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Biomedical risk assessment as an aid for smoking cessation (Review)

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[Intervention Review]

Biomedical risk assessment as an aid for smoking cessation

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ABSTRACT

Background

A possible strategy for increasing smoking cessation rates could be to provide smokers with feedback on the current or potential future biomedical effects of smoking using, for example, measurement of exhaled carbon monoxide (CO), lung function, or genetic susceptibility to lung cancer or other diseases.

Objectives

The main objective was to determine the efficacy of providing smokers with feedback on their exhaled CO measurement, spirometry results, atherosclerotic plaque imaging, and genetic susceptibility to smoking-related diseases in helping them to quit smoking.

Search methods

For the most recent update, we searched the Cochrane Tobacco Addiction Group Specialized Register in March 2018 and ClinicalTrials.gov and the WHO ICTRP in September 2018 for studies added since the last update in 2012.

Selection criteria

Inclusion criteria for the review were: a randomised controlled trial design; participants being current smokers; interventions based on a biomedical test to increase smoking cessation rates; control groups receiving all other components of intervention; and an outcome of smoking cessation rate at least six months after the start of the intervention.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. We expressed results as a risk ratio (RR) for smoking cessation with 95% confidence intervals (CI). Where appropriate, we pooled studies using a Mantel-Haenszel random-effects method.

Main results

We included 20 trials using a variety of biomedical tests interventions; one trial included two interventions, for a total of 21 interventions. We included a total of 9262 participants, all of whom were adult smokers. All studies included both men and women adult smokers at different stages of change and motivation for smoking cessation. We judged all but three studies to be at high or unclear risk of bias in at least one domain. We pooled trials in three categories according to the type of biofeedback provided: feedback on risk exposure (five studies); feedback on smoking-related disease risk (five studies); and feedback on smoking-related harm (11 studies). There was

no evidence of increased cessation rates from feedback on risk exposure, consisting mainly of feedback on CO measurement, in five pooled trials (RR 1.00, 95% CI 0.83 to 1.21; I^2 = 0%; n = 2368). Feedback on smoking-related disease risk, including four studies testing feedback on genetic markers for cancer risk and one study with feedback on genetic markers for risk of Crohn's disease, did not show a benefit in smoking cessation (RR 0.80, 95% CI 0.63 to 1.01; I^2 = 0%; n = 2064). Feedback on smoking-related harm, including nine studies testing spirometry with or without feedback on lung age and two studies on feedback on carotid ultrasound, also did not show a benefit (RR 1.26, 95% CI 0.99 to 1.61; I^2 = 34%; n = 3314). Only one study directly compared multiple forms of measurement with a single form of measurement, and did not detect a significant difference in effect between measurement of CO plus genetic susceptibility to lung cancer and measurement of CO only (RR 0.82, 95% CI 0.43 to 1.56; n = 189).

Authors' conclusions

There is little evidence about the effects of biomedical risk assessment as an aid for smoking cessation. The most promising results relate to spirometry and carotid ultrasound, where moderate-certainty evidence, limited by imprecision and risk of bias, did not detect a statistically significant benefit, but confidence intervals very narrowly missed one, and the point estimate favoured the intervention. A sensitivity analysis removing those studies at high risk of bias did detect a benefit. Moderate-certainty evidence limited by risk of bias did not detect an effect of feedback on smoking exposure by CO monitoring. Low-certainty evidence, limited by risk of bias and imprecision, did not detect a benefit from feedback on smoking-related risk by genetic marker testing. There is insufficient evidence with which to evaluate the hypothesis that multiple types of assessment are more effective than single forms of assessment.

PLAIN LANGUAGE SUMMARY

Does giving people feedback on the effects of smoking on their body help them quit smoking?

Background

Biomedical risk assessment is the process of giving people feedback on the effects of smoking on their body. The physical effects of smoking can be assessed using various measurements, and some people think this could be used as a tool to encourage people to quit smoking. We reviewed the evidence about whether giving adult smokers feedback on the effects of smoking on their body helps them quit smoking.

Study characteristics

This review includes 20 studies using a variety of measurements. One study included two measurements, for a total of 21 measurements assessed. The main feedback measurements we assessed were the level of carbon monoxide in people's breath (a sign of current smoking), measures of lung function (a sign of lung damage from smoking), genetic tests to provide individual risk of cancer, and ultrasound of major arteries in the neck to measure the amount of plaque (a risk factor for stroke). We grouped studies into three categories according to the type of feedback people were given: feedback on exposure to smoking (five studies); feedback on a person's risk for smoking-related diseases (five studies); and feedback on the harms of smoking (11 studies). The studies included a total of 9262 people. All participants were adult smokers, and both men and women were included (although one study performed in a clinic for army veterans included only 4% women). Most studies were conducted in general practices or ambulatory clinics. All of the studies lasted at least six months. The reported evidence is current as of March 2018.

Key results

We did not find evidence that giving smokers feedback on their smoking exposure, their genetic risk of smoking-related disease, or the effects of smoking on their body helps them quit smoking. The most promising results were for giving people feedback on the harm smoking does to their bodies. The studies did not report on harms or side effects of providing feedback. However, given the nature of the measurements (lung or blood tests), we would expect the risk of harms to be low.

Certainty of evidence

Because of problems with the way some of the studies were conducted, we think that further research is likely to change our conclusions.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Biomedical risk assessment compared with standard care or minimal intervention for smoking cessation

Patient or population: people who smoke
Setting: mixed
Intervention: biomedical risk assessment
Comparison: standard care or minimal intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with biomedical risk assessment			
Feedback on smoking exposure *Smoking cessation at longest follow-up over 6 months*	Study population 153 per 1000	**153 per 1000** (127 to 185)	**RR 1.00** (0.83 to 1.21)	2368 (5 studies)	⊕⊕⊕◯[1] **moderate**
Feedback on smoking-related risk *Smoking cessation at longest follow-up over 6 months*	Study population 130 per 1000	**104 per 1000** (82 to 131)	**RR 0.80** (0.63 to 1.01)	2064 (5 studies)	⊕⊕◯◯[1,2] **low**
Feedback on smoking-related harm *Smoking cessation at longest follow-up over 6 months*	Study population 117 per 1000	**147 per 1000** (116 to 188)	**RR 1.26** (0.99 to 1.61)	3314 (11 studies)	⊕⊕⊕◯[3] **moderate**

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for risk of bias: three out of five studies at high risk of bias, and remaining studies at unclear risk of bias.

[2]Downgraded one level for imprecision: fewer than 300 events.

[3]Downgraded one level for imprecision and risk of bias: sensitivity analysis removing studies at high risk of bias produced a statistically significant benefit.

