OVERVIEW

• Addiction is a serious, chronic, relapsing disorder for which multiple evidence based treatments are available.

• Medications should be considered as part of a comprehensive treatment plan, addressing both disordered physiology and disrupted lives.

• Medications should be considered for treatment of: psychiatric sx’s, addictive d/o’s, and co-occurring d/o’s.

• Emerging literature supports use of meds in youth with SUDS and psychiatric comorbidity.
A PRIMER ON THE TREATMENT OF SUBSTANCE USE DISORDERS

PRESENTED BY:

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ADDICTION IS A BRAIN DISEASE
ASAM
“SHORT” DEFINITION OF ADDICTION

• ...A PRIMARY, CHRONIC, RELAPSING DISEASE OF BRAIN REWARD, MOTIVATION, MEMORY AND RELATED CIRCUITRY. DYSFUNCTION IN THESE CIRCUITS LEADS TO CHARACTERISTIC BIOLOGICAL, PSYCHOLOGICAL, SOCIAL AND SPIRITUAL MANIFESTATIONS. THIS IS REFLECTED IN AN INDIVIDUAL PATHOLOGICALLY PURSING REWARD AND/OR RELIEF BY SUBSTANCE USE AND OTHER BEHAVIORS
WHY DO WE CARE ABOUT ADDICTION?

• 1 OUT OF 7 INDIVIDUALS WILL HAVE A SERIOUS SUBSTANCE USE PROBLEM (13.5% LIFETIME PREVALENCE)

• 1 OUT OF 3 AMERICANS ARE DIRECTLY AFFECTED BY ADDICTION

• UP TO 50% OF ADMISSIONS TO THE ER ARE SUBSTANCE-RELATED

• ADDICTION IS A COMMON PROBLEM AMONG PHYSICIANS AND OTHER HEALTH CARE PROVIDERS
Drug Deaths in America Are Rising Faster Than Ever

By JOSH KATZ  JUNE 5, 2017

New data compiled from hundreds of health agencies reveals the extent of the drug overdose epidemic last year.

AKRON, Ohio — Drug overdose deaths in 2016 most likely exceeded 59,000, the largest annual jump ever recorded in the United States, according to preliminary data compiled by The New York Times.

The death count is the latest consequence of an escalating public health crisis: opioid addiction, now made more deadly by an influx of illicitly manufactured fentanyl and similar drugs. Drug overdoses are now the leading cause of death among Americans under 50.

Although the data is preliminary, the Times’s best estimate is that deaths rose 19 percent over the 52,404 recorded in 2015. And all evidence suggests the problem has continued to worsen in 2017.
CURRENTLY ABOUT **2.5 MILLION** US CITIZENS ACTIVELY ADDICTED TO OPIOIDS

1.9 MILLION TO PRESCRIPTION OPIOIDS (79%)

517,000 TO HEROIN (21%)

OPIOID SOCIETAL COSTS - $55 BILLION A YEAR

OPIOID OD QUADRUPLED SINCE 1999 - 54,404 US OD DEATHS IN 2015 - 33,091 (63%) INVOLVED OPIATES

INCREASES RISK FOR HIV, VIRAL HEPATITIS, OTHER INFECTIONS, STDs, ETC.

PLUS MULTIPLE SOCIETAL PROBLEMS

ASAM/ NATIONAL SURVEY ON DRUG USE AND HEALTH (NSDUH); US DEPT OF HHS/CDC / MORBIDITY AND MORTALITY
FACING ADDICTION IN AMERICA

The Surgeon General’s Report on Alcohol, Drugs, and Health
Do Stronger Human Connections Immunise Us Against Emotional Distress?

Right now an exciting new perspective on addiction is emerging. Johann Harri, author of *Chasing The Scream*, recently captured widespread public interest with his Ted talk *Everything You Know About Addiction Is Wrong*, where he concluded with this powerful statement:

"The opposite of addiction is not sobriety. The opposite of"
Biology + Stress + Drugs
Genes Epigenetics IEM's
Especially Trauma
Prescribed Illicit

Risk of Abuse / Addiction
PREVIOUS MEDICAL APPROACHES TO ALCOHOLISM AND DRUG ADDICTION

