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Abrupt nicotine reduction as an endgame policy: a randomised trial

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ABSTRACT

Objective To determine if smokers unmotivated to quit reduce usual cigarette consumption when cigarettes priced according to nicotine content are made available.

Methods Randomised, parallel-group, trial (ACTRN12612000914864) undertaken in Wakatipu/Central Otago, New Zealand. Dependent adult daily smokers unmotivated to quit were randomly allocated to an intervention group provided with 12 weeks supply of free very low nicotine content (VLNC) cigarettes, or to a control group, who were free to purchase their usual cigarette brand over the same period. The primary outcome was change from baseline in the daily mean number of usual cigarettes smoked over the previous week, measured at 12 weeks. Secondary outcomes at 6 and 12 weeks included cigarettes smoked per week (also measured at weeks 1–6 and 9), salivary cotinine, tobacco dependence, smoking satisfaction/craving, behavioural addiction to smoking, autonomy over smoking, motivation to stop, price at which participants would purchase VLNC cigarettes, quitting and adverse events.

Results Thirty-three smokers were randomised (17 intervention, 16 control). A NZ$15 price differential (per pack of 20) based on nicotine content led to a halving in the mean number of cigarettes smoked per day over the previous week, a reduction in tobacco dependence and an increase in quitting. Intervention participants smoked a similar total number of cigarettes (usual plus VLNC) as those in the control group, exposing them to a similar level of toxicants.

Conclusions Smokers unmotivated to quit reduce their usual cigarette consumption (and thus nicotine exposure) when VLNC cigarettes are made available at a significantly reduced price.

INTRODUCTION

Cigarettes with very low nicotine content (VLNC), defined as ≤2 mg nicotine content and ≤0.05 mg nicotine yield per stick, can halve smokers' addiction scores.[1] Furthermore, when used by smokers motivated to quit, with[2–6] as well as without[6–8] nicotine replacement therapy (NRT), the chances of achieving smoking abstinence are increased.[2–4 6 7] Nicotine reduction in cigarettes could be an important component of New Zealand's (NZ) smoke-free 2025 goal (defined as <5% of the adult population smoking). Resistance in NZ to a nicotine reduction policy is unlikely to be strong, given 85% of NZ smokers want the addictiveness of cigarettes reduced.[9] Nicotine reduction could involve selling VLNC cigarettes at a significantly reduced price[10] or by having a mandated reduction in nicotine across all brands simultaneously.[11] Implicit in these strategies are the assumptions that a threshold of nicotine exposure exists, below which addiction is minimised and above which it is sustained (VLNC cigarettes would come under this threshold); and once nicotine content is lowered, it would be difficult for smokers to obtain enough nicotine by increasing their puff frequency/intensity.[12] A key question is whether nicotine reduction should be gradually introduced or involve an immediate reduction to a nicotine level at which no compensatory smoking occurs.[12] It is not known how smokers would react and/or adapt to such changes.

Using a parallel-group trial design we sought to investigate smokers' behaviour under a hypothetical policy scenario of a lower tobacco excise tax on VLNC cigarettes compared with usual cigarettes, so that VLNC cigarettes were substantially cheaper.[10 13] The objective of the pilot study was to obtain sufficient data to inform the sample size calculation for a larger trial. We hypothesised that smokers offered VLNC cigarettes that were cheaper than usual cigarettes would smoke fewer usual cigarettes, have reduced levels of tobacco dependence, make more quit attempts and be more likely to quit.

METHODS

Setting/participants

Smokers from Wakatipu/Central Otago in NZ, who were unmotivated to quit, were recruited between November and December 2012 using media advertising. People were eligible provided they: were aged ≥18 years, were daily smokers, had their first cigarette within 30 min of waking, could provide written consent, had a mobile phone and intended to reside in the region for the next 6 months. Only one person per household was eligible. Pregnant and breastfeeding women were excluded, as were people who only smoked roll-your-own (RYO) tobacco, were current users of NRT products (including electronic cigarettes with nicotine), were currently enrolled in a quit smoking programme and/or used only non-cigarette tobacco products. There were no exclusion criteria related to mental illness, substance abuse and/or use of particular medications. The trial was registered with the Australasian Clinical Trials Network: ACTRN12612000914864.