BACKGROUND

Description of the condition

Smoking is the leading cause of preventable mortality and morbidity in industrialised countries (CDC 2014; Phillips 1995; Sargeant 2001; Yach 2000), and increasingly the smoking epidemic is affecting low- and middle-income countries. This is particularly true for vascular and respiratory diseases, as well as for cancer (DHHS 2004; Doll 2004; Thun 2013). Stopping smoking prolongs life and reduces morbidity (DHHS 1990; Jha 2013). Despite increasing scientific knowledge about health hazards due to cigarette consumption, there is still an increase in prevalence in many countries (Bilano 2015). The gap between knowledge and smoking cessation has been attributed, in part, to smokers' underestimation of their personal risks of smoking-related illness (Krosnick 2017; Lerman 1993; Romer 2001). Although many smokers who are successful in quitting do so on their own (Livingstone-Banks 2019; Schwartz 1987), an increasing proportion use specific aids to support a quit attempt.

Description of the intervention

Evidence is growing on how to help smokers to quit (Fiore 2008; Hartmann-Boyce 2018; Kottke 1988; Lancaster 2017; Stead 2013; West 2000). Interventions that have been shown to help quitting smoking include individual or group counselling, pharmacological therapies, and possibly some forms of self-help materials. Another possible strategy for increasing quit rates is to provide feedback on the physical effects of smoking by physiological measurements. We can conceptually distinguish, in this respect, three different types of feedback: the first one explores biomarkers of smoking exposure (cotinine, carbon monoxide); the second one gives information on smoking-related disease risk (e.g. lung cancer susceptibility according to cytochrome P450 2D6 (*CYP2D6*) genotyping) (Audrain 1997); and the third one depicts smoking-related harm (e.g. atherosclerotic plaque, impaired lung function) (Buist 2002).

How the intervention might work

The rationale for such interventions is to provide personalised motivational feedback to promote risk awareness and to accelerate smoking behaviour change (Curry 1993; Miller 1991). Recognition of personal susceptibility to the adverse effects of smoking may be an important step in the pathway to smoking cessation (McClure 2001; Weinberger 1981; Young 2010). Indeed, most theories related to health behaviour changes (e.g. self-determination theory, theory of planned behaviour, health belief model, transtheoretical model, social cognitive theory, social ecological model, common-sense model) have in common that they recognise an important role to the person's understanding of the potential negative consequences of a given behaviour (Hale 2007; Joseph 2016).

Why it is important to do this review

Individual studies have produced conflicting data on the effect of physiological feedback (Bovet 2002; Buffels 2006; Lerman 1993; McBride 2000; Parkes 2008; Rodondi 2012). This review systematically examined data on smoking cessation rates from randomised controlled trials using feedback on the physiological effect of smoking or on genetic susceptibility to smoking-related diseases.

OBJECTIVES

The main objective was to determine the efficacy of providing smokers with feedback on their exhaled carbon monoxide (CO) measurement, spirometry results, atherosclerotic plaque imaging, and genetic susceptibility to smoking-related diseases in helping them to quit smoking.

The hypotheses to be examined were as follows.

- Feedback on personal characteristics indicating that the effects of smoking, or susceptibility to smoking-related illness, increases rates of smoking cessation.
- Multiple types of measurement (e.g. spirometry and exhaled CO measurement used together) are more effective for smoking cessation than a single form of measurement.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials.

Types of participants

We included studies of any individuals who smoked and who participated in smoking cessation programmes, or in screening for respiratory disease, or in health checkups. There were no restrictions on participant age, motivation to quit, or whether participants were pregnant, were hospitalised, or were suffering from coexistent illness.

Types of interventions

We included studies of any intervention in which a physical measurement, such as exhaled carbon monoxide (CO), spirometry, atherosclerotic plaque imaging, or genetic testing, was used as a way to increase smoking cessation rate. We considered studies in which reporting of these measurements was the only component of an intervention, or was tested as an adjunct to another intervention such as counselling, where the control group received all other components except for the reporting of such measurements. We excluded trials in which the effect of biological measurements was confounded by the use of other components in the active intervention.

Types of outcome measures

The main outcome measure was abstinence from smoking, measured at least six months after the start of the intervention. We used the most conservative measure of quitting at the longest follow-up, preferring biochemically validated results where available. We counted participants lost to follow-up as continuing smokers. We excluded studies that did not provide data on cessation but instead measured intermediate outcomes such as withdrawal symptoms.

Search methods for identification of studies

For this update we searched the Cochrane Tobacco Addiction Group Specialized Register on 27 March 2018 and the US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch) on 3 September 2018 for studies that involved any use of a biomedical test as part of an intervention. At the time of the search, the Register included the results of searches of the Cochrane Central Register of Controlled trials (CENTRAL), Issue 1, 2018; MEDLINE (via Ovid) to update 20180209; Embase (via Ovid) to week 201807; and PsycINFO (via Ovid) to update 20180212. See the Cochrane Tobacco Addiction Group website for full search strategies and a list of other resources.

We used the following topic-related keywords and text terms to identify potentially relevant studies:

patient education, patient compliance, patient counselling, persuasive communication, spirometry, respiratory function, bronchospirometry, carbon monoxide, forced expiratory flow rates, obstructive lung diseases, genetic testing, genetic susceptibility, genetic predisposition, biomarker, feedback.

See Appendix 1 for the full strategy.

Data collection and analysis

Two review authors (out of CC, RB, YM, KS) independently prescreened all search results (abstracts) for possible inclusion or as useful background. Studies were selected for full-text assessment if retained by at least one of the review authors. Two review authors (out of CC, RB, YM, KS) then independently assessed the selected articles for inclusion, resolving any discrepancies by consensus. We have recorded reasons for the non-inclusion of studies in the Characteristics of excluded studies table.

Each review author then extracted and compared the data from the selected studies. This stage included an evaluation of risk of bias. Four review authors independently assessed each study according to the presence and quality of the randomisation process, whether or not trialists and assessors were 'blinded', whether the analysis was appropriate to the study design, and the description of withdrawals and dropouts. We used Covidence for the screening and data extraction (Covidence).

We extracted data, where available, on the following.

- Country and setting (e.g. primary care, community, hospital outpatient/inpatient)
- Recruitment
- Method of selection of participants (e.g. willingness to make a quit attempt)
- Definition of smoker used
- Method of randomisation
- Allocation concealment
- Smoking and demographic characteristics of participants (e.g. average age, sex, average number of cigarettes smoked per day)
- Description of the experimental and control interventions (provider, length, number of visits, etc.)
- Outcomes, including definition of abstinence used, and biochemical validation of cessation
- Proportion of participants with follow-up data
- Whether or not data were analysed on an intention-to-treat basis
- Appropriateness of statistical approach
- Declaration of interest and source of funding

Data synthesis

We expressed results as a risk ratio (RR) for smoking cessation with 95% confidence intervals (CI). Where appropriate, we pooled studies using a Mantel-Haenszel random-effects method. We assessed heterogeneity using the I^2 statistic.

