Management Options for Opioid Dependence

Public Meeting – June 20, 2014

Agenda

Meeting Convened | 10am-10:15am

- *Opening remarks by Commissioner of the Department of Vermont Health Access, Mark Larson*
- *Introduction by Steve Pearson, MD, President, Institute for Clinical and Economic Review*

Presentation of the Evidence and Voting Questions, Q&A | 10:15am – 11:15am

- *Dan Ollendorf, PhD, Chief Review Officer, Institute for Clinical and Economic Review*

Discussion and Public Comments | 11:15am – 11:45am

Q&A with Clinical Experts | 11:45am – 12:15pm

Lunch | 12:15pm – 12:45pm

CEPAC Deliberation and Votes on Evidence Questions | 12:45pm – 1:30pm

Roundtable Discussion | 1:30pm – 3:50pm

Summary and Closing Remarks | 3:50pm – 4pm

New England CEPAC

- Goal:
  - To improve the application of evidence to guide practice and policy in New England
- Structure:
  - Core program of Institute for Clinical and Economic Review (ICER)
  - Evidence review from ICER
  - Deliberation and voting by CEPAC: independent clinicians, scientific review experts, and public members from all six New England states
- Funding:
  - NESCSO
  - Regional private payers
  - Regional provider groups

New England CEPAC

- CEPAC recommendations designed to support aligned efforts to improve the application of evidence to:
  - Practice
    - Patient/clinician education
    - Quality improvement efforts
    - Clinical guideline development
  - Policy
    - Coverage and reimbursement
    - Medical management policies
    - Benefit design

REGULATIONS, RESTRICTIONS, AND ACCESS TO CARE IN NEW ENGLAND

Hungry Heart Documentary

Federal Regulations: Methadone

- Federal law restricts dispensing of methadone to federal- and state- approved Opioid Treatment Program (OTPs)
  - Strict requirements for patient admission, medication dosing, patient assessment, provision of social services, etc.
  - Patients must take methadone under observation, unless patient receives designated take-home privileges
  - Most OTPs only administer methadone, though some provide buprenorphine-containing medications

Federal Regulations: Buprenorphine/Suboxone

- DATA 2000 allows qualified physicians to obtain a waiver to prescribe and/or dispense buprenorphine or Suboxone
  - To receive license, physicians must have a valid DEA registration number, and receive adequate training in the treatment and management of opioid-addicted patients (e.g. certification in Addiction Medicine; completion of 8-hour training program, etc.)
  - Patient caps: physicians cannot treat >30 patients with an addiction treatment concurrently, but after one year can apply for a second waiver to treat up to 100 patients at one time

New England State Regulations

- Each New England state has strict policies related to licensing and accreditation of substance abuse facilities.
- Generally follow federal restrictions for MAT, though New England states have enacted stricter criteria in some areas:
  - Random drug testing
  - Take-home use for patients receiving methadone

New England Legislative Initiatives: Summary

State	Overdose prevention	Safe prescribing of opioid painkillers	Mandatory insurance coverage for MAT	Treatment duration limits for MAT	Increased regulation for Suboxone® prescribers	Jail diversion programs	Care delivery reform
CT	■					■	
ME	■	■		■			
MA	■	■			□	□	
NH		□					
RI	■	□	□				□
VT	■	■			■	■	■

