Relapse to smoking and health-related quality of life: Secondary analysis of data from a study of smoking relapse prevention

Fujian Song1, Max O. Bachmann1, Paul Aveyard2, Garry R. Barton1, Tracey J. Brown1, Vivienne Maskrey1, Annie Blyth1, Caitlin Notley1, Richard Holland1, Stephen Sutton3, Thomas H. Brandon4

1 Norwich Medical School, Faculty of Medicine and Health Science, University of East Anglia, Research Park, Norwich, United Kingdom, 2 Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Primary Care Building, Radcliffe Observatory Quarter, Woodstock Road, Oxford, United Kingdom, 3 Institute of Public Health, University of Cambridge, Cambridge, United Kingdom, 4 Department of Health Outcomes and Behavior, Moffitt Cancer Center, Tampa FL, United States of America

* fujian.song@uea.ac.uk

Abstract

Background
Previous studies have shown that smoking and smoking cessation may be associated with health-related quality of life (HRQoL). In this study, we compared changes in HRQoL in people who maintained abstinence with people who had relapsed to smoking.

Methods
This was a secondary analysis of data from a trial of a relapse prevention intervention in 1,407 short-term quitters. The European Quality of Life -5 Dimensions (EQ-5D) measured HRQoL at baseline, 3 and 12 months. Smoking outcome was continuous abstinence from 2 to 12 months, and 7-day smoking at 3 and 12 months. We used nonparametric test for differences in EQ-5D utility scores, and chi-square test for dichotomised response to each of the five EQ-5D dimensions. Multivariable regression analyses were conducted to evaluate associations between smoking relapse and HRQoL or anxiety/depression problems.

Results
The mean EQ-5D tariff score was 0.8252 at baseline. People who maintained abstinence experienced a statistically non-significant increase in the EQ-5D score (mean change 0.0015, P = 0.88), while returning to smoking was associated with a statistically significant decrease in the EQ-5D score (mean change -0.0270, P = 0.004). After adjusting for multiple baseline characteristics, the utility change during baseline and 12 months was statistically significantly associated with continuous abstinence, with a difference of 0.0288 (95% CI: 0.006 to 0.0571, P = 0.045) between relapsers and continuous quitters. The only difference in quality of life dimensions between those who relapsed and those who maintained abstinence was in the proportion of participants with anxiety/depression problems at 12 months.
(30% vs. 22%, P = 0.001). Smoking relapse was associated with a simultaneous increase in anxiety/depression problems.

Conclusions
People who achieve short-term smoking abstinence but subsequently relapse to smoking have a reduced quality of life, which appears mostly due to worsening of symptoms of anxiety and depression. Further research is required to more fully understand the relationship between smoking and health-related quality of life, and to develop cessation interventions by taking into account the impact of anxiety or depression on smoking.

Background
Cigarette smoking remains the leading preventable cause of premature deaths globally [1]. Results of previous studies have indicated that smoking is negatively associated with quality of life [2, 3], and smoking cessation is associated with reduced depression and anxiety, and improved quality of life [4, 5]. A study found that the level of happiness in ex-smokers who stopped smoking for at least a year was similar to never smokers, and higher than current smokers [6]. However, it is uncertain whether trying and failing to quit increases the level of psychological distress and depression [7–10]. Some studies have reported a significant association between smoking relapse and mental health problems [11, 12], while another study found no greater tendency to relapse for quitters with worsened mental health [13]. Studies showing that relapse is associated with simultaneous changes in quality of life or mood cannot identify the causal direction between them, and these effects may work in both directions.

In a randomised controlled trial, we evaluated the effectiveness of different self-help booklets for preventing smoking relapse in people who had stopped smoking for four weeks, and found no differences between trial arms in smoking relapse at 12 months [14, 15]. Here we compared changes in health-related quality of life (HRQoL) in people who maintained abstinence with people who had relapsed to smoking. We also investigated whether anxiety or depression problems were associated with subsequent smoking relapse, or smoking relapse was associated with subsequent anxiety or depression problems.

