

Institution: Queen Mary University of London (QMUL)
Unit of Assessment: A1 (Clinical Medicine)
Title of case study: Smoking cessation: treating the intractable smoker
<p>1. Summary of the impact</p> <p>There is no ‘magic bullet’ for helping intractable smokers to quit. Rather, the story of this research is one of multiple studies that have built the knowledge base incrementally, allowing Professor of Clinical Psychology Peter Hajek and his team at the Wolfson Institute of Preventative Medicine to produce a targeted, evidence-based model of a specialist treatment that has fed directly into the establishment of the NHS smoking cessation service (NHS-SSS) and national smoking cessation policy (including NICE guidance), and changed clinical practice. The NHS-SSS treats 800,000 smokers per year. The approach is influential globally and has now been used in treating several million smokers and preventing hundreds of thousands of premature deaths.</p>
<p>2. Underpinning research</p> <p>Despite falling rates in many countries, smoking remains one of the biggest killers globally. It costs the NHS £1.5 billion a year. As smoking becomes less socially acceptable, those who continue to smoke are a self-selecting group for whom simple interventions such as brief advice have repeatedly failed. Since 1993, Hajek’s team, the Tobacco Dependence Research Unit (TDRU), at Queen Mary have systematically researched psychological and drug therapies for persistent smokers. Some studies identified effective treatments now used worldwide; others had negative findings, preventing costly but ineffective interventions being implemented.</p> <p>Most smokers in the UK 50 years ago were ‘social smokers’ who were naïve to health promotion and relatively easily influenced by brief interventions. While some people still respond to brief advice (and this remains a key intervention), many smokers today are nicotine dependent and relatively intractable. A substantial proportion have mental health problems, multi-morbidity and/or complex social circumstances. They may require specialist services and active (pharmacological and intensive behavioural) interventions – reflected in the emergence of the NHS-SSS in 1999.</p> <p>The focus of Hajek’s research has been on developing and testing new drug treatments (including balancing the benefits of pharmacotherapies with their potential harms); streamlining complex behavioural interventions so they can be applied on a large scale, and developing and piloting a treatment package that can be disseminated across the NHS.</p> <p>Hajek joined Queen Mary in 1992, bringing along an early version of what was then called the ‘Maudsley Model’ of a specialist smoking cessation intervention developed by himself and colleagues, and establishing the TDRU. TDRU’s work since 1992 has focused particularly on developing a practicable treatment model suitable for nationwide dissemination and undertaking randomised controlled trials, systematic reviews and meta-analyses to inform practical provision of smoking cessation treatments. Importantly, and almost by definition, no magic bullet exists for helping intractable smokers to quit. However, significant findings from the body of work at TDRU from 1993 to 2013 have extended the knowledge base in this challenging area. Of a total of over 100 studies by this Group in the past 20 years, we have selected ten key studies (note: these are <u>illustrative of</u> the kind of work they are doing rather than representing the totality of that work).</p> <p>2a: Systematic reviews</p> <p>The team have completed eight major and several smaller reviews, with statistical meta-analyses where appropriate, some in collaboration with the Cochrane Tobacco Addiction Review Group, and some commissioned by NICE and DH. These helped inform UK and international public health policy and the research agenda. They summarised and synthesised the evidence base on the following questions:</p> <ul style="list-style-type: none"> • What is the efficacy of different approaches to preventing relapse after smoking cessation? Main finding: neither skills training nor extended treatment contact has a sufficiently strong evidence base for routine use in smoking cessation clinics. Other potential approaches were identified which are now pursued by proactive NHS and NIHR funding initiatives (2009) [1]. • Are surgical outcomes worse if smokers quit shortly before elective surgery? Main finding: no significant difference in surgical outcomes between recent quitters and non-quitters (2011) [2].