Key: □ = Introduced ■ = Passed

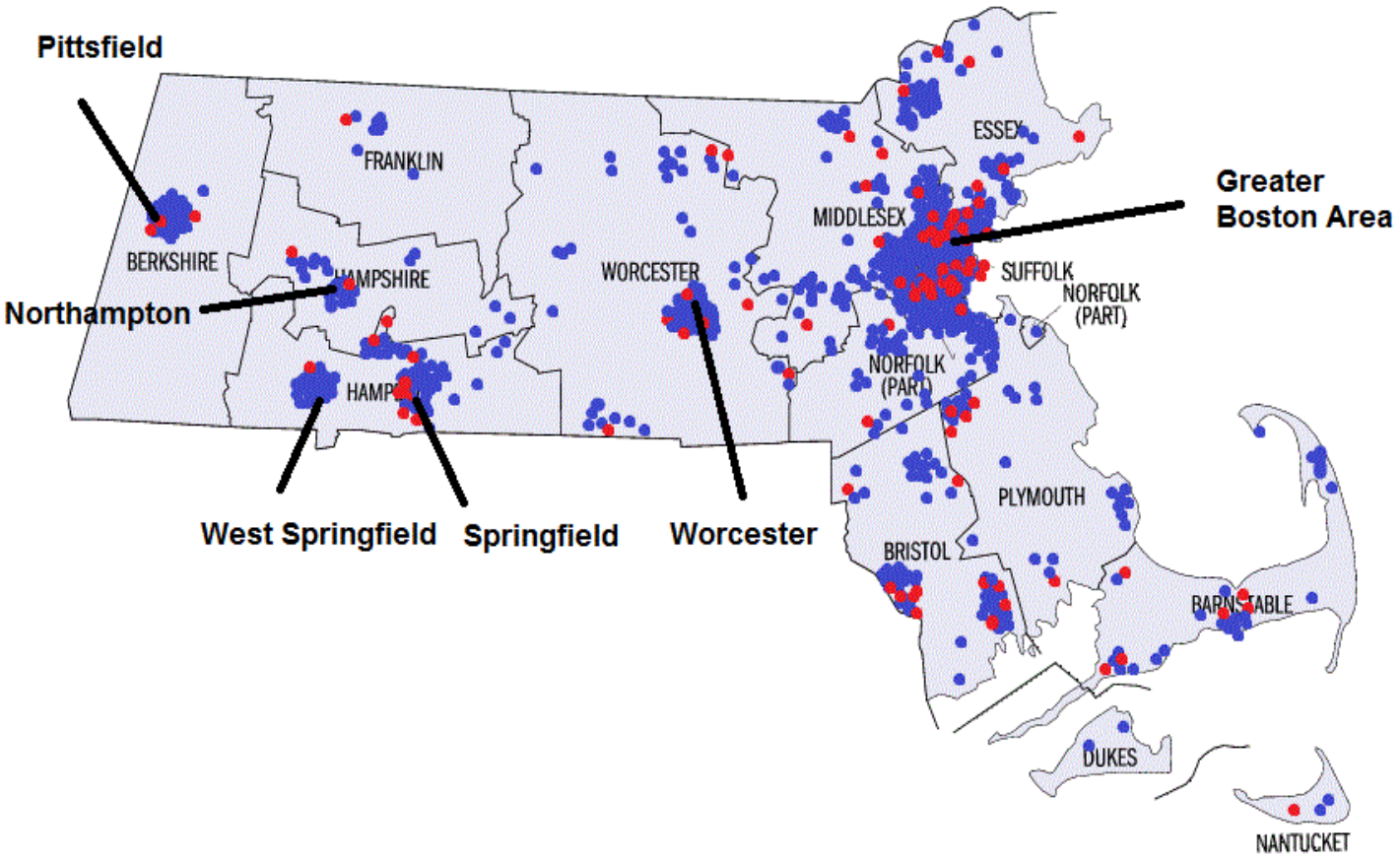
Access to Treatment

- 133,000 New Englanders are abusing or dependent on opioids, of whom 70% meet criteria for treatment but are not currently receiving it
- Availability of both facility-based and office-based opioid dependence treatment falls far short of clinical need
  - 1,193 physicians in New England who can prescribe Suboxone and voluntarily reported their status to SAMHSA, of which approximately one-third have have obtained a waiver to move from a patient cap of 30 to 100 (SAMHSA, 2013)
  - Estimated maximum number of patients who could be treated with Suboxone given current provider capacity is 60,000
- Lack of treatment in US criminal justice system
- Geographic barriers

Geographic barriers to treatment: MA

Red: Opioid Treatment Programs (OTPs)

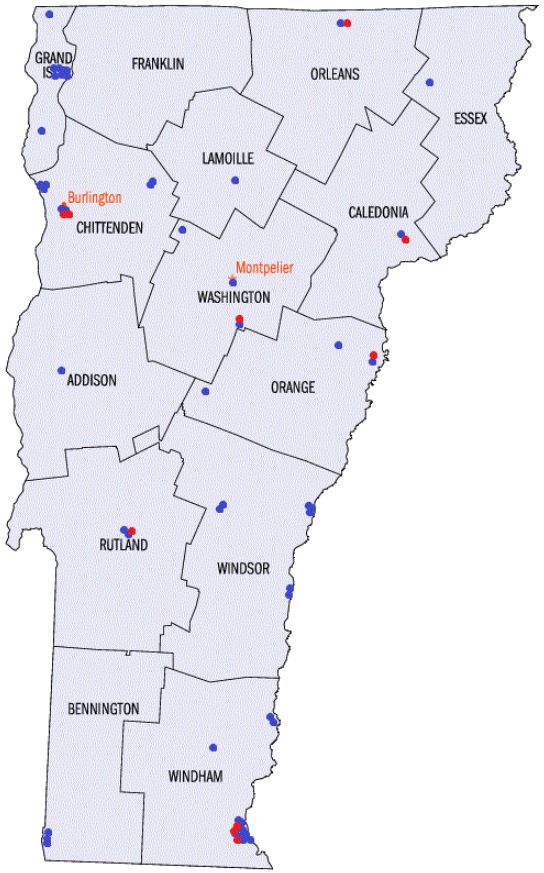
Blue: Suboxone/buprenorphine providers



Geographic barriers to treatment: VT

Red: Opioid Treatment Programs (OTPs)