• BENJAMIN RUSH, MD USED BLEEDING, BLISTERING AND TREATMENT WITH MERCURY LADEN CALOMEL
• DRINK WINE IN WHICH EELS SUCCOCATED
• WATER CURES (HYDROTHERAPY)
• LATER HALF OF 1800S VARIOUS DRUGS: COCAINE, MORPHINE, MJ, HEROIN, ETOH, BROMIDE
• AVERSION THERAPY – 1932 - PRESENT
• ECT, INSULIN SHOCK, PSYCHOSURGERY 1940S – ABOUT 1960S
  ▪ MID- 1900S DRUG INTERVENTIONS: SEDATIVE, TRANQUILIZERS, AMP/METHAMPHETAMINE, LSD, HALLUCINOGENS, HORMONES, CO₂
NY STATE INEBRIATE ASYLUM: 1864
DEEMED A “COMPLETE FAILURE” IN 1979
US FEDERAL NARCOTIC FARMS: 1925 -1950
CONTINUED INTO 1970S

- FEDERAL NARCOTIC FARMS:
  LEXINGTON, KY AND FORT WORTH TEXAS PRIMARY SOURCE OF TREATMENT, 1938 – 1950
- LONG TREATMENT (VOLUNTARY VS INVOLUNTARY)
- LITTLE OR NO FAMILY INVOLVEMENT
- FORCED LABOR
- RELAPSE RATE- VERY HIGH
Federal “Narcotics Farm” - Lexington, KY 1935-1975

Relapse Rate was approximately 95%
DOES ABSTINENCE-BASED TREATMENT WORK?

NATIONAL TREATMENT OUTCOME RESEARCH DATA ON OPIOID ADDICTION PATIENTS

242 PATIENTS IN RESIDENTIAL TREATMENT

34% RELAPSE WITHIN 3 DAYS  45% RELAPSE WITHIN 7 DAYS
50% RELAPSE WITHIN 14 DAYS  60% RELAPSE WITHIN 90 DAYS

MULTIPLE “STUDIES CONSISTENTLY SHOW 2/3 OF PATIENTS IN ABSTINENCE-BASED PROGRAMS RELAPSE”. DR BATKI, MD PROF OF PSY, UPSTATE MED CENTER SYRACUSE
39% wanted to try opioid drugs once more

62% mood was bad

48% ease of access to opioids

62% cravings were too much

37% someone offered them opioids

43% missed the support of the treatment center

Reasons for Relapse
Methadone maintenance treatment, started in 1964, ushered in a new era in the treatment of Opioid Addiction.

Prior to Methadone, the overall relapse rate to heroin use was at least 80%.

APPROVED 1972
**Disulfram At a Glance**

**Chemical name:** Bis(diethylthiocarbamoyl) disulfide.

**Trade name:** Antabuse®.

**U.S. distributor:** Odyssey Pharmaceuticals, Inc., East Hanover, NJ.

**U.S. Food and Drug Administration approval to treat alcohol dependence:** 1951.

**Dosage/How taken:** Tablet by mouth once daily (also may be crushed and mixed with water, coffee, tea, milk, soft drink, or fruit juice).

**How supplied:** Bottles of 100 or 1,000 250 mg tablets or bottles of 50, 100, or 500 500 mg tablets.
PHARMACOTHERAPY USE IN ADDICTION TREATMENT

• IN 2007, 1 IN 3 PEOPLE WITH OPIOID DEPENDENCE USED PHARMACOTHERAPY

• IN 2011, 1 IN 4 PEOPLE WITH ALCOHOL DEPENDENCE USED PHARMACOTHERAPY
MEDIATION ASSISTED TREATMENT/RECOVERY

• USE SPARINGLY AND ONLY WHEN NEEDED

• TREAT SYMPTOMS TO HELP PATIENT STAY IN RECOVERY AND LEARN TOOLS FOR LONG TERM WELLNESS

• SOME MEDS MAY BE LONG TERM, BUT MOST WILL BE SHORT TERM WHILE NEUROGENESIS AND SYNAPTOGENEISS AND NEURAL REPAIR OCCUR, ESPECIALLY IN THE FIRST 3-6 MONTHS OF RECOVERY.

