Using nicotine to help smokers quit

Peter Hajek
Wolfson Institute of Preventive Medicine
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Giving nicotine to smokers: Two chapters of the story

- Nicotine replacement treatments (NRT) were met with a number of concerns and objections.
- Evidence and common sense prevailed and NRT were accepted as safe and effective.
- The second wave of the same idea is having a much tougher ride.
Chapter 1

- Ove Ferno at Leo noted use of oral tobacco in submarine crews unable to smoke, helped Leo develop nicotine chewing gum in 1971, first publication 1973
- Mike Russell instrumental in evidence on nicotine delivery and efficacy
- Gum approved in UK in 1980, in US in 1984
  - Some 10 years from development to use. The gap for much less radical medical innovations is now at least twice as long
What?
Giving nicotine to smokers?

• The initial reaction of many was a surprise
  ■ Is nicotine not the problem smokers are trying to get rid of?
  ■ Isn’t it like giving alcohol to alcoholics?
  ■ Doesn’t it enhance rather than curtail nicotine addiction?

• And
  ■ Isn’t it dangerous? (‘30-60mg lethal’)
  ■ Will it addict non-smokers and children (chewing gum is a kids’ product)
Manufacturers stepped carefully

- Strong medicalisation, numerous caveats, prescription-only, very low dose, warnings about overdose and side effects, use only after quitting, consumption limits
- Dozens of RCTs
- Key additions: patch 1991 (Novartis), nasal spray 1994, back to buccal absorption after that (including inhalator)
Health scares emerged but did not take root

• Case studies of NRT users who got MI
• Claims of adverse effects on BP and HR, ischemia, vasospasm, fibrinogen, atherosclerosis, ‘damage to cells that line blood vessels and the airways’
• ‘Not safe if used beyond three months’
• ‘Oral cancer risk’
• Limited number of zealots and limited media interest, objective studies prevailed
Why not developed into better ‘smoking replacements’?

- Some guesses
  - Solid sales with the existing approach
  - Licensing similar products via bioequivalence much easier than facing the hypertrophied regulatory hurdles generating huge expenditure and uncertain outcome
  - Perhaps also fear of a product becoming popular and rousing the zealots
Better products now appeared, with a population appeal and a promise to eradicate smoking.

They will maintain nicotine use though - backlash from zealots (and from pharma industry).

Old objections now revived and some new generated as well.
Nicotine itself has become a major risk

- Over decades of examining and publicising risks of smoking, effects of nicotine on adolescent brain did not feature
- It now dominates the discourse as the crucial risk and the main justification of anti-vaping regulations
- Denying smokers an easy way out is a small price to pay to protect adolescent brains
The claim is based on animal studies

- Animals damaged by continuous nicotine poisoning close to lethal nicotine levels from early age, unclear relevance
- Mice on N for 7 days and N+C for 4 days went to C place more = gateway (?)
  - No decrease in human cocaine use when smoking rates plummeted
- Plenty of humans use nicotine and there exist relevant human data
If such effects exist, here is where they would show up

- Only male adolescents smoke in some countries, in others there are no sex differences. Do the former have larger sex differences in mental health?
- In some countries, smoking rates in adolescence declined five-fold or more. Did it affect mental health and drug use?
- Huge differences, even small effects should be visible
  - Hope someone will have a look
Old doubts about helpfulness of nicotine revived

- Nicotine just keeps smokers addicted, ‘quitting smoking with nicotine is not really quitting’
- EC not only do not help smokers quit, they prevent quitting
- Using EC to quit can lead to ‘dual use’ and this is worse than smoking
‘Switch to other nicotine source is not quitting’

- The rational goal of tobacco control and smoking cessation is to help smokers avoid smoking-related illness.
- TEC trial: 9% in NRT arm on NRT at 12M, 56% in EC arm on nicotine EC and another 24% on nicotine free EC.
  - Bad if health risks decades later (but these are middle-aged heavy smokers who quit smoking).
  - Good if helps with quitting, weight gain, relapse, withdrawal discomfort, and provide enjoyment.
‘EC undermine quitting’

- Smokers who failed to quit with EC may be less likely to quit a year later – but this self-selected group just showed they are not good at quitting!
- Over 130 RCTs show nicotine helps smokers quit
- Population data: EC help smokers quit
- RCT data: EC help smokers quit
Large RCT cited as showing lack of efficacy

- N=6,006 smoking employees, opt out or included, had to order meds/EC
- EC or meds+EC (?), also 2 types of incentives
- 92% did not order EC and 95% did not ordered meds
- ‘Did not assess efficacy of use, just the offer’

Halpern et al. NEJM 2018
Large RCT that is difficult to interpret

- 6-M ‘quit rates’: 0.1% control, 1% in EC, 0.5% in meds+EC
- Incentives 2.9%, but repeated blood needed to claim $600; abstainers from other arms could have been less likely to bother
- At 12M: 0%, 0.3%, 0.3%, 1.2%

Halpern et al. NEJM 2018
Authors prudent: same for meds and EC; did not test use

UK anti-vaping activist on national TV on his claim that e-cigarettes reduce the probability of quitting: **We just had a large clinical trial published that looked at whether EC help people to quit, and it found it of no additional benefit.**
‘Dual use is worse than smoking’

- Dual users maintain their nicotine intake, but those vaping daily (rather than once a week) reduce their toxin intake.
- In TEC trial, non-quitters in EC arm were significantly more likely to cut cigs/day and CO intake by ≥50% than non-quitters in NRT arm.
- Dual use is better than smoking.
  - May even help with future quitting.
Summary

- NRT faced objections and scares, but evidence and common sense prevailed.

- New nicotine products face much stronger agendas, evidence and common sense are struggling this time round.