'Summary of findings' table

We created a 'Summary of findings' table for our primary outcome in accordance with standard Cochrane methodology. We assessed the certainty of evidence using the five GRADE criteria (study limitations, consistency of effect, imprecision, indirectness, and publication bias).

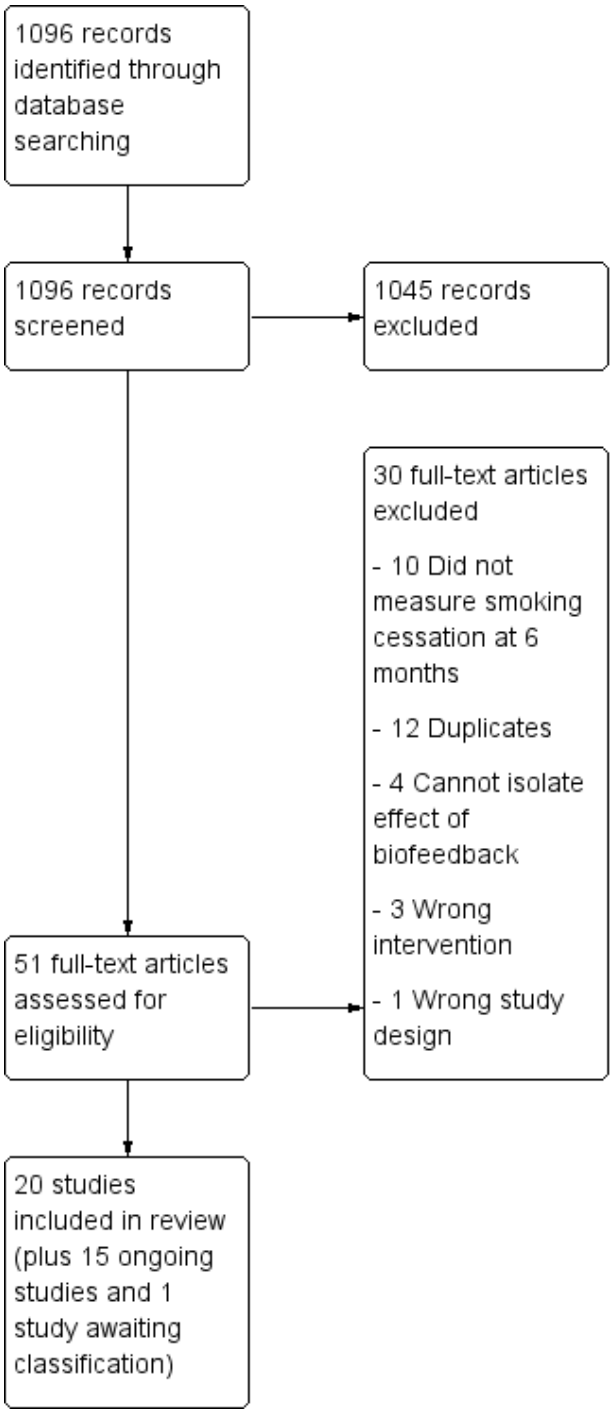
RESULTS

Description of studies

Results of the search

For this update we found 1096 records for screening, from which we identified five new trials, for a total of 20 trials of 9262 people that met our inclusion criteria. The flow of studies is reported in a PRISMA flow diagram (Figure 1). We found 15 studies that were potentially eligible and either ongoing (ACTRN12618000291280; IRCT2017080435257N1; NCT02658032; NCT02840513; NCT02991781; NCT03521141; NCT03583203), or finished but with no published data and no information retrievable through contacting study authors (Martin Lujan 2011; Martin Lujan 2016; NCT01186016; NCT02431611; NCT03377738; Pita Fernandez 2015; Ripoll 2012; Muhammad 2015). Details of these studies can be found in the Characteristics of ongoing studies table. One study was ongoing, but there was insufficient information to assess its eligibility, therefore we assessed it as awaiting classification (NCT02351167).

Figure 1. Study flow diagram for 2019 update.



Included studies

One included study tested two interventions (Audrain 1997). Out of the 21 interventions, five tested feedback on smoking exposure, each measuring the effect of exhaled CO measurements (Audrain 1997; Brunette 2013; Jamrozik 1984; Sanders 1989; Shahab 2011). Five studies tested feedback on smoking-related disease risk; of these, four tested feedback about genetic susceptibility to cancer (Audrain 1997; Hishida 2010; Ito 2006; Nichols 2014), and one tested feedback about genetic susceptibility to Crohn's disease (Hollands 2012). In Audrain 1997, the intervention was feedback about genetic susceptibility combined with CO measurement, which could either be compared to a control group of CO measurement alone, or to a control group without biomarker feedback, thereby testing the combination of the two interventions. Eleven studies assessed feedback on smoking-related harm: four tested the combination of exhaled CO measurement and spirometry (McClure 2009; Risser 1990; Sippel 1999; Walker 1985); five tested the effect of spirometry alone (Buffels 2006; Irizar Aramburu 2013; Segnan 1991), or with the addition of feedback on lung age (Drummond 2014; Parkes 2008); two tested the effect of undergoing an ultrasonography of carotid arteries (and femoral arteries for Bovet 2002) with photographic demonstration of atherosclerotic plaques when present (Bovet 2002; Rodondi 2012).

The trials were conducted in different settings: 11 trials took place in general practice (Buffels 2006; Irizar Aramburu 2013; Jamrozik 1984; Nichols 2014; Parkes 2008; Sanders 1989; Segnan 1991), or outpatient clinics (Bovet 2002; Ito 2006; Rodondi 2012; Sippel 1999); one study took place in the community, recruiting first-degree relatives of probands with Crohn's disease (Hollands 2012); two took place in smoking cessation clinics (Audrain 1997; Walker 1985); one was conducted in a health promotion clinic for army veterans (Risser 1990); one was conducted in a mental health clinic (Brunette 2013); one was conducted in a company (Hishida 2010); and three took place in research institutions (Drummond 2014; McClure 2009; Shahab 2011). Seven trials took place in the USA (Audrain 1997; Brunette 2013; Drummond 2014; McClure 2009; Risser 1990; Sippel 1999; Walker 1985), six in the UK (Hollands 2012; Jamrozik 1984; Nichols 2014; Parkes 2008; Sanders 1989; Shahab 2011), two in Japan (Hishida 2010; Ito 2006), and one trial each took place in Italy (Segnan 1991), Belgium (Buffels 2006), the Seychelles Islands (Bovet 2002), Switzerland (Rodondi 2012), and Spain (Irizar Aramburu 2013).

