

Treatments of substance use disorders in medical settings

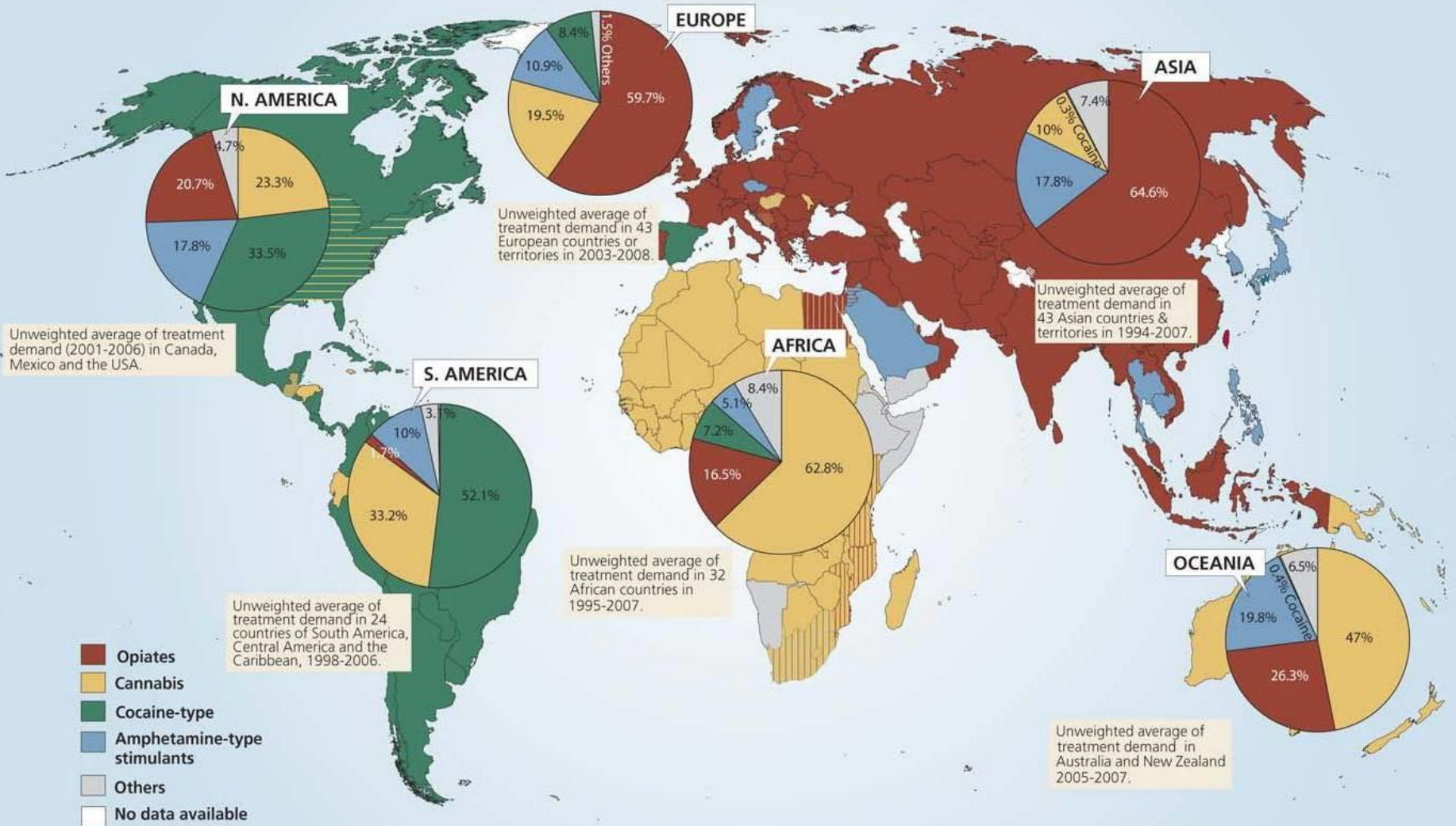
Marek C. Chawarski, Ph.D.

Yale University School of Medicine

Outline

- Epidemiological trends in illicit drug use in Asia
- Opportunities and challenges related to recent changes in health care policies in Asia
- The role of psychosocial interventions substance abuse treatments
- Research on developing medically oriented treatments for substance abuse or dependence disorders
- Advantages of medical treatments over criminal approaches

Treatment demand by type of drug



Note: Data generally account for primary drug use; therefore polydrug use may increase totals beyond 100%.

Sources: UNODC, Annual Reports Questionnaire Data/DELTA and National Government Reports.

