Smoking Cessation: Where are We Now?

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Primary Care Internal Medicine CME 2015
OVERVIEW

- The challenge for treatment
- Newer evidence
  - Safety of varenicline
  - Combining drugs to improve success
  - Electronic cigarettes
- Treating Tobacco as a Chronic Disease

Rigotti NA. Strategies to help a smoker to who is struggling to quit. JAMA 2012;308:1573.
Take Home Message

Treat Tobacco Use Like a Chronic Disease

It needs long-term management and as much of your attention as treating hypertension and diabetes.
WHY TREATING TOBACCO USE MATTERS

- #1 preventable cause of death in the U.S.

- Many people still smoke (18% in US, 15% in MA)
  - Especially people with less education, lower income, psychiatric illness, substance abuse
  - Patterns of tobacco use are changing
    - Many light smokers (<10 cig/day)
    - 22% of cigarette smokers do not smoke every day
    - Small cigars, roll your own (cheaper than cigarettes)
    - Dual use (>1 type of product)

WHY TREATING TOBACCO USE MATTERS

- #1 preventable cause of death in the U.S.
- Many people still smoke
- Cessation reduces mortality
Effect of Smoking Cessation on Survival to 80 Years of Age, By Age at the Time of Quitting Smoking

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WHY TREATING TOBACCO USE MATTERS

- #1 preventable cause of death in the U.S.
- Many people still smoke (18% of US adults)
- Cessation reduces mortality
  - After MI, smoking cessation $\rightarrow$ 36% ↓ in CVD mortality
  - Even after age 65
  - It’s never too early or too late to quit

WHY TREATING TOBACCO USE MATTERS

- #1 preventable cause of death in the U.S.
- Many people still smoke (18% of US adults)
- Cessation reduces mortality
- Tobacco treatment delivered in practice works
A Case

- 55 yo man with HTN, BMI 30, depression (*stable SSRI*)
- Smokes 20 cigarettes/day since age 18
- “I know I should quit, but I’ve tried everything and nothing works.”
- Used nicotine patch for 3 days → “I still wanted a cigarette”
- Used bupropion for 1 month → “I didn’t want to smoke as much…cut down but couldn’t quit”
- “What do you think about the electronic cigarette?”
QUESTIONS

- What’s an electronic cigarette?
- Has he really tried everything?
- What are options for your next step?
69% of current smokers want to quit

52% of smokers try to quit each year

Few succeed long-term (quit for 1 year)

~ 6% succeed without help

25-30% succeed long-term with best treatment

Only 32% of those trying to quit seek help

MMWR November 2011;60:1513
THE CHALLENGE FOR TREATMENT

- We have effective treatments, but...
- We need better treatments
- We need to deliver the treatments we have to more smokers
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SMOKING CESSATION METHODS

2008 US Public Health Service Guideline

- Effective treatments exist
  - Counseling (individual / group / telephone)
  - Pharmacotherapy
  - Combination is better than either one alone

- More is better but even brief intervention works
Nicotine replacement OR

- Skin patch (OTC) 1.9
- Gum (OTC) 1.5
- Lozenge (OTC) 2.0
- Oral inhaler (Rx) 2.1
- Nasal spray (Rx) 2.3

Bupropion SR (Zyban, Wellbutrin SR) 2.0

Varenicline (Chantix) 3.1
NICOTINE REPLACEMENT

- Goal = reduce nicotine withdrawal
- All products about equally effective
- FDA approved use – NEW
  - Can combine NRT products
  - Don’t stop NRT if you smoke
  - Use >12 wks? → Ask your doctor
BUPROPION SR

- Atypical antidepressant - ↑ dopamine in CNS
- Increases cessation rate independent of its antidepressant effect

**Clinical use**
- Start 1 week before quit day (150 mg qd→bid)
- Treat for 3-6 months
- Increases seizure risk (Risk <0.1%)
- Blunts weight gain temporarily
VARENICLINE

- Partial agonist at α4β2 nicotinic receptor
  Receptor subtype that mediates nicotine dependence

- Dual mechanism of action
  - Partial agonist
    Stimulates receptor to treat craving, withdrawal
  - Antagonist
    Prevents nicotine from binding to the receptor →
    Blocks reward, reinforcement of smoking
VARENICLINE

- Clinical use
  - Start 1-4 weeks before quit day
  - Dose ramps up over 1 week to avoid nausea *(to 1 mg bid)*
  - Treat for 3-6 months
  - Most common side effect – nausea, vivid dreams
  - Effective in smokers who are not ready to quit now
  - Concern about adverse psychiatric effects
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FDA Public Health Advisory

July 2009

“[Varenicline] or [bupropion] has been associated with reports of changes in behavior such as hostility, agitation, depressed mood, and suicidal thoughts or actions.”