Randomisation/blinding

Participants were randomised in a 1:1 ratio using block randomisation with varying block sizes of 2 and 4, using sequentially numbered opaque sealed envelopes (produced by a statistician and assigned by a researcher to participants). The trial was not blinded.

Intervention

Participants were randomised to either an intervention or control group approximately 2 weeks before a scheduled 10% increase in tobacco excise tax on 1 January 2013, resulting in the average price of a 20 pack of usual cigarettes being NZ $16.50 compared with an average of NZ$15 at the start of the study. We hypothesised that participants would be more price conscious than usual at this time. Those in the control group were able to purchase their usual brand of cigarettes as normal. Those in the intervention group were provided with 12 weeks supply of VLNC cigarettes at the time of randomisation, to be used ad libitum (MAGIC brand, 22nd Century, USA, with a similar nicotine and tar content to the Quest 3 VLNC cigarettes used in an earlier trial of ours, which reported high acceptability of the cigarettes[5]). The VLNC cigarettes were supplied to participants at no charge, thus creating a large price differential with usual cigarettes. The number of cartons (200 cigarettes/carton) supplied was based on the average number of cigarettes smoked by the participant in the previous week. Labstat Canada undertook verification of the nicotine and tar content of the VLNC cigarettes: mean 0.7 mg nicotine content (SD=0.4 mg); mean 0.04 mg nicotine yield (SD=0.003 mg); mean 3.0 mg tar yield (SD=0.46 mg). The mean nicotine content per cigarette for the 22 most popular cigarette brands in NZ was 8.7 mg (range 5.6–12.4 mg).[10] The VLNC cigarettes used were not available for general sale in NZ or elsewhere.

Outcomes

Baseline data included age, sex, ethnicity, education, smoking history and type of cigarettes smoked (factory/RYO). Participants underwent a run-in period where they reported the number of usual cigarettes smoked during the prior 24 h, for 7 days before their scheduled baseline interview (collected using daily text messages, with paper diary backup). Participants with fewer than 4 days data were excluded and not randomised.

The primary outcome for the trial was change from baseline in the daily mean number of usual cigarettes smoked per day (CPD) over the previous week, measured at 12 weeks. Secondary data included the number of CPD in the prior 24 h, collected daily for weeks 1–6, then at 9 and 12 weeks after randomisation (obtained by text messages, with paper diary backup). This measure included VLNC as well as usual CPD in the intervention group. If no response to a text was received within 4 h, the participant was phoned by a researcher for the information. Data were summed to give the 'number of cigarettes smoked in the previous week'. To offset the costs of replying to study texts, participants were given a $20 food/petrol voucher at the start of the study. An additional $150 food/petrol voucher was provided on completing the 12-week follow-up.

