evidence of required resources	What is the certainty of the evidence of resource requirements (costs)?			
	• Have all-important items of resource use that may differ between the options being considered been identified? • How certain is the evidence of differences in resource use between the options being considered (see GRADE guidance regarding detailed judgements about the quality of evidence or certainty in estimates)? • How certain is the cost of the items of resource use that differ between the options being considered? • Is there important variability in the cost of the items of resource use that differ between the options being considered?	☐ Very low ☐ Low ☐ Moderate ☐ High ☒ **No included studies**		
Cost effectiveness	Does the cost-effectiveness of the intervention favour the intervention or the comparison? The greater the cost per unit of benefit, the less likely it is that an option should be a priority.			
	• Judgements regarding each of the six preceding criteria • Is the cost effectiveness ratio sensitive to one-way sensitivity analyses? • Is the cost effectiveness ratio sensitive to multivariable sensitivity analysis? • Is the economic evaluation on which the cost effectiveness estimate is based reliable? • Is the economic evaluation on which the cost effectiveness estimate is based applicable to the setting(s) of interest?	☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the comparison ☐ Probably favours the intervention ☐ Favours the intervention ☐ Varies ☒ **No included**	No reviews examining cost effectiveness identified	

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		studies		
Health equity, equality and non-discrimination	What would be the impact on health equity, equality and non-discrimination? (WHO INTEGRATE) Health equity and equality reflect a concerted and sustained effort to improve health for individuals across all populations, and to reduce avoidable systematic differences in how health and its determinants are distributed. Equality is linked to the legal principle of non-discrimination, which is designed to ensure that individuals or population groups do not experience discrimination on the basis of their sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socioeconomic status, place of residence or any other characteristics. All recommendations should be in accordance with universal human rights standards and principles. The greater the likelihood that the intervention increases health equity and/or equality and that it reduces discrimination against any particular group, the greater the likelihood of a general recommendation in favour of this intervention.			
	• How are the condition and its determinants distributed across different population groups? Is the intervention likely to reduce or increase existing health inequalities and/or health inequities? Does the intervention prioritize and/or aid those furthest behind? • How are the benefits and harms of the intervention distributed across the population? Who carries the burden (e.g. all), who benefits (e.g. a very small sub-group)? • How affordable is the intervention for individuals, workplaces or communities? • How accessible - in terms of physical as well as informational access - is the intervention across different population groups? • Is there any suitable alternative to addressing the condition, does the intervention represent the only available option? Is this option proportionate to the need, and will it be subject to periodic review?	☐ Reduced ☐ Probably reduced ☐ Probably no impact ☐ Probably increased ☐ Increased ☒ **Varies** ☐ Don't know	• While digital health interventions show effectiveness and can enhance access to health services, they should not be used to replace or detract from provision of other forms of interventions and should ensure patient free and informed consent, safety, confidentiality, privacy and security.	
Feasibility	Is the intervention feasible to implement? The less feasible (capable of being accomplished or brought about) an option is, the less likely it is that it should be recommended (i.e. the more barriers there are that would be difficult to overcome).			
	• Can the option be accomplished or brought about? • Is the intervention or option sustainable? • Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?	☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ **Varies**	feasibility is impacted by resources available especially in LMIC • While there is a lack of information on costs and cost-effectiveness, setting up and sustaining digital health solutions can be costly,	

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		☐ Don't know	while costs for individual users usually not very high.	
Human rights and sociocultural acceptability	Is the intervention aligned with human rights principles and socioculturally acceptable? (WHO INTEGRATE) This criterion encompasses two distinct constructs: The first refers to an intervention's compliance with universal human rights standards and other considerations laid out in international human rights law beyond the right to health (as the right to health provides the basis of other criteria and sub-criteria in this framework). The second, sociocultural acceptability, is highly time-specific and context-specific and reflects the extent to which those implementing or benefiting from an intervention as well as other relevant stakeholder groups consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention. The greater the sociocultural acceptability of an intervention to all or most relevant stakeholders, the greater the likelihood of a general recommendation in favour of this intervention.			
	• Is the intervention in accordance with universal human rights standards and principles? • Is the intervention socioculturally acceptable to patients/beneficiaries as well as to those implementing it? To which extent do patients/beneficiaries value different non-health outcomes? • Is the intervention socioculturally acceptable to the public and other relevant stakeholder groups? Is the intervention sensitive to sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socioeconomic status, place of residence or any other relevant characteristics? • How does the intervention affect an individual's, population group's or organization's autonomy, i.e. their ability to make a competent, informed and voluntary decision? • How intrusive is the intervention, ranging from low intrusiveness (e.g. providing information) to intermediate intrusiveness (e.g. guiding choices) to high intrusiveness (e.g. restricting or eliminating choices)? Where applicable, are high intrusiveness and/or impacts on the privacy and dignity of concerned stakeholders justified?	☐ No ☐ Probably no ☒ **Probably yes** ☐ Yes ☐ Varies ☐ Don't know	• There is not enough data to understand the role of digital interventions for equity, equality and non-discrimination of people using substances: while there is a potential of increasing access to care, it is also possible that not all people can benefit it, what is addressed as problem of "digital divide", which requires further research.	