Methods
This is a secondary analysis of data from a randomised trial (ISRCTN36980856) for smoking relapse prevention [14, 15]. The study was approved for research ethics (UK National Research Ethics Service REC reference: 11/EE/0091, dated 20/04/2011), and all participants were provided detailed information about the study and signed the consent form before participating. Participants were recruited between August 2011 and June 2013, and the follow-up of participants was completed by July 2014. Note that the recruitment start date shown in the ISRCTN registry (01/06/2011) was incorrect, and we confirm that the participant recruitment actually started since August 2011 after the trial’s registration on 25/07/2011. The authors also confirm that all ongoing and related trials for this intervention are registered. The study included 1,407 carbon monoxide (CO) verified quitters at 4 weeks after quit dates in stop smoking clinics. The study excluded quitters who were pregnant, unable to read booklets in English, or younger than 18 years. Participants received either a set of educational booklets or a single leaflet to prevent smoking relapse, and were followed up at 3 and 12 months after the quit date. There was
no difference between trial arms in the occurrence of the primary endpoint in the trial, prolonged abstinence from 4 to 12 months (assessed by self-report of no more than five cigarettes in total, and confirmed by CO<10ppm at the 12 month follow-up). In the current study, we used usual continuous abstinence as the smoking outcome, defined similarly to the primary endpoint but from baseline (1 month after the quit date) to the 12 month follow-up. In addition, we also collected data on 7-day self-report smoking at 3 months and 12 months post quit date.

The European Quality of Life -5 Dimensions- 3 Level (EQ-5D) instrument was used to estimate levels of HRQoL [16]. Participants were asked to complete the EQ-5D questions at baseline (1 month after the quit date), and at 3 and 12 months after the quit date. EQ-5D instrument has 5 dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. For each dimension, there are three possible responses: “no problems”, “some or moderate problems”, and “severe or extreme problems”. In the current study, EQ-5D data were analysed using two methods; utility scores based on EQ-5D and dichotomisation of responses to each of the five EQ-5D dimensions.

Responses to EQ-5D dimensions were converted into a utility score (a scale where death is equal to 0 and full health 1) using the York A1 tariff [17,18]. The York A1 tariff enables a value to be assigned to each EQ-5D health state, where these scores are based on the preferences of a large sample of the UK population. Because the EQ-5D scores are not normally distributed, differences in EQ-5D scores between groups were tested using nonparametric Mann-Whitney test (two sample Wilcoxon rank-sum test). For ordered groups, we used the nonparametric test for trend (an extension of the Wilcoxon rank-sum test) [19]. We also calculated changes in utility score for individual participants between baseline and 3 or 12 months. Although the distribution of EQ-5D original scores was asymmetric, data on changes in utility score from baseline to the follow-up time point was symmetrically distributed. A previous study compared different methods and found that ordinary least squares (OLS) regression model was acceptable for the analysis of EQ-5D tariff data [2]. Therefore, as the main analysis, we performed OLS linear regression analyses to estimate the relationship between the change in utility score, as outcome, and smoking status as explanatory variable, after adjusting for multiple baseline variables. The baseline variables adjusted in the analyses were age, gender, married or living with a partner, unemployed or not, low level of education, free prescription, and the first cigarette within 5 minutes after waking before quitting.

The participants included in the current study were relatively healthy, with a low proportion of “severe or extreme problems” for individual EQ-5D dimensions. Therefore, responses to each of the EQ-5D dimensions were dichotomised into two categories: “no problems” and “some or severe problems” by combining “some to moderate problems” and “severe or extreme problems” [2]. We used chi-square test to analyse the association between the smoking outcome and problems in each of the five EQ-5D dimensions. Because differences in HRQoL scores were attributable mainly to problems in the anxiety/depression dimension, we explored the association between changes in smoking status and changes in anxiety/depression problems.

Stata/IC version 13.1 was used for statistical analyses, and statistical significance was defined as two sided P<0.05.

