Outpatient Management of Nicotine Addiction and Substance Use Disorders

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Why We’re Here

- >20% of deaths in the US are attributable to tobacco, alcohol, and other drug use.
- Addiction is a disease. It should be diagnosed and treated like other diseases.
- >2/3 people with addiction are estimated to be in contact with medical providers.
- Only 1/10 patients get treatment (gap of 20 million).
- Treatment works.

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Figure 1A
Continuum of Substance Use
Percent of Population Age 12+ by Level of Substance Use*

<table>
<thead>
<tr>
<th>Level</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never Used</td>
<td>13.7</td>
</tr>
<tr>
<td>No Current Use</td>
<td>25.3</td>
</tr>
<tr>
<td>Non-Risky Use</td>
<td>14.6</td>
</tr>
<tr>
<td>Risky Use</td>
<td>31.7</td>
</tr>
<tr>
<td>Addiction</td>
<td>15.9</td>
</tr>
</tbody>
</table>

* Includes tobacco, alcohol, illicit drugs and misuse of controlled prescription drugs.
Source: CASA Columbia analysis of The National Survey on Drug Use and Health (NSDUH), 2015.

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Figure 1B
Individuals with Select Medical Conditions Who Receive Treatment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>77.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>73.2</td>
</tr>
<tr>
<td>Migraine</td>
<td>71.2</td>
</tr>
<tr>
<td>All conditions</td>
<td>10.9</td>
</tr>
</tbody>
</table>

‡ All ages: Centers for Disease Control and Prevention (2011).
§ Ages 12 and older: CASA Columbia analysis of The National Survey on Drug Use and Health (NSDUH), 2015.
* Due to data limitations.
It’s (sort of) covered!  
- 1 of 10 essential benefits in the Affordable Care Act  
- Treatment networks, cost sharing, # services

Case

- A 53yo M with a history of CAD, COPD, depression, and low back pain presents for follow-up. He reports that he’s had “enough” and wants to stop smoking. He is interested in “treatment... maybe the patch?”
- He smokes 15 cigarettes per day, including a cigarette upon rising in the morning.
- This will be his first attempt to stop.
Question

- Which of the following is NOT TRUE with regard to nicotine replacement therapy (NRT)?
  - He can not smoke while using NRT
  - They double the patient’s chances of quitting
  - The patient may experience bizarre dreams
  - The patch can be extended beyond 24 weeks to maintain abstinence
Smoking & Health

- Leading cause of preventable death in the United States (CDC)
- Tobacco use is responsible for 1/10 adult death worldwide
- Prevalence has improved (23% in 2000), but still 18% of Americans smoke


About NRT

- 5 forms: patch, gum, lozenge, inhaler, nasal spray
- Data for NRT:
  - 6-month abstinence rates range from 20-27% (vs. 14% in placebo groups)
- Patch
  - >10 cig/day & >100lbs: 6-2-2
    - 21mg patch q day x 6 weeks, then
    - 14mg patch q day x 2 weeks, then
    - 7mg patch q day x 2 weeks
  - Evidence to extend use to 24 weeks, but NOT 52 weeks
- Prepare & educate your patient!
  - Misperception common: 95% of smokers thought wearing the patch while smoking could cause a heart attack
  - Skin irritation (20%) → hairless area & rotate site
  - Nausea (5%) → remove before bed

**NRT continued**

- **Combination Treatment**
  - Outcomes: 35% increase in efficacy (patch + short-acting)
  - Mechanism
    - Patch for tonic craving, but no effect on cue-induced craving
  - How to Use:
    - Gum (up to 24/d)
      - >25 cig/d: 4mg; <25 cig/d: 2mg
      - "Chew & park"
    - Lozenge (up to 20/d)
      - 1st cig <30 min after waking: 4mg
      - Do NOT chew
    - Side effects: nausea, hiccups, heartburn
  - 380 pieces/$45

Ferguson SG et al. Patient Relat Outcome Meas. 2011 Jul;2:

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**Smoking**

- Fast forward 1 year. Your patient tried patch + lozenge but did not find success, though he remains motivated to quit. He asks you about varenicline. Which of the following is true?
  - Varenicline has a black-box warning cautioning against its use in patients with coronary artery disease
  - Varenicline is effective in treating schizophrenics with nicotine dependence
  - Varenicline can not be combined with NRT
  - Varenicline + bupropion is superior to varenicline monotherapy at 1 year
Smoking

