

CTN 0131 Office-based methadone versus buprenorphine to address retention in medication for opioid use disorder treatment

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CDUHR Symposium

April 9, 2024



Project leadership team

Lead investigator

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Co-LI

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Co-Investigators

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- Lisa Marsch PhD
- Richard Schottenfeld MD
- Zoe Weinstein MD MS

Outline

I. Significance

II. Office-based methadone trial preparation

III. Approach

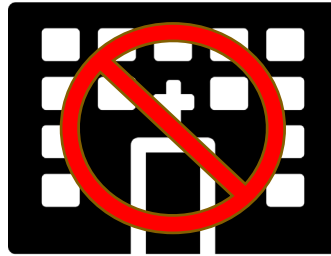
Retention is a challenge

Retention in methadone treatment remains a challenge

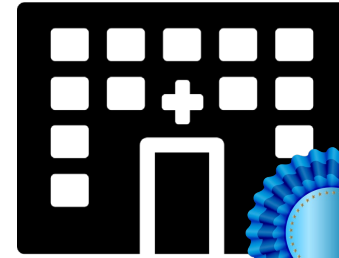
- 60% retained at 12 months overall
- < 50% in many real world settings

Traveling for methadone

Patient with opioid use disorder

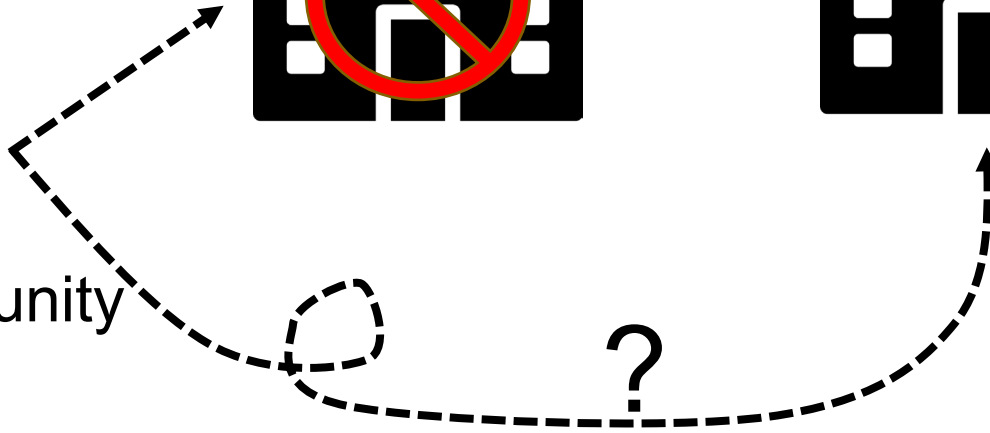


Opioid treatment program



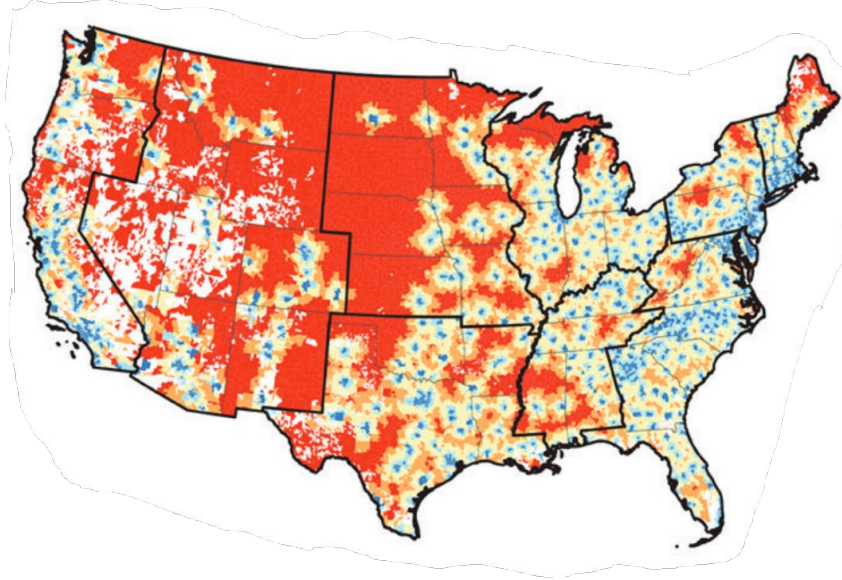
SAMHSA
Certified

Local community

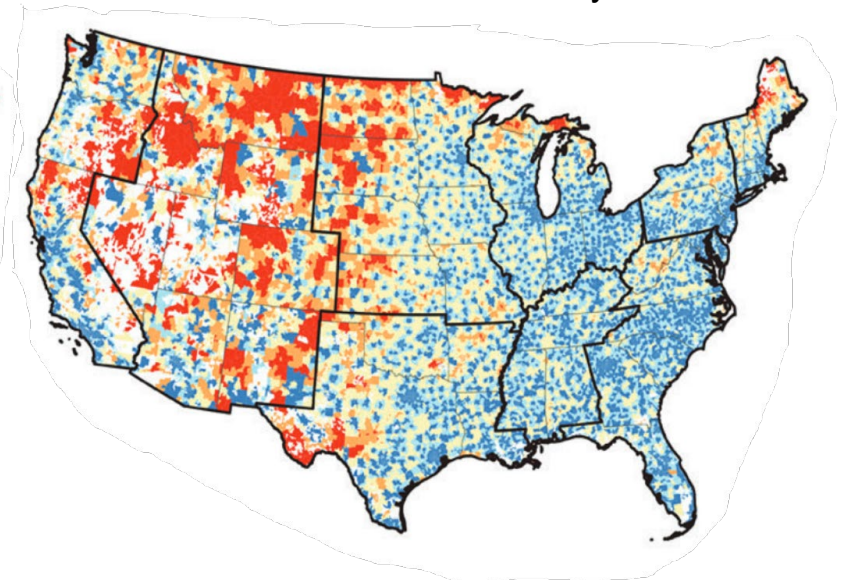


Limited availability

A. Drive time to nearest OTP



B. Drive time to nearest dialysis center



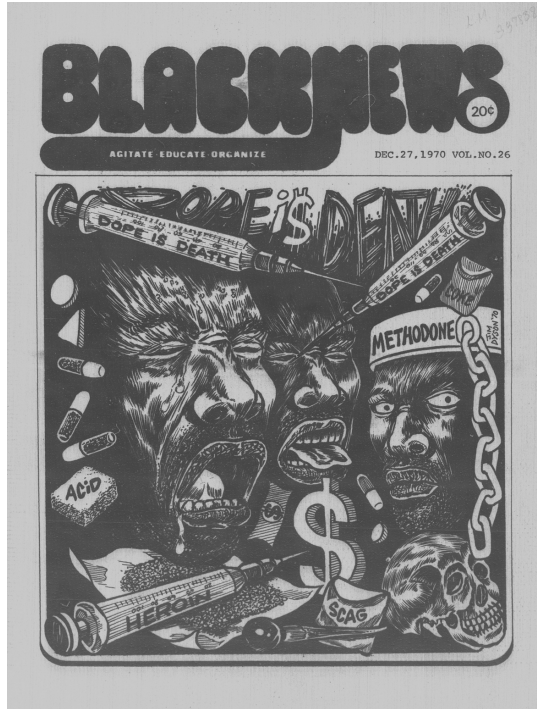
OTP = Opioid treatment program

Time, min



Joudrey et al JAMA Network Open 2022

Community resistance to OTPs



Protest Targets Methadone Clinic Plan

by LAURA GLESBY | Feb 5, 2022 6:00 pm

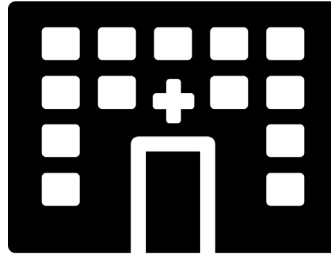
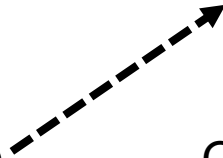
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Office based methadone