Results

The main characteristics of study participants are shown in Table 1. The mean age of the participants was 47.8 years (SD 13.8). Of the 1,407 participants, 52.7% were females, 61.6% married or living with a partner, 52.6% in paid employment, 32.1% with A level or above
Table 1. The main characteristics of study participants.

| Baseline variables       | % (N = 1407) | Baseline EQ-5D utility score: mean (SD) | P value |
|--------------------------|--------------|----------------------------------------|---------|
| Total                    | 100%         | 0.8252 (0.2594)                        |         |
| Age (years):             |              |                                        |         |
| Up to 39                 | 29.5%        | 0.9042 (0.1823)                        | \( P_{\text{trend}} < 0.001 \) |
| 40–59                    | 45.8%        | 0.8028 (0.2817)                        |         |
| 60 & above               | 24.7%        | 0.7701 (0.2739)                        |         |
| Sex:                     |              |                                        |         |
| Female                   | 52.7%        | 0.8153 (0.2681)                        | \( P_{m-w} = 0.084 \) |
| Male                     | 47.3%        | 0.8362 (0.2490)                        |         |
| Marital status:          |              |                                        |         |
| Married/living with partner | 61.6%    | 0.8390 (0.2524)                        | Reference |
| Separated/divorced       | 15.9%        | 0.7742 (0.2922)                        | \( P_{m-w} < 0.001 \) |
| Single                   | 18.2%        | 0.8422 (0.2361)                        | \( P_{m-w} = 0.876 \) |
| Other/unknown            | 4.3%         | 0.7426 (0.2906)                        | \( P_{m-w} < 0.001 \) |
| Ethnic origin:           |              |                                        |         |
| White                    | 98.4%        | 0.8248 (0.2602)                        | \( P_{m-w} = 0.472 \) |
| All other                | 3.6%         | 0.8485 (0.2080)                        |         |
| Employment status:       |              |                                        |         |
| In paid employment       | 52.6%        | 0.9025 (0.1692)                        | Reference |
| Unemployed               | 10.0%        | 0.7132 (0.3007)                        | \( P_{m-w} < 0.001 \) |
| Looking after the home   | 7.4%         | 0.8229 (0.2685)                        | \( P_{m-w} = 0.002 \) |
| Retired                  | 20.3%        | 0.7515 (0.2861)                        | \( P_{m-w} < 0.001 \) |
| Full time student        | 1.2%         | 0.8918 (0.1720)                        | \( P_{m-w} = 0.780 \) |
| Other                    | 8.5%         | 0.6480 (0.3890)                        | \( P_{m-w} < 0.001 \) |
| Education:               |              |                                        |         |
| Degree or equivalent     | 15.2%        | 0.8610 (0.2172)                        | \( P_{\text{trend}} < 0.001 \) |
| A level or equivalent    | 16.9%        | 0.8374 (0.2570)                        |         |
| GCSE or equivalent       | 34.1%        | 0.8477 (0.2425)                        | (excluded) |
| Other                    | 12.4%        | 0.7924 (0.2926)                        | "unknown") |
| None                     | 20.0%        | 0.7627 (0.2877)                        |         |
| Unknown                  | 1.3%         | 0.8414 (0.2458)                        |         |
| Free prescription*:      |              |                                        |         |
| Yes                      | 56.3%        | 0.7702 (0.2947)                        | \( P_{m-w} < 0.001 \) |
| No                       | 43.7%        | 0.8989 (0.1791)                        |         |
| Cigarettes ≥20/day before quitting |         |                                        |         |
| Yes                      | 55.5%        | 0.8086 (0.2750)                        | \( P_{m-w} = 0.020 \) |
| No                       | 44.5%        | 0.8457 (0.2371)                        |         |
| First cigarette after waking up: |         |                                        |         |
| In 5 minutes             | 42.2%        | 0.7848 (0.2924)                        | \( P_{\text{trend}} < 0.001 \) |
| 6–30 minutes             | 42.6%        | 0.8496 (0.2384)                        |         |
| >30 minutes              | 15.2%        | 0.8678 (0.1987)                        |         |
| Previous quit attempts:  |              |                                        |         |
| None                     | 11.1%        | 0.8622 (0.2289)                        | \( P_{\text{trend}} = 0.04 \) |
| 1 attempt                | 26.2%        | 0.8234 (0.2528)                        |         |
| 2 attempts               | 23.7%        | 0.8327 (0.2718)                        |         |
| 3 or more                | 39.0%        | 0.8123 (0.2633)                        |         |
| Longest quit time before:|              |                                        |         |
| Not applicable           | 11.2%        | 0.8622 (0.2289)                        | \( P_{\text{trend}} = 0.008 \) |

(Continued)
education, and 56.3% in receipt of free prescription (free prescription is defined in Table 1). In terms of smoking history, 55.5% of the participants smoked 20 or more cigarettes daily and 42.2% smoked the first cigarette after waking up before the current quit attempt. Of the participants, 88.9% had previously attempted to quit and 71.6% had managed to stop smoking for more than 4 weeks before. The proportion of participants living with a smoking partner was 18.3%.