Injection of heroin and HIV in Asia

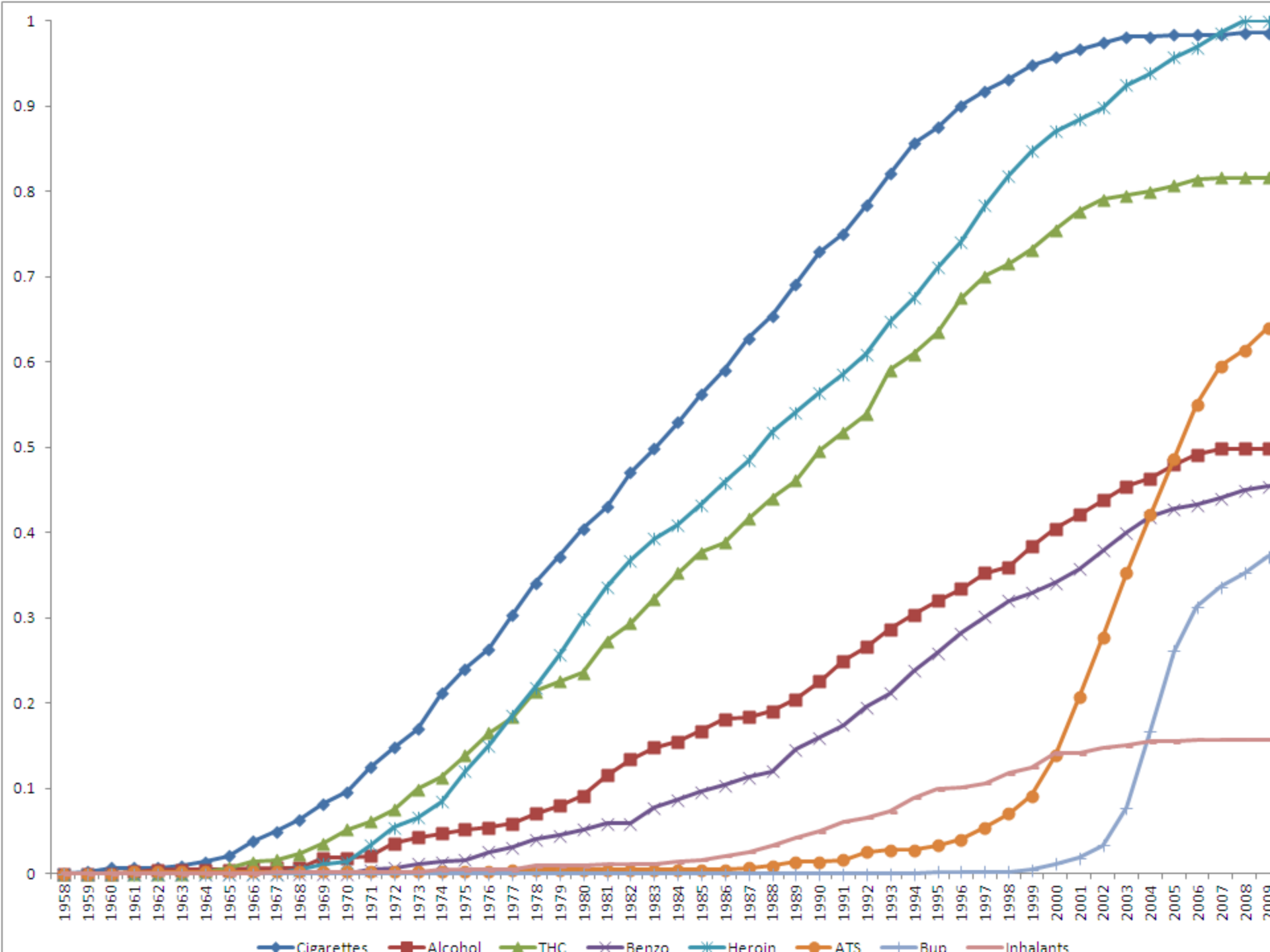
Figure 2: HIV Prevalence & Incidence by Region^{1,2}

Region	Total No. (%) Living with HIV end of 2009	Newly Infected in 2009	Adult Prevalence Rate (15–49), 2009
Global Total	33.3 million (100%)	2.6 million	0.8%
Sub-Saharan Africa	22.5 million (68%)	1.8 million	5.0%
South/South-East Asia	4.1 million (12%)	270,000	0.3%
North America	1.5 million (5%)	70,000	0.5%
Eastern Europe/Central Asia	1.4 million (4%)	130,000	0.8%
Central/South America	1.4 million (4%)	92,000	0.5%
Western/Central Europe	820,000 (2%)	31,000	0.2%
East Asia	770,000 (2%)	82,000	0.1%
Middle East/North Africa	460,000 (1%)	75,000	0.2%
Caribbean	240,000 (0.7%)	17,000	1.0%
Oceania	57,000 (0.2%)	4,500	0.3%

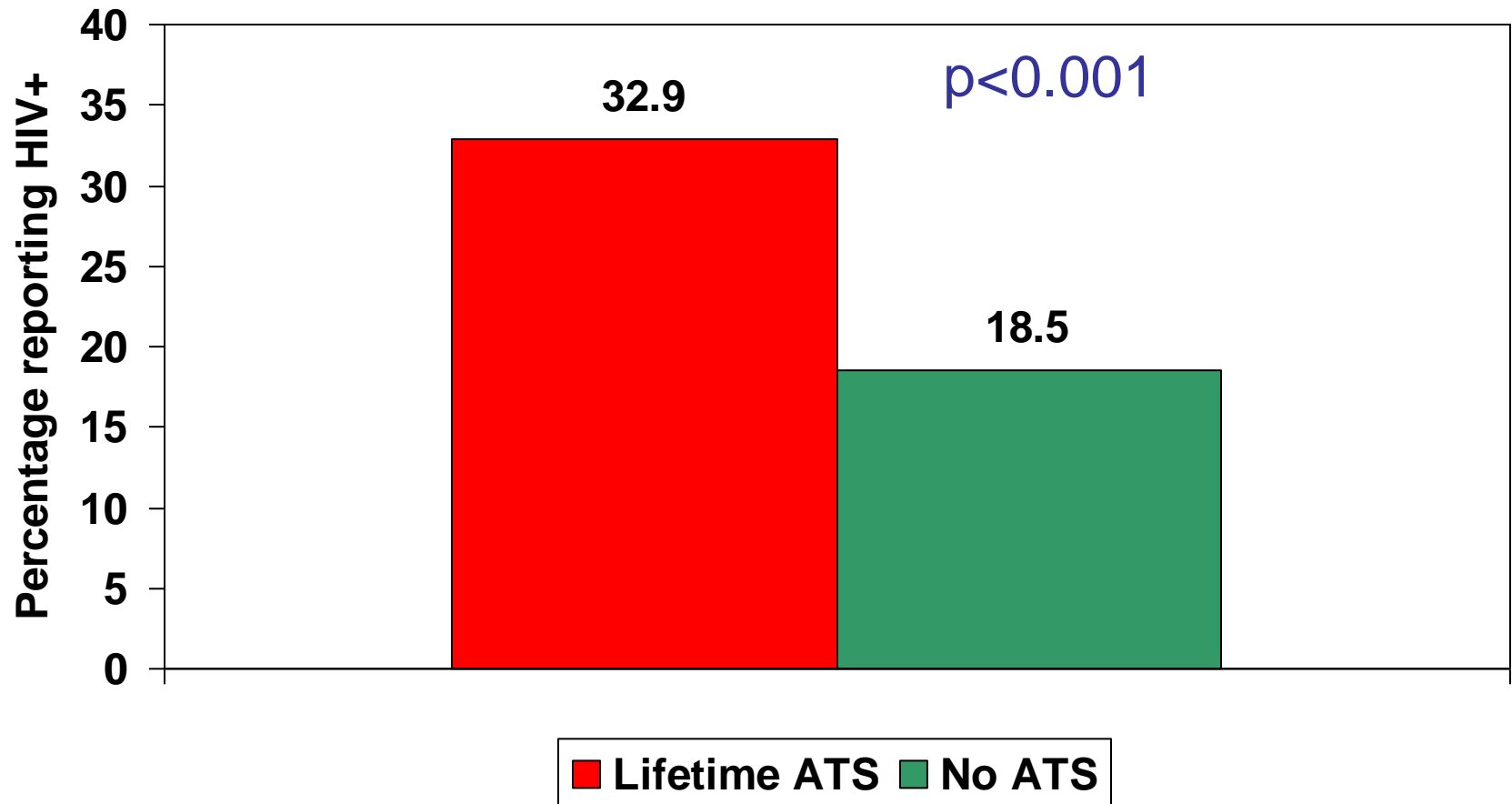
Surveys of active drug abusers in Malaysia