Additional data collected at baseline (face-to-face), 6 weeks (by telephone) and 12 weeks after randomisation (face-to-face) included: tobacco dependence, based on time to first usual cigarette after waking; smoking satisfaction and craving reduction for usual cigarettes (modified Cigarette Evaluation Questionnaire (mCEQ);[14] behavioural dependence on smoking (Glover Nilsson Smoking Behavioural Questionnaire—GN-SBQ);[15] the Autonomy Over Tobacco Scale (AUTOS);[16] the single-item Motivation to Stop Scale;[17] and adverse events. Participants were asked about the number of attempts they made to give up smoking their usual cigarettes in the past 3 months (asked at baseline) or since baseline (asked at 6 and 12 weeks). Quitting was defined as having stopped smoking usual cigarettes for ≥24 h. Seven-day point prevalence abstinence was defined as the proportion of participants who consumed no usual cigarettes in the previous 7 days (people in the intervention group were also asked about consumption of VLNC cigarettes). Continuous abstinence was defined as self-report of smoking not more than 5 usual cigarettes since randomisation. Method of quitting was also asked. Participants were asked at baseline and 12 weeks about what price they would purchase VLNC cigarettes at. Finally, we collected 1 mL saliva samples from participants at baseline, 6 and 12 weeks, and batch-tested them for cotinine. Samples were extracted via protein precipitation with internal standard (D4-nicotine) in acetonitrile, followed by dilution with water. Samples were then analysed on an Agilent 1200 series high-performance liquid chromatograph and eluted via solvent gradient from a Phenomenex Synergi Polar-RP 80 A 4 μm 150×4.6 mm column, with mass spectral detection by an ABSciex 3200 QTrap mass spectrometer. The assay was quantitative between 5 and 10 000 ng/mL with a limit of detection of 0.5 ng/mL. The extraction efficiency of the method was reported as approximately 95%, with a precision of better than 5%. Samples were collected at varying times of the day. At the end of the study, quitting support was offered to all participants still smoking.

Sample size/analysis

Sixty participants (30 per arm) were sought over a 6-week period. Data were collected on paper-based forms, entered into Excel and then imported to SAS. Analyses were undertaken on an intention-to-treat and per-protocol basis (excluding withdrawals and those lost to follow-up). Primary outcome data were non-normally distributed and thus median and IQR data are presented. Change from baseline for the continuous outcomes were analysed using t tests if data were normally distributed, or Mann-Whitney tests if data were non-normally distributed (quitters were removed for these analyses). Repeated measures analysis using mixed models was conducted to compare the total number of cigarettes smoked by the control group (usual) and total number smoked by the intervention group (usual plus VLNC cigarettes) at all visits. All tests of significance were two-tailed. Participants lost to follow-up were presumed to have not reduced their level of smoking of usual cigarettes.

RESULTS

Overall, 54 people responded to the advertising, with 18 ineligible and 3 excluded after the 7-day run-in. A total of 33 eligible callers were randomised. Only one person (in the control group) was lost to follow-up at 12 weeks. No withdrawals or pregnancies occurred (figure 1) and no differences were seen in baseline variables between the two arms (table 1). Compliance with replying to the text messages and/or use of the backup diary was high (82% control, 89% intervention). Two adverse events were reported (one in each group) but neither was attributable to the intervention (upper respiratory tract infection, broken tooth).

Number of usual and VLNC cigarettes smoked

The intervention group halved their daily median number of usual CPD over the previous week at all time points, in comparison to no change in CPD in the control group (figure 2). There was a significant reduction in the daily median number of usual CPD over the previous week from baseline to 6 weeks in the intervention group compared with the control group, with this finding reflected in the salivary cotinine readings (table 2). However, for the primary outcome of change from baseline to 12 weeks in the daily median number of usual CPD over the

