Health Technology Assessment Programme

National Institute for Health Research

NETSCC, HTA
18 March 2014

The NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), based at the University of Southampton, manages evaluation research programmes and activities for the NIHR

Health Technology Assessment Programme
National Institute for Health Research
Evaluation, Trials and Studies Coordinating Centre
University of Southampton, Alpha House
Enterprise Road, Southampton, SO16 7NS

tel: +44(0)23 8059 5586
fax: +44(0)23 8059 5639

email: hta@hta.ac.uk
web: www.hta.ac.uk

HTA No. 13/70/01: Cannabis cessation therapy for adults who use cannabis regularly: Protocol for systematic review short report

1. Title of the project:

Cannabis cessation therapy for adults who use cannabis regularly: Protocol for systematic review short report

2. Name of TAR team and project 'lead'

TAR Team:

School of Health and Related Research (ScHARR), The University of Sheffield.

Project Lead:

Dr Katy Cooper, Research Fellow in Evidence Synthesis

Health Economics and Decision Science, ScHARR, University of Sheffield

Regent Court, 30 Regent Street, Sheffield S1 4DA

Tel: 0114 2220773

Fax: 0114 2724095

E-mail: k.l.cooper@sheffield.ac.uk

3. Plain English summary

Cannabis is a widely used drug in the Western world. In one study reporting cannabis use in European countries, use for 20 or more days per month ranged from 3.5% to 44.1%, with the figure for the UK being 3.9%.[1] Cannabis use is often defined as acute (occasional) or chronic, with chronic usage being defined as daily usage over a period of years.[2] Cannabis dependence, also known as cannabis abuse disorder, can develop from chronic usage, and is defined as impaired control over use and difficulty in ceasing use.[2] Cannabis abuse disorder is a recognised psychiatric diagnosis, often diagnosed via the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria[3] and the International Classification of Diseases (ICD-10).[4]

Both acute and chronic cannabis use are associated with an increased risk of medical and psychological problems. Acute effects include hyperemesis syndrome, impaired coordination and performance, anxiety, suicidal ideations/tendencies, and psychotic symptoms.[4] Chronic effects include mood disorders, exacerbation of psychotic disorders in vulnerable people, cannabis use disorders, withdrawal syndrome, neurocognitive impairments, cardiovascular and respiratory and other diseases.[5]

Providing treatment to chronic users of cannabis to reduce or cease their usage is a fairly recent occurrence. Until the 1980's it was thought that chronic cannabis use did not lead to dependence, and treatment was therefore not required.[6] Since then, research has looked to evaluate the use of a wide variety of psychological and psychosocial interventions, such as motivational interviewing (MI), cognitive behavioural therapy (CBT) and contingency management.[7] Guidance from the National Institute for Health and Care Excellence (NICE) states that pharmacological interventions for chronic cannabis users are not well developed and so psychosocial interventions are the mainstay of effective treatment.[8] There is limited evidence to suggest which of the many psychological and psychosocial interventions are the most effective at reducing cannabis use. UK guidelines for the treatment of chronic users, developed by the Department of Health, state that clinicians should consider motivational interventions in mild cases and structured treatment with key working in more heavy users, while cognitive behavioural therapy should be used in cases with co-morbidity with depression and anxiety.[9] European best practice guidance, produced by the European Monitoring Centre for Drugs and Drug Addiction, recommends the use of multidimensional family therapy, whereas individual sessions of CBT are stated as being 'likely to be beneficial".[10]

4. Decision problem

The aim of this assessment is to systematically review the evidence for the clinical effectiveness of psychological and psychosocial interventions for cannabis cessation in adults who use cannabis regularly.

Population and setting

The relevant population will include individuals ≥ 18 years of age, who are regular users of cannabis and have received treatment for their cannabis use in a community or outpatient setting. Studies focussing specifically on treating cannabis users within prisons or the criminal justice system or in inpatient settings will be excluded.

Interventions to be assessed

Studies involving behavioural interventions (psychological or psychosocial) will be included.

Relevant comparators

Comparators will include other interventions, waiting list control, treatment as usual, or no treatment.

Key outcomes

The key outcomes for this review are: frequency and intensity of cannabis use; severity of dependence; motivation to change; level of cannabis-related problems (including medical and other); attendance, retention and drop-out rates; and recommendations for future research.

5. Review methods for synthesis of evidence of clinical effectiveness

A review of the clinical effectiveness evidence will be undertaken systematically following the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (http://www.prisma-statement.org/). The review will assess the effectiveness of psychological and psychosocial interventions for cannabis cessation in adults who use cannabis regularly.

