Breaking the Chains of Nicotine Dependence - A Breakthrough Approach

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Smoking Cessation in 2001

- Smoking contributes to all 4 leading causes of death in industrialised countries.

- The benefits of smoking cessation are undisputed and start from day 1 of quitting.

- Nicotine is a highly addictive substance and this addiction remains the greatest stumbling block to smoking cessation.

- There are a wide range of therapies now available with one year efficacy at 30% or more.
The bad news
Smoking in China

• Overall prevalence rates
  – 61% men and 7% women
  – highest in government staff, peasants and workers

• Predicted mortality
  – 50 million young persons alive today will be eventually killed by tobacco use
Smoking in China

- Mortality from smoking similar to Western countries
  - 50% of smokers die of a smoking related death
  - 25% of smokers die between 35 yo - 69 yo

- Smoking related deaths in China
  - 45% die from COPD, 15% from lung cancer, 8% CHD
Smoking = nicotine addiction

- Medically recognised addiction (DSM-IV, ICD-10)
- Nicotine addiction = heroin or cocaine addiction
- Neurobiological condition where nicotine effects both reward and withdrawal pathways in the brain
Nicotine is highly addictive

- Mildly pleasant stimulation initially, but it follows the behaviour very quickly (fast positive reinforcement)
- Leads to tolerance, so that higher doses are needed for the same effect
- Leads to brain changes so that smokers feel discomfort when nicotine level is low (negative reinforcement)
- Smoking relieves this discomfort and creates an illusion of positive effects.
Quitting smoking is the ONLY way to reduce tobacco-related deaths in the medium term and is the best thing that smokers can do to improve their own individual health risks.
The good news
Smoking- benefits of quitting

- Smoking cessation at 50 yo reduces the risk of dying within 15 years by 50%
- Effects on health after last cigarette
  - 20 mins = BP and HR drop to normal
  - 48hrs = no nicotine left in body
  - 5 years = risk of heart attack falls by half
  - 10 years = risk of heart attack same as never smoked
  - 10 years = risk of lung cancer falls by half
  - 20 years = risk of lung cancer similar to never smoked
FALL IN DEATH RATE FROM LUNG CANCER AFTER STOPPING SMOKING

DOLL, R. and PETO, R. BRITISH MEDICAL JOURNAL, 1979. Photograph 8
FALL IN DEATH RISK FROM CORONARY HEART DISEASE AFTER STOPPING SMOKING

U.S. PUBLIC HEALTH SERVICE
THE HEALTH CONSEQUENCES OF SMOKING, 1979. Photograph 4
Nicotine withdrawal syndrome

- **Main relevant subjective symptoms:**
  - Mood changes: Irritable/aggressive, depressed, restless. Lasts on average under 4 weeks. Can be severe.
  - Urges to smoke: Frequency usually declines within weeks, but bouts of strong urges can occur long-term. Similar to or greater than cravings for other addictive drugs.
  - Increased hunger: Usually until the new body weight stabilises, over several months. The average weight gain is about 5kg over the first year.
Most smokers quit by themselves

But there are now a range of effective aids which can make the task of quitting easier
The 5 A’s of smoking cessation

• **Ask** - about current and past tobacco use
• **Assess** - motivation to quit, lung function
• **Advise** - rewards of smoking cessation (hazards of smoking) - personalise
• **Assist** - prepare to quit, set date, discuss treatment options and behavioural aspects
• **Arrange** - referral to smoking cessation therapist, pharmacotherapy
Ask

- Identify the smokers and those they expose (spouses, children, work-mates)
- Obtain a smoking history (pack years, quit attempts, reasons for failing)
- Update smoking status with each visit/admission
Stages of Readiness to Quit

- **Nonsmoker**
- **Smoker**
- **Ex smoker**

Addiction and relapse are processes within the cycle.