• MY WHOLE PHILOSOPHY IS STABILIZING UNTIL THE FOUNDATION IS BUILT, THEN MOVING AWAY FROM MEDICATIONS WHEN POSSIBLE.
PHARMACOTHERAPY IN SUBSTANCE USE DISORDERS

• TREATMENT OF WITHDRAWAL (DETOX)
• TREATMENT OF PSYCHIATRIC SYMPTOMS OR CO-OCCURRING DISORDERS
• REDUCTION OF CRAVINGS AND URGES
• SUBSTITUTION THERAPY
• PREVENTION
• OVERDOSE REVERSAL
Dopamine Pathways

Functions
- Reward
- Pleasure, Euphoria
- Motor Function (fine tuning)
- Compulsion
- Perseveration
- Decision Making
- Mental Focus
- Motivation
- Attachment

Serotonin Pathways

Functions
- Mood
- Mental
- Well-being
- Memory
- Processing
- Sleep
- Cognition
MEDICATION ASSISTED TREATMENT/RECOVERY: ALCOHOL DEPENDENCE

FDA-APPROVED:
• DISULFURAM (ANTABUSE)
• PO NALTREXONE (REVIA)
• IM NALTREXONE (VIVITROL)
• ACAMPROSATE (CAMPRAL)

NON-FDA-APPROVED:
• TOPIRAMATE (TOPAMAX)
• ONDANSETRON (ZOFRAN)
• BACLOFEN
MEDICATIONS FOR OPIOID DEPENDENCE

• DETOXIFICATION
  • OPIOID-BASED AGONIST (METHADONE, BUPRENORPHINE)
  • NON-OPIOID BASED (CLONIDINE*, SUPPORTIVE MEDICATIONS)
  • ANTAGONIST-BASED (NALTREXONE: “RAPID”)

• RELAPSE PREVENTION
  • AGONIST MAINTENANCE (METHADONE)
  • PARTIAL AGONIST MAINTENANCE (BUPRENORPHINE)
  • ANTAGONIST MAINTENANCE (NALTREXONE)
OPIOID DETOXIFICATION

• MEDICATIONS USED TO ALLEVIATE WITHDRAWAL SYMPTOMS
  • OPIOID AGONISTS (METHADONE, BUPRENORPHINE)
  • OTHER SUPPORTIVE MEDICATIONS
    • CLONIDINE, TIZANIDINE, LOFEXIDINE (ALPHA-2 AGONISTS)*
      • CAUTION: HYPOTENSION
      • COMFORT MEDICATIONS INCLUDING ANTIDIARRHEALS, ANTIEMETICS,
        PAIN MEDICATIONS, MUSCLE RELAXANTS, BENZODIAZEPINES

*OFF-LABEL USE.

OPIOID RECEPTOR BLOCKADE: GOALS

• REDUCE SYMPTOMS AND SIGNS OF WITHDRAWAL
• REDUCE OR ELIMINATE CRAVING
• BLOCK EFFECTS OF ILLICIT OPIOIDS
• RESTORE NORMAL PHYSIOLOGY
• PROMOTE PSYCHOSOCIAL REHABILITATION AND NON-DRUG LIFESTYLE
OPIOID RECEPTOR ACTIVATION

![Graph showing receptor activation vs. log dose of opioid]

- **Full Agonist** (methadone)
- **Partial Agonist** (buprenorphine)
- **Antagonist** (naltrexone/naloxone)
METHADONE

• ORALLY ACTIVE SYNTHETIC μ-OPIOID FULL AGONIST
• QUICK ABSORPTION, SLOW ELIMINATION, LONG HALF-LIFE
• EFFECTS LAST 24 HOURS; ONCE-DAILY DOSING MAINTAINS CONSTANT BLOOD LEVEL
• PREVENTS WITHDRAWAL, REDUCES CRAVING AND USE
• FACILITATES REHABILITATION
• REQUIRES GOING TO A CLINIC
• LIMITED AVAILABILITY
**BUPRENORPHINE**

- **SUBLOCADE™, SUBOXONE®, SUBUTEX®, ZUBSOLV®, BUNAVAIL®**
- **FDA APPROVED: 2002, AGE 16+ YEARS**
- **MANDATORY CERTIFICATION FROM DEA (100 PATIENT LIMIT)**
- **OFFICE-BASED, EXPANDS AVAILABILITY**
- **ANALGESIC PROPERTIES**
- **CEILING EFFECT**
- **MECHANISM: M-OPIOID PARTIAL AGONIST**