Methods of recruitment were heterogeneous between studies. Among the six studies conducted in general practice, one recruited patients at their first visit (Jamrozik 1984); another screened outpatients on specific days (Segnan 1991); two screened patients during the recruitment period (Buffels 2006; Sanders 1989); and two invited known smokers by post (Parkes 2008; Nichols 2014). One study recruited smokers among outpatients in primary care clinics (Sippel 1999); one study recruited outpatients at a cancer centre hospital (Ito 2006); and one study recruited patients referred to a mental health treatment clinic (Brunette 2013). Four studies recruited smokers by media advertisement (Audrain 1997; Rodondi 2012; Shahab 2011; Walker 1985). The remaining studies recruited smokers participating in a health survey (Bovet 2002); employees who identified themselves as smokers in a questionnaire used for an annual workplace checkup (Hishida 2010); veterans that responded to a mailed invitation to attend a health promotion clinic (Risser 1990); and participants of a cohort study of people with a history of injecting drugs (Drummond 2014). Two studies combined diverse methods of recruitment. One study used media advertisement, outpatient recruitment, data from health plan records, a quitline register, and a purchased e-mail list of smokers (McClure 2009), and another asked probands to identify first-degree relatives through three routes, first approaching probands receiving care through hospital services, secondly contacting them by mail using Crohn's disease databases at 42 participating hospitals, and finally placing advertisements in the newsletters of associations (Hollands 2012). One study did not specify the method of recruitment (data were obtained after contacting the study author; the study is not yet published) (Irizar Aramburu 2013). Participation rates (i.e. the proportion of those approached who agreed to take part in the trial) were seldom recorded.

All studies included male and female adults who were smokers at the time of inclusion. Only 10 studies provided a definition of being a smoker at the time of inclusion (Audrain 1997; Bovet 2002; Drummond 2014; Hollands 2012; Irizar Aramburu 2013; Ito 2006; McClure 2009; Nichols 2014; Rodondi 2012; Shahab 2011). The mean age of the participants when given varied between 31.7 and 53.0 years. The proportion of women in the trials varied between 4% and 65%. The mean number of cigarettes smoked per day varied between 11.9 and 29.2. The mean number of cigarettes smoked per day tended to be highest in the trials set in a smoking cessation clinic (29.2 per day in Walker 1985 and 22.7 per day in Audrain 1997) or among veterans (23.5 per day in Risser 1990). Levels of nicotine addiction as assessed by the Fagerström score were provided in three studies (Heatherton 1991), and ranged from 3.5 to 5.4 (Drummond 2014; Nichols 2014; Rodondi 2012); proportions of participants in the various stages of change according to Prochaska and Di Clemente were only provided in five studies (Prochaska 1983), with the proportion of participants in the preparation stage ranging from 17% to 37.5% (Audrain 1997; Ito 2006; McClure 2009; Parkes 2008; Sippel 1999).

The therapist delivering the intervention was a physician in five trials (Bovet 2002; Buffels 2006; Irizar Aramburu 2013; Jamrozik

1984; Segnan 1991); a nurse in four trials (Hishida 2010; Risser 1990; Rodondi 2012; Sanders 1989); a specific study staff member in seven trials (Audrain 1997; Drummond 2014; Ito 2006; Parkes 2008; Shahab 2011; Sippel 1999; Walker 1985); a trained health educator or research counsellor in two trials (Hollands 2012; McClure 2009); the principal investigator with help from trained smoking cessation practitioners in one study (Nichols 2014); and the intervention and feedback was web based in one study (Brunette 2013). Further details on the included studies can be found in the Characteristics of included studies tables.

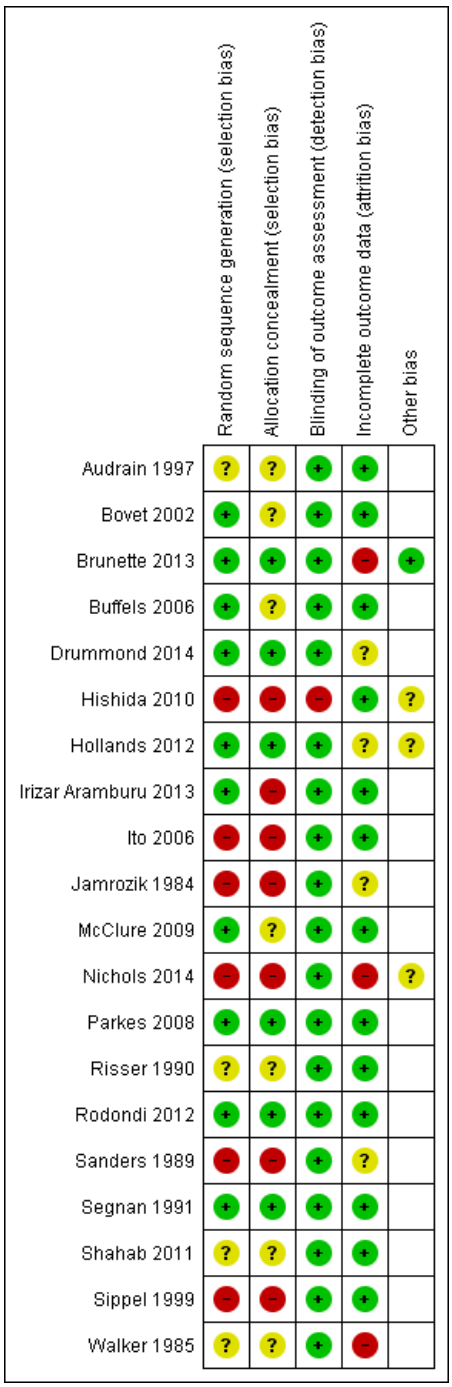
Excluded studies

For this update, we excluded 31 studies at full-text screening, and listed a total of 61 excluded studies. The primary reasons for exclusion were because the effect of the biomedical assessment could not be evaluated separately from the rest of the cessation intervention; the study had less than six months follow-up; or the study was not a true randomised trial. The excluded studies along with reasons for their exclusion can be found in the Characteristics of excluded studies table.

Risk of bias in included studies

We judged all but three included studies to be at high or unclear risk of bias in at least one domain (Parkes 2008; Rodondi 2012; Segnan 1991). 'Risk of bias' judgements for each study are displayed in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Only six of the 20 included trials reported an adequate procedure for both randomisation and allocation concealment (Brunette 2013; Drummond 2014; Hollands 2012; Parkes 2008; Rodondi 2012; Segnan 1991). Eight studies did not report the method of randomisation, or provided insufficient information to assume that allocation was adequately concealed (Audrain 1997; Bovet 2002; Buffels 2006; McClure 2009; Nichols 2014; Risser 1990; Shahab 2011; Walker 1985). Five studies reported inadequate allocation sequences, with allocation by day, week, or month of attendance (Hishida 2010; Ito 2006; Jamrozik 1984; Sanders 1989), or by odd-/even-numbered questionnaire at the time of check-in (Sippel 1999). In one of these studies, 120 participants were allocated to the wrong group and were excluded from further analysis (Sanders 1989).