- Between 2006 and 2008 we conducted a series of surveys among not-in-treatment injection drug users in three cities in Malaysia (Penang, Kuala Lumpur, and Johor Bharu)
 - 1st survey: October - November 2006
 - 2nd survey: June - September 2006
 - 3rd survey: January - March 2008 (wave 1) and October 2008 - March 2009 (wave 2)
- A total of 732 IDUs were surveyed
 - 680 males and 53 females
- Participants were recruited in neighborhoods with high concentration of drug use (e.g., shooting galleries, needle and syringe exchange programs)
- Collected information included demographics, drug use history and current patterns of use, self-reported HIV status, behavioral risks, and urine toxicology screens





ATS abuse and HIV status







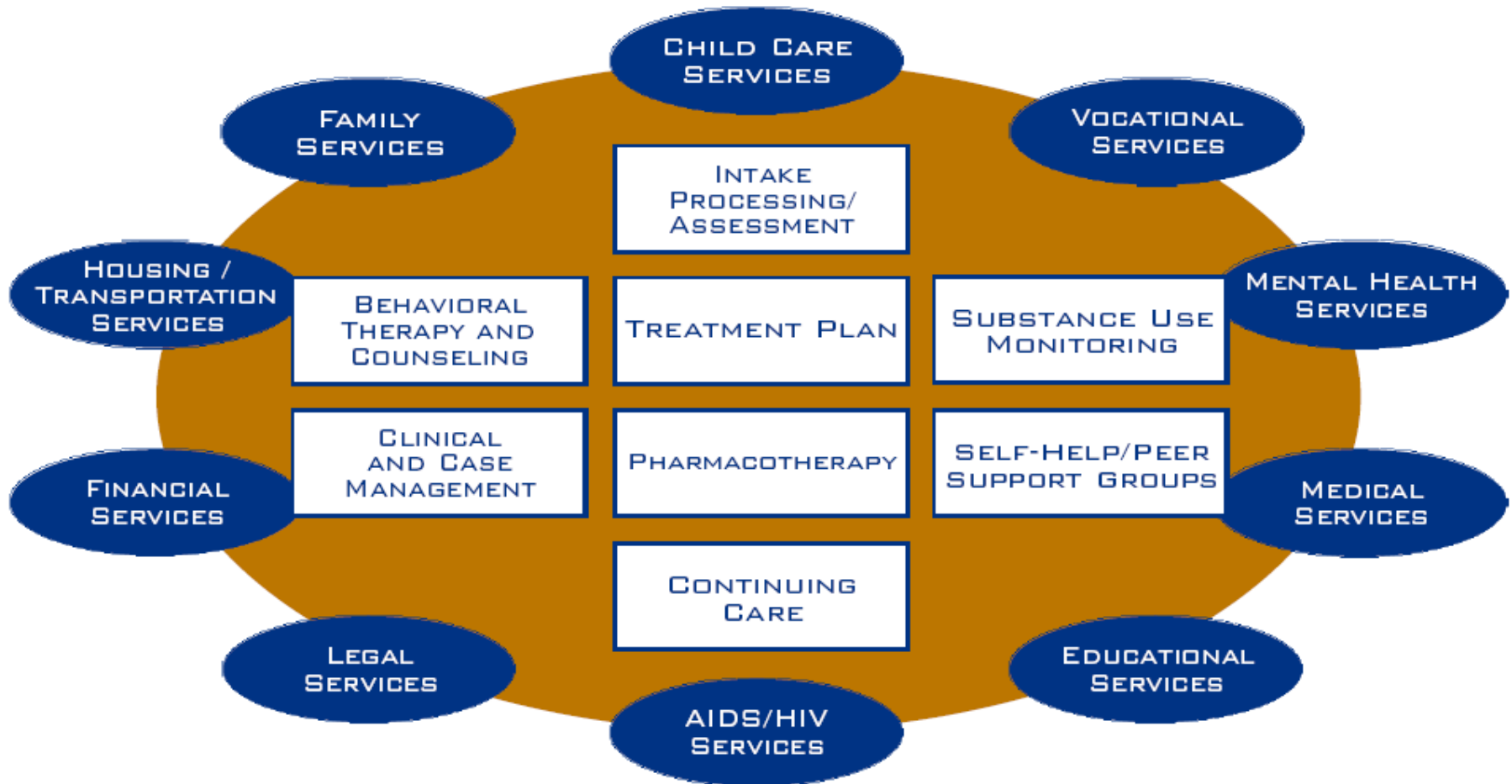
LIFE

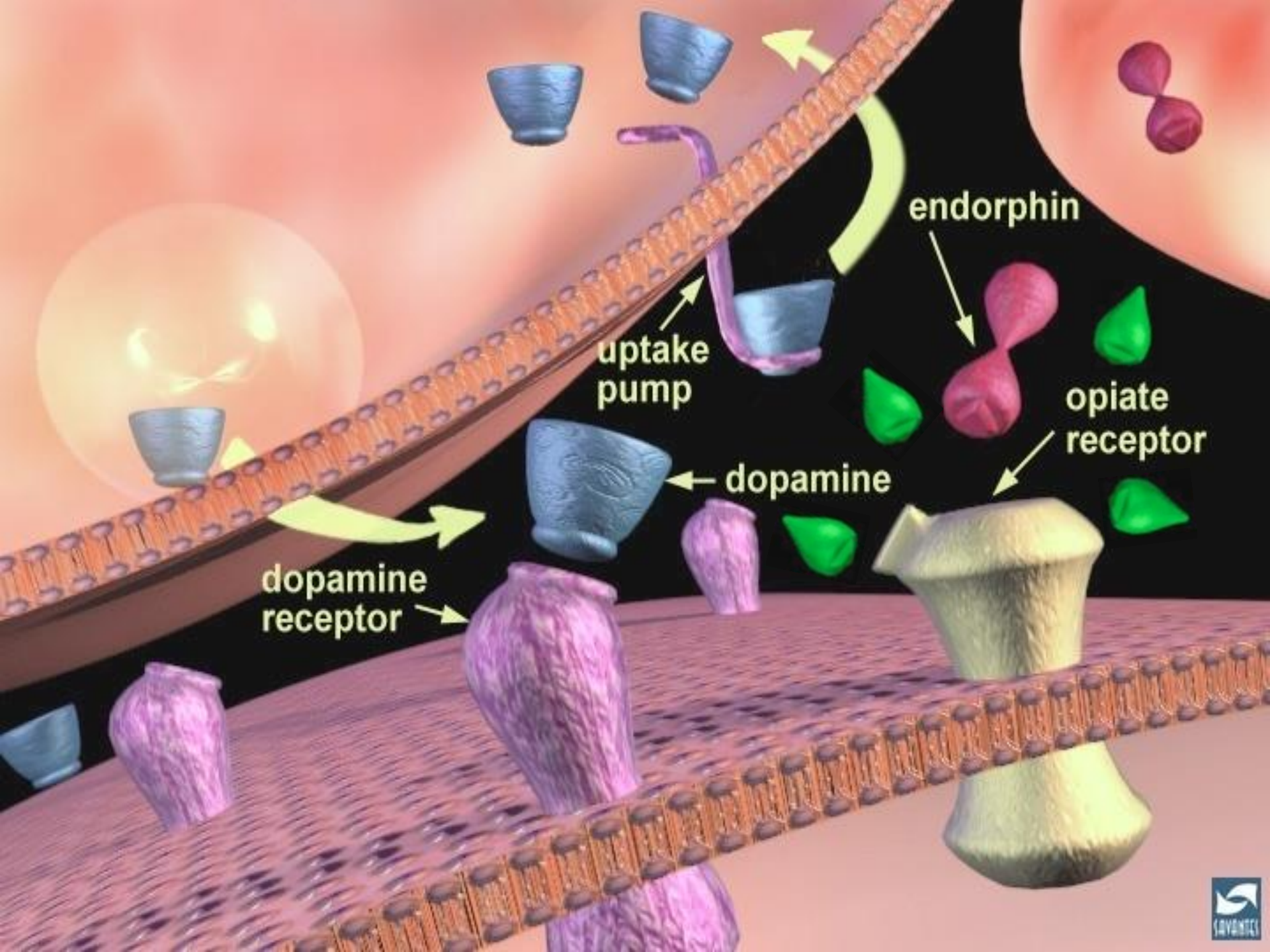
Failure of criminal approaches

- Criminalization of drug use, penitentiary type prevention/treatment efforts, and supply/demand reduction efforts failed to curtail escalation of drug abuse and related problems in Asia
- Rapid increase of HIV infections in the 1990s, fuelled by injection drug use, prompted many countries in Asia to revise and expand their approaches and policies toward substance abuse problems
- Despite initially strong opposition against medical treatments for drug abuse problems in many Asian countries, based on social, cultural, and religious grounds, the failure of primarily criminal approaches opened doors for the introduction of medically based treatments for drug abuse or dependence disorders
- Currently, many countries in Asia utilize a dual approach combining both criminal/penitentiary approaches and medical treatments