Blue: Suboxone/buprenorphine providers

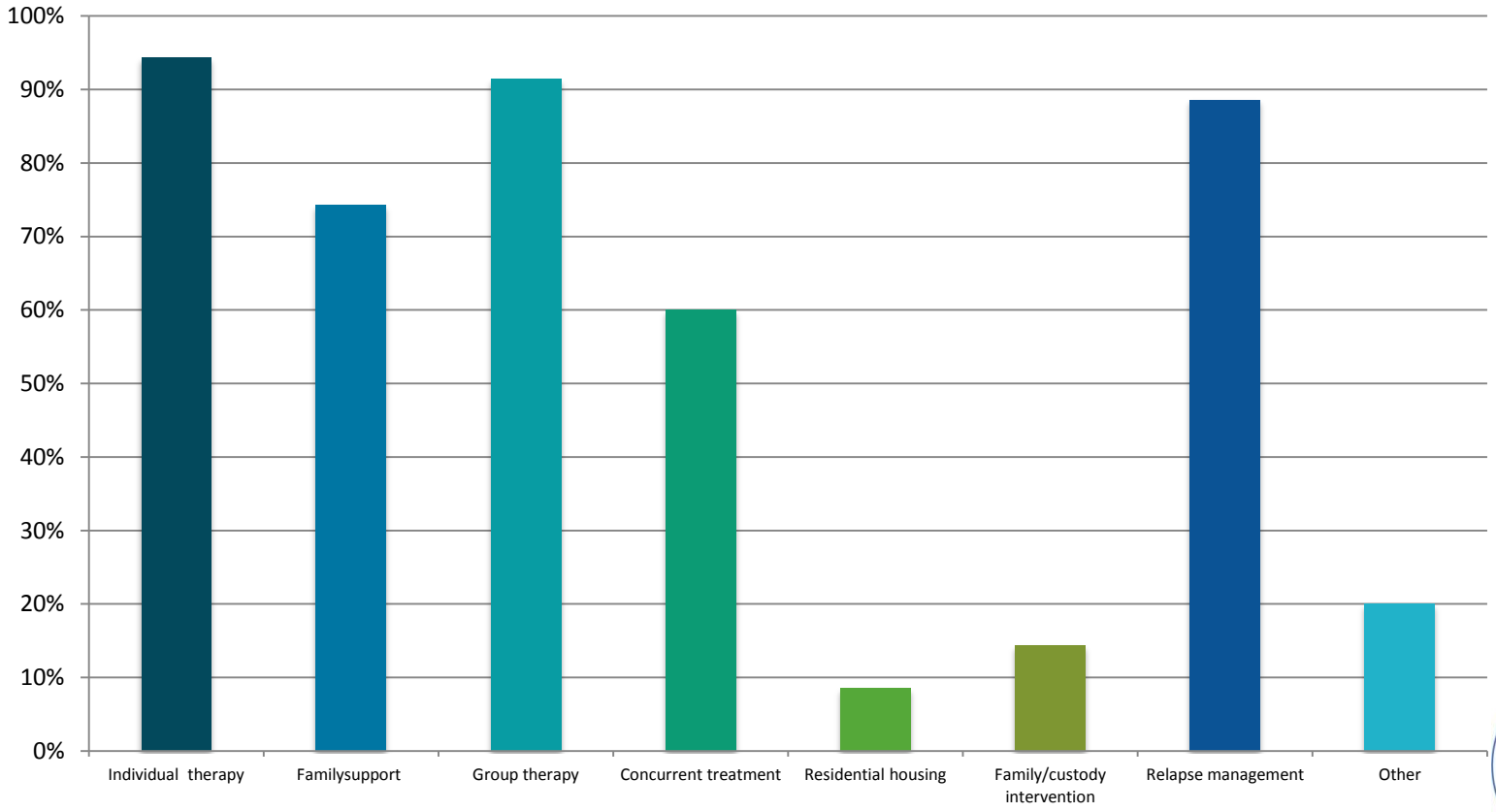


ICER Survey Results

- Survey of 32 treatment programs in New England (represented OTPs, OBOTs, residential treatment providers, and outpatient counseling programs)
- Services provided:
  - Nearly all respondents offered some form of MAT
  - 30% of treatment centers had protocols in place that established limits on dosing and/or treatment duration
  - Only ~30% of survey respondents offering MAT had written protocols in place to support physicians in determining which treatment agent to use

ICER Survey Results

Survey results of supportive services provided at treatment centers in New England (n=32)



ICER Survey Results: Barriers to providing high quality treatment

Obstacle/Treatment challenge	Significant or very significant barrier
Insurance coverage for opioid treatment	**57%**
Efficiency of referral pathways for treatment	**47%**
Regulatory structure and restrictions	**46%**
Community reaction to placement of treatment centers	**37%**
Communication/coordination across different health providers	**34%**
Recruiting/retaining qualified staff	**33%**
Staff or resource levels to address co-morbid conditions	**30%**
Availability of time and resources to asses treatment outcomes	**27%**
Patient/family attitudes regarding need for treatment	**23%**
Tailoring treatment program to client needs	**13%**

EVIDENCE PRESENTATION

Outline

- Evidence on:
  - Maintenance vs. detoxification
  - Comparative effectiveness of medications
  - Dosing/duration considerations, key program components, innovative delivery models
- Economic impact of management options for opioid dependence
- Potential budgetary impact of expanding access to treatment in New England
- Guidelines and coverage policies

REVIEW OF PUBLISHED EVIDENCE

"Framing Questions"

- Maintenance vs. detox (and other drug-free treatment)
- Suboxone vs. methadone vs. naltrexone
- Dosing and duration considerations
- Key components of treatment
- Innovative delivery models

MAINTENANCE VERSUS DETOXIFICATION

Maintenance vs. Detox

- 2009 Cochrane review and meta-analysis (11 RCTs, ~2,000 patients)*
  - Better retention and lower use of illicit opioids for maintenance
  - No statistical differences in criminal activity or mortality
- POATS study†: Greater treatment success with 4-month Suboxone regimen (~50%) vs. 4-week regimen (7%)

*Mattick, 2009 (Document CD002209)

†Weiss et al., Arch Gen Psych 2011

Maintenance vs. Detox

- RCT of 152 adolescents undergoing 2-week (detox) vs. 12-week Suboxone treatment*:
  - Retention at 3 months better for maintenance (70% vs. 21%, p<.001)
  - Illicit opioid use lower for maintenance (38% vs. 55%, p<.001)