“FDA is requiring the manufacturers of both products to add a new Boxed Warning:

People who … experience any serious and unusual changes in mood or behavior or who feel like hurting themselves or someone else should stop taking the medicine and call their healthcare professional right away.”

VARENICLINE SAFETY

The dilemma

- Stopping smoking produces nicotine withdrawal symptoms (*depressed mood, anxiety, and irritability*).
- When these symptoms occur in a smoker who is stopping smoking on varenicline, did the drug or did quitting smoking cause the symptom?
- Case reports cannot answer this question.
- 2015 meta-analysis of 39 double-blind RCTs of varenicline → no excess of depression or suicidal thoughts (but few had patients with mental illness).*

*Thomas KH, BMJ 2015;350:h1109
Varenicline Safety

Trials in Patients with Psychiatric Co-morbidity

In Both Studies:

- Varenicline was well tolerated.
- Did not worsen psychiatric symptoms.
- Did not increase suicidal ideation.

**Depression\(^1\)**

- (n=525)
- Week 9-12: 36 (OR: 3.35, 95% CI: 2.16-5.21)
- Week 9-52: 20 (OR: 2.36, 95% CI: 1.40-3.98)

**Schizophrenia\(^2\)**

- (n=127)
- Week 12: 19 (OR: 4.74, 95% CI: 1.03-21.78, p = 0.46)
- Week 24: 11 (OR: 6.18, 95% CI: 0.75-50.71, p = 0.09)

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VARENICLINE SAFETY
Observational Study (Thomas et al, BMJ 2013)

UK Clinical Practice Research Datalink
- Population based data: 5.4 million patients (8.5% of UK)
- EHR data linked to UK mortality data and hospital data

Patients starting smoking medication (9/06 – 10/11)
- NRT \( (n=81,545) \)
- Bupropion \( (n=6741) \)
- Varenicline \( (n=31,260) \)

Outcome: fatal and non-fatal self-harm (suicide), new antidepressant prescription over 3 months follow-up

Result: No evidence of increased risk of suicidal outcomes for varenicline vs NRT, bupropion vs NRT
VARENICLINE SAFETY
Population-based Observational Study (Molero et al, BMJ 2015)

- Entire population of Sweden over age 15 (~8 million)
  - 69,757 people prescribed varenicline from 2006-2009
  - Compared outcomes in them vs. rest of the population

- No difference in main outcomes
  - New psychiatric diagnoses
  - Suicidal behavior
  - Traffic accidents, criminal offenses

- Small increase
  - Anxiety (HR 1.23, 95% CI 1.01-1.51)
  - Depression (HR 1.31 (95% CI 1.06-1.63)
  - But only in those with pre-existing diagnoses
Varenicline may increase risk of psychiatric symptoms in some patients. The risk is not well defined.

Prescribing any drug requires balancing risks and benefits.
- Varenicline is one of the most effective drugs available to treat tobacco dependence
- Continuing to smoke is clearly hazardous

**FDA Drug Safety Communication** – October 2011

“The Agency continues to believe that the drug’s benefits outweigh the risks.”

**Bottom line:** Patients given varenicline must be followed
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PLASMA NICOTINE LEVELS

Cigarettes vs. Nicotine Replacement Products

- Cigarette (1-2 mg)
- Nasal spray (1 mg)
- Gum (4 mg)
- Patch (21 mg)
NICOTINE REPLACEMENT

Long-acting, slow onset → skin patch

- Constant nicotine level to avoid withdrawal
- Simplest to use, best compliance
- User has no control of dose

Short-acting, faster onset

→ oral (gum, lozenge, inhaler)
→ nasal (spray)

- User controls dose
- Nicotine blood levels fluctuate more
- Requires more training to use properly
New Ways to Use NICOTINE REPLACEMENT

- Combine short- and long-acting forms
- Treat longer to prevent relapse
- Continue patch after a “slip”
- Start patch before quit day
- “Reduce to quit” (gradual reduction)

Current Pharmacotherapy Options


Drug vs. Placebo

Nicotine Replacement (NRT)

Bupropion

Varenicline

Combination NRT

Odds Ratio (95% Credible Interval)  # of Studies (Direct Comparisons)

Nicotine Replacement (NRT)

1.84 (1.71, 1.99)  119

Bupropion

1.82 (1.6, 2.06)  36

Varenicline

2.88 (2.4, 3.47)  15

Combination NRT

2.73 (2.07, 3.65)  2

Favors placebo  Favors active drug

Posterior Median Odds

0.5 1 1.5 2 2.5 3 3.5 4
Current Pharmacotherapy Options


- All drugs > placebo
  - Single NRT, combination NRT, varenicline, bupropion

- Tier 1: Single NRTs, bupropion

- Tier 2: Varenicline, combination NRT
  - Varenicline ~ combination NRT? No direct trial evidence

- Is there a Tier 3?
Combining Drugs Across Classes

Is there a Tier 3?

