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The available evidence in the field of treatment of opiate: The experience of developing the WHO clinical guidelines

Background, Objectives and Methods

Systematic reviews (SRs) published by Cochrane Drugs and Alcohol Group (CDAG) were used as background to develop WHO guidelines on treatment of opioid dependence.

Objective: To assess to what extent the available evidence in SRs published by the CDAG can inform treatment policy.

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Methods

Methods: to compile GRADE profiles based on the 15 SRs of CDAG (CLIB 3, 2006) on opioid use disorders using the GRADE methodology.

The areas identified by WHO panel were:

1.Management of opioid intoxication and overdose
2. Management of opioid withdrawal
3. Management of opioid dependence

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Management of opioid intoxication and overdose

- no SR on this issue

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Management of opioid withdrawal

Outcome	
severity and duration of withdrawal symptoms	Critical
side effects	Critical
completion of treatment	Critical
mortality	Critical
patients who have relapsed at follow-up at 12 months	Critical
Cost of treatment	Critical
use of primary substance during treatment	Important but not critical
use of other drugs during treatment	Not important
patients who have relapsed at follow-up > 12 months	Not important

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METHODS

3. Management of opioid dependence

The panel identified 20 different outcomes for this area, 8 of these were considered critical

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Outcome	
Retention in treatment	Critical
Side effects	Critical
Mortality	Critical
Level of social functioning	Critical
Quality of life	Critical
HIV seroconversion	Critical
Hepatitis seroconversion	Critical
patient satisfaction	Critical
use of primary substance	Important but not critical
patients who have relapsed at follow-up at 12 months	Important but not critical
patients who have relapsed at follow-up > 12 months	Important but not critical
frequency of high risk behaviours	Important but not critical
criminal and delinquent behaviour	Important but not critical
use of other drugs	Important but not critical
relapse rate in abstinence oriented treatment program	Not important
disability	Not important
psychiatric comorbidity	Not important
compliance with treatment	Not important
diversion of medication (not naltrexone)	Not important
cost of treatment	Not important

RESULTS

Detoxification treatments

- 7 Cochrane reviews were published on opiate detoxification treatments

- 7 clinical questions, were identified for this area and for each clinical questions in the reviews were available answers related to different outcomes;

- For 2/ 9 of the identified outcomes (cost of treatment and patients who have relapsed at follow-up > 12 months), there were no data available in the published reviews. These two outcomes were not considered critical by the panel.

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RESULTS

1. Should Tapered methadone vs any other tapered pharmacological treatment be used in any opioid user?

Outcome	Results	Quality of evidence
completion of treatment	favour methadone n.s.	moderate
severity and duration of withdrawal symptoms	data not pooled	low
side effects	data not pooled	moderate
use of primary substance	favour methadone s.s.	moderate
relapsed at follow up	favour methadone n.s.	low

2. Should Tapered methadone vs tapered buprenorphine be used in all opioid dependent patients?

Outcome	Results	Quality of evidence
completion of treatment	no differences	moderate
side effects	favour methadone n.s.	moderate

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RESULTS

3. Should tapered methadone vs alpha2 adrenergic agonists be used in all opioid dependent patients?

Outcome	Results	Quality of evidence
completion of treatment	favour methadone n.s.	moderate
side effects,	favour methadone n.s.	moderate
relapsed at follow up	no differences	moderate

4. Should Opioid antagonists with minimal sedation be used for opioid withdrawal?

Outcome	Results	Quality of evidence
completion of treatment	no differences	moderate
severity and duration of withdrawal symptoms,	data not pooled	low
side effects,	favour control n.s.	very low
relapsed at follow up	favour treatment n.s.	low

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RESULTS

5. Should Opioid antagonist under heavy sedation be used for opioid withdrawal?

Outcome	Results	Quality of evidence
completion of treatment	favour treatment n.s.	high
severity and duration of withdrawal symptoms	data not pooled	low
life threatening adverse events	favour control n.s.	high
relapsed at follow up	no differences	high

7. Should Inpatients detoxification treatments vs outpatient detoxification treatments be used in opiate dependent patients?

Outcome	Results	Quality of evidence
completion of treatment	favour outpatient s.s.	very low
relapsed at follow up	favour outpatient n.s.	very low

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RESULTS

6. Should Any pharmacological detoxification treatment plus psychosocial treatment vs any pharmacological detoxification treatment alone be used in opioid dependent patients requiring detox?