*Woody et al., JAMA 2008

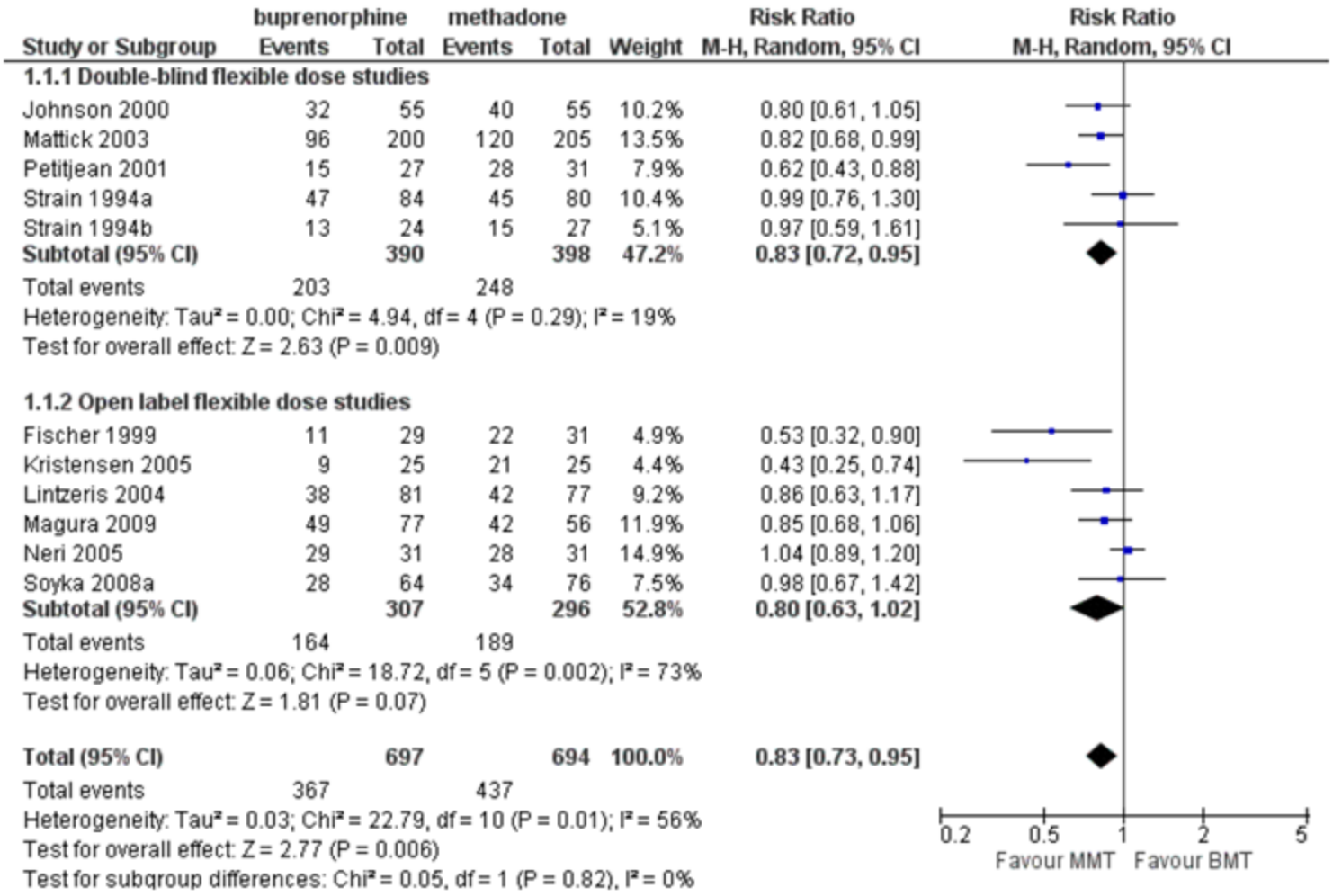
COMPARATIVE EFFECTIVENESS OF MANAGEMENT OPTIONS FOR OPIOID DEPENDENCE

Suboxone vs. Methadone

- 2014 Cochrane review and meta-analysis (20 RCTs, ~2,800 patients)*
  - Patients in both treatment arms received identical levels of support services
  - No statistical differences in mortality, illicit opioid use, criminal activity
  - Better retention for methadone (52% vs. 63% at 3-12 months of follow-up; rate ratio=0.83; 95% CI=0.72, 0.95)

*Mattick, 2014 (Document CD002207)