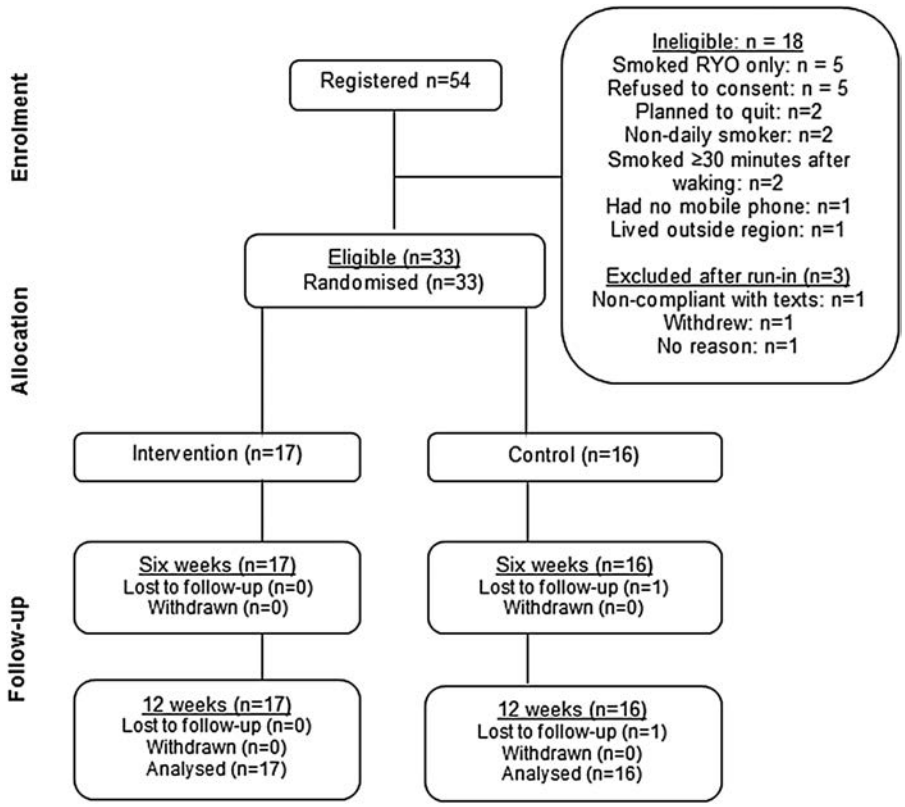

Figure 1 Flow chart of recruitment and retention of participants (RYO, roll-your-own).

previous week the reduction observed was not statistically significant (p=0.066), with salivary cotinine readings once again supporting these findings (table 2). A similar result was seen with per-protocol analysis (data not presented). Overall, participants in the intervention group smoked a similar total amount of CPD (usual plus VLNC cigarettes) as participants in the control group over the 12-week period (repeated measures p=0.692) but replaced the usual cigarettes they stopped smoking with VLNC cigarettes.

Effect of the tobacco excise tax increase on smoking behaviour

Participants were randomised on average 2.5 weeks before the tobacco excise tax increase (intervention: mean=2.55 weeks, SD=0.98; control: mean=2.54 weeks, SD=1.07). In the control group, the tax increase had no observed effect on the daily mean number of usual CPD over the previous week (figure 2). However, intervention participants reduced the number of usual CPD at week 3, and by week 4 were smoking more VLNC than usual cigarettes. The number of VLNC cigarettes smoked gradually decreased over the 12-week period, while the number of usual CPD slowly increased (figure 2).

Tobacco and smoking dependence

Participants were heavily tobacco dependent at baseline but by 12 weeks dependence had reduced, more so for those in the intervention group than the control group (seven vs two participants, respectively, extended their time to first usual cigarette to >30 min from waking). We observed a greater reduction in the mean total AUTOS score from baseline to 6 and 12 weeks in the intervention group than the control group, although this was not statistically significant (table 2). We found a statistically significant reduction in mean scores for the GN-SBQ in the intervention group compared with the control at 6 and 12 weeks (table 2). No significant difference between the groups was noted for the mCEQ at 6 and 12 weeks, with the exception of craving reduction, which had a greater reduction from baseline to 12 weeks in the control group (table 2).

Quitting behaviour

The change from baseline to 12 weeks in motivation to stop smoking was not significantly different in the intervention group (mean=0.60, SD=1.18) compared with the control group (mean=0.29, SD=0.99, p=0.447). However, participants in the intervention group were more likely to have made a quit attempt during the 12-week study period (seven participants), compared with those in the control group (one participant, Fisher's exact test p=0.041). In the intervention group, two participants had quit smoking usual cigarettes and no participants had quit smoking usual as well as VLNC cigarettes (7-day point prevalence abstinence at 12 weeks). In comparison, one participant had quit smoking usual cigarettes in the control group. In terms of continuous abstinence at 12 weeks, two participants in the intervention group had quit smoking usual cigarettes compared with one in the control group.