A “Cadillac” drug treatment program

Components of Comprehensive Drug Abuse Treatment





endorphin

uptake pump

dopamine

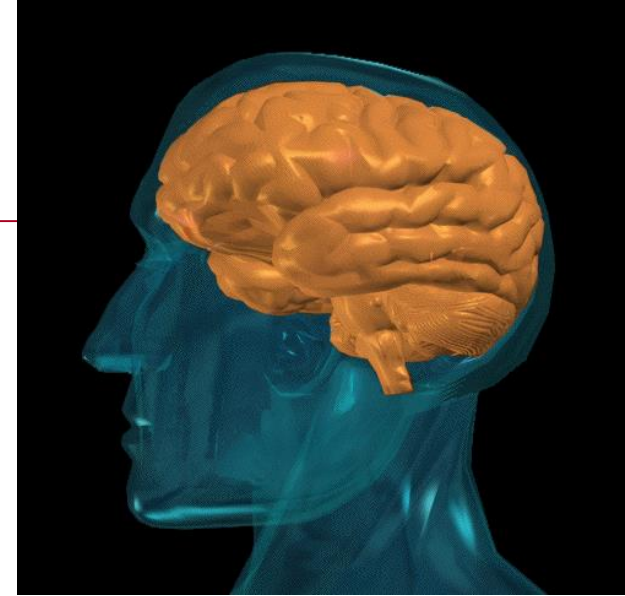
opiate receptor

dopamine receptor

Drug use behaviors = disease symptoms

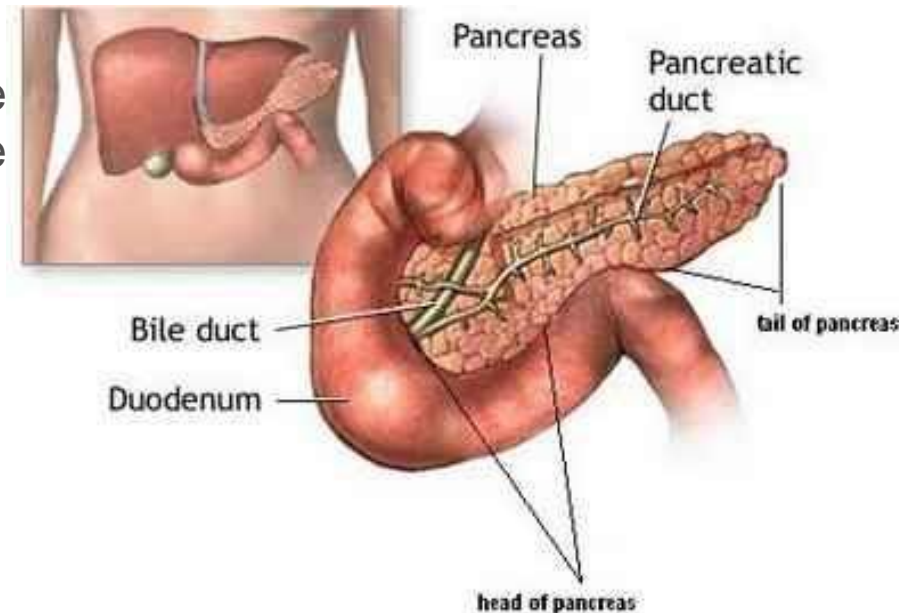
Medical perspective

- Drug use results in dysregulation of important brain functions leading to
 - Preoccupation with drugs, cravings
 - Continued use despite adverse effects
 - Loss of control - compulsive use, inability to stop or abstain, use more than intended or when didn't intend to use
- Prolonged drug use can cause physiologic dependence
 - Tolerance
 - Withdrawal after abstaining
- A simplified, medical model, with the health care professional (doctor, therapist, or counselor) as an expert who provides the 'patient' with diagnosis, prophylaxis, prognosis and cure, offers a compelling treatment conceptualization for effective recovery from the disease of opiate dependence



A “Toyota” drug treatment program

- Taking medications to reduce/stabilize symptoms of the disease; discontinuing exposure to harmful effects of illicit substances
- Monitoring of treatment progress or for symptoms recurrence/worsening
 - Frequent urine testing
 - Ongoing visits with medical professionals to monitor treatment progress and to adjust or change treatment as necessary
- Lifestyle changes
 - Changing daily behavioral patterns and activity levels to adopt a lifestyle supportive of prolonged recovery
 - Avoiding situations that can increase likelihood of symptoms reoccurrence
- Outpatient treatment
 - Active involvement of the patient in his/her own treatment
 - Support from the family, friends, or society of the patient’s recovery efforts

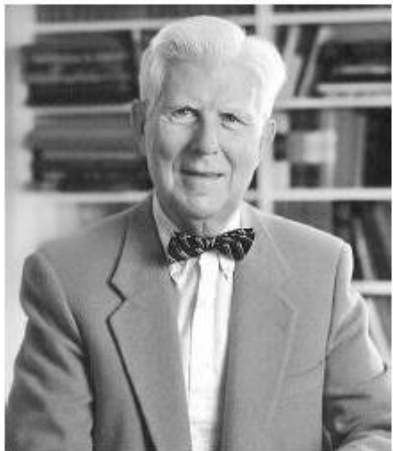


Behavioral Drug and HIV Risk Reduction Counseling (BDRC)

- BDRC is an integrated drug abuse and HIV risk reduction behavioral intervention premised on social learning theory
 - uses small-step/small-success approach to implementing behavioral changes aimed at engaging patients in rewarding activities and interactions that are unrelated to or incompatible with drug use
- BDRC educates patients about the disease of opiate dependence, and the effective medical treatments for this disease
 - to improve their treatment engagement and compliance, to improve their knowledge and coping skills, and to increase their involvement in activities alternative to drug use
- Focuses on a limited number of problem areas immediately related to drug use
 - offers a prescriptive approach for addressing these problems with short-term goal-setting and behavioral contracts
- Delivered by nursing or other medical personnel who do not have advanced training in psychology or social work
 - particularly suitable for settings where trained and experienced therapists are not available

Foundations of BDRC

- Cognitive Behavioral Therapy (or cognitive behavior therapy, CBT) pioneered by Aaron Temkin Beck (born 1921) and Albert Ellis (1913 – 2007)
 - CBT is an umbrella term for therapies that share a theoretical basis in learning theories and cognitive psychology and use methods of change derived from these theories
- Social Learning Theory and the concept of self-efficacy originated by Albert Bandura (born 1925)
- Locus of control concept proposed by Julian Rotter (born 22 October 1916)



BDRC features

- Individualized, educational, directive, and prescriptive
- Medically oriented
 - Medical understanding of the disease of opiate dependence
 - Medical approach to recovery
- Uses short-term behavioral contracts aimed at improving treatment adherence and getting patients to make initial lifestyle changes, including
 - Cessation/reduction of drug use
 - Cessation/reduction of drug- and sex-related risk behaviors
- Provides immediate feedback and positive reinforcement of patient progress
 - Positively- or gain-framed health promotion messages increase the likelihood of patient adherence to treatment recommendations and engagement in recommended/prescribed behavioral change
- Links the initial treatment gains with long-term recovery goals

Study overview – Muar, Malaysia

- **Specific aims**

- To evaluate whether the efficacy of Physician Management (PM) and non-contingent, one-week supplies of take-home buprenorphine (Standard BUP) is improved by providing additional manual-guided behavioral drug and HIV risk reduction counseling (BDRC) with abstinence-contingent take-home buprenorphine (ACB)

- **Methods**

- 16 week pilot randomized clinical trial enrolling treatment seeking heroin-dependent volunteers (N=26) conducted in Muar, Malaysia

- **Primary outcomes**

- Retention
- Proportion of opioid positive urine tests (at least weekly) and days per week of self-reported drug use
- HIV risk behaviors assessed by AIDS Risk Inventory (ARI) administered at baseline and treatment completion