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About Varenicline

- **Mechanism of action**: partial agonist nicotine receptor → relieve withdrawal, block reinforcing effects from smoking
- **Dosing**
  - 0.5mg PO q day x3d, then 0.5mg PO bid x4d, then 1mg PO bid
  - Stop smoking after 1 week
- **Prescribing**
  - Chantix starter pack. Take as directed. Disp #1 package, 0 refills.
  - Chantix continuing pack. Take as directed. Disp #-- package(s), #-- refills
Varenicline Safety

- Black box warning for serious neuropsychiatric events
  - Found from postmarketing & case-control studies
    - 2 pooled studies of 17 RCTs, 7 large uncontrolled observational trials, 4 large controlled observational trials no signal found for suicidality
  - Varenicline is effective in patients with psychiatric disorders (schizophrenia, BPD, SAD, depression)
  - Recent FDA update to label about combining varenicline and alcohol (decreased tolerance, increased drunkenness, black-outs)
- Varenicline is not associated with increased CV events


Varenicline Efficacy: New Evidence

- Varenicline + NRT superior to varenicline alone at 6 mos.
- Varenicline + buproprion not superior to varenicline monotherapy
- Varenicline effective in contemplative patients*


Table 2. Continuous Carbon Monoxide-Confirmed Smoking Abstinence Rates for Periods of the Study

<table>
<thead>
<tr>
<th>Period</th>
<th>Varenicline Group (n = 760)</th>
<th>Placebo Group (n = 750)</th>
<th>Risk Difference, % (95% CI)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary End Point</strong>a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 15-24</td>
<td>244 (32.1)</td>
<td>52 (6.9)</td>
<td>25.2 (21.4-29.0)</td>
<td>4.6 (3.5-6.1)</td>
</tr>
<tr>
<td><strong>Secondary End Points</strong>b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 21-24</td>
<td>287 (37.8)</td>
<td>94 (12.5)</td>
<td>25.2 (21.1-29.4)</td>
<td>3.0 (2.4-3.7)</td>
</tr>
<tr>
<td>Weeks 21-52</td>
<td>205 (27.0)</td>
<td>74 (9.9)</td>
<td>17.1 (13.3-20.9)</td>
<td>2.7 (2.1-3.5)</td>
</tr>
<tr>
<td><strong>Post-Hoc End Point</strong>c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weeks 15-52</td>
<td>182 (24.0)</td>
<td>45 (6.0)</td>
<td>18.8 (14.5-21.4)</td>
<td>4.0 (2.9-5.4)</td>
</tr>
</tbody>
</table>

Case

Which of the following is true about e-cigarettes?

- They are FDA approved for smoking cessation therapy
- The nicotine delivery device is regulated as a medical device by the FDA
- Randomized controlled trials show efficacy for smoking cessation superior to nicotine replacement therapy
- E-cigarettes have been shown to increase lung airflow resistance
E-cigarettes

- Not FDA-approved for treatment of nicotine dependence
- Not regulated by the FDA as a medical device (no oversight of good manufacturing practices)
- 2 RCTs for use in smoking cessation
  - Tobacco abstinence improved at 12 weeks (11% vs. 4%) but no difference at 6, 12 mos.
  - E-cig v. NRT v. placebo e-cig: Nicotine e-cig superior to placebo (7% vs. 4%), but not NRT
- Small safety trials show increased airway resistance after usage
- Long term effect of exposure to chemicals in e-cig unknown


Bupropion

- Efficacious for smoking cessation (OR 1.85)
- Combination NRT = varenicline > bupropion and mono NRT
### Summary

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosing</th>
<th>OR</th>
<th>Pearls</th>
</tr>
</thead>
</table>
| Combination NRT   | 6-2-2 patch 21mg q day x6 weeks, then 14mg q d x2 weeks, then 7mg qd x2 wk Lozenge: 2-4mg q1-2 h (up to 20/day) | 2.73 | • Can continue patch to 24 weeks (if covered).  
• Rotate site; take off before bed |
| Varenicline       | Starter pack (take as directed), then Continuation pack (take as directed) Quit time: 1 week after start | 2.89 | • Consider if pre-contemplative  
• Can combine with NRT  
• Black box neuropsych side effects & suicidality |
| Bupropion         | 150mg ER PO q day x3 days, then 150mg ER BID. Quit time: 1 week after start | 1.85 | • Contra-indicated for hx seizure disorder  
• Black box neuropsych side effects & suicidality  
• Weight loss |
| NRT, monotherapy  | As above                                                               | 1.9 |                                                                                             |