4.3. Summary of judgements

Table 7. Summary of judgements

Priority of the problem	- Don't know	- Varies		- No	- Probably No	- Probably Yes	✓ **Yes**
Desirable effects	- Don't know	- Varies		- Trivial	✓ **Small**	- Moderate	- Large
Undesirable effects	- Don't know	- Varies		- Large	- Moderate	- Small	✓ **Trivial**
Certainty of the evidence	- No included studies			✓ **Very low**	- Low	- Moderate	- High
Values				- Important uncertainty or variability	✓ **Possibly important uncertainty or variability**	- Probably no important uncertainty or variability	- No important uncertainty or variability
Balance of effects	- Don't know	- Varies	- Favours comparison	- Probably favours comparison	- Does not favour either	✓ **Probably favours intervention**	- Favours intervention
Resources required	✓ **Don't know**	- Varies	- Large costs	- Moderate costs	- Negligible costs or savings	- Moderate savings	- Large savings
Certainty of the evidence on required resources	✓ **No included studies**			- Very low	- Low	- Moderate	- High
Cost–effectiveness	✓ **No included studies**	- Varies	- Favours comparison	- Probably favours comparison	- Does not favour either	- Probably favours intervention	- Favours intervention
Equity, equality and non-discrimination	- Don't know	✓ **Varies**	- Reduced	Probably reduced	- Probably no impact	- Probably increased	- Increased
Feasibility	- Don't know	✓ **Varies**		- No	- Probably No	- Probably Yes	- Yes
Human rights and sociocultural acceptability	- Don't know	- Varies		- No	- Probably No	✓ **Probably Yes**	- Yes

✓Indicates category selected, -Indicates category not selected

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Appendix I: mhGAP process note

mhGAP Guideline Update: Notes on process for identifying level of evidence review required v2_0 (13/12/2021)