Study design

- Standard buprenorphine induction protocol
- Random assignment to
 - Non-contingent weekly take-home doses (PM+Standard BUP) or
 - Abstinence-contingent take-home doses (BDRC+ACB) with additional weekly Behavioral Drug and Risk Reduction Counseling (BDRC)
- All study participants received buprenorphine mono tablets (Subutex), ~ 12 mg daily
- All participants received Physician Management (PM)

Abstinence-contingent dosing

- All participants in BDRC+ACB group initially received directly observed medications
- Based on documented abstinence (rapid urine tests) at any time during treatment, the BDRC+ACB group received take-home doses
 - Amount of take-home supply escalating from one day to one week if continuously abstinent
- Participants testing opioid positive reverted to directly observed doses (3 times per week dosing) until documented abstinence

BDRC counseling

- Participants in the BDRC+ACB group received weekly manual-based BDRC individual counseling (45-60 minutes) provided by trained drug counselors
- Counseling fidelity and counselor adherence to the manual monitored via biweekly supervision sessions with BDRC manual author (MCC)
- BDRC counseling targeted
 - Treatment adherence (both to medication regimen and psychosocial interventions)
 - Reduction/cessation of drug use
 - Drug-and sex related risks for HIV or other infections
 - Behavioral changes necessary to achieve and maintain drug abstinence
- BDRC counselors linked progress made in treatment with longer term recovery goals

BDRC counselors

- 3 nurse counselors with 5 years of drug counseling experience trained to provide BDRC
 - BDRC training included
 - Didactic workshops
 - Case conferences
 - 3 or more closely supervised practice cases
- Ongoing bi-weekly supervision with the study PI

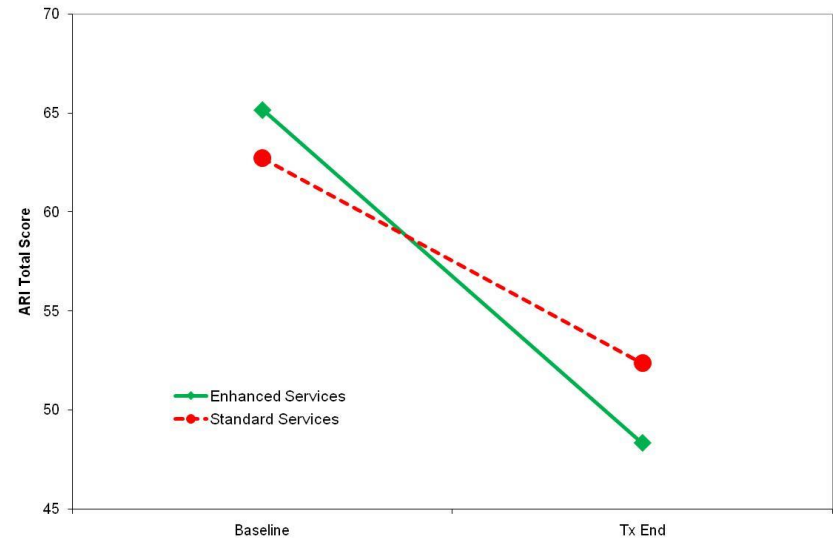
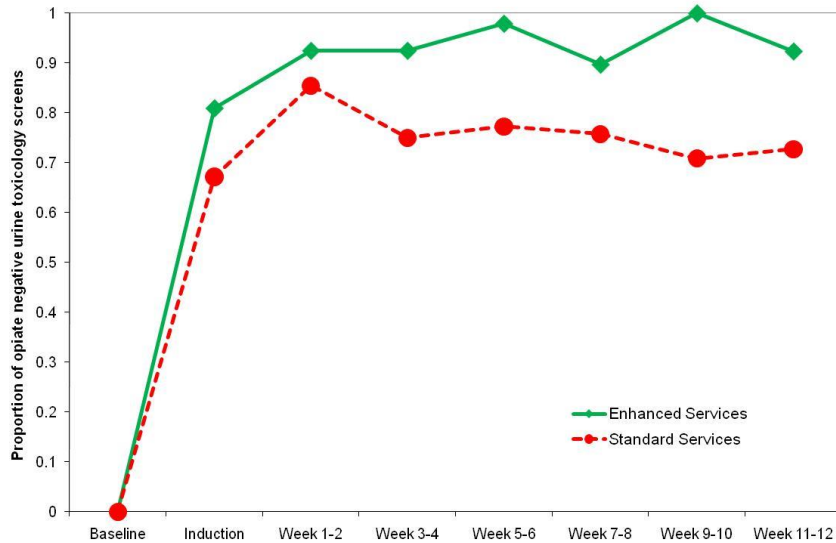
Physician Management (PM)

- The first visit lasted 45 minutes, followed by weekly 10-12 minute visits
- Intervention focused on medication adherence, medication efficacy, and potential side effects
- Urine toxicology results reviewed at each visit and brief advice given on how to become or remain abstinent
- Provided by general practitioner with 3 years of experience in treating substance abuse patients

Sample characteristics (N=26), Muar

Age – Mean (SD)	39.9 (8.6)
Male	24/26 (92%)
Years of opiate use – Mean (SD)	18.8 (8.6)
Days of opiate use in the past 30 – Mean (SD)	24 (8.9)
Lifetime IDU	18/26 (69%)
Current IDU (past 30 days)	10/26 (38%)
Lifetime needle sharing	14/26 (54%)
Current needle sharing (past 30 days)	11/26 (42%)
Multiple concurrent sex partners (lifetime)	4/26 (15%)
Consistent condom use	1/26 (4%)
Lifetime ATS abuse	20/26 (77%)
Lifetime benzodiazepine abuse	13/26 (50%)
Lifetime marijuana abuse	22/26 (85%)
Unemployed	4/26 (15%)
Less than 9 years of education	20/26 (77%)
Single	19/26 (73%)

