How best to get your patients to stop smoking

Dr Alex Bobak
GP and GPSI in Smoking Cessation
Wandsworth, London
4 IN 10 CANCERS CAN BE PREVENTED

These are proven ways to reduce the risk of cancer.

Numbers and circle sizes show the maximum numbers of cancer cases that could be prevented each year in the UK.

LIFESTYLE

- Eat Fruit & Veg
  - Reduce: 13,100
- Keep Healthy Weight
  - Reduce: 18,100
- Drink Less Alcohol
  - Reduce: 12,800
- Be SunSmart
  - Reduce: 11,500
- Eat Less Processed & Red Meat
  - Reduce: 6,130
- Be Active
  - Reduce: 1,900
- Eat Less Salt
  - Reduce: 1,700
- Be Smoke Free
  - Reduce: 64,500
Smoking can cause at least 14 different types of cancer.
Smokers want to stop

All smokers

~70% want to stop\textsuperscript{1}

~30% try each year\textsuperscript{2}

~2–3% succeed in stopping each year\textsuperscript{3}

2. West R Getting serious about stopping smoking 1997.
3 Keys to stopping successfully:

- Wanting to stop smoking

But for 95-97% of smokers, wanting to stop is not enough\(^1\) – they need:

- Good quality support

- Evidence-based treatments

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## Long-term cessation rates

<table>
<thead>
<tr>
<th></th>
<th>No Pharmacotherapy</th>
<th>Pharmacotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Willpower alone</td>
<td>3-5%</td>
<td>4-6%</td>
</tr>
<tr>
<td>Support (trained adviser)</td>
<td>10-15%</td>
<td>20-30%</td>
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</table>
Proven smoking cessation interventions

- Brief advice from a healthcare professional (especially a GP)
- Behavioural support
- Pharmacotherapy
  - Nicotine Replacement Therapy
  - Bupropion (Zyban)
  - Varenicline (Champix)
Giving advice to smokers

Smoking advice from a healthcare professional (HCP), especially a GP, can be one of the most important triggers for a quit attempt.
What is the most common advice which GPs give to smokers?

Advice to stop smoking
Problems with ‘advice to stop’

- Negative message
- Nagging
- Nothing new
- Encourages conflict and denial
- Frustrating for both doctor and smoker
- Takes longer
- Puts you off doing it again
Ideas for a better form of advice?

Advice on HOW to stop smoking
# Long-term cessation rates

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<th>No Pharmacotherapy</th>
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<tbody>
<tr>
<td><strong>Willpower alone</strong></td>
<td>3-5%</td>
<td>4-6%</td>
</tr>
<tr>
<td>(46% of attempts(^1))</td>
<td></td>
<td>(49% of attempts(^1))</td>
</tr>
<tr>
<td><strong>Support (trained adviser)</strong></td>
<td>10-15%</td>
<td>20-30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.6% of attempts(^2))</td>
</tr>
</tbody>
</table>

Concept of Very Brief Advice (VBA) for smokers

1. Establish and record smoking status (QOF):
   “Do you smoke?/Are you still smoking?”

2. Advise how to stop:
   “The best way to stop is with support and treatment”

3. Offer support and treatment (QOF):
   “When you are ready just make an appointment with…….who is great!”
VBA DELIBERATELY DOES NOT:

• advise smokers to stop

• ask how much or what they smoke

• even ask if they want to stop
Benefits of very brief advice (VBA):

- Brief! (<30 seconds or it won’t be used)
- Records smoking status (future VBA as 70%+ relapse)
- Opportunistic (suitable for almost any consultation)
- Positive (or you put them off trying)
- Not confrontational or nagging (not telling them to stop)
- Informative (saying how to stop)
- Engaging (new information)
- Evidence-based
- Satisfies QOF
- NOT a smoking cessation consult (that’s for next time)
- Very simple: MINIMUM EFFORT, MAXIMUM REWARD
Modules on VBA:

- RCGP module:
  www.elearning.rcgp.org.uk
  “Behaviour change in cancer prevention”

- National Centre for Smoking Cessation and Training module:
  www.ncsct.co.uk/VBA

- BMJ Learning website
  search “VBA”
Support options in order of likely effectiveness:

- Group
- One-to-one
- Telephone helpline
- Text messaging programmes
- Stop smoking websites
- Stop smoking books
- Smartphone apps
Keys to good quality support in a General Practice:

- The advisor
- The consultations
Keys to a successful advisor

- Willing
- Available
- Flexible
- Empathetic
- Skilled listener and communicator
- Positive
- Motivational
- Realistic
- Knowledge of smoking cessation
- Cost-effective

* i.e. should be carefully selected, not just delegated
Keys to successful consultations

- Minimal delay
- Smoker owns the attempt
- Choice of support and treatment options
- Systems to make treatments easy to obtain
- Same advisor throughout
- Not telling smoker to stop but how to stop
- Routine use of CO monitoring
- Expect and normalise failure
- Enough time
- Good record keeping (Targets!)
Pharmacotherapy for nicotine dependence

- Nicotine Replacement Therapy (NRT)
- Bupropion (Zyban)
- Varenicline (Champix)
Nicotine Replacement Therapy
(NRT)
Nicotine replacement therapy

- Available in nine different forms
- Based on nicotine weaning\(^1\)
- Significantly reduces withdrawal symptoms and cravings vs placebo\(^2\)
- Significantly increases smoking cessation rate vs placebo (odds ratio = 1.58)\(^3\)
- Standard regime is to start NRT on quit date
- Treatment lasts 8–12 weeks
- Combination use now routine

NRT - Use and dosage

- Gum: up to 15 or 25/day 2mg, 4mg or 6mg
- Patch: 16 or 24 hours Variety, all of 3 strengths
- S/L tabs: up to 40/day 2mg
- Lozenges: min 8 max 15/day 2mg or 4mg
- Mini lozs: up to 15/day 1.5mg or 4mg
- Inhalator: 6-12 cartridges/day 10mg
- Nasal Spray: up to 64 sprays/day 1mg
- Oral Spray: up to 64 sprays/day 1mg
- Oral Strips: up to 15 oral films/day 2.5mg
Plasma nicotine levels – contrast between cigarettes and NRT

Adapted from: Tobacco Advisory Group of the Royal College of Physicians 2000.
Considerations for patients using NRT

- USE ENOUGH!
  - Avoid under-dosing and irregular use

- LONG ENOUGH!
  - Don’t stop early, continue 8–12 weeks

- NOT A PUFF!
  - Slower and less efficient source of nicotine than cigarettes so cannot compete
Bupropion
(Zyban)
Bupropion SR

- Non-nicotine prescription tablet originally developed to treat depression¹

- Modifies dopamine levels and noradrenergic activity¹

- Significantly increases smoking cessation rate vs placebo (odds ratio = 1.94)²

Patient assessment for bupropion

- **INDICATIONS:**
  - Adults motivated to stop smoking

- **CONTRAINDICATIONS**
  - History of seizures
  - History of eating disorder
  - History of bipolar disorder
  - CNS tumour
  - Acute alcohol or benzodiazepine withdrawal
  - Severe hepatic cirrhosis

- Bupropion should not be used in pregnancy
- Bupropion and its metabolites are secreted in breast milk
- For full details refer to the SPC at www.medicines.org.uk/emc

Patient assessment for bupropion

● INTERACTIONS
  - Antidepressants
  - Antiepileptics
  - Antivirals
  - Atomoxetine
  - Dopaminergics
  - Hormone antagonists

● CAUTIONS
  - Elderly
  - Predisposition to seizures eg drugs which lower seizure threshold, head trauma, diabetes
  - Hepatic impairment
  - Renal impairment
Dose of bupropion

<table>
<thead>
<tr>
<th>Days</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 6</td>
<td>150mg once daily</td>
</tr>
<tr>
<td>7 – 14</td>
<td>150mg twice daily</td>
</tr>
<tr>
<td>15+</td>
<td>150mg twice daily</td>
</tr>
</tbody>
</table>

Quit date

- Standard course 7-9 weeks
- Can be used for longer off license
Adverse events on bupropion

- Insomnia: Bupropion 24, Placebo 12
- Headache: Bupropion 11, Placebo 11
- Dry mouth: Bupropion 18, Placebo 10
- Nausea: Bupropion 13, Placebo 6

Bupropion in smokers with CVD. McRobbie 2001
Varenicline
(Champix)
Varenicline – partial nicotine agonist