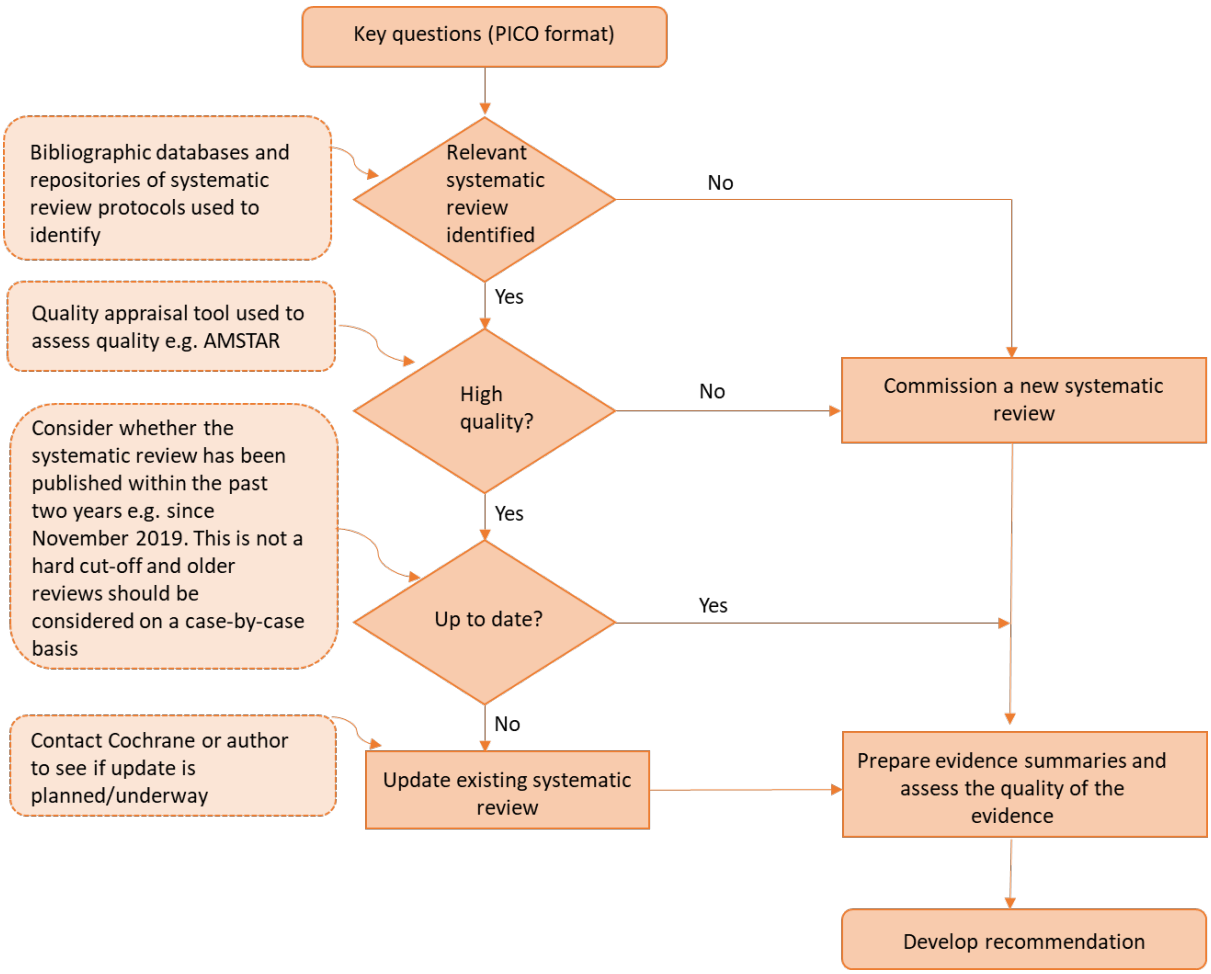
This document is intended to provide guidance to focal points on the level of evidence review required as part of the evidence retrieval process for the mhGAP guideline update process. As a general rule, the update process should be informed by existing high quality systematic reviews. The process for evidence retrieval and synthesis is fully outlined in chapter 8 of the WHO handbook for guideline development https://apps.who.int/iris/handle/10665/145714.

Three main categories of evidence review are proposed in this document:

1) Existing relevant, up to date, high quality systematic review(s) provide the evidence required. **An existing systematic review is sufficient to prepare the evidence summaries**. It may be possible to include more than one systematic review for the same PICO, as different reviews may match different outcomes of a PICO. However, if more than one systematic review is available for the same PICO outcome, one review should be selected, based on quality, relevance, search comprehensiveness and date of last update. The selection process should be transparently reported, with justification of choices.
2) Existing high quality systematic reviews are either out of date or do not fully address the PICO, though it is considered that the review can be updated to meet these requirements. **An update of an existing systematic review is required before the evidence summaries can be prepared**. The update process may require addition of new studies published after the review, or inclusion of outcomes not covered by the existing reviews.
3) Existing systematic reviews are either not of sufficiently high quality or cannot be updated to fully address the PICO. **A new systematic review is required before the evidence summaries can be prepared**

Figure 1 below details the process to identify which level of evidence review is required to support the evidence retrieval process for a PICO.

Fig. 1. Is a new systematic review needed



All key questions are currently in PICO format as presented in the Appendix of the planning proposal PICOs. Subsequent steps include the following:

1. **Identify and evaluate existing systematic reviews**: Identify one or more systematic review(s) to address each PICO question. Existing systematic reviews will inform the guideline development process, whether or not a new systematic review or an update of an existing review is required, and the evidence review team will detail existing systematic reviews in each case. The method for identifying existing systematic reviews should be fully detailed in the evidence summary and include the following sources:
    a. Search of bibliographic databases, such as PubMed/MEDLINE, Embase, PsychInfo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHIL, Scopus, African Index Medicus, Index Medicus for the Eastern Mediterranean Region, Index Medicus for the South-East Asian Region, Latin American and Caribbean Health Sciences Literature, and Western Pacific Region Index Medicus.
    b. Search of repositories of systematic reviews protocols, including PROSPERO, Open Science Framework (OSF), and Cochrane.
2. **Assess if systematic review is up to date:** It is preferred that identified systematic reviews have been published within the past two years e.g. since November 2019. This is not a hard cut-off and older reviews should be considered on a case-by-case basis, particularly those covering the time period since the last update of the mhGAP guideline in 2015. It is acknowledged that COVID has led to a pausing of many mental health research activities over the past two years, and this may also impact the availability of systematic reviews

within the preferred two year period. For any reviews that fall outside the two year period, the guideline methodologist will advise on suitability.