Summary of findings, Muar pilot



- Both groups reduced illicit opiate use during treatment ($F(7, 154)=38.1, p<0.001$); reductions were significantly larger in the BDRC+ACB group than in the PM+Standard BUP group ($F(1, 22)=5.0, p<0.05$)
- Both groups significantly reduced HIV risk behaviors during treatment as compared to pre-treatment assessment ($F(1, 22)=11.4, p<0.05$)
 - Reductions in HIV risks were larger in the BDRC+ACB group than in the PM+Standard group (27% vs. 16% reductions from the baseline levels, respectively) but these differences did not reach statistical significance ($p=0.87$)

Study overview – Wuhan, China

- **Methadone dosing**

- All study participants received methadone doses from their MMT programs, following the standard dosing protocols in the MMT programs in Wuhan
- The average daily dose of methadone was 45 mg; all doses were dispensed at the clinics under the direct observation of the clinic staff

- **Medical and psychosocial services**

- During MMT treatment, patients may schedule brief visits with a physician, nurse, or a counselor on an “as needed” basis to address concerns or a crisis
- Participants assigned to MMT+BDRC also received weekly, manual-guided BDRC in individual sessions lasting 45-60 minutes

- **Primary outcomes**

- Opiate use based on urine tests
- HIV risk behaviors (self-report using AIDS Risk Inventory, a structured interview)

Study participants, Wuhan

- Treatment seeking volunteers eligible for and entering methadone maintenance treatment (MMT) were enrolled after providing informed, voluntary consent
 - All individuals eligible for MMT were also eligible to participate in the study
 - 86 individuals expressed interest in study participation; 54 completed the screening process; 9 were excluded because of their imminent plans to move in search of a new job
 - 45 individuals signed informed consent and were enrolled into the protocol
 - The first 8 study participants, 4 at each MMT clinic, 2 for each counselor, were training cases assigned to MMT+BDRC condition in order to give the nurse counselors opportunity to continue improving their mastery of the newly learned BDRC intervention
 - The remaining 37 participants were randomly assigned to either Standard MMT (n=17) or MMT+BDRC (n=20) using a simple randomization procedure

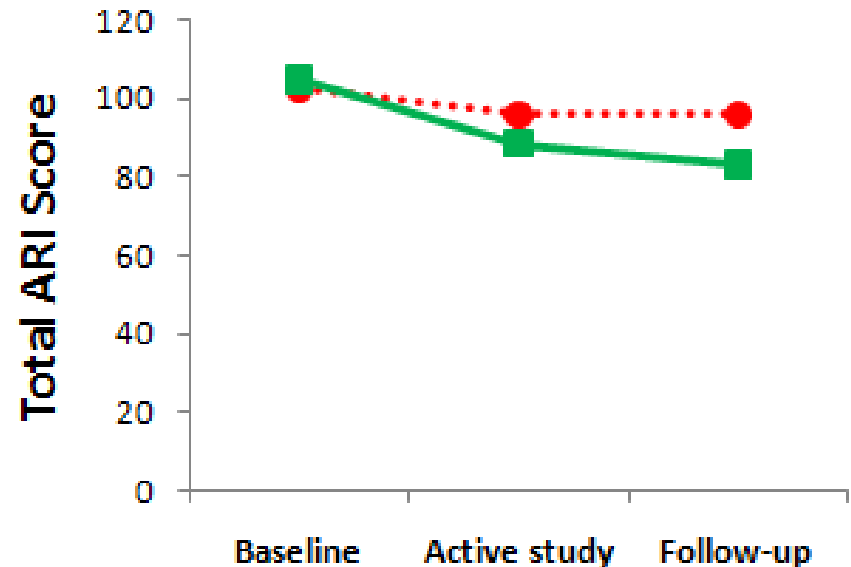
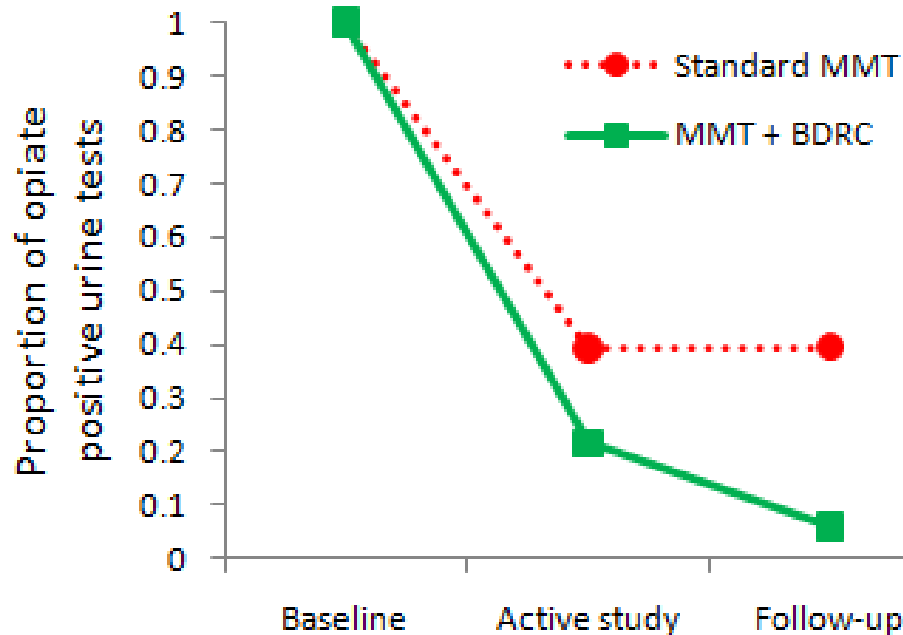
BDRC counselors

- 4 nurse counselors from two MMT clinics in Wuhan, China
 - All with minimal prior drug counseling experience
- BDRC training included
 - A didactic workshop
 - 2 supervised practice cases
 - Ongoing supervision
 - Case conferences (video or phone teleconferences)
 - Occasional face-to-face supervisory discussions with the study PI

Randomized sample (N=37), Wuhan

Baseline Characteristics	MMT (n=17)	MMT+BDRC (n=20)
Age	37.0 (7.5)	36.4 (7.0)
Males	15 (88%)	15 (75%)
Education less than high school	12 (71%)	18 (90%)
Unemployed	8 (47%)	15 (75%)
Married	6 (35%)	7 (35%)
IDU	15 (88%)	14 (70%)