The number of people who completed the EQ-5D-3L questionnaire was 1348 (95.8%) at baseline, 1290 (91.7%) at the 3 month follow-up and 1171 (83.2%) at the 12 month follow-up. The mean EQ-5D tariff score was 0.8252 at baseline. In bi-variable analyses, EQ-5D scores at baseline were statistically significantly associated with age, divorced or separated, employment status, education level, in receipt of free prescription, heavy smokers before quitting, and previous quit history (Table 1). Results of multivariable regression analysis found that EQ-5D scores at baseline were independently and negatively associated with age (P < 0.001), being female (P = 0.002), unemployment (P < 0.001), and first cigarette within 5 minutes of waking (P < 0.001), after adjusting for other baseline characteristics.

After excluding three participants who died before the 12 month follow up, the proportion of continuous abstinence from baseline to 12 months was 32.4%. The mean EQ-5D utility scores at different time points are shown in Table 2. The differences in EQ-5D utility score between relapsers and continuous quitters were statistically non-significant at baseline and 3 months, but were statistically significant at 12 months (P = 0.040). The mean change in EQ-5D utility score between baseline and 12 months was -0.0270 (significantly deteriorated, P = 0.004) for relapsers and 0.0015 (non-significantly

### Table 1. (Continued)

| Baseline variables | % (N = 1407) | Baseline EQ-5D utility score: mean (SD) | P value |
|--------------------|-------------|----------------------------------------|---------|
| <1 week            | 6.3%        | 0.8311 (0.2634)                        |         |
| 1–4 weeks          | 10.9%       | 0.8496 (0.2506)                        |         |
| >4 weeks, <6 months| 33.1%       | 0.8210 (0.2656)                        |         |
| ≥ 6 months         | 38.5%       | 0.8115 (0.2631)                        |         |
| Living with a smoking partner: | | | |
| Yes                | 18.3%       | 0.8327 (0.2530)                        | P<sub>m-w</sub> = 0.656 |
| No                 | 81.7%       | 0.8235 (0.2609)                        |         |

P<sub>trend</sub>—the nonparametric test for trend across ordered groups (an extension of the Wilcoxon rank-sum test. P<sub>m-w</sub>—Mann-Whitney test (two sample Wilcoxon rank-sum test).

* Free prescription—The charge for a single prescription is £8.05 in the UK. Some people are entitled to free prescriptions because of their age (60 or over, or under 16, or aged 16 to 18 in full-education), income (on Income Support or qualified via other benefits or tax credits), or medical condition. GCSE—The General Certificate of Secondary Education.

### Table 2. Mean EQ-5D utility scores at baseline and follow-ups by smoking status.

| Time point  | All participant | Abstinent at 12 months | Relapsed at 12 months | P value |
|-------------|-----------------|------------------------|-----------------------|---------|
|             | N               | Mean                   | n                     | Mean    |         |
| Mean utility scores at different time points | | | | | |
| Baseline    | 1348            | 0.8252                 | 442                   | 0.8289  | 903     | 0.8234  | 0.412 |
| At 3 months | 1290            | 0.8255                 | 451                   | 0.8247  | 836     | 0.8261  | 0.873 |
| At 12 months| 1171            | 0.8072                 | 451                   | 0.8307  | 720     | 0.7924  | 0.040 |

Two sample Wilcoxon rank-sum (Mann-Whitney) test was used for the test of mean utility scores at different time points, and t-test for the change in utility scores.
improved, P = 0.883) for continuous quitters. After adjusting for multiple baseline characteristics, the utility change during baseline and 12 months was statistically significantly associated with continuous abstinence, with a difference of 0.0288 (95% CI: 0.0006 to 0.0571, P = 0.045) between relapers and continuous quitters.