Impact case study (REF3b)

- Do any alternative therapies not currently used by the NHS show efficacy or a promise that they might be effective? Main findings: Hypnosis, acupuncture, gradual cessation gadgets and several herbal remedies lack efficacy. The 'Alan Carr method' awaits evaluation.
- What is the efficacy of cytosine in smoking cessation? Main finding: Cytosine is effective. Given its low cost and good safety profile, its licensing should be expedited. (2013) [3]
- What is the relationship between an individual's rate of nicotine metabolism and their risk of dependence, severity of withdrawal symptoms and chance of successful quitting? Main finding: there is currently limited evidence that individual variation in nicotine metabolism can be used to tailor pharmacotherapy, but further studies are warranted.
- What is the efficacy and safety of aversive therapy (eg 'rapid smoking') as an aid to quitting? Main finding: primary studies were positive but generally of poor quality and publication bias may have occurred, hence the evidence base for this approach is weak.
- Are there any risks associated with nicotine withdrawal and use of nicotine replacement treatments in secondary care and in pregnancy? Main finding: NRT is safe in secondary care though its use in ICUs to prevent delirium is not warranted. NRT is safer than smoking in pregnancy, but with standard dosing and brief support, it lacks efficacy.
- What are the optimal treatment approaches for use in secondary care and in pregnancy? Main finding: brief interventions with or without medications are not effective, but treatments providing support for over four weeks have good evidence of efficacy.
- What is the efficacy and safety of interventions to reduce post-cessation weight gain? Main finding: whilst some pharmacotherapies appear to have short-term success, these benefits are not reliably sustained long term and significant side effects may occur. Dieting in the initial period of cigarette withdrawal may undermine the quit attempt (2012) [4].

2b: Randomised controlled trials (RCTs)

Hajek's team have published over 20 RCTs since 1993. Selected examples are:

- Brief interventions vs usual care during routine hospital admissions to promote smoking cessation. Main finding: no advantage over usual care. (2002) [5]
- Comparison of five different nicotine replacement therapy (NRT) products. Main finding: current NRT products are equally effective and have low abuse potential. (1999) [6]
- Efficacy of routine stop-smoking and relapse prevention interventions in pregnancy versus usual care. Main finding: brief interventions lack efficacy in this setting.
- Nicotine lozenge vs placebo in smoking cessation (pivotal trial). Main finding: Nicotine lozenges are effective.
- Varenicline vs placebo used for 4 weeks prior to quitting. Main finding: Varenicline pre-loading reduces enjoyment of smoking and smoke intake and facilitates smoking cessation. (2011) [7]
- Combining varenicline with nicotine patch or placebo patch. Main finding: Nicotine patch does not increase varenicline efficacy (2013) [8]
- Efficacy of nicotine mouth spray vs nicotine lozenges. Main finding: mouth spray was significantly better than lozenges at reducing urge to smoke.
- Efficacy of nicotine pouch vs placebo (pivotal trial). Nicotine pouch is effective.
- Ondansetron vs placebo in reducing withdrawal symptoms in smoking cessation. Main finding: no advantage over placebo.
- Varenicline vs placebo as maintenance following successful abstinence at 3 months (pivotal trial). Main finding: extended treatment improves long-term outcomes. (2006) [9]

2c: Cohort studies (17 in total since 1993; below are examples focusing on one research topic pioneered by Hajek's team: long-term use of NRT)

- Prevalence of long-term use of nicotine chewing gum among smokers treated at routine services. Main finding: 6% use gum at one year, primarily exceptionally heavy smokers who seem to need long-term help to maintain abstinence, gum use reduces weight gain.
- Effect of NRT cost on long-term use. Main finding: making NRT free had no major effect on the occurrence of their long-term use.
- Long-term use of different NRT products. Main finding: dependence potential is proportional to the speed of nicotine delivery.

2d: Standardisation of outcome measures

On the basis of many years' experience summarising different primary studies, Hajek's team proposed a standard set of outcome criteria to be followed by all studies to make comparison and synthesis easier. The standard is increasingly used by researchers worldwide (2005) [10].