Inclusion/exclusion criteria

Population and setting

The relevant population will include participants aged ≥ 18 years, who are regular users of cannabis. The review will focus on studies in a community or outpatient setting.

Studies focussing on the following sub-populations will be excluded:

- Studies in the setting of the criminal justice system – i.e. prisons, following release (on-parole) or within the court system;
- Studies where the majority of participants are young people (< 18 years of age). In studies of mixed age groups, data for subgroups aged ≥ 18 years will be extracted if available, or if not then the study will be included if ≥ 80% of participants are aged ≥ 18 years, or where this data is not available then where the mean age of participants is ≥ 18 years, at baseline.
- Studies where participants are treated in an inpatient setting, i.e. the patient received treatment for regular cannabis use while occupying a hospital ward or within an emergency department.
- Studies in which the intervention is provided to participants other than the cannabis user (e.g. parents or partners).
- Studies in very specific sub-populations (such as indigenous communities or HIV patients).

For studies covering abuse of more than one substance (i.e. poly-substance abuse, involving other drugs or alcohol), the following approach will be taken:

- Studies will only be included if they report cannabis-use outcomes (rather than any drug use) for the sub-population who are cannabis users.
- Studies in which the entire population is dependent on alcohol, cocaine, opiates, amphetamines, or receiving methadone maintenance will be excluded (since these are quite specific populations and less relevant to cannabis cessation).

Subgroups

When analysing the results of the included studies we will undertake subgroup analyses by the following attributes where data allows:

- Intensity of cannabis use at baseline
- Intensity of use of alcohol or tobacco at baseline
- Poly-substance abuse – studies involving participants who suffer from poly-substance dependence or abuse;
- Psychiatric illness – studies involving participants who have a 'dual diagnosis', i.e., are regular cannabis users and have a psychiatric illness;
- Mode of enrolment onto intervention/treatment– studies involving different modes of enrolment (e.g. referred by health professional; response to advert).

Included interventions

Behavioural interventions will include psychological or psychosocial interventions, delivered in an outpatient or community setting, aiming to reduce or cease participants' use of cannabis. Examples include:

- Cognitive behavioural therapy (CBT) – a form of "talking therapy" that aims to manage cannabis use by changing the way the participant thinks or behaves.[11]
- Motivational interviewing (MI) – a patient centred approach that aims to improve motivation to change and resolve ambivalence to change;[12]
- Motivational enhancement therapy (MET) - a variant of motivational interviewing that is manual-based;[13]
- Brief motivational interventions – a variant of motivational interviewing that is undertaken over a short period of time;[9]
- Contingency management – providing patients with tangible rewards in return for a reduction or cessation in drug taking;[9]
- Case management – a strategy to improve the coordination and continuity of the delivery of services to a patient;[14]
- Relapse therapy / relapse prevention therapy – based on CBT, enables clients to cope with high risk situations that may lead to drug taking.[15]

Combinations of therapies: (for example, combinations of CBT and MI therapies).

Mode of delivery: Therapies delivered face-to-face or via the internet/telephone will be included.

Additional interventions: If additional interventions are identified during this review, they will be included if relevant to a UK setting, following consultation with our clinical advisors.

Comparators

Comparators will include other psychosocial interventions, waiting list control, treatment as usual, or no treatment. Studies comparing a psychosocial intervention to a drug treatment will be excluded since assessment of drug treatments for cannabis cessation is beyond the scope of this review.

Outcomes

The key outcomes for this review are:

- Frequency and intensity of cannabis use, via self-report, with or without confirmation by biological analysis (urinalysis, hair/saliva analysis)
    - Number of days, amount per day: before, during and after the intervention;
    - Number (%) reporting abstinence following intervention;
- Severity of dependence/abuse measured via standard questionnaires (e.g. Addiction Severity Index,[16] Severity of Dependence Scale[17])
- Motivation to change (e.g. as measured by the Readiness to Change Questionnaire (RCQ)[13])
- Level of cannabis-related problems: medical problems, legal problems, social and family relations, employment and support, assessed by questionnaires such as the Cannabis Problems Questionnaire;[18]
- Attendance, retention and drop-out rates; measured as number of sessions attended, number (%) completing whole treatment period;
- Recommendations for future research.

Included study types

Only randomised controlled trials (RCTs) will be included in this review.