3. **Appraise quality of systematic review:** Use the AMSTAR-2 quality appraisal tool to assess the quality of the identified systematic review(s) https://amstar.ca/docs/AMSTAR-2.pdf . This includes consideration of the extent to which the PICO is fully addressed by the systematic review(s) identified.

By following the process outlined in figure 1, and steps 1-3 above, the FP and evidence review team will have sufficient evidence to assess which of the three main categories of evidence review apply to each PICO under consideration:

1) Existing systematic reviews are sufficient to prepare the evidence summaries
2) An update of an existing systematic review is required before the evidence summaries can be prepared
3) A new systematic review is required before the evidence summaries can be prepared

Appendix II: Search terms used to identify randomized controlled trials

Search string for PubMed:
“Substance-Related Disorders"[MeSH Terms] OR “substance-related disorders“[All Fields] OR “drug abuse”[MeSH Terms] OR “drug abuse”[All Fields] OR “drug use”[All Fields] OR “addiction”[All Fields] OR “drug dependence”[All Fields] OR “substance use”[All Fields] OR “multiple drug abuse”[MeSH Terms] OR “multiple drug abuse”[All Fields] OR “multiple addiction”[All Fields] OR “polydrug”[All Fields] OR “heroin dependence”[MeSH Terms] OR “heroin”[All Fields] OR “cocaine dependence”[MeSH Terms] OR “cocaine”[All Fields] OR “crack”[All Fields] OR “morphine addiction”[MeSH Terms] OR "Morphine Dependence"[MeSH Terms] OR “morphine”[All Fields] OR “opiate addiction”[MeSH Terms] OR “opium”[All Fields] OR “opiate”[All Fields] OR “opioid”[All Fields] OR “benzodiazepine dependence”[MeSH Terms] OR “benzodiazepine”[All Fields] OR “narcotic*”[All Fields] OR “prescription drug misuse”[All Fields] OR “prescription drug abuse”[All Fields] OR “ecstasy”[All Fields] OR "Opioid-Related Disorders"[MeSH Terms] OR "Amphetamine-Related Disorders"[MeSH Terms] OR "Cocaine-Related disorders"[MeSH Terms] OR "Prescription Drug Misuse"[MeSH Terms] OR "Cannabis"[Mesh] OR "Marijuana Abuse"[Mesh] OR "Marijuana Smoking"[Mesh] OR “Cannabis”[All Fields] OR “Marijuana Abuse”[All Fields] OR “Marijuana Smoking”[All Fields] OR “marihuana”[All Fields] OR “marijuana”[All Fields] OR “marijuana”[Mesh]
AND
“Internet"[Mesh] OR “internet”[All Fields] OR “online”[All Fields] OR “web”[All Fields] OR “e-health”[All Fields] OR “Mobile Applications"[Mesh] OR “mobile phone”[All Fields] OR “smartphone”[All Fields] OR “mobile device”[All Fields] OR "Computers"[Mesh] OR “computer”[All Fields] OR “app”[All Fields] OR "Therapy, Computer-Assisted"[Mesh] OR “computer-assisted”[All Fields] OR "Drug Therapy, Computer-Assisted"[Mesh] OR “telemedicine”[All Fields] OR "Telemedicine"[Mesh]
AND
Randomization filter