Suboxone vs. Methadone



Study or Subgroup	buprenorphine Events	Total	methadone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Double-blind flexible dose studies						
Johnson 2000	32	55	40	55	10.2%	0.80 [0.61, 1.05]
Mattick 2003	96	200	120	205	13.5%	0.82 [0.68, 0.99]
Petitjean 2001	15	27	28	31	7.9%	0.62 [0.43, 0.88]
Strain 1994a	47	84	45	80	10.4%	0.99 [0.76, 1.30]
Strain 1994b	13	24	15	27	5.1%	0.97 [0.59, 1.61]
Subtotal (95% CI)		**390**		**398**	**47.2%**	**0.83 [0.72, 0.95]**
Total events	203		248			
Heterogeneity: Tau² = 0.00; Chi² = 4.94, df = 4 (P = 0.29); I² = 19%						
Test for overall effect: Z = 2.63 (P = 0.009)						
1.1.2 Open label flexible dose studies						
Fischer 1999	11	29	22	31	4.9%	0.53 [0.32, 0.90]
Kristensen 2005	9	25	21	25	4.4%	0.43 [0.25, 0.74]
Lintzeris 2004	38	81	42	77	9.2%	0.86 [0.63, 1.17]
Magura 2009	49	77	42	56	11.9%	0.85 [0.68, 1.06]
Neri 2005	29	31	28	31	14.9%	1.04 [0.89, 1.20]
Soyka 2008a	28	64	34	76	7.5%	0.98 [0.67, 1.42]
Subtotal (95% CI)		**307**		**296**	**52.8%**	**0.80 [0.63, 1.02]**
Total events	164		189			
Heterogeneity: Tau² = 0.06; Chi² = 18.72, df = 5 (P = 0.002); I² = 73%						
Test for overall effect: Z = 1.81 (P = 0.07)						
Total (95% CI)		**697**		**694**	**100.0%**	**0.83 [0.73, 0.95]**
Total events	367		437			
Heterogeneity: Tau² = 0.03; Chi² = 22.79, df = 10 (P = 0.01); I² = 56%						
Test for overall effect: Z = 2.77 (P = 0.006)						
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%						

*Mattick, 2014 (Document CD002207)

Suboxone vs. Methadone

- Single retrospective study of methadone vs. buprenorphine in 61 adolescents*:
  - Longer retention in treatment for methadone (mean 354 vs. 58 days, $p<.01$)

*Bell et al., Drug and Alcohol Review 2006

Naltrexone

- 2011 Cochrane review and meta-analysis (6 RCTs, ~400 patients)*
  - Oral naltrexone no better than placebo for any major outcome, including retention
- Buprenorphine superior to oral naltrexone in single 24-week RCT in 126 patients†:
  - Time in treatment (mean 117 vs. 84 days, p=.022)
  - Time w/o heroin use (mean 51 vs. 24 days, p=.028)

*Minozzi, 2011 (Document CD001333)

†Schottenfeld et al., Lancet 2008

Naltrexone

- No head-to-head comparisons of injectable, extended-release naltrexone (Vivitrol®) vs. oral naltrexone or any maintenance treatment
- Single, placebo-controlled RCT of 250 patients followed for 24 weeks*:
  - Better time in treatment vs. placebo (median 168 vs. 96 days, p=.004)
  - Higher rate of abstinence while in treatment (36% vs. 23%, p=.022)

*Krupitsky et al., Lancet 2011

DOSING AND DURATION CONSIDERATIONS

Dosing and Duration

- Higher doses of methadone and Suboxone associated with better outcomes
- Apparent thresholds beyond which outcomes no longer improve:
  - ~100 mg for methadone
  - 16-32 mg for Suboxone
- Expert input suggests that dosing remains individualized, and thresholds from older studies may no longer be applicable

Dosing and Duration

- Attempts to taper maintenance medication to abstinence have been largely unsuccessful
- Observational studies suggest that longer and gradual tapers have better chance for success
- Recent RCT of 3 Suboxone taper durations followed by oral naltrexone in 70 patients showed promise for 4-week taper*:
  - 50% abstinence in treatment after 12 weeks vs. 16% and 20% for 2- and 1-week tapers (p=.03)