This work was undertaken mainly by Hajek and his staff at TDRU. The main external collaborator was Prof Robert West at UCL and other members of the UK Centre of Tobacco Control Studies, Public Health Centre of Excellence, of which TDRU is the key member researching treatments for dependent smokers. Funding was from MRC, NIHR, NHS, charities and manufacturers of stop-smoking medication. Researchers on the author lists below who were working at Queen Mary at the time of the research include Hajek, McRobbie, Burrows, Meadow, Taylor, Mills and Myers.

3. References to the research (10 papers selected from over 100 from this research stream):

1. Hajek P, Stead LF, West R, Jarvis M, Lancaster T. Relapse prevention interventions for smoking cessation. *Cochrane Database of Systematic Reviews* 2009; CD003999. doi: 10.1002/14651858.CD003999.pub3
2. Myers K, Hajek P, Hinds C, McRobbie H. Stopping smoking shortly before surgery and postoperative complications: a systematic review and meta-analysis. *Archives of Internal Medicine* 2011; 171: 983-989. doi: 10.1001/archinternmed.2011.97
3. Hajek P, McRobbie H, Myers K. Efficacy of cytisine in helping smokers quit: systematic review and meta-analysis. *Thorax* 2013; doi: 10.1136/thoraxjnl-2012-203035.
4. Farley AC, Hajek P, Lycett D, Aveyard P. Interventions for preventing weight gain after smoking cessation. *Cochrane Database of Systematic Reviews* 2012; CD006219. doi: 10.1002/14651858.CD006219.pub3
5. Hajek P, Taylor TZ, Mills P. Brief intervention during hospital admission to help patients to give up smoking after myocardial infarction and bypass surgery: randomised controlled trial. *BMJ* 2002; 324: 87-89.
6. Hajek P, West R, Foulds J, Nilsson F, Burrows S, Meadow A. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. *Archives of Internal Medicine* 1999; 159: 2033-8.
7. Hajek P, McRobbie H, Myers K, Dhanji A, Stapleton J. Use of varenicline for four weeks before quitting smoking. Decrease in ad-lib smoking and increase in smoking cessation rates. *Archives of Internal Medicine* 2011; 171: 770-7.
8. Hajek P, Myers K, Dhanji A, McRobbie H. Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone? A randomised controlled trial. *BMC Medicine* 2013; 11:140 doi:10.1186/1741-7015-11-140.
9. Tonstad S, Tønnesen P, Hajek P, Williams K, Billing C, Reeves K. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA* 2006; 296: 64-71.
10. West, R., Hajek, P., Stead, L., & Stapleton, J. (2005). Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction* 2005; 100: 299-303.

4. Details of the impact**4a: Reframing the paradigm of smoking cessation**

One cumulative impact from 20 years of research at TDRU has been a shift in professional (and, to a lesser extent, public) understanding of the problem of persistent smoking. Doctors and others are now more likely to acknowledge that giving up smoking is not a simple issue of willpower; people who do not quit readily on brief advice are likely to have complex physiological, cognitive or social circumstances that militate against successful quitting. This paradigm shift was recognized in 2008 when the official US guideline on tobacco control was updated: "*Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit. Effective treatments exist, however, that can significantly increase rates of long-term abstinence*" [1]. The justification of this statement was argued in a parallel editorial in the *Annals of Internal Medicine* [2].

4b: Improving treatments for dependent smokers

This research has contributed to advances in pharmacological and behavioural treatments of dependent smokers used worldwide. For example: pivotal trials contributed to the licensing approvals of nicotine lozenge, varenicline (reference 8 above) and mouth spray; and the trial of varenicline pre-loading (reference 7 above) is changing clinical practice currently. The 'Maudsley'

Impact case study (REF3b)

Model of intensive stop-smoking treatment refined and piloted within TDRU is now used across NHS-SSS and abroad. More effective treatments of intractable smokers are contributing to the reduction in smoking-related morbidity and mortality in this group. Because tobacco dependence is closely linked to social disadvantage, this is also contributing to reducing health inequalities.