For specific EQ-5D dimensions, smoking status at 12 months was not statistically significantly associated with problems in mobility, self-care, usual activity, and pain or discomfort at baseline and the follow-ups (Fig 1). Of the five EQ-5D dimensions, only problems in anxiety/depression at 12 months was statistically significantly associated with smoking relapse (30% for relapses vs. 22% for continuous quitters, P = 0.001).

The relationships between smoking reported at the two follow-ups and some/severe problems in anxiety or depression dimension are shown in Table 3. Anxiety/depression problems at baseline were not significantly associated with smoking relapse at 3 months (P = 0.112) or at

---

**Fig 1.** Proportion of participants with some/severe problems in different EQ-5D dimensions by continuous abstinence. In each EQ-5D dimension the “some problems” and “severe problems” were combined as “some/severe problems”. Differences in “some/severe problems” between the relapse and abstinent was statistically significant only for anxiety/depression dimension at 12 months (P = 0.001).

https://doi.org/10.1371/journal.pone.0205992.g001
12 months (P = 0.841), and anxiety/depression problems at 3 months were not significantly associated with smoking relapse at 12 months (P = 0.354). Smoking relapse at 3 months was not statistically significantly associated with anxiety/depression problems at 12 months (OR 1.22, 95% CI 0.87 to 1.71; P = 0.246). However, smoking relapse at 3 or 12 months was statistically associated with anxiety/depression problems at the same time points (Table 3).

Fig 2 shows the proportion of participants with anxiety/depression problems by further subgrouping smoking status at baseline, 3 and 12 months. The proportion of anxiety/depression problems among participants who remained abstinent at both 3 and 12 months was 27% at baseline, and somewhat reduced to 22% at 3 months and 23% at 12 months. For participants who did not smoke at 3 months but smoked at 12 months, the proportion of anxiety/depression problems was higher at 12 months (31%), compared with that at baseline (27%) and 3 months (23%). It is interesting to note the fluctuation of anxiety/depression problems among participants who smoked at 3 months and did not smoke at 12 months; the proportion of anxiety/depression problems was somewhat high at baseline (32%), considerably increased at 3 months (45%), and then much reduced at 12 months (24%). Participants who reported smoking at both 3 and 12 months had a high proportion of anxiety/depression problems at baseline (36%) and at the two follow-ups (42% and 36% respectively).

Discussion

In the current study, the mean EQ-5D utility score was 0.8252 (SD 0.2594) at baseline and 0.8072 (SD 0.2456) at 12 months, which is similar to the score reported for a representative sample of English former smokers, 0.8225 (SD 0.2512) [2]. It was found that EQ-5D utility at baseline was negatively associated with certain participant characteristics, including older age, being female, unemployed, and heavy smoking before quitting. At follow-up, those who had relapsed had a lower quality of life, while those maintaining abstinence had a small and non-significant increase in HRQoL. The difference in HRQoL between the relapsers and continuous quitters at follow-up was statistically significant, and due to changes in anxiety or depression, with no evidence of changes in other EQ-5D dimensions.

A study of the English general population found that heavy smokers had poorer HRQoL in all five EQ-5D dimensions compared with never smokers [2]. In the current study of short-term quitters, analyses of EQ-5D dimensions revealed that the differences in HRQoL between relapsers and continuous quitters were mainly attributable to problems in the anxiety/depression dimension. This finding was consistent with those from a previous study that examined the relationship between smoking cessation and HRQoL using the EQ-5D [20]. The association between anxiety/depression and smoking or smoking cessation is complex, and results from different studies are often inconsistent. For example, a recent study did not find a long-

Table 3. Results of logistic regression analyses of associations between anxiety or depression problems and smoking status at baseline, 3 and 12 months.

| Any anxiety/depression problems | Odds ratio (95% confidence interval); P value |
|---------------------------------|---------------------------------------------|
|                                 | Smoking at 3 months | Smoking at 12 months |
| At baseline                     | 1.27 (0.95–1.70); P = 0.112 | 1.03 (0.80–1.31); P = 0.841 |
| At 3 months                     | 2.28 (1.63–3.17); P < 0.001 | 1.13 (0.87–1.47); P = 0.354 |
| At 12 months                    | 1.22 (0.87–1.71); P = 0.246 | 1.49 (1.14–1.95); P = 0.003 |