Patient with opioid use disorder

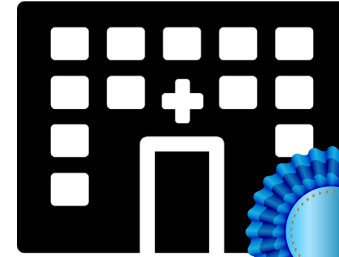


Office based practice



Community pharmacy

Opioid treatment program



SAMHSA
Certified

Local community

Methadone medical maintenance

MEDICAL MAINTENANCE FEASIBILITY STUDY

Don C. Des Jarlais, Herman Joseph,
Vincent P. Dole, Marie E. Nyswander

INTRODUCTION

Background

Since 1964, methadone maintenance has evolved from a small re-
search project into the largest single modality for the treatment
of heroin addiction (Des Jarlais and Uppal 1980, Dole and
Nyswander 1976, Lowinson 1981). This evolution has been shaped by

Published 1985

Methadone medical maintenance

Original Contribution

October 10, 2001

Methadone Maintenance in Primary Care A Randomized Controlled Trial

David A. Fiellin, MD; Patrick G. O'Connor, MD, MPH; Marek Chawarski, PhD; et al

» [Author Affiliations](#)

JAMA. 2001;286(14):1724-1731. doi:10.1001/jama.286.14.1724

Methadone medical maintenance



ELSEVIER



MEDICAL MAINTENANCE

Drug and Alcohol Dependence

Volume 65, Issue 2, 1 January 2002, Pages 137-148



A multicenter randomized evaluation of methadone medical maintenance

Van L King^a  , Kenneth B Stoller^a, Michael Hayes^b, Annie Umbricht^c, Marian Currens^b,
Michael S Kidorf^a, James A Carter^a, Robert Schwartz^{d e}, Robert K Brooner^a

Methadone medical maintenance





Journal of Substance Abuse Treatment

Volume 31, Issue 4, December 2006, Pages 385-393



Regular article

A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model

Van L. King M.D. ^a  , Michael S. Kidorf Ph.D. ^a, Kenneth B. Stoller M.D. ^a,
Robert Schwartz M.D. ^{b c}, Kenneth Kolodner Sc.D. ^a, Robert K. Brooner Ph.D. ^a

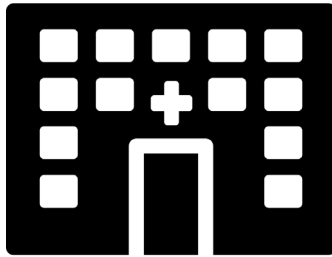
Office based methadone

- Is methadone treatment safe and effective when *initiated* within office-based settings?

Methadone provision within United States and Canada



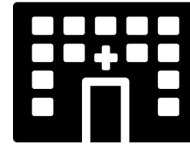
Opioid treatment program



Federally
Certified



Addiction specialist



Office-based



Community pharmacy

Stigma of methadone in the US

Special Communication

Methadone Maintenance Treatment

treatment.

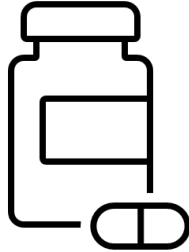
An unfortunate consequence of the early enthusiasm for methadone treatment is today's general disenchantment with chemotherapy for addicts. What was not anticipated at the onset was the nearly universal reaction against the concept of substituting one drug for another, even when the second drug enabled the addict to function normally. Statistics showing improved health and social