*Sigmon et al., JAMA Psychiatry 2013

KEY PROGRAM COMPONENTS

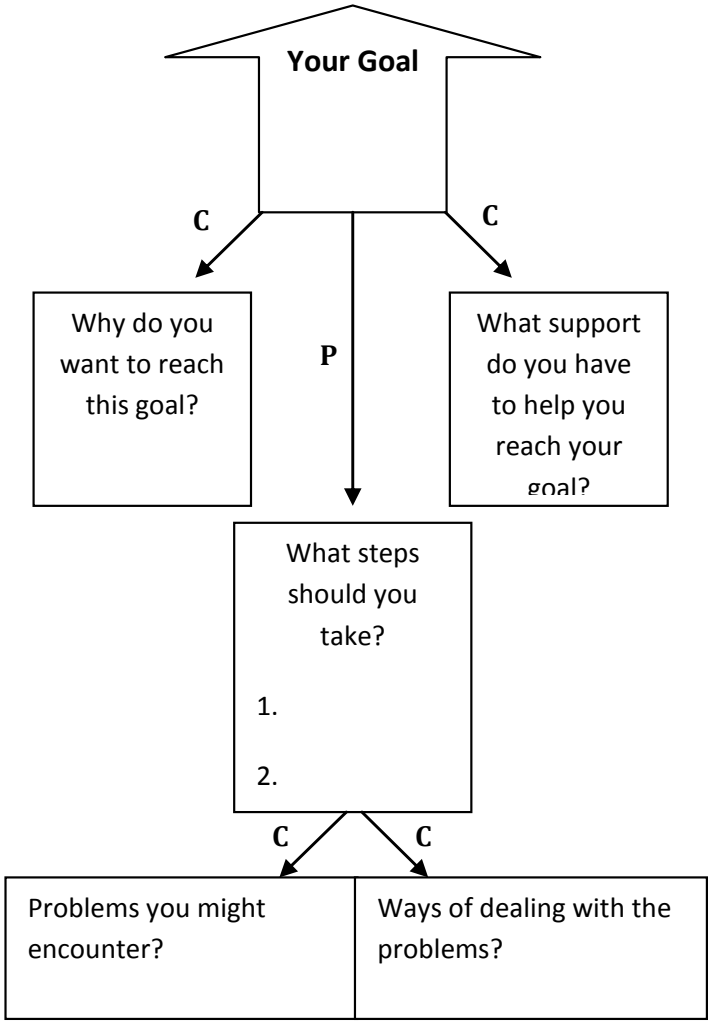
Program Components

- Positive incentives associated with better retention and more drug-free urine tests vs. standard care:
  - E.g., contingency vouchers for monetary payment, gift cards, etc.
- Negative incentives also associated with better retention and adherence to counseling, but not reduced opioid use:
  - E.g., mandatory dose tapers for missed appointments

Program Components

- Evidence is mixed on benefit of active, goal-oriented therapeutic approaches (e.g., cognitive-behavioral therapy):
  - Subpopulations more adherent to counseling schedules more likely to benefit
- Brief, clinician-led counseling may be sufficient in many circumstances
- Some evidence that visual guides to goal-setting and tracking may be effective

Visual Treatment Guide Example*



*Czuchry et al., J Psychoactive Drugs 2009

INNOVATIVE DELIVERY MODELS

Innovative Delivery Models

- Pilot studies of office-based take-home methadone dosing result in comparable or better outcomes vs. standard facility-based treatment
  - Conducted primarily in clinically-stable, employed patients with social supports
- Other pilot studies in more unstable patients showed comparable retention but greater levels of illicit opioid use and methadone diversion

Innovative Delivery Models

- Flexible approaches to Suboxone management also show comparable outcomes compared to facility-based treatment
- An RCT comparing facility-, office-, and group therapy-based Suboxone management in 94 patients showed better retention in the office and group therapy arms:*
  - Retention at 20 weeks: 21%, 33%, and 52% for facility, office, and group therapy arms (p=.05)

*Miotto et al., J Addict Med 2012

Innovative Delivery Models

- Alternative methods to deliver counseling appear to provide comparable effectiveness to in-person approaches, e.g.:
  - Telephonic coaching
  - Group therapy by videoconference
- Addition of specific interventions to increase employability appear to result in modest improvements in employment

ECONOMIC EVALUATION: COHORT MODEL

Cohort Model: Methods

- Purpose: to assess the comparative value of maintenance, taper-based, and abstinence-based treatment of opioid dependence
- Evaluated 2-year outcomes and in hypothetical cohorts of 1,000 patients
- Four possible outcomes:
  - In treatment
  - Out of treatment, drug free
  - Out of treatment, relapsed
  - Dead

Cohort Model: Methods

- Strategies:
  - Methadone maintenance
  - Suboxone maintenance
  - Suboxone 4-week taper to oral naltrexone
  - Suboxone 4-week taper to Vivitrol
  - Vivitrol alone after detox
  - Oral naltrexone alone after detox

Cohort Model: Methods

- Medical Costs:
  - Drug therapy for substance abuse
  - Other substance abuse services
  - All other healthcare services
- "Social" Costs:
  - Lost productivity
  - Law enforcement
  - Victimization (e.g., property damage, vandalism, injury-related expenses)

Cohort Model: Key Assumptions

Assumption	Rationale
Outcomes driven by initial treatment strategy only	*Lack of detailed, time-dependent data on therapy switch and/or readmission to treatment*
Competing mortality risks (beyond those related to in- vs. out-of-treatment status) not considered	*Unlikely to affect outcomes in short-term model*
Certain social costs (e.g., caregiver burden) not included	*Cost components consistent with other published economic evaluations*
Absolute increase in retention of 5% for taper to Vivitrol vs. oral naltrexone	*Assumption; no available data*
Rate of "drug-free" patients constant (modifiable only by differential rate of death)	*Counterintuitive to assume that higher rates of treatment "drop out" would translate to higher rates of drug-free individuals*
No benefit of methadone in reducing productivity loss	*Assumption that need for daily in-person dosing and intensive treatment would counteract any potential for improved employment*

Cohort Model: Results

Outcome/Cost	MMT	BMT	SUB/VIV Taper	SUB/Oral NTX Taper	Vivitrol Alone	Oral NTX Alone
Treatment outcome (per 1,000):						
In treatment	630	523	550	500	416	277
Relapsed	185	292	265	315	400	538
Drug –free	177	176	177	176	173	169
Died	8	9	8	9	12	16
Cost ($, per patient):						
Drug therapy	699	3,655	8,553	1,249	6,585	665
Other SA services	14,017	7,043	4,146	4,297	2,985	2,446
Other health care	23,926	25,993	25,454	26,441	28,109	30,844
SUBTOTAL	***38,642***	***36,691***	***38,153***	***31,988***	***37,679***	***33,954***
Social costs	92,068	102,337	98,033	105,917	119,239	141,076
TOTAL	***130,710***	***139,028***	***136,187***	***137,905***	***156,918***	***175,030***