Due to the demonstrative nature of the intervention, participants and those delivering the intervention could not be blinded to allocation, therefore we did not assess performance bias, and assessed detection bias independent of blinding. We judged the risk of detection bias to be low if abstinence was biochemically verified, or if the intervention and control groups received similar amounts of face-to-face contact. If abstinence was not biochemically verified and the intervention group received more face-to-face contact than the control group, then we judged the risk of detection bias to be high because the results may be prone to differential misreport. We judged only one study to be at high risk of detection bias based on these criteria (Hishida 2010); we assessed the remaining studies as at low risk of bias.

Three trials used urinary cotinine level to validate smoking cessation at follow-up (Parkes 2008; Sanders 1989; Segnan 1991). One study used the same validation procedure but only on a subsample of self-reported ex-smokers (Jamrozik 1984). Two studies used expired air carbon monoxide (Risser 1990; Walker 1985). One study used serum cotinine level (Rodondi 2012); one study used saliva cotinine (Hollands 2012); and two studies used both exhaled CO and salivary cotinine (Drummond 2014; Nichols 2014). Nine studies did not use any biochemical validation (Audrain 1997; Bovet 2002; Brunette 2013; Buffels 2006; Hishida 2010; Ito 2006; McClure 2009; Shahab 2011; Sippel 1999). Only seven studies explicitly mentioned that assessors were blinded to allocation at the time of outcome determination (Bovet 2002; Brunette 2013; Parkes 2008; Risser 1990; Rodondi 2012; Shahab 2011; Sippel 1999).

In three studies (Audrain 1997; Nichols 2014; Walker 1985), it was not possible to determine the initial allocation of the participants who were subsequently lost to follow-up, and the analysis had to be performed per protocol. This may have overestimated cessation rates for the individual studies, but impact on meta-analysis results were probably limited given the limited number of participants in those three studies. In one study (Hishida 2010), those who were allocated to the intervention group but who subsequently declined to participate in biomarker testing were included in the baseline characteristics table, but were excluded from further analyses.

Effects of interventions

See: **Summary of findings for the main comparison** Biomedical risk assessment compared with standard care or minimal intervention for smoking cessation

Results are given as risk ratios (RRs) for smoking cessation at the latest recorded follow-up time (six to 12 months) between intervention and control groups, with 95% confidence intervals (CI). An RR greater than one favours the intervention group. We classified trials into three analyses by type of intervention: those that provided feedback on smoking exposure, those that provided feedback on smoking-related disease risk, and those that provided feedback on smoking-related harms. Results of the analyses are reproduced in Figure 3, Figure 4, and Figure 5.

Figure 3. Forest plot of comparison: 1 All interventions, outcome: 1.1 Smoking cessation - feedback on smoking exposure.

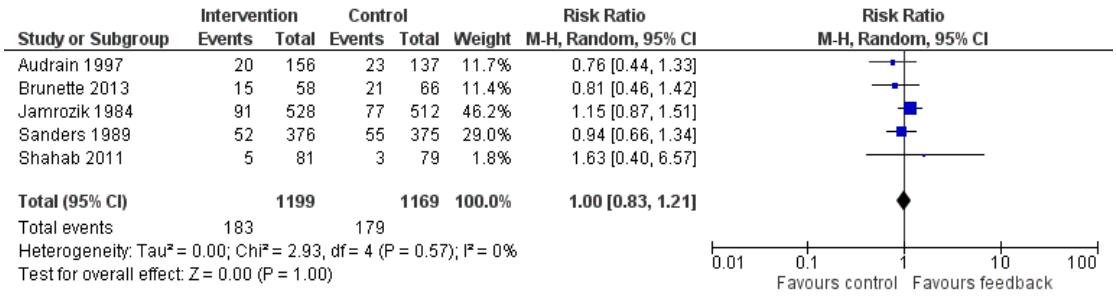


Figure 4. Forest plot of comparison: 1 All interventions, outcome: 1.2 Smoking cessation - feedback on smoking-related disease risk.

