Does cigarette reduction while using nicotine replacement predict quitting?

Observational evidence from the Rapid Reduction Trial

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In smoking cessation many pharmacotherapies can safely be given to quitters before quit day, for example:

- Varenicline—evidence of efficacy (Cahill et al. 2013)
- Nicotine replacement (NRT) sometimes used in this way—not as standard. Evidence of efficacy inconclusive (Lindson & Aveyard 2011)

Pre-quit pharmacotherapy may break learned associations between smoking and pleasure, leading to reduced consumption.
Smoking reduction occurs in smokers asked to smoke ad lib whilst using pre-quit pharmacotherapy (Lindson & Aveyard 2011; Hajek et al. 2011)

Reduction may in turn be associated with quitting altogether

Hajek et al. (2011) - ad lib smokers who reduced their smoking (cotinine) by 50%+ during varenicline use were more likely to quit

Rose et al. (2010) - ad lib smokers whose exhaled carbon monoxide (CO) levels decreased by more than 55.6% whilst using nicotine patches more likely to quit.

Figure from: Hajek P, McRobbie HJ, Myers KE, Stapleton J, Dhanji A. Use of varenicline for 4 weeks before quitting smoking. Decrease in adlib smoking and increase in smoking cessation rates. Arch Intern Med 2011; 171 (8): 770-777
Background

• If quitting success is only likely in smokers responding to pre-quit medication by reducing consumption cessation advisors could use this to direct treatment
  
  – Reaction to medication could be monitored, and discontinued if no response
  – Length of pre-quit treatment could be tailored, according to time taken to reach reduction target

• This study adds to existing evidence by looking at the effect of behavioural instructions during the pre-quit period
  
  – Reducing cigarette consumption ‘vs’ smoking as usual
  – Is the association between smoking reduction and quitting moderated by medication use and/or the behavioural instruction?
Aims

To look for further evidence of an association between pre-quit smoking reduction, whilst using NRT over a two week period, and future abstinence.

Explore this further by investigating the impact of pre-quit behavioural instructions
Method

• Observational analysis of an RCT: The Rapid Reduction Trial (RRT); N=697
  
  – Participants randomised to: 1) two weeks of nicotine patches whilst advised to smoke as normal, OR 2) two weeks of nicotine patches plus acute NRT whilst advised to reduce smoking, before quitting completely

• Setting: Primary care in the West Midlands, UK

• Participants: smoking 15+ cigarettes per day (cpd) and motivated to quit

• Key variables:
  
  – Reduction in smoking consumption (cpd & exhaled carbon monoxide (CO), between baseline and quit day two weeks later. Measured continuously and dichotomously (<50% vs ≥50%)
  
  – Smoking abstinence defined using Russell Standard (RS) (West et al. 2005) at 4 week and 6 month follow-up, validated using exhaled CO <10ppm
Analyses

• Logistic regression used to determine if changes in smoking were associated with abstinence, with and without adjusting for potential confounders

• Adjusted for following baseline variables: gender, age, ethnicity, qualifications, employment, age started smoking, nicotine dependence, saliva cotinine, number of previous quit attempts, length of longest quit attempt, living with smoker, confidence in quitting, trial arm, trial arm preference

• Unadjusted analyses split by trial arm to test whether associations varied by behavioural treatment allocation

• Analyses conducted using IBM SPSS Statistics 22
Results

- Participants evenly split between males and females, a mean age of 49, smoked 20 cpd, and had an FTND of 6 (highly addicted)

- 421 and 517 of the total 697 participants provided the required cpd and CO data respectively

<table>
<thead>
<tr>
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<th>Abrupt Arm</th>
<th>Reduction Arm</th>
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<tbody>
<tr>
<td>% Cpd reduction; mean (sd)</td>
<td>28 (27)</td>
<td>69 (18)</td>
</tr>
<tr>
<td>% CO reduction; mean (sd)</td>
<td>20 (33)</td>
<td>48 (67)</td>
</tr>
<tr>
<td>Cpd reduction ≥ 50%; n/N (%)</td>
<td>52/237 (21.9%)</td>
<td>161/184 (87.5%)</td>
</tr>
<tr>
<td>CO reduction ≥ 50%; n/N (%)</td>
<td>49/291 (16.8%)</td>
<td>132/226 (43.7%)</td>
</tr>
</tbody>
</table>