Logistic regression analysis using smoking at 3 or 12 months as the dependent variable, and adjusted for age, sex, married or not, unemployment, low education (GCSE or lower), receipt with free prescription, and the first cigarette in 5 minutes after waking up.

https://doi.org/10.1371/journal.pone.0205992.t003
term impact of smoking cessation on depression, although depression reduced possibility of quitting [21]. Because smokers often use cigarettes to attempt to cope with stress and anxiety, many smokers and some health professionals mistakenly believe that smoking cessation will worsen stress and anxiety symptoms [22]. This belief may arise because tobacco withdrawal symptoms include anxiety and depression immediately after abstinence, although withdrawal symptoms last only a few weeks [23]. However, many previous studies found that failed quit attempts may increase anxiety or depression [7–9, 24, 25], and successful smoking cessation reduces stress and anxiety [4–6, 22].

A prospective study published in 1990 examined the relation between changes in stress levels and changes in smoking status, and concluded that the relation was possibly bidirectional [5]. Although the association between changes in smoking status and changes in stress levels was consistently observed in other studies [22, 26], the causal direction remains uncertain. In a
recent study by Taylor and colleagues [13], deterioration in mental health after achieving and maintaining abstinence until four months did not predict relapse to smoking by 12 months. In the current study, we found that smoking relapse was accompanied with increased anxiety or depression problems measured at the same time. However, anxiety or depression problems at baseline or at 3 months were not associated with smoking relapse at 12 months (Table 3, Fig 2). It is also interesting to note that relapse to smoking by 3 months was associated with an increase in anxiety and depression at that time, while returning to abstinence by 12 months was associated with reduced anxiety and depression at 12 months (Fig 2).

The effects of anxiety or depression on smoking relapse may occur promptly with little delay, so that smoking is closely associated with the present, rather than the previous, mental status. This may explain why deterioration in mental health did not predict smoking relapse after eight months in a previous study [13]. However, as a failed quit attempt, relapse to smoking itself is likely a stressful incident. In contrast to the immediate effects of anxiety and depression on smoking relapse, the beneficial effects of smoking cessation on anxiety or depression may not be perceived immediately and may often be complicated by withdrawal symptoms. Consequently, people with mental illness have a higher smoking prevalence and are less likely to quit than people without mental illness [27]. Although accumulating evidence suggests that smoking cessation improves mental health and reduces stress or depression in long term, more efforts are required to manage stress and other depressive symptoms in smoking cessation interventions, whilst emphasising these potential longer mental health benefits.

**Strengths and limitations**

This is the first study to examine changes in EQ-5D based HRQoL in a large number of people who had quit smoking for several weeks after receiving smoking cessation treatment. The study provided data on EQ-5D based utility scores by smoking relapse status, which will help evaluations of long-term cost-effectiveness and cost-utility of smoking cessation and tobacco control interventions [28]. By measuring EQ-5D status at baseline, 3 and 12 months, and collecting data on smoking status at 3 and 12 months, we were able to investigate the association between changes in smoking status and changes in HRQoL (specifically, changes in anxiety/depression problems).

We found that the difference in changes in HRQoL between relapers and continuous quitters was statistically significant, although the clinical and public health importance of the difference was unclear. We focused on the association between smoking relapse and HRQoL in the present study. However, it should be stressed that smoking relapse is also associated with other demographic or socioeconomic factors, including age, marital status, employment status, and living with a partner who smokes [14]. The participants of the current study were predominately white (98%), reflecting the ethnic composition of the area; pregnant women, people younger than 18 years and those who were unable to read English were excluded [14], so that the results of the current study may not be generalizable to these groups. As mood and smoking status were assessed infrequently, this study alone cannot clarify the causal pathway. The current study was observational in nature, and we could not rule out the existence of other factors or events that were associated with both relapse to smoking and changes in EQ-5D responses.

**Conclusions**

Relapse to smoking is associated with reduced quality of life measured by EQ-5D, which seems mainly attributable to problems of anxiety and/or depression. Further research is required to more fully understand the relationship between smoking and health-related quality of life, and
to develop cessation interventions by taking into account the impact of anxiety and depression on smoking.