4c: Clinical and policy clarity on what does not work

Some TDRU trials and reviews have shown negative or ambiguous results, curtailing widespread implementation of ineffective interventions. For example, the RCT of brief intervention in routine hospital admission (reference 5 above) showed no significant improvement in quit rate. A similar study showed negative impact of midwife-led advice in pregnant women. The effect of these negative studies is that, increasingly, busy clinicians are not expected to deliver smoking cessation efforts to persistent smokers in settings where such interventions would be ineffective [3].

4d: Change in NICE guidelines and other official advice

- Hakek was co-opted onto the Programme Development Group for the NICE Public Health Guidance for smoking cessation (PH10). He undertook a rapid review of non-NHS treatments for smoking cessation as part of the guideline development process, incorporating the various reviews done by TDRU and others [4]. PH10 superseded previous NICE reviews of individual therapies and aimed for the first time to review the totality of possible therapies.
- Hakek advised the guideline development group for Public Health Guidance 34 Quitting Smoking in Pregnancy and Following Childbirth [5]. He wrote a 'Rapid review of interventions to prevent relapse in pregnant ex-smokers', which was appended to the NICE guidance.
- The series of studies on long-term use of nicotine replacement treatments (eg refs 10 and 11 above) were instrumental in relaxing NRT licensing and allowing long-term NRT use. Prior to this research it was believed that NRT should be prescribed only for short periods.
- Research from TDRU has influenced smoking cessation policy beyond the UK. For example, the World Health Organisation Policy Recommendations cites Hajek's research [6].

4d: Policy investment in specialised smoking cessation services

This work contributed to significant policy shift towards specialist smoking cessation services. NHS-SSS, established in 1999, is unique internationally as a support for smokers motivated to quit but unable to do so unaided [7]. The service provision framework employed by the smoking cessation clinics was originally based on the Maudsley model developed by Hajek *et al* and subsequently refined by him at QMUL in collaboration with others. It consists of regular meetings (group or one to one) with a trained adviser using structured, withdrawal-oriented support with smoking cessation medications. The NHS-SSS, which treats 800,000 smokers annually, operates in dialogue with a number of specialist teams, including TDRU, who continue to undertake studies whose findings directly inform the refinement and extension of the clinical service.

5. Sources to corroborate the impact

1. Treating Tobacco Use and Dependence: 2008 Update. U.S. Department of Health and Human Services. Rockville (MD): Public Health Service; May 2008.
<http://guideline.gov/content.aspx?id=12520#Section420>
2. Steinberg MB, Schmelzer AC, Richardson DL, Foulds J: The case for treating tobacco dependence as a chronic disease. *Annals of Internal Medicine* 2008; 148: 554-556.
3. Fiore MC, Baker B. Should Clinicians Encourage Smoking Cessation for Every Patient Who Smokes? Smoking Cessation for Every Patient Who Smokes. *JAMA* 2013; 309: 1032-33.
4. NICE Public Health Guidance 10. Smoking Cessation Services (2008).
www.nice.org.uk/PH010
5. NICE Public Health Guidance 26. Quitting Smoking in Pregnancy and Following Childbirth (2010). <http://guidance.nice.org.uk/PH26/Guidance/pdf/English>
6. World Health Organization. Policy recommendations for smoking cessation and treatment of tobacco dependence. Geneva: World Health Organization (2003, still current).
www.who.int/tobacco/resources/publications/tobacco_dependence/en/
7. Bauld L, Bell K, McCullough L, Richardson L, Greaves L. The effectiveness of NHS smoking cessation services: a systematic review. *Journal of Public Health* 2010; 32: 71-82.
8. Mardle T, Merrett S, Wright J, Percival F, Lockhart I. Real world evaluation of three models of NHS Smoking Cessation Service in England. *BMC Research Notes* 2012; 5: 9.