Participants' views on price

At baseline, participants in both groups had very similar views on what price they would purchase VLNC cigarettes at instead of usual cigarettes (figure 3). However, after 12 weeks of access to the VLNC cigarettes, participants in the intervention group were reluctant to purchase the cigarettes unless there was a significant price differential (figure 3).

DISCUSSION

Results from this small pilot trial indicate that when a $15–$16 price differential based on nicotine content is offered for cigarettes, smokers will reduce the amount of usual cigarettes they

Table 1 Baseline characteristics

Variables	Intervention group N=17 (%)	Control group N=16 (%)
Gender		
Female	11 (65)	7 (44)
Ethnicity		
Non-Māori	15 (88)	15 (94)
Māori	2	1
Age at baseline (years)		
Mean (SD)	41.8 (16.8)	37.8 (14.1)
Highest level of education		
<Year 12	7 (41)	5 (31)
≥Year 12	10 (59)	11 (69)
Type of tobacco smoked		
Factory made only	11 (65)	7 (44)
Factory as well as roll-your-own	6 (35)	9 (56)
Age started smoking (years)		
Mean (SD)	14.1 (2.5)	15.0 (2.6)
Number of usual CPD		
Mean (SD)	16.3 (6.7)	17.3 (6.5)
Salivary cotinine (ng/mL)		
Median (IQR)	24 (17–46)	36 (24–63)
Motivation to stop scale		
Median (IQR)	3 (3–4)	4 (2–4)
mCEQ (mean, SD)		
Satisfaction	4.2 (1.4)	4.4 (1.0)
Psychological reward	4.1 (1.7)	4.5 (1.3)
Aversion	1.4 (0.6)	1.5 (0.6)
Sensations	2.9 (2.1)	3.3 (1.3)
Craving	5.5 (1.3)	6.1 (1.0)
GN-SBQ (mean, SD)	21.3 (6.4)	25.5 (6.3)
AUTOS (mean, SD)		
Total score	24.1 (8.9)	26.4 (5.9)
Withdrawal symptoms	7.3 (2.8)	7.9 (2.3)
Psychological dependence	8.9 (3.0)	9.7 (1.9)
Cue-induced cravings	7.9 (3.7)	8.9 (2.7)

Motivation to stop was measured on a scale of 1–7, where 1=I don't want to stop smoking, 2=I think I should stop smoking but don't really want to, 3=I want to stop smoking but haven't thought about when, 4=I really want to stop smoking but I don't know when I will, 5=I want to stop smoking and hope to soon, 6=I really want to stop smoking and intend to in the next 3 months, and 7=I really want to stop smoking and intend to in the next month.
mCEQ=Modified Cigarette Evaluation Questionnaire. Each subscale was scored 1–7, where 1 is not at all, 2 is very little, 3 is a little, 4 is moderately, 5 is a lot, 6 is quite a lot and 7 is extremely.
GN-SBQ=Glover Nilsson Smoking Behavioural Questionnaire. Scored 0–4 for each question with 11 questions. Total score=44. Scores of <12=mild behavioural dependence, 12–22=moderate behavioural dependence, 23–33=strong behavioural dependence, >33=very strong behavioural dependence.
AUTOS=Autonomy Over Tobacco Scale. Each question is scored 0–3, where: 0=not at all, 1=a little, 2=pretty well and 3=very well. The total questionnaire has 12 questions, with a maximum score of 36. Each subscale has 4 questions, with a maximum score of 12.
CPD, cigarettes smoked per day.

smoke and replace them with VLNC cigarettes. As a result, smokers will reduce their total nicotine intake, although they would remain exposed to similar levels of toxicants and their associated health risks. Findings support the hypothesis that a price differential based on the nicotine content of tobacco can lead to reduced tobacco dependence and increased quitting behaviour. Under such a policy smokers are likely to use both types of cigarettes (usual and VLNC) in order to achieve a balance between craving and cost.[10 18] Such dual use has been observed in other trials where free VLNC cigarettes were provided, but participants still had access to their usual brand cigarettes.[6 7 19]