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### Resources for Quitting

- **Quitlines**
  - California: 1-800-NO-BUTTS
    - Can get 4 weeks of nicotine patches
    - Medicaid patients eligible for $20 gift card
    - Multi-lingual
      - Chinese: 1-800-838-8917
      - Korean: 1-800-556-5564
      - Spanish: 1-800-45-NO-FUME (1-800-456-6386)
      - Vietnamese: 1-800-778-8440
      - Tobacco Chewers: 1-800-844-CHEW (1-800-844-2439)
  - Every state has a quitline – access by calling 1-800-QUIT-NOW & the person gets transferred to their state quitline
    - 1-855-DEJELO-YA (Quit it now) for Spanish speakers
    - [www.asiansmokersquitline.org](http://www.asiansmokersquitline.org)
Case

- 45yo M with a history of obesity, DM, and HTN presents for a follow-up visit. You broach the topic of alcohol and he explains he drinks “socially.”
- His exam is notable for hypertension (152/93), BMI of 31, and telangiectasias on the nose and cheeks.
- Recent labs show a hemoglobin A1c is 7.5 and a lipid panel: TC 175, HDL 52, LDL 130, and TG of 290.

Case continued

- After exploring what “social drinking” means, you explain the following about safe drinking limits:
  - Men should not exceed 6 drinks per day
  - Men should not exceed 14 drinks per week
  - Men should not exceed 3 drinks per day
  - Men should not exceed 20 drinks per month
  - There are no medical recommendations about safe drinking limits
Case continued

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  - Men should not exceed 20 drinks per month
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Alcohol Use Disorders

- Each day, 6 people die from alcohol poisoning
  - Most are age 35-64 years, most are men
  - Disproportionately more deaths among Native American/Alaska Natives
- 4th leading preventable cause of death in the US
- Only 19% of patients with lifetime alcohol use disorder have been treated

Grant B, et al. JAMA Psychiatry, 2015
A Plug for Universal Screening

- USPSTF recommends clinicians screen for alcohol misuse and provide persons engaged in risky or hazardous drinking with brief behavioral counseling to reduce misuse (B)
- Most patients with alcohol use disorders (69-98%) are not detected by physicians
- Physicians are less likely to detect problems when screening tools are not used universally or in patients for whom they do not expect to have alcohol problems (women, white, higher SES)
- Lab testing is not sufficiently sensitive or specific


The Spectrum of Alcohol Use

- 13% Harmful use, alcohol abuse
- 13% Alcohol dependence
- 7-20% of outpatients
- >50% of health consequences

What are Healthy Alcohol Limits?

- Increased risks for alcohol-related problems occur for:
  - Men < 65 who drink more than 4 standard drinks in a day (or more than 14 per week)
  - All women or men >65 who drink more than 3 standard drinks in a day (or more than 7 per week)

What’s a Standard Drink?

In the U.S., a standard drink is any drink that contains about 14 grams of pure alcohol (about 0.6 fluid ounces or 1.2 tablespoons).
Diagnosis of Substance Use Disorders

- DSM-IV – abuse and dependence
  - Abuse (≥1 of the following; "4 Rs"):
    - Risky use
    - Relationship problems
    - Role failure
    - Run-ins with the law
  - Dependence (≥3 of the following; "4 Cs"):
    - withdrawal
    - tolerance
    - Loss of Control
    - repeated attempts to quit
  - Continued use despite harm
    - Med/psych problems from use
  - Compulsion
    - ↑ time spent using
    - give up activities to use
  - Craving

- DSM-5: substance use disorder
  - Mild (2-3), moderate (4-5), or severe (≥6) depending on # criteria in last 12 mos.
    - Risky use
    - Relationship problems
    - Role failure
    - Exceed own limits
    - Withdrawal
    - Tolerance
    - Loss of Control
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    - Compulsion to use
      - ↑ time spent using
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7-20% of outpatients >50% of health consequences

The Spectrum of Alcohol Use

7-20% of outpatients >50% of health consequences
Building Motivation for Change

- **Brief Intervention**
  - **Summarize** your assessment of substance use and its complications and consequences
  - **Feedback**: Would it be ok if I shared some information with you about the health effects of drinking/drug use? What do you make of that?
  - **Assess Readiness**
    - Low motivation: Build it
      - Pros/Cons: So on the one hand you like beer, but you don’t like the cost of a DUI. Is that right?
      - Importance Ruler: You said cutting back on drinking was an importance level of 3/10. How come you didn’t say 0?
      - Extremes: What might happen if you keep smoking?
    - High motivation: Action plan
      - You seem ready to make a change. What are your goals and how can you accomplish them?
      - Here are some strategies that have helped others... What might be the next step for you?