- Does combining drugs of different classes improve quit rates?

- 2 placebo controlled randomized trials were published in 2014
  - Each started with varenicline
  - 1 added bupropion (vs. placebo)
  - 1 added nicotine patch (vs. placebo)
Adding Bupropion or NRT to Varenicline

**Add bupropion**

- Week 12 (End of Treatment): OR: 1.49, CI: 1.05-2.12, P=.03
- Week 26: OR: 1.52, CI: 1.04-2.22, P=.03
- Week 52: OR: 1.39, CI: 0.93-2.07, P=.11

**Add nicotine patch**

- Week 12 (End of Treatment): OR: 1.85, CI: 1.19-2.89, P=.007
- Week 24: OR: 1.98, CI: 1.25-3.14, P=.004

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What is this woman doing?

No, she’s not smoking a cigarette. She’s vaping.
ELECTRONIC CIGARETTE

A nicotine delivery device that looks like a cigarette

- Invented in China in 2003
- Rapid growth in US sales since ~ 2010
- Not FDA regulated as device or drug
- The products are evolving to look less like cigarettes

Nicotine + propylene glycol
ELECTRONIC CIGARETTES

Many Questions, Few Answers

- How much nicotine do they actually deliver?
- Who is using them?
  - Current smokers >> exsmokers, rarely nonsmokers
- How many people are using them?
  - No good national data for adults.
  - Apparent rapid increase in prevalence, especially in 2013
- Why are they using them?
  - To quit smoking or reduce health risk
  - Use where they can’t smoke cigarettes
ELECTRONIC CIGARETTES
Many Questions, Few Answers

- They should be less harmful cigarettes that burn tobacco, but are they harmless?
  - What else is in the heated vapor?

- Will they help people stop smoking?
  - 1 randomized controlled trial so far *
  - E-cig vs. nicotine patch in smokers who wanted to quit
  - Both treatments had similar low quit rates

- If not, will they be harm reduction products?
  - Is long-term e-cig use or or “dual use” less risky?

* Bullen C et al, Lancet, 2013; 382:1629
ELECTRONIC CIGARETTES
Public Health Concerns

- Will they appeal to youth, who transition to cigarettes?
  “Gateway hypothesis”
What's Your Taste?

Choose E-cigarette Cartridge From 7 Delicious Flavors by XEO E-cigarettes!!

World's Most Powerful E-cigarette Available in 7 Flavors!!

Tastes your Mouth Crave For, Which Flavor you Smoke?

XEO
SLIM. CHARGED. READY TO GO.

AVAILABLE NATIONWIDE!

Visit us at blucigs.com/store-locator

blu ELECTRONIC CIGARETTES

Now Available in Retail Stores Nationwide

blucigs.com/store-locator/
Past 30 day tobacco product use by high school students

ELECTRONIC CIGARETTES

Public Health Concerns

- Will they appeal to youth, who transition to cigarettes?
- Will their use undermine no-smoking norms?
  - Should they be allowed where smoking is prohibited?
ELECTRONIC CIGARETTES

Public Health Concerns

- Will they appeal to youth, who transition to cigarettes?
- Will their use undermine no-smoking norms?
  - Should they be allowed where smoking is prohibited?
- Will they distract smokers who could quit from doing so?
WHY QUIT?

SWITCH TO BLU

blu is the smart choice for smokers wanting a change. Take back your freedom to smoke when and where you want without ash or smell. blu is everything you enjoy about smoking and nothing else.

Nobody likes a quitter, so make the switch today.

Visit blucigs.com
ELECTRONIC CIGARETTES

Public Health Concerns

- Will they appeal to youth, who transition to cigarettes?
- Will their use undermine no-smoking norms?
  - Should they be allowed where smoking is prohibited?
- Will they distract smokers who could quit from doing so?
- Is the nicotine in e-cigs a poison risk for young children?
- Could products be adapted to deliver other drugs?
ELECTRONIC CIGARETTES

The bottom line

- E-cigarettes are a “disruptive technology” *
- Will they be a net public health benefit or harm?
- Research to answer the question is needed
  - Long-term effects on health
  - Efficacy as a cessation tool
  - Monitor patterns of use nationally
- FDA regulations are urgently needed

ELECTRONIC CIGARETTES

Question for you

Should you recommend them to smokers?