Outcome	Results	Quality of evidence
completion of treatment	favour treatment s.s.	high
use of opiate during the treatment	favour treatment n.s.	moderate
relapsed at follow up	favour treatment s.s.	high
use of other substances	favour treatment n.s.	low
mortality	favour treatment n.s.	very low

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RESULTS

Maintenance treatments

- 8 Cochrane reviews were published on opiate detoxification treatments

- 14 clinical questions, were identified for this area and for each clinical questions in the reviews were available answers related to different outcomes;

- For 12/20 of the identified outcomes (Quality of life, HIV seroconversion, hepatitis seroconversion, patient satisfaction, patients who have relapsed at follow-up > 12 months, relapse rate in abstinence oriented treatment program, disability, psychiatric comorbidity, compliance with treatment, diversion of medication (not naltrexone), and cost of treatment) there were no data available in the published reviews, four of these were considered critical by the panel

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RESULTS

1. Should methadone maintenance high dose (60-109 mg/day) vs methadone maintenance medium doses (40-59 mg/day) be used for opioid dependence?

Outcome	Results	Quality of evidence
retention in treatment	favour high doses s.s.	high
opioid abstinence	favour high doses n.s.	moderate
criminal behavour	favour high doses n.s.	moderate
mortality	favour high doses n.s.	very low

Comparing

2. Methadone maintenance high doses (60-109 mg/day) vs methdaone maintenance low doses (1-39 mg/day)

3. Methadone maintenance very high doses (>109 mg/day) vs methadone maintenance high doses (60-109 mg/day)

4. Methadone maintenance medium doses (40-59 mg/day) vs methadone maintenance low doses 1-39 mg/day)

Results are always in favour of higher dosages

and

5. Methadone maintenance treatment vs placebo

Results of high quality in favour of methadone

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RESULTS

6.Should buprenorphine maintenance flexible doses vs methadone maintenance flexible doses be used for opioid maintenance treatment?

Outcome	Results	Quality of evidence
retention in treatment	favour methadone s.s.	high
use of opiate during the treatment	no differences	high
use of other drugs	no differences	high
criminal behavour	no differences	moderate

Comparing

7.Low doses buprenorphine vs low doses methadone,
8.High Dose buprenorphine versus high dose methadone
Results always in favour of methadone for retention in treatment, similar for the other outcomes
and
9. Buprenorphine maintenance treatment vs placebo
Results of high quality in favour of buprenorphine

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RESULTS

10. Should Heroin maintenance treatments vs Methadone maintenance treatments be used for chronic opiate dependents?

Outcome	Results	Quality of evidence
relapsed to street heroin	favour treatment n.s.	very low
retention in treatment	favour control n.s.	very low
mortality	favour control n.s.	very low
criminal behavour	favour treatment n.s.	very low
social functioning	favour treatment n.s.	very low

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RESULTS

11. Should Oral Naltrexone be used for Opioid dependence?

Outcome	Results	Quality of evidence
retention in treatment	favour naltrexone n.s.	moderate
use of opiate	favour naltrexone s.s.	high
relapse at follow up	favour naltrexone n.s.	moderate
side effects	favour placebo n.s.	low
criminal behavour	favour naltrexone s.s.	moderate

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RESULTS

12. Should Psychosocial plus pharmacological maintenance treatments vs Pharmacological maintenance treatments alone be used for Opioid dependence?

Outcome	Results	Quality of evidence
retention in treatment	favour control n.s.	high
use of opiate	favour treatment s.s.	high
retention at follow up	favour control n.s.	high
abstinent at follow up	favour control n.s.	low

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RESULTS

14. Should Substitution treatment be used for prevention of HIV infection or reduction of high risk behaviours?

Outcome	Results	Quality of evidence
frequency of high risk behaviours as:		
injecting behaviours	favour treatment s.s..	low
sexual behaviours	favour treatment s.s..	low

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Results on Grading quality: 15 reviews; 21 profiles

Outcome	Number of times for which the outcome was considered in the 21 profiles	Quantitative measures	Quality of evidence
completion of treatment/retention in treatment	19/21	19/19	7/19 high, 10/19 moderate, 2/19 very low
side effects of treatment	7/21	5/7	1/7 high, 4/7 moderate, 1/7 low, 1/7 very low
mortality	6/21	6/6	1/6 high, 5/6 very low
severity and duration of withdrawal symptoms	3/21	0/3	3/3 low
patients who have relapsed at follow-up (different length)	9/21	9/9	3/9 high, 2/9 moderate, 3/9 low, 1/9 very low
Level of social functioning	2/21	2/2	1/2 moderate, 1/2 low
use of primary substance during treatment	10/21	10/10	6/10 high, 4/10 moderate
use of other illicit substances during treatment	8/21	8/8	3/8 high, 1/8 moderate, 4/4 low
retention in treatment at 12 months	1/21	1/1	1/1 high
frequency of high risk behaviours	1/21	1/1	1/1 low
criminal and delinquent behaviour	5/21	5/5	1/5 high, 3/5 moderate, 1/5 very low

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Results on Grading quality: 15 reviews; 21 profiles

Quality of evidence of the information available in the 15 reviews published by CDAG Group

Quality of evidence	N°	%
High	23/71	32,4
moderate	25/71	35,2
Low	13/71	18,3
very low	10/71	14,1

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