Part blocking
• Reduces the pleasurable effects of smoking and potentially the risk of full relapse after a temporary lapse

Part Stimulating
• Relieves craving and withdrawal symptoms

Recruitment to abstinence

Point prevalence abstinence (%)

Time (weeks)

Drug treatment

Varenicline (n=352)
Bupropion SR (n=329)
Placebo (n=344)

* p<0.001 Varenicline vs Placebo
# p<0.001 Varenicline vs Bupropion SR
** p=0.13 Varenicline vs Bupropion SR

Patient assessment for varenicline:

- INTERACTIONS
  - No clinically meaningful drug interactions

- CAUTIONS
  - Breastfeeding
  - History of mental illness
    - No specific contraindications
    - Monitor mental state
Patient assessment for varenicline:

- **INDICATIONS:**
  - Adults motivated to stop smoking

- **Not recommended** in patients with end stage renal failure

- **Should not be used** during pregnancy

What about nausea?

- Up to a third get nausea
- Warn before prescribing
- Usually self-limiting
- Take with food or water
- Can use anti-emetics \textit{?}prochlorperazine (Stemetil)
- Adjust dose

Dose of varenicline

<table>
<thead>
<tr>
<th>Days</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 3</td>
<td>0.5mg once daily</td>
</tr>
<tr>
<td>4 – 7</td>
<td>0.5mg twice daily</td>
</tr>
<tr>
<td>8 – 14</td>
<td>1mg twice daily</td>
</tr>
<tr>
<td>15+</td>
<td>1mg twice daily</td>
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</table>

- Standard course 12 weeks
- Licensed for up to 24 weeks use
Smoking cessation treatment for depression, suicide, and self harm in England: Research Datalink: prospective cohort study

Kyla H Thomas National Centre for Clinical Research, Aspire Research and Consultancy, Oxford, UK. "Data is from a national Research Datalink: prospective cohort study of adult smokers in England. The study included 349 English general practices, 119,546 adult smokers, 81,545 NRT, 6,741 bupropion, and 31,260 varenicline. "

45.7% had used antidepressants

BMJ 2013;347:f5704 doi: 10.1136/bmj.f5704 (Published 11 October 2013)
Results and Conclusions

- No evidence that patients prescribed varenicline or bupropion had higher rates of fatal or non-fatal self harm or treated depression compared with those on prescribed nicotine replacement therapy.

- “These findings should be reassuring for users and prescribers of smoking cessation medicines.”
Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Prof Robert M Anthenelli, MD, Prof Neal L Benowitz, MD, Prof Robert West, PhD, Lisa St Aubin, DVM, Thomas McRae, MD, David Lawrence, PhD, John Ascher, MD, Cristina Russ, MD, Alok Krishen, MS, Prof A Eden Evins, MD

Published Online: 22 April 2016

8144 smokers
4028 non-psych; 4116 psych
16 countries, 6 continents
30th Nov 2011–13th Jan 2015

2037 varenicline
2034 bupropion
2038 NRT
2035 placebo
# Primary Outcome Measure: Neuropsychiatric AE Composite Endpoint

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Participants with Events n/N, %</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Varenicline</td>
<td>Bupropion</td>
<td>NRT</td>
<td>Placebo</td>
</tr>
<tr>
<td>Non-psychiatric</td>
<td>13/990 1.3%</td>
<td>22/989 2.2%</td>
<td>25/1006 2.5%</td>
<td>24/999 2.4%</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>67/1026 6.5%</td>
<td>68/1017 6.7%</td>
<td>53/1016 5.2%</td>
<td>50/1015 4.9%</td>
</tr>
<tr>
<td>Overall (both</td>
<td>80/2016 4.0%</td>
<td>90/2006 4.5%</td>
<td>78/2022 3.9%</td>
<td>74/2014 3.7%</td>
</tr>
<tr>
<td>cohorts)</td>
<td></td>
<td></td>
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</table>

Efficacy: Continuous Abstinence Rates (CARs) Non-Psychiatric and Psychiatric Cohorts