- Many unanswered questions about safety, efficacy for quitting
- Tell smokers that they are not FDA approved
- Probably less harmful than combustible cigarettes
- Recommend trying “clean nicotine” first
- Don’t recommend but don’t discourage if smokers insist

Do not permit use in hospitals or health care facilities

E-cig use is not permitted at MGH

Consistent with American Heart Association guideline, Circulation, Aug. 26, 2014
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TREATING TOBACCO IN HEALTH CARE
2008 U.S. Public Health Service Guidelines – 5A’s

- Routine advice to quit is effective
- Brief counseling is more effective

- **ASK** all patients about smoking
- **ADVISE** all smokers to quit
- **ASSESS** smoker’s readiness to quit
- **ASSIST** smokers to quit
- **ARRANGE** follow-up care
The model of ambulatory practice is changing

- A team effort
- Create a system of care
- Embed it into routine practice flow
- Link to resources outside the office
**TREATING TOBACCO IN THE OFFICE**

*U.S. Public Health Service Guidelines – 5A’s*

<table>
<thead>
<tr>
<th>5A’s</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASK</strong></td>
<td>Done by office staff <em>(vital sign)</em></td>
</tr>
<tr>
<td><strong>ADVISE</strong></td>
<td>Core clinician role</td>
</tr>
<tr>
<td><strong>ASSESS</strong></td>
<td></td>
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<tr>
<td><strong>ASSIST</strong></td>
<td>Fax / email referral to Quitline</td>
</tr>
<tr>
<td><strong>ARRANGE</strong></td>
<td>or health system resource</td>
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</tbody>
</table>
ASK

About smoking

“Do you ever smoke cigarettes?”

“Meaningful use” of electronic health records requires smoking status documentation

About secondhand smoke exposure
A NEWER WAY TO ‘ASSESS’

- Don’t ask a smoker if they are ready to quit
- Just offer treatment

“Quitting smoking can be hard, but there is good treatment and I can help you. Would you like to try?”
REFERRAL RESOURCES

- **Telephone Quitline**
  - *Proactive* multisession counseling
  - Convenient, private, free
  - **1-800-QUIT NOW**

- **Text messaging**
  - http://smokefree.gov/smokefreetxt

- **Websites**  (www.tytostop.org)

- **Smartphone apps**
QUITWORKS system

Staff fax referral form to Quit line

Quit line calls smoker to offer counseling + NRT

Quit line gives doctor feedback on patient

Massachusetts Referral Form

Patients: Complete this section

- First Name
- Last Name
- Are you 18 or older? [Yes] [No]
- Mailing Address
- City
- State
- Zip
- Phone Number
- When should we call? [Morning] [Afternoon] [Evening] [No preference]
- Language Preference: [English] [Spanish] [Other (specify)]
- May we leave a message? [Yes] [No]
- Primary Insurance of Tobacco User: [Blue Cross Blue Shield MA] [Tufts Health Plan] [Harvard Pilgrim] [MassHealth/Medicaid] [Other]

I authorize this provider to release the information on this referral form to QuitWorks so that I may be contacted and participate in the QuitWorks program. I also authorize QuitWorks to disclose information about my progress in attempting to quit smoking to the health care provider listed on this form.

Health Care Providers: Complete this section

- Referring Provider: [ ] Phone Number
- Facility: [ ] Fax Number
- Address: 
- Send feedback report to: [Same as above] [ ]
- Name
- Phone Number
- Fax Number
- PEDIATRICS ONLY: [Mother] [Father] [Other (specify)]
- Patient’s relationship to child:
- Child/Children’s name: [to help with recordkeeping]

This form can be downloaded from WWW.QUITWORKS.ORG

Fax this form toll-free to 1-866-560-9113
MEDICATION COVERAGE BY HEALTH INSURERS

Massachusetts

- Medicaid – *all* FDA-approved meds!
  Even OTC nicotine gum, patch, lozenge
  Requires prescription but no prior approval

- Private insurance
  Most cover Rx only but that will be changing
A Case: Revisited

- What’s an electronic cigarette?

- Has he really tried everything?
  - NRT at adequate dose or in combination
  - Bupropion + NRT
  - Varenicline (if psychiatric status stable)
  - Behavioral support – key to bolster self-confidence

- Candidate for lung cancer CT screening
SUMMARY

- Treating smoking = chronic disease management
- Use combinations
  - Drugs + counseling
  - Combine drugs
- Use the systems being built to help you
  - Quitline  **(1-800-QUIT NOW)**
  - QuitWorks fax referral system
- Keep trying
- New harm reduction products are here to stay