- **RESIST THE RIGHTING REFLEX!!! No Fixin’!!**

Treatment Options for Alcohol Use Disorders

- Mutual support groups
- Self-Management strategies
- Residential treatment
- Social Supports
- Medication Assisted Treatment

www.findtreatment.samhsa.gov
Case

- 46yo M with a history of chronic low back pain, obesity, and depression presents for follow-up. He is scheduled for a cholecystectomy in the next 4 weeks. He is drinking ½ pint of whiskey per day after work, which is more than he used to drink, and he’s been having problems with his partner as a result of his alcohol use. He wants to cut back, and possibly quit. He has no history of alcohol withdrawal. He is housed and has family support.
- His labs are notable for an AST of 53 and ALT of 62 (ULN <40).

Case

- Which of the following would you recommend for his alcohol use disorder:
  - Inpatient detoxification therapy
  - Oral naltrexone
  - Oral acamprosate
  - IM naltrexone
  - Disulfiram
Case

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  - Disulfiram

Medications for treatment of alcohol use disorders

- Naltrexone (PO, IM)
- Disulfiram
- Acamprosate
- "off label"
  - Topiramate
**Naltrexone (ReVia; Vivitrol)**

- Mech. of Action:
  - μ opioid receptor antagonist → block dopamine release in the "reward pathway" → eliminate reinforcing effects of alcohol

- Who
  - Moderate to severe alcohol use disorder. Motivated.
  - ≥4 days of abstinence (or after detox)
  - NOT using chronic opioids
  - LFTs <3X ULN

**Efficacy of Naltrexone**

- Meta-analysis of 53 studies (n=9140)
  - NNT = 20 to prevent 1 person from returning to any drinking
  - NNT = 12 to prevent 1 person from returning to heavy drinking (≥4 drinks/d for women and ≥5 drinks/d for men)
  - IM naltrexone: reduction in heavy drinking days

Naltrexone Dosing & Monitoring

- **Dosing:**
  - ½ tablet q day x 1 week, then 1 tab (50mg) po q day. Take after eating or with food.
  - IM: 380mg q 4 weeks

- **Monitoring**
  - Check baseline LFTs, then q month
  - Consider baseline urine drug screen
  - Treat for 3-4 months. If abstinence, consider stopping treatment.
  - If tolerating med but still drinking, consider increase to 100mg daily

- **Side effects**
  - Start-up syndrome: nausea, vomiting, abdominal pain, h/a (~30%)
  - Black box: hepatotoxicity

Acamprosate (Campral)

- **Mechanism of Action:**
  - Unclear; inhibits NMDA receptor → dec glutaminergic excitation associated with intake and withdrawal

- **Who:**
  - Moderate-severe alcohol use disorders; opioids ok
  - Abstinent

- **Efficacy:**
  - Equivalent to naltrexone
  - Decreased risk any drinking versus placebo (RR 0.88); NNT = 9
  - European studies
**Dosing & Monitoring**

- **Dosing**
  - 666mg PO tid (333mg tablets)
  - Adjust for renal insufficiency (contra-indicated for CrCl <30)
  - Take with or without food

- **Side effects**
  - Diarrhea, fatigue

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**Disulfiram (Antabuse)**

- Mech of action: blocks aldehyde dehydrogenase → acetaldehyde → aversive reaction
- **Who:**
  - Highly motivated patients
  - No etoh for at least 12-24 hours
  - Non-alcoholic mouthwashes
- **Dosing**
  - 500mg po q day for 1-2 weeks
- **Side effects**
  - Metallic taste in mouth, fatigue, reaction
**Topiramate***