Excluded study types

The following study types will be excluded:

- Non-randomised studies;
- Narrative reviews, editorials, opinion pieces;
- Reports written in a language other than English or published as meeting abstracts, where insufficient methodological details are reported in the abstract to allow critical appraisal of study quality and extraction of study characteristics and key outcomes.

Search strategy

A comprehensive search will be undertaken to systematically identify RCTs of psychological or psychosocial interventions for cannabis cessation in regular users of cannabis. The search strategy will comprise the following elements:

- Searching electronic databases and web sites for grey literature
- Contact with experts in the field
- Scrutiny of bibliographies of relevant reviews and retrieved papers.

A list of electronic databases and examples of websites to be searched is provided in Table 1. The search strategy will be adapted across databases. Language and date restrictions will not be applied. Searches in the major databases will be restricted by study type (i.e. RCTs and systematic reviews). An example MEDLINE search strategy is provided in Appendix 1.

Table 1: Data sources – electronic databases and grey literature

Electronic database sources

- MEDLINE(R) In-Process & Other Non-Indexed Citations and MEDLINE(R) (Ovid) 1948 to present
- EMBASE (Ovid) 1980 to present
- Psychological Information Database PsycINFO (Ovid) 1806 to present
- The Cochrane Library including the Cochrane Database of Systematic Reviews (CDSR), Cochrane Register of Controlled Trials (CENTRAL), Health Technology Assessment (HTA) and Database of Abstracts of Review of Effects (DARE) Databases 1898 to present

Grey literature and internet sources

- ISI Web of Knowledge Conference Proceedings Index
- ClinicalTrials.gov (http://www.clinicaltrials.gov/)
- metaRegister of Controlled Trials (mRCT) (http://www.controlled-trials.com/mrct/)
- Websites – UK and international professional societies and drug abuse organisations sites include but are not limited to:
    - United Nations Office on Drugs and Crime http://www.unodc.org/
    - DrugScope http://www.drugscope.org.uk/
    - American Society of Addiction Medicine (ASAM) http://www.asam.org/
    - National Institute on Drug Abuse http://www.drugabuse.gov/
    - Canadian Centre on Substance Abuse http://www.ccsa.ca/Eng/Pages/Home.aspx
    - Canadian Society of Addiction Medicine http://www.csam-smca.org/

Data extraction strategy

Titles and abstracts of citations identified by the searches will be screened for potentially relevant studies by one reviewer and a 10% sample checked by a second reviewer (and a check for consistency undertaken). Full texts will be screened by two reviewers. We will extract and summarise details of studies identified for inclusion using a data extraction sheet. One reviewer will perform data extraction of each included study. All numerical data will be checked against the original article by a second reviewer. Any disagreements will be resolved through discussion. Where studies comprise duplicate reports (parallel publications), the most recent and relevant report will be used as the main source, and additional reports checked for extra information. Where studies are included in existing high-quality systematic reviews, data will be extracted from the review and checked in the original article.

Quality assessment strategy

Methodological quality of included RCTs will be assessed using the Cochrane Collaboration risk of bias assessment criteria. This tool addresses specific domains, namely: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective outcome reporting.[19]

Methods of analysis/synthesis

Data will be tabulated and summarised in a narrative review. Meta-analysis may not be feasible as it is likely that there will be high heterogeneity in interventions, comparators and outcomes. However, where possible, we will pool data in a meta-analysis using Cochrane RevMan software (version 5.2; RevMan 2012). Outcomes reported as continuous data will be estimated using a mean difference (MD) with 95% confidence interval (95% CI). Outcomes reported as dichotomous data will be estimated as risk ratios (RRs) with associated 95% CI. Clinical heterogeneity across RCTs (that is the degree to which RCTs appear similar in terms of participants, intervention type and duration and outcome type) and statistical heterogeneity will be considered prior to data pooling. Methods for meta-analysis will be those described in the Cochrane Handbook.[19] Pooled effect estimates from meta-analyses that are undertaken will be summarised and presented figuratively.

Service user involvement

Service users' views will be sought to inform the systematic review. Service users will be recruited by the clinical advisors. The review team, KC and RC, will meet with service users twice during the project – once near the beginning of the study to introduce the study and discuss the planned data extraction, and once nearing the end of the review to discuss elements of the draft report. Service users will be reimbursed for time and travel expenses.