Cohort Model: Results

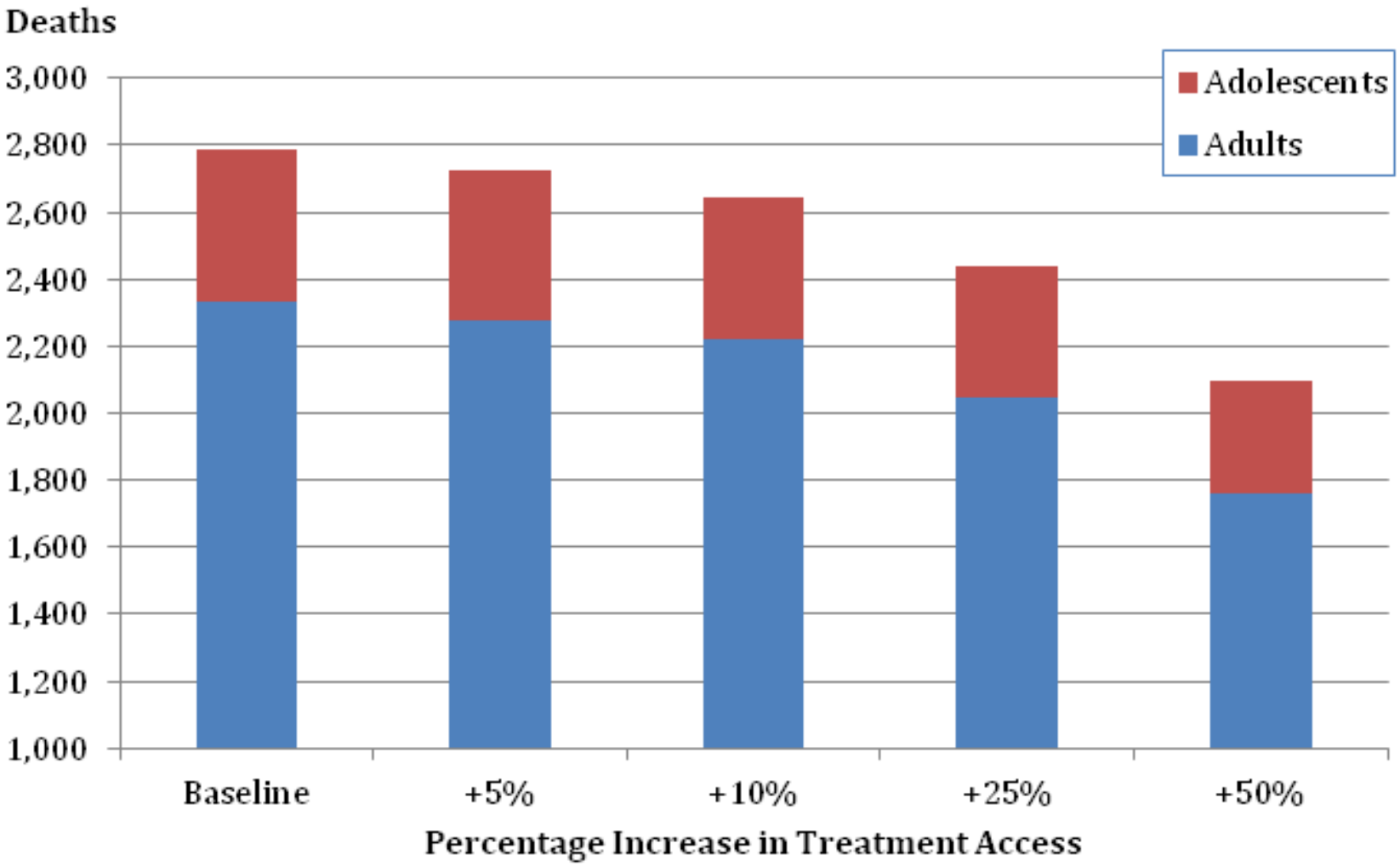
- Cost (healthcare only) per relapse averted:
  - $11,000-$15,000 for maintenance/taper approaches vs. oral naltrexone
  - $18,000 for methadone vs. Suboxone
  - Levels <$50,000 considered cost-effective in other evaluations of mental health interventions
- Cost per death averted very high in all comparisons
- When total costs considered, all other treatment options less costly and more effective than oral naltrexone