- 44% and 19% of participants were abstinent at 4 week and 6 month follow-up respectively
Results

Cigarettes per day (cpd) reduction
• No association between cpd and abstinence at 4wk & 6mth follow-up, measured continuously or dichotomously, in the adjusted or unadjusted analyses

• E.g. the odds ratio for association between degree of cpd reduction & 4 wk abstinence was 1.02 (95%CI=0.92 to 1.13)

Exhaled carbon monoxide (CO) reduction
• For every 10% reduction in CO participants were 9% more likely to be abstinent at 4wk follow-up (adjusted); OR=1.09 (95%CI=1.03 to 1.15)

• Unadjusted analyses showed modest association between reducing by 50%+ and quitting at 4wks. Didn’t persist in the adjusted model

• No significant associations observed with 6mth abstinence
# Results

Associations between smoking reduction and abstinence at 4 weeks and 6 months post-quit, split by trial arm (abrupt versus reduction)

<table>
<thead>
<tr>
<th></th>
<th>Four week follow-up</th>
<th>Six month follow-up</th>
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<tr>
<td></td>
<td>Odds of abstinence</td>
<td>Odds of abstinence</td>
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<td></td>
<td>abrupt arm</td>
<td>in reduction arm</td>
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<td></td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
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<td>Trial arm x</td>
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<td>reduction</td>
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<tr>
<td>Continuously measured cpd reduction</td>
<td>1.04 (0.95 to 1.14)</td>
<td>1.27 (1.08 to 1.51)</td>
</tr>
<tr>
<td>Dichotomously measured cpd reduction</td>
<td>0.99 (0.53 to 1.85)</td>
<td>2.18 (0.89 to 5.34)</td>
</tr>
<tr>
<td>Continuously measured CO reduction</td>
<td>1.05 (0.98 to 1.11)</td>
<td>1.03 (0.98 to 1.09)</td>
</tr>
<tr>
<td>Dichotomously measured CO reduction</td>
<td>0.87 (0.47 to 1.60)</td>
<td>2.52 (1.47 to 4.35)</td>
</tr>
</tbody>
</table>

- Bonferroni correction (Bonferroni 1936) applied: p=0.05/8 tests= p=0.01

- One significant interaction - no associations in abrupt trial arm; however a 50%+ reduction in CO was predictive of abstinence at 4wks in reduction arm
Results

The interaction effect between reduction in exhaled carbon monoxide (CO) levels and trial arm, on the probability of smoking abstinence at four week follow-up.
Conclusions

• In this observational study of data from a 2-armed RCT comparing abrupt quitting to reducing smoking to quit pre-quit smoking reduction occurred in both trial arms.

• Cpd reduction was not associated with quitting success, but there was moderate evidence that CO reduction may be associated with an increased probability of quitting at 4wk, but not 6mth, follow-up.

• This was explained by increased probability of quitting in the reduction arm, although the abrupt arm were not more likely to be abstinent at four weeks if they reduced their CO levels.

• Findings contradict previous literature, which found smoking reduction predicted quitting success when using pre-quit pharmacotherapy (Hajek et al. 2011; Rose et al. 2009; Rose et al. 2010).
Conclusions

• Larger smoking reductions in the reduction arm were likely due to the behavioural instruction to reduce

• The interaction effect suggests this instruction, rather than NRT pretreatment, was associated with abstinence

• Effects were modest and should be treated with caution

• Evidence for a benefit of nicotine preloading is still inconclusive (Lindson & Aveyard 2011), and should be established before further investigation

• Mechanisms of the effects of varenicline should be further examined to see if they can be used to guide treatment
Thanks to…

• **British Heart Foundation** - the Rapid Reduction Trial funders

• Co-authors and investigators on the Rapid Reduction Trial: **Paul Aveyard, Robert West and Susan Michie**

• All of the **researchers and participants** who worked on the trial in particular **Miriam Banting** who also helped with data cleaning
References

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