**Supporting information**

**S1 Dataset.** Data from the SHARPISH trial for smoking relapse and health-related quality of life.

(TXT)

**Acknowledgments**

We thank staff from NHS Norfolk and Norfolk Community Health & Care NHS Trust for providing advice on the development of the trial protocol. We thank stop smoking advisors from NHS stop smoking services in Norfolk, Lincolnshire, Suffolk, Hertfordshire, Great Yarmouth and Waveney for recruiting quitters to the study. The trial was conducted in collaboration with the Norwich Clinical Trials Unit whose staff provided input into the design, conduct and analysis (Tony Dyer–randomisation and data management).

**Author Contributions**

**Conceptualization:** Fujian Song, Thomas H. Brandon.

**Data curation:** Fujian Song.

**Formal analysis:** Fujian Song, Garry R. Barton.

**Funding acquisition:** Fujian Song.

**Investigation:** Fujian Song, Max O. Bachmann, Paul Aveyard, Garry R. Barton, Tracey J. Brown, Vivienne Maskrey, Annie Blyth, Caitlin Notley, Richard Holland, Stephen Sutton, Thomas H. Brandon.

**Methodology:** Fujian Song, Max O. Bachmann, Paul Aveyard, Garry R. Barton, Richard Holland, Stephen Sutton, Thomas H. Brandon.

**Supervision:** Fujian Song.

**Writing – original draft:** Fujian Song.

**Writing – review & editing:** Max O. Bachmann, Paul Aveyard, Garry R. Barton, Tracey J. Brown, Vivienne Maskrey, Annie Blyth, Caitlin Notley, Richard Holland, Stephen Sutton, Thomas H. Brandon.

**References**

1. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2013. Geneva: The World Health Organization 2013.

2. Vogl M, Wenig CM, Leidl R, Pokhrel S. Smoking and health-related quality of life in English general population: implications for economic evaluations. *BMC Public Health* 2012, 12:203. https://doi.org/10.1186/1471-2458-12-203 PMID: 22429454

3. Goldenberg M, Danovitch I, LeHak WW. Quality of life and smoking. *Am J Addict* 2014, 23:540–562. https://doi.org/10.1111/j.1521-0391.2014.12148.x PMID: 25255868

4. Taylor G, McNeill A, Gilrington A, Farley A, Lindson-Hawley N, Aveyard P. Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ* 2014, 348:g1151. https://doi.org/10.1136/bmj.g1151 PMID: 24524926

5. Cohen S, Lichtenstein E. Perceived stress, quitting smoking, and smoking relapse. *Health Psychol* 1990, 9:466–478. PMID: 2373070
6. Shahab L, West R. Differences in happiness between smokers, ex-smokers and never smokers: cross-sectional findings from a national household survey. *Drug Alcohol Depend* 2012, 121:38–44. https://doi.org/10.1016/j.drugalcdep.2011.08.011 PMID: 21906891

7. van der Deen FS, Carter KN, Wilson N, Collings S. The association between failed quit attempts and increased levels of psychological distress in smokers in a large New Zealand cohort. *BMC Public Health* 2011, 11:598. https://doi.org/10.1186/1471-2458-11-598 PMID: 21798059

8. McClave AK, Dube SR, Strine TW, Kroenke K, Caraballo RS, Mokdad AH. Associations between smoking cessation and anxiety and depression among U.S. adults. *Addict Behav* 2009, 34:491–497. https://doi.org/10.1016/j.addbeh.2009.01.005 PMID: 19217720

9. Torres LD, Barrera AZ, Delucchi K, Penilla C, Perez-Stable EJ, Munoz RF. Quitting smoking does not increase the risk of major depressive episodes among users of Internet smoking cessation interventions. *Psychol Med* 2010, 40:441–449. https://doi.org/10.1017/S0033291709990560 PMID: 19627638

10. Shahab L, Andrew S, West R. Changes in prevalence of depression and anxiety following smoking cessation: results from an international cohort study (ATTEMPT). *Psychol Med* 2014, 44:127–141. https://doi.org/10.1017/S0033291713000391 PMID: 23907203

11. Hawkins J, Hollingworth W, Campbell R. Long-term smoking relapse: a study using the British household panel survey. *Nicotine Tob Res* 2010, 12:1228–1235. https://doi.org/10.1093/ntr/ntq175 PMID: 21036960