Expertise in this TAR team

TAR Centre

The ScHARR Technology Assessment Group (ScHARR-TAG) undertakes reviews of the effectiveness and cost-effectiveness of healthcare interventions for the NHS R&D Health Technology Assessment Programme on behalf of a range of policy makers, including the National Institute for Health and Care Excellence. Much of this work, together with our reviews for the international Cochrane Collaboration, underpins excellence in healthcare worldwide. A list of publications can be found at: http://www.sheffield.ac.uk/scharr/sections/heds/collaborations/scharr-tag/reports.

6. Competing interests of authors

The authors do not have any competing interests.

7. Timetable/milestones

Milestone	Date
Draft protocol	31st Jan 2014
Final protocol	28th Feb 2014
Progress report	25th April 2014
Assessment report	30th May 2014

8. Appendices

Appendix 1: Draft search strategy (Ovid MEDLINE)

Medline and Medline In-Process & Other Non-Indexed Citations: Ovid. 1946 to Present

1. Substance-Related Disorders/
2. (cannabis$ or marijuana or marihuana or hashish).ab,ti.
3. 1 and 2
4. exp marijuana abuse/
5. ((cannabis$ or marijuana or marihuana or hashish) adj2 (misuse or abuse$ or addict$ or depend$ or disorder$ or use$)).ab,ti.
6. or/3-5
7. ((cannabis$ or marijuana or marihuana or hashish) adj3 (therap$ or treatment$)).ab,ti.

8. (cessation adj2 (therap$ or treat$)).ab,ti.
9. exp psychotherapy/
10. psychotherap$.ab,ti.
11. ((psychodynamic or psychosocial) adj2 (therap$ or treatment$ or intervention$ or program$)).ab,ti.
12. exp Behavior Therapy/
13. ((behavio$ or cognitive$) adj3 (therap$ or treatment$ or management or intervention$ or program$)).ab,ti.
14. cbt.ab,ti.
15. exp Counseling/
16. counsel$.ab,ti.
17. exp Mind-Body Therapies/
18. ((relaxation or imagery) adj2 (therap$ or technique$)).ab,ti.
19. (guided adj2 imagery).ab,ti.
20. biofeedback.ab,ti.
21. (family adj2 therap$).ab,ti.
22. (motivation$ adj3 (therap$ or interview$)).ab,ti.
23. ((case or contingency) adj2 (therap$ or management)).ab,ti.
24. ((coping skill$ or cbst or self control or assertive$) adj2 (training or therap$)).ab,ti.
25. aversi$ therap$.ab,ti.
26. covert sensiti?ation.ab,ti.
27. or/7-26
28. 6 and 27
29. meta-analysis as topic/
30. (meta analy$ or metaanaly$).tw.
31. Meta-Analysis/
32. (systematic adj (review$1 or overview$1)).tw.
33. "Review Literature as Topic"/
34. or/29-33
35. (cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab.
36. ((reference adj list$) or bibliograph$ or hand-search$ or (relevant adj journals) or (manual adj search$)).ab.
37. ((selection adj criteria) or (data adj extraction)).ab.
38. "review"/
39. 37 and 38
40. comment/ or editorial/ or letter/

41. Animals/
42. Humans/
43. 41 not (41 and 42)
44. 40 or 43
45. 34 or 35 or 36 or 39
46. 45 not 44
47. 28 and 46
48. Randomized controlled trials as Topic/
49. Randomized controlled trial/
50. Random allocation/
51. randomized controlled trial.pt.
52. Double blind method/
53. Single blind method/
54. Clinical trial/
55. exp Clinical Trials as Topic/
56. controlled clinical trial.pt.
57. multicenter study.pt.
58. or/48-57
59. (clinic$ adj25 trial$).ti,ab.
60. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$ or mask$)).tw.
61. Placebos/
62. Placebo$.tw.
63. randomly allocated.tw.
64. (allocated adj2 random).tw.
65. or/59-64
66. 58 or 65
67. Case report.tw.
68. Letter/
69. Historical article/
70. 67 or 68 or 69
71. exp Animals/
72. Humans/
73. 71 not (71 and 72)
74. 70 or 73
75. 66 not 74
76. 28 and 75

9. Team members' contributions

Project management and systematic reviewing

Katy Cooper, Senior Research Fellow, ScHARR. KC has extensive experience in undertaking systematic reviews of health technologies. KC will lead the project and undertake the review of effectiveness. She will co-ordinate the review process including: protocol development, co-ordinating the searches, assessing studies for eligibility, data extraction and quality assessment of included studies, data checking and analysis (where appropriate), and development of the final report.