- **Not ready (40%)**
- **Unsure (40%)**
- **Ready (20%)**
Assess

- Determine the smokers readiness to quit (not ready, unsure, ready)
- Establish the presence of any end organ damage (CHD, PVD, cerebrovascular disease)
- Check lung function by spirometry
Advise

• Provide clear supportive messages

• Emphasise both the benefits and pitfalls of continued smoking

• Personalise the message for each smoker
Assist

- Encourage cutting down
- Explore barriers to quitting
- Discuss treatment options
- Plan a quit date
Arrange

- Referral to smoking cessation therapist or group
- Prescribe nicotine replacement therapy and/or bupropion (Zyban)
- Regular follow up to advise on pharmacotherapy (doses, side-effects)
Stages of Readiness to Quit

Nonsmoker

Addiction

Smoker

Ask

Assess

Advise

Assess

Advise

Assist

Arrange

Ex smoker

Relapse

Not ready

40%

Unsure

40%

Ready

20%
Aids to Smoking Cessation

- NON PHARMACOLOGICAL
  - Self-help materials
  - Simple Advice from a Health Professional
  - Behavioral counseling
  - Hypnosis
  - Acupuncture
Aids to Smoking Cessation

- PHARMACOLOGICAL
  - Nicotine Replacement Therapy
  - Bupropion
  - Clonidine
  - Other antidepressants
  - Mecamylamine
  - Lobeline
  - Herbal Preparations
Advice from Doctors and Nurses

- 31 trials (more than 26,000 smokers)
- Primary care, hospital wards, outpatient clinics, industrial clinics
- SIMPLE ADVICE INCREASES THE QUIT RATE
- Odds Ratio 1.69 (95% CI: 1.45 to 1.98)
- More intensive advice slightly more effective
- Main effect is to motivate a quit attempt
Behavioral Counseling

• Specialised smoking cessation clinics or counselors
• BOTH ONE-TO-ONE TREATMENT OR GROUP THERAPY WORK
• Counseling more effective than brief advice
• No difference between different psychological approaches (except aversion therapy which is ineffective)
• No difference between effectiveness of group therapy or individual counseling
• Groups are probably more cost effective
Other Non-pharmacological Therapies

• Hypnosis
  – no more effective than other behavioral interventions

• Acupuncture
  – any short-term effects are likely to be placebo related
Relative effectiveness of therapies

<table>
<thead>
<tr>
<th>“Therapy”</th>
<th>Odds ratio</th>
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</thead>
<tbody>
<tr>
<td>Self help materials</td>
<td>1.0 - 1.5</td>
</tr>
<tr>
<td>Simple advise by health workers</td>
<td>1.4 - 1.9</td>
</tr>
<tr>
<td>Behavioural counselling/groups</td>
<td>1.6 - 2.7</td>
</tr>
<tr>
<td>NRT</td>
<td>1.6 – 2.8</td>
</tr>
<tr>
<td>Bupropion</td>
<td>1.9 – 3.9</td>
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</tbody>
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Acupuncture in 16 RCT showed no benefit over “sham” acupuncture
Nicotine replacement therapy (NRT)

- NRT is recommended for up to 3 months
- NRT has a great safety record
- Doubles success rates of behavioural therapies
- Gum/patch/inhalar/nasal spray/lozenges
- Similar efficacy for all types
- Customised to smokers preference
# Meta-analysis of nicotine replacement therapy trials

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Peto Odds Ratio</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gum (46 trials, N=16,482)</td>
<td>1.63</td>
<td>1.48 - 1.78</td>
</tr>
<tr>
<td>Patch (30 trials, N=14,638)</td>
<td>1.77</td>
<td>1.58 - 1.97</td>
</tr>
<tr>
<td>Intranasal spray (4 trials, N=887)</td>
<td>2.27</td>
<td>1.61 - 3.20</td>
</tr>
<tr>
<td>Inhaler (4 trials, N=976)</td>
<td>2.08</td>
<td>1.43 - 3.04</td>
</tr>
<tr>
<td>Sublingual tablet (2 trials, N=488)</td>
<td>1.73</td>
<td>1.07 - 2.80</td>
</tr>
<tr>
<td><strong>All NRT formulations</strong></td>
<td><strong>1.72</strong></td>
<td><strong>1.60 - 1.84</strong></td>
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Efficacy of NRT