A Ten-Year Perspective

Vincent P. Dole, MD, Marie E. Nyswander, MD

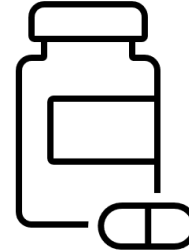
JAMA 1976

Comparative effectiveness in the setting of illicit fentanyl analog use



Buprenorphine

Versus



Methadone

Outline

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III. Approach

Office-based clinical team

Office-based practice

- Two to three experienced buprenorphine prescribers

Community pharmacy

- Open six or more days a week
- One or more study pharmacist

Study sites

1. Highland Hospital Bridge Clinic at Alameda Health System, Oakland, CA
2. Outpatient Buprenorphine Induction Clinic, UCSF, San Francisco, CA
3. Office Based Addiction Treatment Program, BMC, Boston, MA
4. Division of Addiction Sciences P.R.O.A.C.T, Huntington, WV
5. Rapid Start Clinic, Kaiser Permanente Colorado, Denver, CO
6. Hennepin Healthcare Addiction Medicine, Minneapolis, MN

DEA regulatory exception

Obtained exemption to 21 CFR 1306.04(c) for each study site

Required exemptions per site:

- 2-3 prescribers
- 1 or more pharmacies

Additional outreach

- SAMHSA
- State opioid treatment authorities (SOTAs)

Methadone formulation

- 5 mg and 10 mg tablets
- 40 mg diskettes (preferable if available)
- No liquid

Methadone treatment structure

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Prescriber Visit	x	*x	At least 2 days					At least 2 of 7 days						
Pharmacy Visit	At least 6 of 7 days							At least 5 of 7 days						

Prescribing Clinician

- ✓ Methadone dose titrated by office-based prescriber
- ✓ Prescriptions will be written for between 1-28 days
- ✓ Days 8-168: Office visits at least 28-days

Pharmacy

- ✓ Prior to dispensing take-home dose a pharmacist will observe ingestion of 1 dose at each visit
- ✓ Tablet formulation will be used

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Study overview

Hybrid Type 1 effectiveness/implementation study

Pragmatic trial design

Study aims

Aim 1: Training aim

- Train approximately 6 large office-based BUP sites to provide office-based methadone with pharmacy administration and/or dispensing

Training and pilot

- In person training site prescribing and pharmacy team
- Monthly learning collaborative
- Successfully pilot office-based methadone with three patients