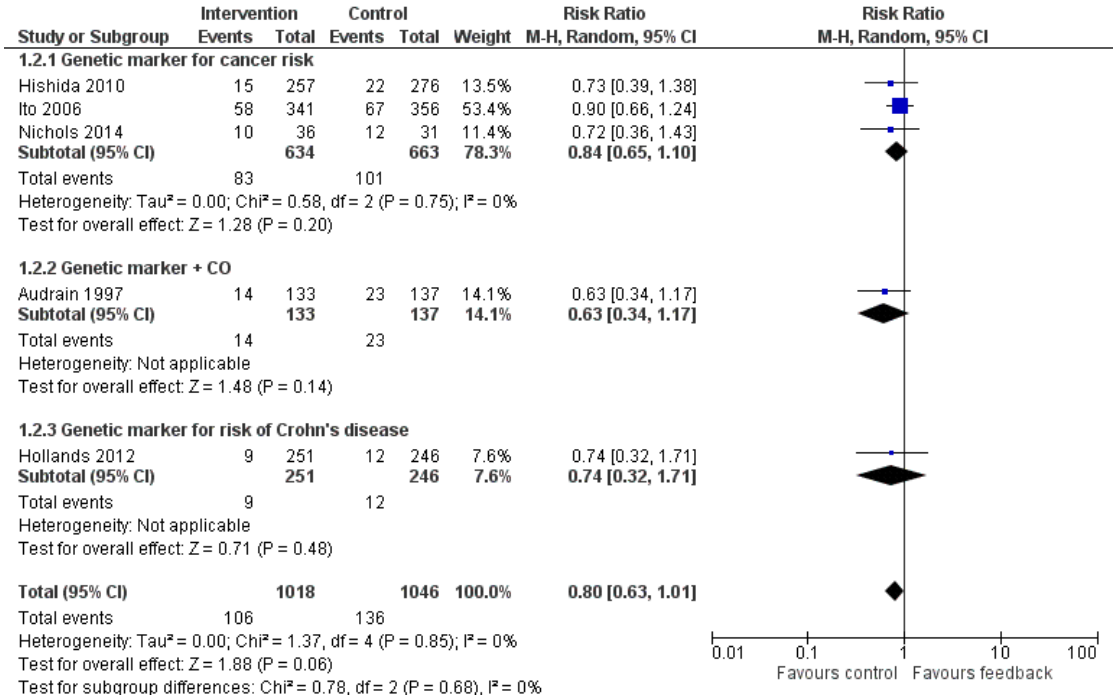
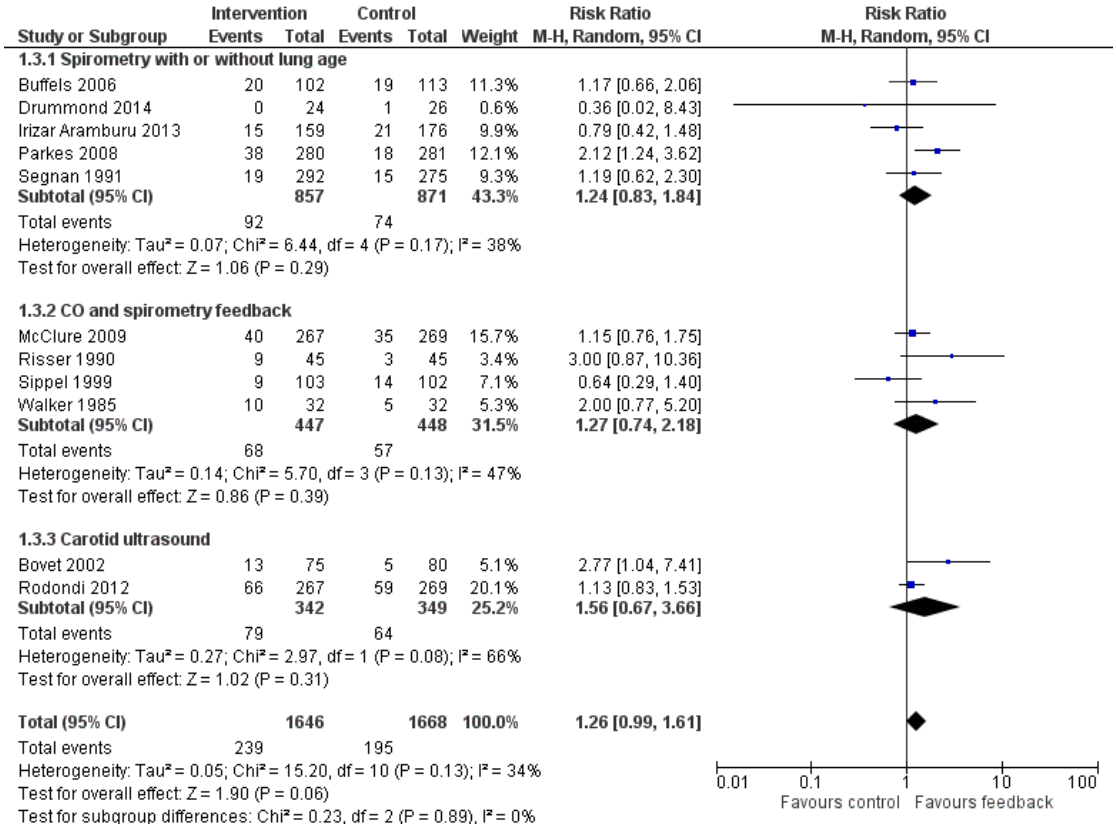


Figure 5. Forest plot of comparison: 1 All interventions, outcome: 1.3 Smoking cessation - feedback on smoking-related harm.



Feedback on smoking exposure

Five studies isolated the effect of demonstrating levels of exhaled CO on smoking cessation rate (Audrain 1997; Brunette 2013; Jamrozik 1984; Sanders 1989; Shahab 2011). There was no evidence of a significant benefit from these pooled studies (RR 1.00, 95% CI 0.83 to 1.21; I^2 = 0%; n = 2368; Analysis 1.1; Figure 3).

Feedback on smoking-related disease risk

Three trials studied measurements of genetic susceptibility to smoking-related cancer (Hishida 2010; Ito 2006; Nichols 2014), and one measured the genetic susceptibility to Crohn's disease (Hollands 2012). We pooled all five trials and found no evidence of a significant benefit from these pooled studies (RR 0.80, 95% CI 0.63 to 1.01; I^2 = 0%; n = 2064; Analysis 1.2; Figure 4).

We pooled the three trials testing feedback on the genetic susceptibility to smoking-related cancers and found no evidence of a significant benefit from these pooled studies (RR 0.84, 95% CI 0.65 to 1.10; I^2 = 0%; n = 1297; Analysis 1.2.1). Hollands 2012 did not detect a benefit from feedback on genetic susceptibility to Crohn's disease (in relatives of individuals suffering from Crohn's disease) (RR 0.74, 95% CI 0.32 to 1.71; n = 497).

Feedback on smoking-related harms

Eleven studies provided feedback on smoking-related harm. Pooling all 11 studies narrowly missed a significant effect on smoking cessation (RR 1.26, 95% CI 0.99 to 1.61; I^2 = 34%; n = 3314; Analysis 1.3; Figure 5). However, a sensitivity analysis removing the three studies at high risk of bias did detect an effect (RR 1.36, 95% CI 1.07 to 1.74; I^2 = 24%; n = 2710; *analysis not shown*).

Five studies provided feedback based on spirometry results (Buffels 2006; Drummond 2014; Irizar Aramburu 2013; Parkes 2008; Segnan 1991). There was no evidence of a significant benefit from spirometry with or without feedback on lung age when the five studies were pooled (RR 1.24, 95% CI 0.83 to 1.84; I^2 = 38%; n = 1728; Analysis 1.3.1). Four trials used exhaled CO measurement and spirometry together (McClure 2009; Risser 1990; Sippel 1999; Walker 1985). None of these trials detected a significant

effect independently, and there was no evidence of a significant benefit when these studies were pooled (RR 1.27, 95% CI 0.74 to 2.18; I^2 = 47%; n = 895; Analysis 1.3.2). Two trials tested ultrasonography of carotid (and femoral) arteries (Bovet 2002; Rodondi 2012). There was no evidence of a significant benefit from these pooled studies (RR 1.56, 95% CI 0.67 to 3.66; I^2 = 66%; n = 691; Analysis 1.3.3).

Multiple versus single forms of measurement

Only one study directly compared multiple forms of measurement with a single form of measurement (Audrain 1997). The study did not detect a significant difference in effect between measurement of CO plus genetic susceptibility to lung cancer and measurement of CO only (RR 0.82, 95% CI 0.43 to 1.56; n = 189; Analysis 2.1). The other included studies were too clinically heterogenous to allow indirect comparisons of multiple versus single forms of measurement.