- All of the trials of NRT have included some form of (at least) brief advice to smokers.
- Most effective if targeted to smokers motivated to quit and with high levels of nicotine dependency.
- Little evidence about role of NRT amongst smokers with low dependency (<10-15/day).
Nicotine replacement therapy: caution

- Should not be given for unstable cardiac disease
  - poorly controlled hypertension
  - unstable angina
- Close monitoring when given with bupropion
Nicotine replacement therapy: summary

- Clinical trials show NRT is effective, safe and very well tolerated.
- Greatest efficacy when doses are optimised to maintain serum nicotine levels
- Administered using one or a combination of preparations tailored to suit the smoker
Bupropion (Zyban)

Atypical antidepressant that inhibits neuronal uptake of noradrenaline and dopamine
Bupropion

- Slow release form licensed in USA, parts of Europe, New Zealand
- EFFECTIVE WHEN OFFERED WITH BEHAVIOURAL SUPPORT (OR 2.73, CI: 1.90-3.94)
- More effective than nicotine patch alone
- Its effectiveness can be further increased by addition of Nicotine Replacement Therapy
Bupropion & Nicotine Patch Study

- End of Treatment and One Year Abstinence n = 893

% Pt. Abstinence

Dosage and Administration

- Patients should set a **quit date** within the first 2 weeks of treatment with Zyban, generally in the second week.
- **Start Zyban ≥ 7 days before target quit date**
  - 150 mg every morning for first 3 days
  - For most patients, titrate to recommended and maximum dose of 300 mg/day (150 mg b.i.d., ≥ 8 hours between doses)
- Doses above 300 mg/day should not be used
- **Continue Zyban 150 mg b.i.d. for at least 7 weeks**
- Continue treatment for certain individuals (eg. relapse)
Side effects of Bupropion

- **Dry mouth** (10% vs. 5% placebo)
- **Insomnia** (35% vs. 20% placebo)
  - delay p.m. dose > 4 hours before going to bed
- **Seizures** (1/1000 anticipated... however)
  - NONE in any of the smoking cessation trials
Bupropion and seizures

- Bupropion does not cause seizures
- Bupropion lowers the seizure threshold comparable to other antidepressants
- Although the reported seizure rate on bupropion is 1/1000 clinical trials involving over 3,000 patients reported no seizures.
Bupropion: contraindications

- Seizures or past history of seizures
- During pregnancy or breast feeding
- History of - bulimia or anorexia nervosa
  - severe head injury
- Concomitant use with anti-depressants
Bupropion: caution

- Patients with severe liver disease or cirrhosis
- Concomitant use with drugs metabolised by
  - CYP 2B6 eg cyclophosphamide
  - CYP 2D6 eg flecainide, metoprolol, anti-psychotics
Bupropion: Summary

- Clinical trials show Bupropion is currently the most effective agent for smoking cessation
- Bupropion is well tolerated, non-addictive and has no withdrawal symptoms
- Screening patients for contraindications is necessary for safe prescribing
Zyban - GlaxoSmithKline New Zealand
Smoking Cessation: NZ perspective

- Adopted US guidelines
- NRT is sold direct to consumer
- NRT now subsidized by the government
- Smoking cessation products are advertised on TV
- Various organizations are funding
  - training of cessation therapist
  - running of cessation clinics
- Government subsidy on zyban under review
My opinion

- Is Bupropion safe?
- NRT vs Bupropion?
- Is direct to consumer (DTC) marketing appropriate for smoking cessation drugs?
- Can the GP do this on their own?
- Who should pay?
Smoking Cessation in 2001: Summary

- Smokers are coming under increasing pressure
  - restrictions on where smoking is allowed
  - greater taxes on cigarettes
  - adverse effects of passive smoking

- There is now a range of effective pharmacological preparations and non-pharmacological approaches for smoking cessation.
Thank you