Summary of findings, Wuhan pilot



- Both groups significantly reduced HIV risk behaviors ($p < 0.001$) and the reductions were significantly greater for the MMT+BDRC group than for the Standard MMT group ($p < 0.05$)
- The overall proportion of opiate-positive urine tests was significantly lower in the MMT+BDRC group than in the Standard MMT group during both in the 3 month active phase of study protocol and during the follow up ($p < 0.001$)

Current RTC in Wuhan

- **Specific aim:** To compare the efficacy of MMT combined with one of three manual-guided counseling approaches
 - Behavioral Drug and HIV Risk Reduction Counseling (BDRC)
 - Educational Counseling (EC)
 - Counseling approximating what is provided as treatment as usual (TAU) in China
- **Participants**
 - 300 treatment seeking volunteers entering MMT in Wuhan, randomly assigned to one of 3 randomization groups (above)
- **Study interventions**
 - 4 months of active treatment and 6 months of follow-up
- **Primary outcomes**
 - Reduction of drug- and sex-related HIV risk behaviors
 - Reduction of frequency of heroin or other illicit opiate use, and duration of opiate abstinence
- **Secondary outcomes**
 - Treatment retention
 - Reductions in other illicit drug use
 - Improvements of functional status of MMT patients

Educational Counseling (EC)

- EC uses a **didactic** lecture-discussion format to **educate/inform** the patient about core concepts/topics related to the disease of opiate dependence and successful recovery
- The content of EC sessions **closely matches the content/scope of the BDRC** educational components (focusing on HIV and other blood borne and infectious diseases, opiate dependence and its treatment)
- EC is **not individualized**, does not include or require extensive evaluation of the individual participant's problems, does not include development of an individualized treatment plan, does not make use of behavioral contracts, and does not include extensive feedback and evaluation of the participant's progress by the counselor

HPTN#058 in Thailand and China

- The HIV Prevention Trials Network (HPTN) protocol #058, “A Phase III randomized controlled trial to evaluate the efficacy of drug treatment in prevention of HIV infection among opiate dependent injectors,”
 - PI: Dr. David S. Metzger, University of Pennsylvania
- Primary Aim
 - To assess the efficacy of drug treatment in reducing the incidence of HIV infection among heroin injectors; primary outcome: **HIV seroconversion**
- Secondary Aim
 - To assess frequency of drug use, risk behaviors, and mortality
- Study Population
 - HIV negative opiate dependent injectors in Thailand and China (N=1400)
- Study Interventions
 - Long-term (1 year) Suboxone maintenance (n=700)
 - 3x/week, directly observed ingestion at the study clinics
 - Short-term (~20 days) Suboxone taper (repeated at 6 months if needed/wanted) (n=700)
 - 3x/week, directly observed ingestion at the study clinics
 - BDRC once per week during the first three months and monthly thereafter (1 year total) for all study participants in individual counseling sessions 45-60 minutes long

HPTN#058 in Thailand and China

- Study Sites
 - Chiang Mai, Thailand
 - Nanning and HengXian in Guangxi province, China
 - Urumqi, Xinjiang province, China
- BDRC Counselors
 - Nurses, drug counselors, other medical and non-medical personnel (social-workers, outreach workers, educators)
 - Minimal training and experience in provision of psychosocial or behavioral interventions for drug abusing patients
 - Training involved multiday didactic workshops, case presentations/review, educational video training sessions, supervised practice cases, ongoing re-training and supervision via monthly conference calls and study site visits
- Study has been closed to enrollment of new patients
 - No preliminary results are yet available

BDRC in MMT programs in Jakarta, Indonesia

- Primary Aim
 - To evaluate the efficacy of BDRC on retention in methadone treatment, reductions of illicit drug use, and reductions in the use of contaminated injection equipment
- Secondary Aims
 - To evaluate the costs of BDRC and relate these costs to its measured benefits
 - To assess and monitor HIV prevalence and incidence rates in the study sample
- Study Population
 - Opiate dependent individuals entering MMT clinics in Jakarta, Indonesia (N=300)
- Study Interventions
 - Treatment as usual (TAU): standard MMT with minimal counseling
 - MMT with BDRC counseling once every two weeks during the first six months and monthly thereafter (one year total)

Summary

- The results of pilot randomized clinical trials support the feasibility and potential efficacy of providing behavioral drug and HIV risk reduction counseling (BDRC) in OMT programs in Malaysia, China, or elsewhere in Asia
 - HIV risk behaviors and illicit opiate use decreased at greater rates for patients who were provided BDRC in addition to standard drug treatment services
- With its focus on a limited number of problem areas, prescriptive approach for addressing specific problems with short-term goal-setting and behavioral contracts, and efficacy when provided by nursing or other trained medical personnel who do not have advanced training in psychology or social work, BDRC seems particularly suitable for settings masters or doctoral level therapists are not available

Criminal vs. medical perspective

- Criminal approaches and penitentiary type prevention/treatment efforts failed to curtail the escalation of drug abuse and related problems (e.g., HIV/AIDS) in Asia
- Extensive scientific research supports a simplified medical perspective on drug abuse that reduces stigmatization of the problem and offers a straightforward medically-based treatment
- Medication assisted treatments (MAT) for drug abuse/dependence disorders
 - Greatly improved efficacy
 - Marked reductions in illicit drug use
 - Marked reductions in criminal activity
 - Dramatic reductions in mortality rates
 - Decreased incidence of HIV infection
 - Improvements in overall health status
 - Acceptable and liked by patients
 - No long-term adverse health effects

Summary

- Drugs alter critical neurochemical processes in the brain resulting in dysregulation of important brain functions and the development of the disease of opiate dependence
- Substance abuse/dependence disorder is a chronic medical condition with high risk of persistence, relapse and recurrence, similar to diabetes, hypertension or other chronic medical disorders
- A medical conceptualization of substance abuse or dependence disorder and the corresponding medical treatment model reduces the stigmatization and increases the likelihood of engaging the patient in an active recovery process leading to sustained abstinence and full rehabilitation from drugs