12. Zvolensky MJ, Bakhshaie J, Sheffer C, Perez A, Goodwin RD. Major depressive disorder and smoking relapse among adults in the United States: a 10-year, prospective investigation. *Psychiatry Res* 2015, 226:73–77. https://doi.org/10.1016/j.psychres.2014.11.064 PMID: 25650047

13. Taylor G, McNeill A, Aveyard P. Does deteriorating mental health after smoking cessation predict relapse to smoking? *BMC Public Health* 2015, 15:1150. https://doi.org/10.1186/s12889-015-2473-z PMID: 26589146

14. Blyth A, Maskrey V, Notley C, Barton GR, Brown TJ, Aveyard P, et al. Effectiveness and economic evaluation of self-help educational materials for the prevention of smoking relapse: randomised controlled trial. *Health Technol Assess* 2015, 19:1–70, v-vi.

15. Maskrey V, Blyth A, Brown TJ, Barton GR, Notley C, Aveyard P, et al. Self-help educational booklets for the prevention of smoking relapse following smoking cessation treatment: a randomized controlled trial. *Addiction* 2015, 110:2006–2014. https://doi.org/10.1111/add.13080 PMID: 26235659

16. Brooks R. EuroQol: the current state of play. *Health Policy* 1996, 37:53–72. PMID: 10158943

17. Dolan P: Modelling valuations for EuroQol health states. *Med Care* 1997, 35:1095–1108. PMID: 9366889

18. Dolan P, Roberts J. Modelling valuations for EQ-5D health states: an alternative model using differences in valuations. *Med Care* 2002, 40:442–446. PMID: 11961478

19. Cuzick J. A Wilcoxon-type test for trend. *Stat Med* 1985, 4:87–90. PMID: 3992076

20. Chen PC, Kuo RN, Lai CK, Tsai ST, Lee YC. The relationship between smoking status and health-related quality of life among smokers who participated in a 1-year smoking cessation programme in Taiwan: a cohort study using the EQ-5D. *BMJ Open* 2015, 5:e007249. https://doi.org/10.1136/bmjopen-2014-007249 PMID: 25953727

21. Shahab L, Gilchrist G, Hagger-Johnson G, Shankar A, West E, West R. Reciprocal associations between smoking cessation and depression in older smokers: findings from the English Longitudinal Study of Ageing. *Br J Psychiatry* 2015, 207:243–249. https://doi.org/10.1192/bjp.bp.114.153494 PMID: 25999339

22. McDermott MS, Marteau TM, Hollands GJ, Hankins M, Aveyard P. Change in anxiety following successful and unsuccessful attempts at smoking cessation: cohort study. *The British Journal of Psychiatry* 2013, 202:62–67. https://doi.org/10.1192/bjp.bp.112.114389 PMID: 23284151

23. Hughes JR. Effects of abstinence from tobacco: valid symptoms and time course. *Nicotine Tob Res* 2007, 9:315–327. https://doi.org/10.1080/14622200701188919 PMID: 17365764

24. Berlin I, Chen H, Covey LS. Depressive mood, suicide ideation and anxiety in smokers who do and smokers who do not manage to stop smoking after a target quit day. *Addiction* 2010, 105:2209–2216. https://doi.org/10.1111/j.1360-0443.2010.03109.x PMID: 20840207

25. Manning BK, Catley D, Harris KJ, Mayo MS, Ahlulwala JS. Stress and quitting among African American smokers. *J Behav Med* 2005, 28:325–333. https://doi.org/10.1007/s10865-005-9004-9 PMID: 16049631

26. Hajek P, Taylor T, McRobbie H. The effect of stopping smoking on perceived stress levels. *Addiction* 2010, 105:1466–1471. https://doi.org/10.1111/j.1360-0443.2010.02979.x PMID: 20528815
27. Cook BL, Wayne GF, Kafali EN, Liu Z, Shu C, Flores M. Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation. JAMA 2014, 311:172–182. https://doi.org/10.1001/jama.2013.284985 PMID: 24399556

28. NICE. Guide to the methods of technology appraisal 2013. NICE article [PMG9]. National Institute of Health and Clinical Excellence (NICE) 2013.