Robin Chatters, Research Associate, ScHARR. RC has experience of undertaking systematic reviews in areas such as Health Services Research and Public Health. RC will assist KC in undertaking the systematic reviewing. He will be involved in protocol development, assessing studies for eligibility, data extraction and quality assessment of included studies, data checking and analysis (where appropriate), and development of the final report.

Information specialist

Ruth Wong, Information Specialist, ScHARR. RW has experience of undertaking literature searches for the ScHARR Technology Assessment Group systematic reviews and other external projects. RW will be involved in developing the search strategy and undertaking the electronic literature searches.

Clinical advisors

Mr Matt Knight, Manager – Alcohol and Drugs, Public Health England
Matt.knight@phe.gov.uk
Tel: 0113 2265041

Dr Olawale Lagundoye, Consultant in Addiction Psychiatry, Sheffield Health and Social Care
Olawale.Lagundoye@shsc.nhs.uk
Tel: 0114 3050546

Mr Mick Holmes, Team Leader, Sheffield Adult Treatment Service
mick.holmes@turning-point.co.uk
Tel: 0114 275 5973

Clerical and administration

Gill Rooney, Project Administrator. GR will assist in the retrieval of papers and in preparing and formatting the report.

Service user representation

Service users will be recruited by the clinical advisors for input into the early stages of the project and draft report.

10. References

1. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Prevalence of daily cannabis use in the European Union and Norway. *EMCDDA*, Lisbon, November 2012.
2. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet* 2009; 374: 1383–91.
3. Diagnostic and Statistical Manual of Mental Disorders. 4th Edition. June 2000.
4. World Health Organization (WHO). ICD-10: International Statistical Classification of Diseases and Related Health Problems. 10th Revision, 2010.
5. Karila L, Roux P, Rolland B, Benyamina A, Reynaud M, Aubin HJ, Lançon C. Acute and Long-Term Effects of Cannabis Use: A Review. Curr Pharm Des. 2013 Aug 29. [Epub ahead of print]
6. McRae AL, Budney AJ, Brady KT. Treatment of marijuana dependence: a review of the literature. *Journal of Substance Abuse Treatment* 2003;24(4):369–76.
7. Denis C, Lavie E, Fatseas M, Auriacombe M. Psychotherapeutic interventions for cannabis abuse and/or dependence in outpatient settings. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art.No.:CD005336. DOI: 10.1002/14651858.CD005336.pub2.
8. National Institute for Health and Care Excellence (NICE). NICE Clinical Guideline 51: Drug misuse: Psychosocial interventions. *NICE* 2007.
9. Department of Health (England) and the devolved administrations (2007). *Drug Misuse and Dependence: UK Guidelines on Clinical Management*. London: Department of Health (England), the Scottish Government, Welsh Assembly Government and Northern Ireland Executive
10. Best Practice Portal: Treatment Options for Cannabis Users. European Monitoring Centre for Drugs and Drug Addiction. http://www.emcdda.europa.eu/best-practice/treatment/cannabis-users. Date accessed: 6th Jan 2014.
11. NHS Choices. Cognitive behavioural therapy. http://www.nhs.uk/conditions/Cognitive-behavioural-therapy/Pages/Introduction.aspx. Date accessed: 6th Jan 2014.
12. Miller RW, Rollnick S. Motivational interviewing: preparing people to change addictive behavior. New York, NY: The Guilford Press; 1991.
13. Smedslund G, Berg RC, Hammerstrøm KT, Steiro A, Leiknes KA, Dahl HM, Karlsen K. Motivational interviewing for substance abuse. *Cochrane Database of Systematic Reviews* 2011, Issue 5. Art.No.:CD008063. DOI: 10.1002/14651858.CD008063.pub2.

14. Hesse M, Vanderplasschen W, Rapp R, Broekaert E, Fridell M. Case management for persons with substance use disorders. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD006265. DOI: 10.1002/14651858.CD006265.pub2.
15. Maddock C, Babbs M. Interventions for cannabis misuse. *Advances in Psychiatric Treatment* 2006;12:432–439.
16. McLellan A, Luborsky L, Woody GE, O'Brien CP. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *The Journal of Nervous and Mental Disease* 1980;168(1):26–33.
17. Swift W, Copeland J, Hall W. Choosing a diagnostic cut-off for cannabis dependence. *Addiction* 1998;93(11):1681–92.
18. Copeland J, Swift W, Rees V. Clinical profile of participants in a brief intervention program for cannabis use disorder. *Journal of Substance Abuse Treatment* 2001;20(1):45–52.
19. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.