Search string for Embase:
‘Substance-Related Disorders’/exp OR ‘substance-related disorders’ OR ‘drug abuse’/exp OR ‘drug abuse’ OR ‘drug use’ OR ‘addiction’ OR ‘drug dependence’ OR ‘substance use’ OR ‘multiple drug abuse’/exp OR ‘multiple drug abuse’ OR ‘multiple addiction’ OR ‘polydrug’ OR ‘heroin dependence’/exp OR ‘heroin’ OR ‘cocaine dependence’/exp OR ‘cocaine’ OR ‘crack’ OR ‘morphine addiction’/exp OR ‘Morphine Dependence’ OR ‘morphine’ OR ‘opiate addiction’/exp OR ‘opium’ OR ‘opiate’ OR ‘opioid’ OR ‘benzodiazepine dependence’/exp OR ‘benzodiazepine’ OR ‘narcotic*’ OR ‘prescription drug misuse’ OR ‘prescription drug abuse’ OR ‘ecstasy’ OR ‘Opioid-Related Disorders’ OR ‘Amphetamine-Related Disorders’ OR ‘Cocaine-Related Disorders’ OR ‘Prescription Drug Misuse’ OR ‘Cannabis’/exp OR ‘Marijuana Abuse’/exp OR ‘Marijuana Smoking’/exp OR ‘Cannabis’ OR ‘Marijuana Abuse’ OR ‘Marijuana Smoking’ OR ‘marihuana’ OR ‘marijuana’ OR ‘marijuana’/exp
AND
‘Internet’ OR ‘internet’ OR ‘online’ OR ‘web’ OR ‘e-health’ OR ‘Mobile Applications’ OR ‘mobile phone’ OR ‘smartphone’ OR ‘mobile device’ OR ‘computer’ OR ‘app’ OR ‘Computer-Assisted’ OR ‘telemedicine’
AND
'randomized controlled trial'/de

Search string for PsycInfo
DE “Substance-Related Disorders" OR “substance-related disorders“ OR DE “drug abuse” OR “drug abuse” OR “drug use” OR “addiction” OR “drug dependence” OR “substance use” OR DE “multiple drug abuse” OR “multiple drug abuse” OR “multiple addiction” OR “polydrug” OR DE “heroin dependence” OR “heroin” OR DE “cocaine dependence” OR “cocaine” OR “crack” OR DE “morphine

addiction” OR DE "Morphine Dependence" OR “morphine” OR DE “opiate addiction” OR “opium” OR “opiate” OR “opioid” OR DE “benzodiazepine dependence” OR “benzodiazepine” OR “narcotic*” OR “prescription drug misuse” OR “prescription drug abuse” OR “ecstasy” OR DE "Opioid-Related Disorders" OR DE "Amphetamine-Related Disorders" OR DE "Cocaine-Related Disorders" OR DE "Prescription Drug Misuse" OR DE "Cannabis" OR DE "Marijuana Abuse" OR DE "Marijuana Smoking" OR “Cannabis” OR “Marijuana Abuse” OR “Marijuana Smoking” OR “marihuana” OR “marijuana” OR DE “marijuana”
AND
DE “Internet" OR “internet” OR “online” OR “web” OR “e-health” OR DE “Mobile Applications” OR “mobile phone” OR “smartphone” OR “mobile device” OR DE "Computers” OR “computer” OR “app” OR "Computer-Assisted” OR "Telemedicine"
AND
Randomized Controlled Trial.pt. OR Pragmatic Clinical Trial.pt. OR exp Randomized Controlled Trials as Topic/ OR "Randomized Controlled Trial (topic)"/ OR Randomized Controlled Trial/ OR Randomization/ OR Random Allocation/ OR Double-Blind Method/ OR Double Blind Procedure/ OR Double-Blind Studies/ OR Single-Blind Method/ OR Single Blind Procedure/ OR Single-Blind Studies/ OR Placebos/ OR Placebo/ OR (random* or sham or placebo*).ti,ab,hw. OR ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw. OR ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw.

Search string for CENTRAL

"Substance-Related Disorders" OR "Heroin Dependence" OR "Morphine Dependence" OR "Opioid-Related Disorders" OR "Morphine Dependence" OR "Amphetamine-Related Disorders" OR "Cocaine-Related Disorders" OR "Prescription Drug Misuse" OR "drug abuse" OR "drug use" OR "addiction" OR "drug dependence" OR "substance use" OR "multiple drug abuse" OR "multiple addiction" OR polydrug OR "heroin dependence" OR "heroin" OR "cocaine dependence" OR "cocaine" OR "crack" OR "morphine addiction" OR "morphine" OR "opiate addiction" OR "opium" OR "opiate" OR "opioid" OR "benzodiazepine dependence" OR "benzodiazepine" OR "narcotic*" OR "prescription drug misuse" OR "prescription drug abuse" OR "ecstasy" OR "Cannabis" OR "Marijuana Abuse" OR "Marijuana Smoking" OR “marihuana” OR “marijuana”
AND
“Internet" OR “online” OR “web” OR “e-health” OR “Mobile Applications” OR “mobile phone” OR “smartphone” OR “mobile device” OR “computer” OR “app” OR "Computer-Assisted” OR "Telemedicine"