This study was conducted in line with CONSORT guidelines, text messaging was used to limit recall bias, and we used a measure of nicotine dependence (AUTOS) that did not rely on the number of overall CPD. The fact that the measured severity of addiction decreased in the intervention group, despite no change in the number of CPD, demonstrates the utility of the AUTOS for research involving manipulation of methods of nicotine delivery. Although not measured, compensation was unlikely to have occurred given the extremely low levels of nicotine present in the cigarettes.[4] Some limitations of the study should be acknowledged. First, the study was limited by its small sample size, so it was not possible to adjust for baseline variables or to correct for multiple tests. Nevertheless, we found a consistent trend for the majority of outcomes in favour of the intervention group. These data will help to estimate sample sizes for more definitive studies. Second, lack of blinding in the trial means there may be reporting bias. Third, findings may not be applicable to groups with high smoking rates, such as Māori (indigenous NZers) and smokers with comorbid alcohol or mental health problems, as the study involved few such people. Previous research has shown that Māori smokers motivated to quit and smokers with

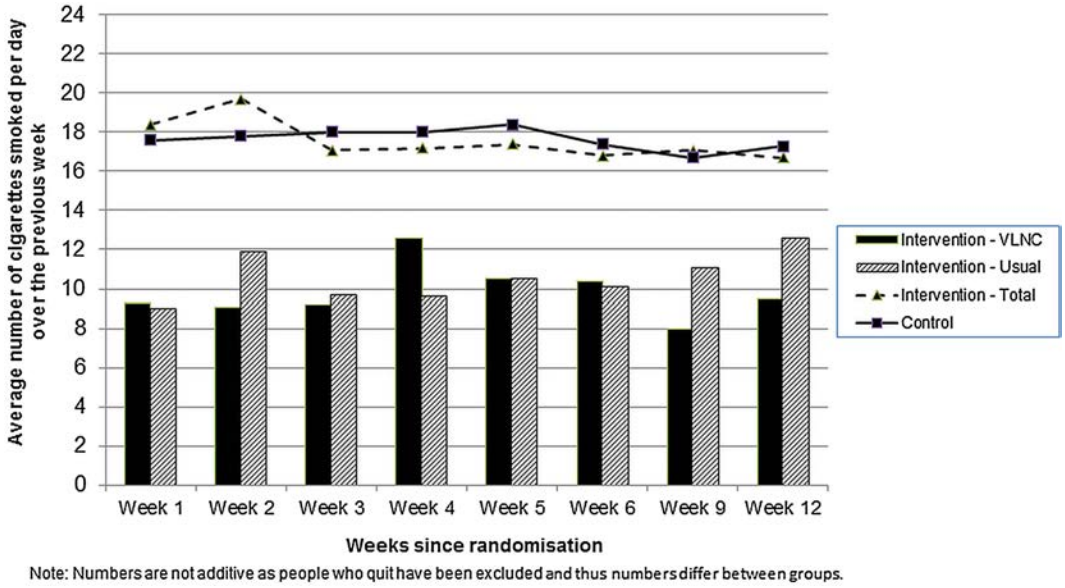

Figure 2 Cigarettes smoked per day over the previous week.