- Mech of action: inhibits excitatory glutamate receptors, inhibits DA release, and enhances GABA function.
- Efficacy: fewer drinking days, fewer heavy drinking days, fewer drinks/d
- Who:
  - Alcohol dependent; ?PTSD
  - Not necessarily abstinent
- Dosing
  - 25mg po q day x1 week, then 50mg po q day x1 week, then 25mg qAM and 50mg q PM...max 300mg/d [slow, over 6-8 weeks]
- Side effects
  - Changes in taste, anorexia, memory/concentration problems, weight loss

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**Opioid Use Disorders**

*Figure 7.2 Specific Illicit Drug Dependence or Abuse in the Past Year among Persons Aged 12 or Older: 2013*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Numbers in Thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>4,280</td>
</tr>
<tr>
<td>Pain Relievers</td>
<td>855</td>
</tr>
<tr>
<td>Cocaine</td>
<td>331</td>
</tr>
<tr>
<td>Heroin</td>
<td>409</td>
</tr>
<tr>
<td>Stimulants</td>
<td>413</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>277</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>152</td>
</tr>
<tr>
<td>Sedatives</td>
<td>99</td>
</tr>
</tbody>
</table>

National Survey on Drug Use and Health (NSDUH), 2013. Available at: [www.samhsa.gov](http://www.samhsa.gov)
HIV outbreak in Scott County, Indiana related to prescription Opana
Diagnosis of Opioid Use Disorders

- DSM-5: substance use disorder
  - continuum
  - Mild (2-3), moderate (4-5), or severe (≥6) depending on # criteria in last 12 mos.
    - Risky use **
      - Relationship problems
      - Role failure
      - Exceed own limits **
      - Withdrawal
      - Tolerance
      - Loss of Control
    - Repeated attempts to quit
    - Compulsion to use
      - ↑ time spent using
      - Give up activities to use
    - Continued use despite harm
      - Med/psych problems from use
    - Craving

ER visit for sedation
Partner difficulties – comments about pain med usage
Job loss
No functional impvmt (i.e., job)
- Doctor shopping;
- multiple prescribers;
- ER visits;
- Non-adherence to treatment plan

Hypogonadism; OSA; depression


Treatment of Opioid Use Disorders

- Methadone maintenance treatment
  - Full, mu opioid receptor agonist → blocks effects of opioids, dec craving
  - Outcomes: dec heroin use; dec HIV, dec mortality, dec criminal behavior
  - Disadvantages: schedule, cost, stigma, availability
- Treatment program locator: http://dpt2.samhsa.gov/treatment/directory.aspx

SCHOOL OF MEDICINE * UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
Treatment of Opioid Use Disorders

- Buprenorphine
  - Partial agonist at mu opioid receptor: occupies receptor and eliminates withdrawal, but also competitively inhibits full agonists. Ceiling effect.
  - Long-half life: 24-60 hours (q day dosing)
  - Forms: buprenorphine (Subutex), buprenorphine-naloxone pills or film (Suboxone)
  - Approved for office-based treatment of opioid use disorders through the Drug Addiction Treatment Act (DATA, 2000)
  - Good patients: medically and psychiatrically stable, coverage for the med, not dependent on other drugs
  - Down-sides: less supervision, diversion
  - Get certified! (x-license)
    - 8 hour web-based training
      - http://www.aaap.org/education-training/buprenorphine/
  - Physician locator:
    - http://buprenorphine.samhsa.gov/bwns_locator/

- Naltrexone
  - Opioid receptor antagonist
  - High relapse rate after discontinuation
  - Requires highly motivated patient
Summary

- Several treatments are available for nicotine dependence and the best outcomes have been shown for combination NRT and varenicline.
- Varenicline may be efficacious in patients contemplating quitting.
- E-cigarettes are not FDA-approved for treatment of nicotine dependence.
- Remember healthy alcohol limits for men (4 in a day, 14 per week) and women + adults >65yo (3 in a day, 7 per week)
- For stable patients with moderate-severe alcohol use disorders, consider treatment with naltrexone (IM or PO, no opioids), acamprosate, topiramate, or disulfiram

Summary continued

- Contra-indications to naltrexone include: liver function tests >3-4 x ULN, and chronic or upcoming opioid use.
- Dependence to prescription opioids is more common than to heroin.
- Effective treatments for opioid use disorders include methadone maintenance, buprenorphine, or naltrexone.
- Primary care providers may do office-based treatment of opioid use disorders with buprenorphine-naloxone after completing the requisite training for an x license.
Disclosures

I have nothing to disclose