DISCUSSION

Summary of main results

Due to the scarcity of evidence of sufficient quality, we cannot make definitive statements about the effectiveness of biomedical risk assessment as an aid for smoking cessation. Most studies were small and did not detect significant effects. We pooled studies based on the type of feedback they provided. The most promising results relate to spirometry and carotid ultrasound, where moderate-certainty evidence, limited by imprecision and risk of bias, did not detect a statistically significant benefit, but confidence intervals very narrowly missed one, and the point estimate favoured the intervention. A sensitivity analysis removing those studies at high risk of bias did detect a benefit. Moderate-certainty evidence limited by risk of bias did not detect an effect of feedback on smoking exposure by CO monitoring. Low-certainty evidence, limited by risk of bias and imprecision, did not detect a benefit from feedback on smoking-related risk by genetic marker testing. There is insufficient evidence with which to evaluate the hypothesis that multiple types of assessment are more effective than single forms of assessment. Results are summarised in Summary of findings for the main comparison.

Only two studies detected statistically significant intervention effects. One of these was a trial in primary care that used spirometry and immediate feedback of the results using a graphical display (Parkes 2008). Intervention participants were told their "lung age" if this was older than their chronological age. The control group also had spirometry and feedback, but the results were given by letter in terms of standard measures of lung function, with no mention of lung age. All participants were advised to quit and offered a referral to intensive support. Contact time was longer in the intervention group because of the verbal feedback. Giving the spirometry results in terms of lung age resulted in an increase in the cessation rate at 12 months from 6.4% to 13.6%. In considering the strength of evidence and generalisability of this trial, it should also be noted that the outcome was limited to point-prevalence abstinence, and information was lacking about the comparability of the study sample with the entire recruitment population. Another study, retrieved in the current update, also assessed spirometry with lung age feedback (compared with spirometry results in a standardised written format) but in a research cohort of intravenous drug users (Drummond 2014). The sample size was small (50 participants), and the study did not show a significant benefit of this approach.

The other study with a statistically significant positive effect used pictures of ultrasound photographs of atherosclerotic plaques (Bovet 2002). Participants were randomised to undergo ultrasonography (n = 74) or not (n = 79). Those with ultrasonographic demonstration of atherosclerotic plaques (n = 20) were given photographs of their plaques with a relevant explanation, whereas the others did not benefit from any further procedure. This study's external validity can be questioned, as the sample was made up predominantly of male light smokers (average 10 to 12 cigarettes a day). Another study using a similar feedback method had a larger sample (536 smokers), a larger proportion of women (45%), and heavier smokers as participants (an average of 20 cigarettes smoked per day) (Rodondi 2012). This study did not show a statistically significant effect of the intervention. The authors noted in their discussion that they included only smokers with a motivation to quit and that they used a very intensive smoking cessation programme in both the intervention and control groups.

While the evidence does not directly support the use of biomedical risk assessment for smoking cessation, more research is needed before we can be confident in this result.

Overall completeness and applicability of evidence, and limitations of the review

Cochrane methods are designed to minimise bias in the review process. However, due to the nature of the intervention, there were some difficulties in finding suitable evidence. In most of the included studies, the biomedical testing component was added to intensive quit-smoking sessions, with counselling lasting up to 60 minutes and completed by written material and reinforcement sessions or follow-up phone calls. The incremental effect of biomedical risk assessment might have been diluted by the high intensity of the 'standard' care used. It is also possible that the changes in motivational stages induced by biomedical risk assessment are too subtle to be characterised as directly leading to a successful quit attempt. Data from those studies do not permit verification of this hypothesis. However, given the increasing evidence that the transtheoretical model of behaviour change is not a mandatory prerequisite for a smoking cessation intervention to be effective

(Cahill 2010; Riemsma 2003), we do not consider this lack of intermediate data to be a major concern.

Biomedical risk assessment was also conceptualised as a part of multicomponent interventions (with components other than biomedical risk assessment) by some authors of studies identified by our search strategy (Borrelli 2002; Borrelli 2005; Ferketich 2012; Hajek 2002; Humerfelt 1998; Kotz 2009; Martucci 2010; McBride 2002; McClure 2013; Prokhorov 2008; Richmond 1986). Even though four of these studies demonstrated effects significantly favouring intervention versus control groups, they did not isolate the specific effect of biomedical feedback. The retrieved studies also did not provide us with sufficient data to adequately examine our second research hypothesis, that feedback with different types of measurements is more effective for smoking cessation than feedback of a single measurement.

Another possible explanation for the absence of effectiveness of biomedical risk assessment provided in addition to counselling could be the potentially counterproductive effect of communicating normal results to smokers. Six included studies provided some insight about smoking cessation rates in subgroups according to test results. Sippel 1999, Buffels 2006, and Parkes 2008 did not find any correlation between smoking cessation and abnormal spirometry results. Bovet 2002, which overall detected significantly higher cessation rates in participants offered ultrasonography, found a statistically non-significant lower smoking cessation rate among the subgroup of participants without plaques at ultrasonography than among participants in the control group. Rodondi 2012 found that, in the ultrasonography group, cessation rates did not differ according to the presence or absence of atherosclerotic plaques. Parkes 2008 noted that anecdotally some smokers were motivated by having normal results because it helped them feel it was "not too late" to quit. Ito 2006 found some evidence that among participants without cancer, those told they had increased susceptibility to cancer were more likely to quit. This particular question, and the way to handle and communicate normal results, has yet to be answered.

Trials demonstrating smoking-related harms using spirometry (especially when combined with lung age) or carotid ultrasound tended to show a stronger effect on smoking cessation, though this effect was not significant. This could be explained by the fact that direct and concrete demonstration of manifest harm might be more likely to motivate smokers to quit smoking, according to the Leventhal Common Sense Model (Hale 2007). It might be more straightforward for a smoker to establish a causal link between smoking and a direct and "noticeable" harm such as lung damage (increased lung age) or carotid plaques. Inversely, feedback on smoking exposure, using indirect and more obtuse measures such as CO, might not be sufficient to motivate a change in behaviour. Genetic feedback might be even more difficult to understand and counterproductive in the sense that people might believe that risks are not modifiable due to the deterministic aspect of genetics.

Two other trials used demonstration of smokers' children's exposure to environmental tobacco smoke by measuring the child's urinary cotinine level (abstinence was a secondary outcome) and demonstration of Latino caregivers' asthmatic children's exposure to secondhand CO (Borrelli 2010; Wakefield 2002), with RRs of 0.26 (95% CI 0.02 to 2.33) and 0.90 (95% CI 0.72 to 1.12), respectively. A third study evaluated the efficacy of personalised feedback during foetus ultrasound on pregnant smokers (Stotts 2009), and again did not detect a benefit (RR 1.31, 95% CI 0.66 to 2.58). We excluded these studies from our analysis because our research hypothesis was that smokers, although adept at estimating the risks of smoking in terms of morbidity and mortality, are prone to underestimate their own risk with regard to smoking (Lerman 1993; Romer 2001). It therefore seemed to us that providing biomarker feedback about someone else's health (even one's own children or foetus) would act differently and may not contribute to counteracting this personal optimistic bias. In any event, these trials did not detect benefits for the interventions tested.