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US FOOD AND DRUG ADMINISTRATION. DRUGS@FDA: FDA APPROVED DRUG PRODUCTS. WWW.ACCESSDATA.FDA.GOV/SCRIPTS/CDE/R/DAF/INDEX.CFM.
BUPRENORPHINE

- CEILING EFFECT
- MECHANISM: M-OPIOID PARTIAL AGONIST
- LOWER ABUSE POTENTIAL
- SAFER IN OVERDOSE (BECAUSE OF CEILING EFFECT AND NALOXONE)
MEDICATION ASSISTED TREATMENT/RECOVERY: OPIOID DEPENDENCE: DETOX

40 HEROIN ADDICTS RANDOMIZED TO:

- 1 WEEK DETOX FOLLOWED BY PLACEBO AND COUNSELING
- 1 YEAR BUP MAINTENANCE AND COUNSELING

HEROIN USE

- BUPRENORPHINE DETOX, PLACEBO MAINTENANCE = 100% RELAPSED - 4/20 DIED!!
- BUPRENORPHINE MAINTENANCE = 75% (SD 60%) OPIOID NEGATIVE URINE DRUG SCREENS. 0/20 DEATHS
In one study, all patients who were detoxed and counselled relapsed with about 50 days. Those receiving maintenance medication with counselling demonstrated a lower rate of relapse.
STUDIES OF MAT WITH SUBOXONE – HOW LONG SHOULD IT BE USED?

MAT WITH SUBOXONE FOR 7 DAYS VS 28 DAYS IN 990 PTS WITH OPIOID SUD

- SIMILAR RELAPSE RATES EITHER WAY ABOUT 87% AT THREE MONTHS (LING 2009)

- MAT WITH SUBOXONE FOR 3 MO…
  60% OPIOID FREE AT 1 YEAR (KATZ 2009/GALANTER 2003)

- MAT WITH SUBOXONE FOR 6 – 9 MO
  90% OPIOID FREE AFTER ONE YEAR (DID NOT LOOK AT OTHER DRUGS) (BADGAIYAN 2015)
NALTREXONE

• REVIA®
• FDA APPROVED: 1994
• DOSING: 50 MG PO QD (START AT 25 MG QD)
• MECHANISM: M-OPIOID ANTAGONIST
  • DECREASES POSITIVE REINFORCING EFFECTS
  • DECREASES CUE-INDUCED CRAVINGS
• RESULTS: HIGHER RATES OF ABSTINENCE, SIGNIFICANT PERCENTAGE OF OPIOID-FREE WEEKS, DECREASED CRAVING
IM NALTREXONE

• VIVITROL™
• FDA APPROVED: 2006
• INTRAMUSCULAR INJECTION ONCE MONTHLY
• NO NEED FOR ORAL LEAD-IN
• MECHANISM: M-OPIOID ANTAGONIST
COMPARATIVE EFFECTIVENESS OF EXTENDED-RELEASE NALTREXONE VS BUPRENORPHINE-NALOXONE FOR OPIOID RELAPSE PREVENTION (X:BOT): A MULTICENTER, OPEN-LABEL, RCT

• NIDA FUNDED
• N=570 RANDOMLY ASSIGNED
• 24 WEEKS
• “…IT IS MORE DIFFICULT TO INITIATE PATIENTS TO [EXTENDED-RELEASE NALTREXONE] THAN [SUBLINGUAL BUPRENORPHINE-NALOXONE], AND THIS NEGATIVELY AFFECTED OVERALL RELAPSE. HOWEVER, ONCE INITIATED, BOTH MEDICATIONS WERE EQUALLY SAFE AND EFFECTIVE.”
EXTENDED-RELEASE NALTREXONE VS SUBLINGUAL BUPRENORPHINE-NALOXONE FOR RELAPSE PREVENTION IN OPIOID USE DISORDER