<table>
<thead>
<tr>
<th></th>
<th>Weeks 9–12</th>
<th>Weeks 9–24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Psychiatric Cohort</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varenicline (n=1005)</td>
<td>38.0*</td>
<td>26.1*</td>
</tr>
<tr>
<td>Bupropion (n=1001)</td>
<td></td>
<td>26.4*</td>
</tr>
<tr>
<td>NRT (n=1013)</td>
<td>25.5*</td>
<td>18.8*</td>
</tr>
<tr>
<td>Placebo (n=1009)</td>
<td></td>
<td>18.5*</td>
</tr>
<tr>
<td><strong>Psychiatric Cohort</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varenicline (n=1032)</td>
<td>29.2*</td>
<td>19.3*</td>
</tr>
<tr>
<td>Bupropion (n=1033)</td>
<td></td>
<td>20.4*</td>
</tr>
<tr>
<td>NRT (n=1025)</td>
<td></td>
<td>13.7*</td>
</tr>
<tr>
<td>Placebo (n=1026)</td>
<td></td>
<td>13.0**</td>
</tr>
</tbody>
</table>

* *p<0.0001 vs. placebo
** *p=0.0007 vs. placebo

1. Anthenelli R et al Lancet 2016: http://dx.doi.org/10.1016/S0140-6736(16)30272-0
EAGLES conclusions

- No significant increase in neuropsychiatric AEs in varenicline or bupropion compared with NRT patch or placebo

- Varenicline more effective than placebo, NRT patch and bupropion

- Bupropion and NRT patch more effective than placebo
Cost-effectiveness of NRT, bupropion and varenicline
From NICE guidance, 2002

“Both bupropion and NRT are considered to be among the most cost-effective of all healthcare interventions”

“Estimates of cost-effectiveness... are below £2000 per Life Year Gained”
Cost-effectiveness of varenicline

- From NCSCT guidance, 2012

- “The incremental cost-effectiveness ratio of varenicline compared with no pharmacotherapy has been estimated at between £950 and £1,140 per QALY gained”

- “Prolonging treatment duration from 12 to 24 weeks has also been shown to be cost-effective, resulting in an ICER of £622 per QALY”

Cost Per Quality Adjusted Life Year Gained

- £24,000: Statins - starting treatment at 60 years
- £14,000: Statins - starting treatment at 70 years
- £494: Smoking cessation interventions (estimate 1)
- £3,554: Smoking cessation interventions (estimate 2)

* Intensive statin therapy over standard dose therapy in patients with acute coronary syndrome

NHS Annual Expenditure (£millions)

(approx. £ millions expenditure annually)

The real world!

2007–2015 English NHS Stop Smoking Services Data
English Stop Smoking Services % 4 week quit rates (DoH)

As all smokers should be given the optimum chance of success in any given quit attempt, licensed pharmacotherapy, currently nicotine replacement therapy (NRT), varenicline (Champix) and bupropion (Zyban) should all be made available in combination with intensive behavioural support. Varenicline or combination NRT offers smokers the best chances of quitting, and unless clinically contraindicated, should be available as first-line treatments to all clients.\textsuperscript{1}
Numbers Needed to Treat (NNT) to Obtain 1 Long-Term Quitter?

- Brief advice = 40\(^{(1)}\)
- Adding medication to behavioural support.....
- NRT = 23\(^{(2)}\)
- Bupropion = 20\(^{(2)}\)
- Varenicline = 10\(^{(2)}\)

Numbers Needed to Treat (NNT) to Prevent a Premature Death?

- Brief advice = 80
- Adding medication to behavioural support.....
- NRT = 46
- Bupropion = 40
- Varenicline = 20
E-Cigarettes Summary

- About 3 million users in the UK (2017)
- 20-30 times safer than smoking
- High false perception of harm
- At least as effective as NRT for smoking cessation
- Unregulated so great variability
- Unlikely to cause any risk from passive vaping
- May be addictive
- No specific brands can be recommended as no trial data
- One product (e-Voke from British American Tobacco) is licensed for smoking cessation though not yet on the market
E-cigarette recommendations

- First recommend varenicline, combination NRT and bupropion for cessation – and if smokers won’t use these, only then should you sanction use of e-cigarettes

- Advise complete cessation of smoking with e-cigarettes not smoking reduction (45% e-cig users continue to smoke)\(^1\)

- Always recommend support- NHS stop smoking advisors paid the same to support quit attempts with e-cigs

1. Use of e-cigarettes (vapourisers) among adults in Great Britain. Action on Smoking and Health. May 2017