Table 2 Change from baseline in continuous outcomes

	Intervention (n=17)	Control (n=15)	p Value
Change in number of usual CPD in the previous week			
6 weeks (median, IQR)	−5.29 (−10.50 to −2.00)	−0.55 (−1.71 to 1.11)	0.002*
12 weeks (median, IQR)	−2.00 (−6.57 to −0.43)	−0.64 (−3.68 to 0.43)	0.066*
Change in salivary cotinine (ng/mL)†‡			
6 weeks (mean, SD)	−9.5 (23.5)	16.4 (32.4)	0.022
12 weeks (mean, SD)	10.9 (23.0)	17.1 (22.1)	0.495
Change in mCEQ‡ (6 weeks)			
Satisfaction (median, IQR)	−0.50 (−1.00 to 0.33)	−0.33 (−0.67 to 0)	0.922*
Psychological reward (mean, SD)	−0.41 (1.41)	−0.69 (0.92)	0.520
Aversion (median, IQR)	0.5 (0 to 1.5)	0 (−0.5 to 0)	0.022*
Sensations (mean, SD)	0 (−2 to 1)	0 (0 to 1)	0.346*
Craving (median, IQR)	0 (−1.5 to 0.5)	0 (−2 to 1)	0.857*
Change in mCEQ‡ (12 weeks)			
Satisfaction (median, IQR)	−0.33 (−0.67 to 0.67)	−0.50 (−1 to 0)	0.230*
Psychological reward (mean, SD)	−0.80 (1.46)	−0.63 (1.02)	0.719
Aversion (median, IQR)	0 (−0.5 to 0)	0 (−0.5 to 0)	0.623*
Sensations (mean, SD)	−0.33 (2.61)	0.50 (1.22)	0.287
Craving (median, IQR)	0 (−1 to 0)	−1 (−1 to 1)	0.036*
Change in GN-SBQ‡			
6 weeks (mean, SD)	−4 (−5 to 0)	−3 (−5 to −1)	0.366*
12 weeks (mean, SD)	−5.29 (4.89)	−1.71 (3.52)	0.036
Change in AUTOS‡ (6 weeks)			
Total score (mean, SD)	−4.5 (−7.0 to −2.5)	−3.0 (−6.0 to 0)	0.259*
Withdrawal symptoms (mean, SD)	−2.0 (−3.0 to −0.5)	−1.0 (−3.0 to 0)	0.416*
Psychological dependence (median, IQR)	−1.5 (−3.5 to 0)	−1.0 (−2.0 to 0)	0.270*
Cue-induced cravings (mean, SD)	−2.0 (−2.5 to 0)	−1.0 (−2.0 to 0)	0.293*
Change in AUTOS‡ (12 weeks)			
Total score (mean, SD)	−5.53 (5.55)	−2.00 (4.51)	0.072
Withdrawal symptoms (mean, SD)	−2.53 (2.56)	−0.64 (1.65)	0.027
Psychological dependence (median, IQR)	−2.00 (−3.00 to −1.00)	−1.00 (−2.00 to 0)	0.162*
Cue-induced cravings (mean, SD)	−0.93 (1.49)	−0.50 (1.91)	0.500

All tests of significance are between group comparisons and t tests (unless otherwise indicated).
*Mann-Whitney test.
†One baseline extreme outlier in the control group was excluded from analysis.
‡People who quit have been excluded (three quitters at 12 weeks: two in the intervention group and one in the control group; and one quitter in the intervention group was excluded at 6 weeks).
AUTOS, Autonomy Over Tobacco Smoking Scale; CPD, cigarettes smoked per day; GN-SBQ, Glover Nilsson Smoking Behavioural Questionnaire; mCEQ, modified Cigarette Evaluation Questionnaire.