- 12-WEEK MULTICENTER OUTPATIENT OPEN-LABEL RCT, N=159
- 5 URBAN ADDICTION CLINICS IN NORWAY (2012–2015)
- N=80 EXTENDED-RELEASE NALTREXONE AND N=79 BUPRENORPHINE-NALOXONE → N=105 COMPLETED
- BUPRENORPHINE-NALOXONE MEAN DOSE 11.2 MG
- RANDOMIZATION OCCURRED AFTER DETOXIFICATION COMPLETED
- NO SIGNIFICANT DIFFERENCES BETWEEN GROUPS IN
  - PROPORTION TOTAL NUMBER OF DAYS OPIOID NEGATIVE URINE TESTS
  - RETENTION
  - USE OF HEROIN AND OTHER ILLICIT OPIOIDS
  - EXTENDED-RELEASE NALTREXONE PATIENTS REPORTED LESS HEROIN CRAVING, MORE TREATMENT SATISFACTION

NALTREXONE/VIVITROL

• NALTREXONE SYNTHESIZED IN 1963, APPROVED FOR OPIOID ADDICTION IN 1984
• VIVITROL (INJECTABLE NALTREXONE) APPROVED FOR ALCOHOL ADDICTION IN 2006

• DAILY ORAL OR 1X MONTHLY INJECTABLE
• COVERED BY MEDICAID/MEDICARE IN MOST STATES
Patients treated with VIVITROL and counseling had a SIGNIFICANTLY HIGHER PERCENTAGE OF OPIOID-FREE WEEKS.

- During weeks 5–24

Confirmed abstinence = negative urine drug test and no self-reported opioid use

Median placebo patients (with psychosocial support) had 35% cumulative opioid-free weeks. Median VIVITROL patients (with psychosocial support) had 90% cumulative opioid-free weeks.

In the prespecified subset (n=53, 8% of the total study population) patients who abstained for 7 days prior to the first injection had

92% FEWER HEAVY-DRINKING DAYS

- Median heavy-drinking days per month
- The same treatment effects were not evident among the subset of patients (n=571, 92% of the total study population) who were actively drinking at the time of treatment initiation
- Baseline for both VIVITROL 380 mg and placebo was 15.2 heavy-drinking days per month

• CONCLUSIONS AND RELEVANCE: EXTENDED-RELEASE NALTREXONE WAS AS EFFECTIVE AS BUPRENORPHINE-NALOXONE IN MAINTAINING SHORT-TERM ABSTINENCE FROM HEROIN AND OTHER ILLICIT SUBSTANCES AND SHOULD BE CONSIDERED AS A TREATMENT OPTION FOR OPIOID-DEPENDENT INDIVIDUALS.
Secondary End Points, Cravings

Subjective opioid craving declined rapidly from baseline in both treatment groups.

Average opioid craving was initially less for the XR-NTX group ($P=0.0012$ at week 7) than for the BUP-NX group, then converged by week 24 ($P=0.20$)

Craving was self-reported with an opioid-craving VAS, range 0–100.

VAS=visual analog scale

HOW TO CHOOSE A MEDICATION
EVIDENCE-BASED TREATMENTS

• MOTIVATIONAL ENHANCEMENT/CONTINGENCY MANAGEMENT
• MATRIX MODEL
• COGNITIVE-BEHAVIOR THERAPY
• COMMUNITY REINFORCEMENT (PLUS VOUCHERS)
• FAMILY BEHAVIORAL THERAPY
• MUTUAL HELP GROUP
• 12-STEP FACILITATION
• INTENSIVE REFERRAL
• PHARMACOTHERAPY

Biology + Stress + Drugs → Risk of Abuse / Addiction

- Genes
- Epigenetics
- IEMs
- Especially Trauma
- Prescribed
- Illicit
LEVEL OF CARE

• HARM REDUCTION
• COMMUNITY
• OUTPATIENT
• INTENSIVE OUTPATIENT (IOP)
• PARTIAL HOSPITALIZATION (PHP)
• RESIDENTIAL TREATMENT PROGRAM
• AMBULATORY DETOX
• HOSPITAL-BASED TREATMENT PROGRAM
LEVEL OF CARE

- HARM REDUCTION – “MEET PATIENT WHERE THEY ARE AT”
- COMMUNITY – SBIRT (SCREENING, BRIEF INTERVENTION, AND REFERRAL TO TREATMENT)
- OUTPATIENT – COUNSELING, THERAPY, MEDICATIONS
- INTENSIVE OUTPATIENT (IOP)
- PARTIAL HOSPITALIZATION (PHP)
- RESIDENTIAL TREATMENT PROGRAM
- AMBULATORY DETOX
- HOSPITAL-BASED TREATMENT PROGRAM
WHAT YOU NEED TO PROVIDE COMPREHENSIVE ADDICTION TREATMENT:

- X NUMBER, DEA WAIVER (?)
- THERAPISTS/COUNSELORS
- TREATMENT PROGRAMS TO REFER TO AND FROM
  - FACILITATED REFERRAL BEST
- COMMUNITY-BASED SUPPORT PROGRAMS
  - 12 STEP, INCLUDES REFUGE RECOVERY, SELF-MANAGEMENT AND RECOVERY TRAINING (SMART), ALCOHOLICS ANONYMOUS (AA), ETC.
- PEER SUPPORT
CLINICAL MANAGEMENT OF COMORBID DISORDERS

• INDIVIDUALIZE AND INTEGRATE TREATMENT FOR COMORBID DISORDERS WHENEVER POSSIBLE

• CONSIDER DEVELOPMENTAL NEEDS AND STAGES

• CONSIDER RANDOM DRUG TESTING

• CONSIDER NEED FOR HIGHER LEVEL OF CARE

• CONSULT ADDICTION MEDICINE SPECIALIST IF NECESSARY
MEDICATION MANAGEMENT IN COMORBID DISORDERS

• AMBIVALENCE IS COMMON
• WHEN DO WE USE MEDICATIONS IN PATIENTS WITH OUD?
• WHEN TO INITIATE PHARMACOTHERAPY WHEN DIAGNOSIS IS UNCLEAR?
  • WITH PSYCHOSIS, MODERATE TO SEVERE DEPRESSION, OR MANIA, TREAT SOONER

• STRATEGIES INCLUDE
  • COMMUNICATE FREQUENTLY WITH CAREGIVERS
  • VERBALIZE CLEAR EXPECTATIONS (RE: MEDICATION OUTCOMES, CONFIDENTIALITY)
  • EXPECT POSSIBILITY OF MISUSE AND DRUG INTERACTIONS
  • SCHEDULE FREQUENT FOLLOW-UPS

IF YOU’RE GOING TO FLY THE PLANE...

• **MY GOAL**
  • LOWEST AMOUNT OF MEDICATION
  • SAFEST CHOICE OF MEDICATION
  • MOST EFFECTIVE MEDICATION
  • DECREASE/STOP MEDICATIONS WHEN CAN
    • **EG, BUPRENORPHINE UNTIL READY TO STOP, THEN USE THE PODESTA PROTOCOL TO TAKE THEM OFF COMFORTABLY**

• **COMPARE TO DIABETES**
  • LIFESTYLE CHANGE
  • HABIT CHANGE
  • DIET CHANGE

• **TIME FRAME**
  • VERY SHORT-TERM
  • MEDIUM TIME (3 MONTHS TO 2 YEARS)
  • LONG-TERM
CURRENT OPIOID MAT CONTROVERSIES/QUESTIONS

• WHICH PATIENTS SHOULD BE OFFERED MAT AND WHEN IN THEIR TREATMENT COURSE SHOULD THEY BE OFFERED IT?

• HOW LONG DO YOU CONTINUE MAT?

• MAT VS ABSTINENCE AND IS THERE A HAPPY MEDIUM?

• LONG-TERM SIDE EFFECTS?

• IS A PATIENT WHO USES MEDICATION TO MAINTAIN SOBRIETY IN “REAL RECOVERY” (AND DOES IT MATTER)?

• NO FDA APPROVED MEDICATIONS FOR ADDICTIONS OTHER THAN OPIOID AND ALCOHOL
COST EFFECTIVENESS OF TREATMENT

• COST TO SOCIETY OF DRUG ABUSE IS $200 BILLION/YEAR

• TREATMENT IS LESS EXPENSIVE THAN INCARCERATION
  • METHADONE MAINTENANCE = $4700/YEAR
  • IMPRISONMENT = $18400/YEAR

• OTHER STUDIES SHOW THAT EVERY $1 INVESTED IN TREATMENT CAN YIELD UP TO $7 IN SAVINGS
IN CONCLUSION

• Addiction is a serious, chronic, and relapsing disorder; use multiple evidence-based treatments.

• Medications should be considered as part of a comprehensive treatment plan, addressing both disordered physiology and disrupted lives.

• Medications should be considered for treatment of psychiatric symptoms, addictive disorders, and comorbid disorders.