ECONOMIC EVALUATION: POPULATION BUDGET IMPACT

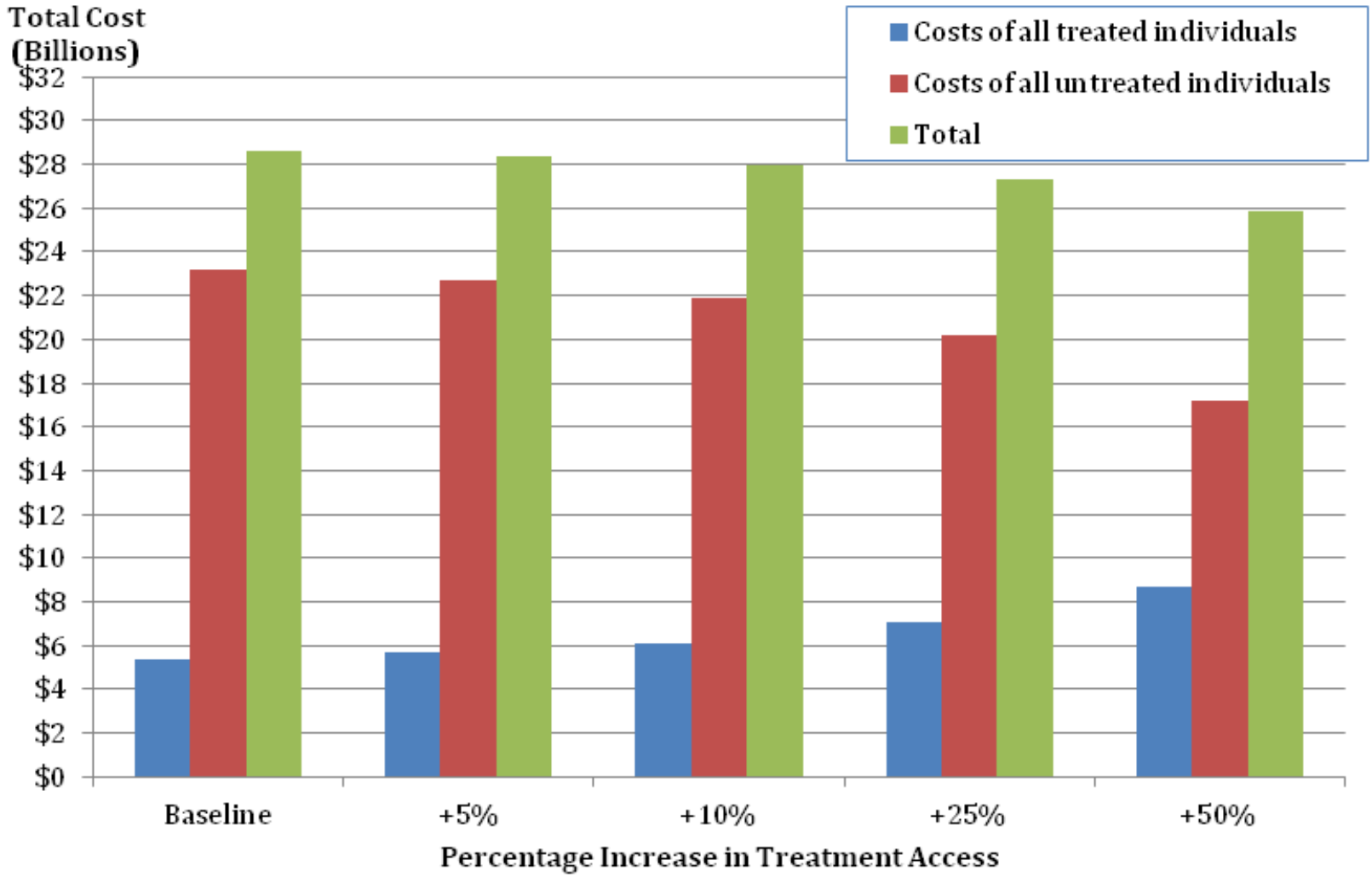
Budget Impact Model: Methods

- Numbers of opioid-dependent persons estimated from state-based SAMHSA survey data:
  - Stratified by whether in vs. out of treatment
- Two-year estimates of substance abuse-related deaths, health care costs, and total costs
- Evaluation of change in numbers of deaths and costs associated with moving alternative numbers of patients into Suboxone maintenance

Budget Impact Model: Substance Abuse-Related Deaths over 2 Years



Budget Impact Model: Change in Total Costs over 2 Years



CLINICAL GUIDELINES

Clinical Guidelines

- ASAM, AATOD, APA, NIDA, SAMHSA, AMCP
- Methadone considered underutilized, some enthusiasm for office-based expansion
  - Cautionary language regarding abuse potential
- Support for Suboxone based on comparable performance, potential for increased access, and lower abuse potential
- Naltrexone recommended for motivated individuals participating in ancillary support services
  - Liver function testing recommended for Vivitrol

COVERAGE POLICIES

Coverage Policies

- No major restrictions on methadone coverage
- Limits on Suboxone use:
  - Dose (16 mg/day): MA, ME, VT Medicaid, BCBSMA
  - Duration (24 mo): ME
  - Monthly quantity limits (30-90 tab equivalent) by many regional and national payers
  - Enrollment in ancillary services for many regional and national payers
- Vivitrol limits:
  - Fail-first on oral naltrexone: ME Medicaid, Anthem/Wellpoint
  - 3-6-month initial treatment authorization: VT Medicaid, ConnectiCare

VHA PBM Formulary Guidance and Mental Health Services Package

- Patient suitability for OBOT or OTP care setting determined by the patient's:
  - existing psychosocial supports
  - co-occuring psychiatric disorders
  - dependence on depressants
  - previous success/failed attempts with opiod agonists
  - expected compliance with treatment
  - co-occuring pain syndrome
- MAT: treatment with buprenorphine or methadone must be available to all patients with opioid dependence, and must be considered as part of treatment plan for all such patients
- MAT must be provided in conjunction with psychosocial supportive services

PUBLIC COMMENTS

Public Comments

- Dosing: improved outcomes with higher doses for methadone and buprenorphine than the standards outlined in the report
- Additional barriers to treatment:
  - Arbitrary restrictions from treatment programs (e.g. strict entry criteria)
  - Underinsurance of maintenance therapy, expensive co-pays
  - Dosage and treatment duration limits from payers
- Legislative updates in Vermont: Jail diversion, prescription monitoring, treatment requirements for MAT, etc.
- Support for MAT as a first-line treatment approach based on demonstrated effectiveness and value