Study aims

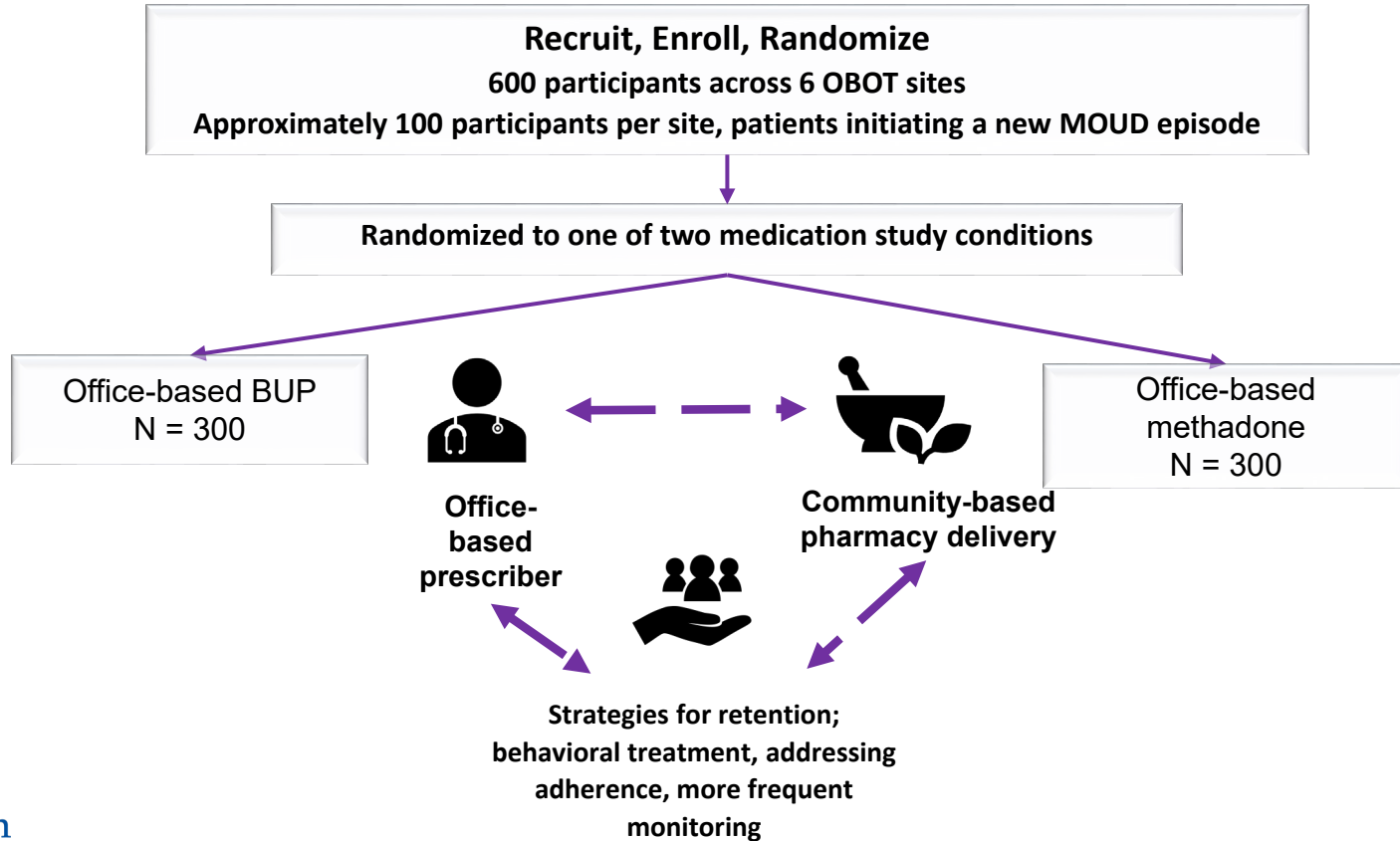
Aim 2: Effectiveness aim

- Office-based methadone versus office-based BUP on retention in treatment (as randomized) during the 168 days post-randomization

Aim 3: Implementation aim

- Identify implementation barriers, facilitators and acceptability at the patient, provider and health-systems level for office-based methadone

Study overview



Effectiveness aim eligibility

Include

- 18 and older and DSM-5 OUD
- Starting new MOUD treatment episode

Exclude

- More than 72 hours of MOUD in the 7 days prior to randomization as a “bridge” to the new OUD treatment episode

Eligibility continued

Exclude

- Known contraindication to methadone
- Pregnant by urine hCG and does not agree to prenatal ob/gyn care
- Actively suicidal or severely cognitively impaired precluding informed consent
- Requiring residential or inpatient treatment services as determined by site clinician
- Unable to provide reliable locator information
- Unwilling to follow study procedures
- Prior enrollment in the current study
- Currently enrolled in another research study which will conflict with study procedures
- Currently in jail, prison or other overnight facility or have pending legal action that could prevent participation in study activities
- Unable to conduct research assessments in English

Effectiveness aim outcomes

Primary

- Number of days until MOUD treatment discontinuation (as randomized) during the 168 days post-randomization

Selected secondary

- Days in any MOUD treatment
- Days with self-reported opioid, stimulant, and benzodiazepine use
- Participant satisfaction

Implementation aim eligibility

Interviews and focus groups with:

- Study site clinicians and staff involved in the treatment of patients with OUD along with healthcare administrators and regulators
- Patients randomized to office-based methadone

Study timeline

Activities	Approximate Month (0-60)					
	0-7	8-12	13-18	19-24	25-42	43-60
Site Selection	X					
ClinicalTrials.gov Registry	X					
Finalize Training Materials	X					
Site Endorsement	X					
Begin Enrollment		X				
Enrollment Ends						X
Ongoing Intervention		X	X	X	X	
Data Accrual		X	X	X	X	
Database Cleaning and Lock						X
Data Analyses						X
Presentations and Publications						X

Thank you

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