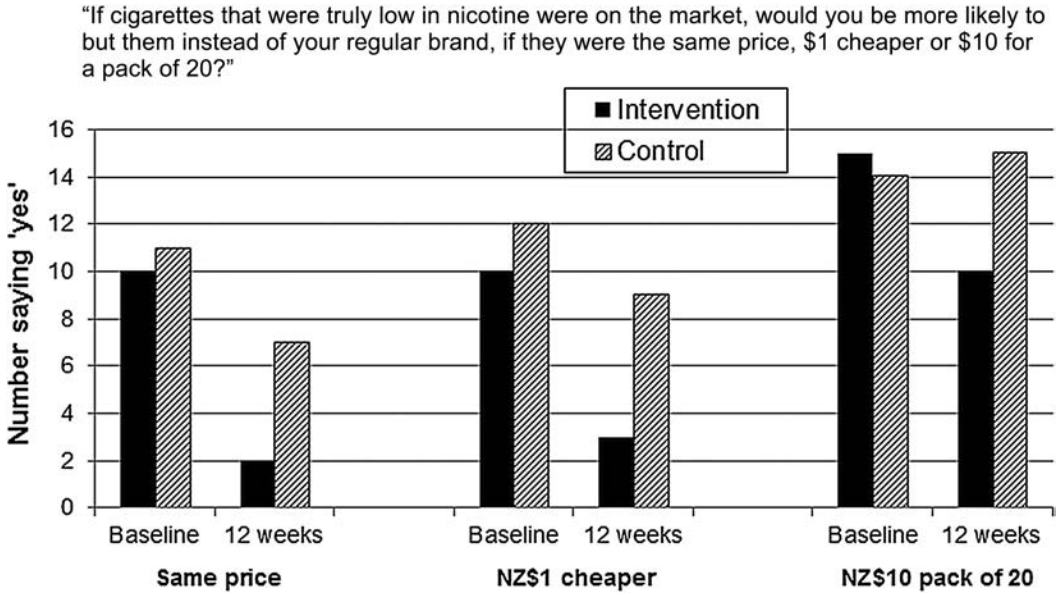

Figure 3 Participants' views on nicotine reduction.

schizophrenia also reduce their levels of tobacco dependence, reduce the amount of usual CPD and quit smoking using VLNC cigarettes.[5 20] Finally, the baseline cotinine results were much lower than previously reported averages given the number of CPD. Although cotinine levels are known to vary with time of day, how recently a cigarette was smoked, and by environmental, physiological and genetic factors,[21 22] the reason for the low levels is unknown.

Although exploratory, these findings help inform nicotine reduction policy in 2 ways. First, cost is a strong driver for the use of VLNC cigarettes by smokers unmotivated to quit, a finding reflected in cigarette price breakpoint studies.[23 24] Since addiction is maintained by consumption of usual cigarettes and use of VLNC cigarettes leads to a change in expectations around price of purchase, a one-step abrupt reduction in tobacco excise for VLNC cigarettes seems likely to be the better option should VLNC cigarettes be made available. Second, a mandated reduction in nicotine across all combusted tobacco products simultaneously (with no price reduction) is likely to be a strong policy option, as it avoids the issue of dual use. This policy would need to be supported by testing of brands for nicotine content to ensure no mislabelling. Any black market in usual cigarettes that occurred would likely increase the price of usual tobacco even further, though alternative nicotine smoking-simulation products (such as e-cigarettes) may dampen such demand.

What this paper adds

- Despite finding very low nicotine content (VLNC) cigarettes less appealing, smokers unmotivated to quit are willing to smoke VLNC cigarettes and fewer usual cigarettes, but only if there is a favourable price differential.
- Use of VLNC cigarettes by smokers unmotivated to quit reduces their level of tobacco dependence and leads to increased quitting activity.
- A mandated reduction in nicotine across all brands simultaneously appears a better policy option as it avoids the issue of dual use of VLNC and usual cigarettes.

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Contributors All authors conceived the original idea for the trial, sought funding and wrote the protocol. CH and TF managed the day-to-day running of the trial, including participant follow-up. VP provided statistical advice for the trial and carried out all data analyses. The paper was written by NW with input from all co-authors. NW will act as guarantor for the paper.

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Competing interests NW has provided consultancy to the manufacturers of smoking cessation medications, received honoraria for speaking at a research meeting and received benefits in kind and travel support from a manufacturer of smoking cessation medications. CB has received in-kind benefits from the manufacturer of smoking cessation medications. MG has provided consultancy to the manufacturers of smoking cessation medications. NW, CB, MG, ML and CH have previously undertaken a smoking cessation trial that involved the use of very low nicotine content cigarettes, purchased from Vector Group Ltd, USA.

Patient consent Obtained.

Ethics approval Ethics approval for this trial was obtained from the Northern B Health and Disability Ethics Committee (Ethics Number 12/NTB/48).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement We provide permission to share the information provided in this report.

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