A promising new approach could be for dental practitioners to use a point-of-care test for salivary nicotine metabolites. A short-term randomised controlled trial compared smoking cessation after eight weeks among participants who received either counselling with immediate or delayed (at the end of the study) feedback on salivary nicotine level (Barnfather 2005). The risk ratio for smoking cessation is close to being statistically significantly in favour of those who received immediate feedback: RR of 3.40 (95% CI 1.00 to 11.61). Trials with longer-term follow-up are needed to confirm this effect (Coleman 2005).

Despite broad inclusion criteria regarding the type of participants, we found only scarce data exploring the effect of biomedical risk assessment on hospitalised patients or acutely ill individuals. It is possible that such a specific context and the presence of coexistent illnesses could facilitate a modification of risk perception. One study included participants both with and without cancer (Ito 2006). Reported subgroup analyses did not detect benefits either for participants with cancer (RR 0.65, 95% CI 0.43 to 1.02) or for participants without cancer (RR 1.22, 95% CI 0.63 to 2.36).

Some recent studies used connected devices such as mobile-phone applications (ACTRN12618000291280; NCT02840513; NCT03583203), or provided web-based feedback (Brunette 2013). Biofeedback on lung damage or risk of lung cancer, or both, is a well-represented intervention in ongoing studies (NCT02658032; NCT03521141; NCT03583203).

Certainty of the evidence

The certainty of the evidence using GRADE criteria was low to moderate, depending on feedback category. The evidence on interventions providing feedback on risk exposure was of moderate certainty, limited by risk of bias because three of the five studies were at high risk of bias, and the remaining studies were at unclear risk of bias. The evidence on interventions providing feedback on smoking-related disease risk was of low certainty, limited by

risk of bias and imprecision because fewer than 300 events were recorded. The evidence on interventions providing feedback on smoking-related harm through spirometry or carotid ultrasound was of moderate certainty, limited by imprecision and risk of bias because the confidence intervals only narrowly missed a statistically significant benefit, and a sensitivity analysis excluding studies at high risk of bias did detect one.

Agreements and disagreements with other studies or reviews

An earlier non-systematic review was conducted on the use of biomarkers in smoking cessation (McClure 2001). This work aimed to review the theoretical rationale and empirical evidence regarding this practice, and therefore did not specifically focus on the assessment of the efficacy of biomarker feedback as a way to increase rates of long-term smoking cessation. The review therefore included non-randomised trials (Haddow 1991; Kilburn 1990; Loss 1979; Scott 1990); trials providing multicomponent interventions that precluded the isolation of the specific effect of biomarker feedback (Bauman 1983; Lerman 1997; Richmond 1986); trials comparing the effect of abnormal test results versus normal test results rather than test versus no test (Li 1984); and trials reporting outcomes other than smoking cessation. One study identified by McClure as "in press" appears never to have been published (Hoffman 1998), and we were unable to obtain further information despite several attempts to contact the authors. Four studies mentioned by McClure were also included in our review (Audrain 1997; Jamrozik 1984; Risser 1990; Walker 1985). Our review includes 16 trials not in the McClure review (Bovet 2002; Brunette 2013; Buffels 2006; Drummond 2014; Hishida 2010; Hollands 2012; Irizar Aramburu 2013; Ito 2006; McClure 2009; Nichols 2014; Parkes 2008; Rodondi 2012; Sanders 1989; Segnan 1991; Shahab 2011; Sippel 1999). When focusing on efficacy data, McClure 2001 concluded that biomarker feedback may enhance the likelihood of cessation because a trend for increased abstinence was found in three randomised trials (Hoffman 1998; Risser 1990; Walker 1985). The fact that two of these trials, Walker 1985; Risser 1990, are subject to major methodological limitations (small samples, inadequate randomisation procedures), and that the report of Hoffman 1998 remains unpublished, calls for great caution in drawing such conclusions.

AUTHORS' CONCLUSIONS

Implications for practice

We found little evidence about the effects of biomedical risk assessment as an aid for smoking cessation. However, the current evidence base does not support the use of biomedical risk assessment as an aid for smoking cessation. The most promising results relate to spirometry and carotid ultrasound, where moderate-certainty evidence, limited by imprecision and risk of bias, did not detect a statistically significant benefit, but confidence intervals very narrowly missed one, and the point estimate favoured the intervention. A sensitivity analysis removing those studies at high risk of bias did detect a benefit. Moderate-certainty evidence limited by risk of bias did not detect an effect of feedback on smoking exposure by carbon monoxide monitoring. Low-certainty evidence, limited by risk of bias and imprecision, did not detect a benefit from feedback on smoking-related risk by genetic marker testing. There is insufficient evidence with which to evaluate the hypothesis that multiple types of assessment are more effective than single forms of assessment.

Implications for research

There is room for improvement in the methodological quality of studies aimed at evaluating the efficacy of biomedical risk assessment as an aid to smoking cessation. In particular, further studies assessing feedback on smoking-related harm could be more beneficial than those assessing feedback on smoking exposure or smoking-related disease risk. Future studies should aim to have adequate sample sizes; conceal allocation following the randomisation procedure; use a standard definition of a smoker and of abstinence from smoking; systematically use biochemical validation of smoking abstinence; and include of all those lost to follow-up in the denominator of each group (on an intention-to-treat basis).

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Audrain 1997

Methods	**Setting:** "smoking clinic", USA **Recruitment:** press **Selected:** advertisement: "free smoking-cessation study"
Participants	550 smokers (defined as >= 5 cpd for >= 1 year) out of 1104 eligible; mean age 44 years, 62.8% female, 83.9% white, mean cpd: 22.7 **Stage of change:** Preparation stage: 37.5%, mean Fagerström score: 5.4 **Therapist:** trained health educator
Interventions	**Control:** QSC group: 60-minute Quit-Smoking Consultation (QSC) (quit plan, gaining support) **Intervention 1:** Exposure Biomarker (CO) Feedback (EBF) plus 10-minute motivational counselling before QSC. **Intervention 2:** Susceptibility Biomarker (CYP2D6) Feedback plus 10-minute motivational intervention plus EBF plus QSC
Outcomes	Definition of abstinence: 30-day abstinence Duration of follow-up: 12 months Biochemical validation of non-smokers: none
Identification	
Notes	**Source of funding:** Grant ROI CA63562 from the National Institutes of Health, National Cancer Institute

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised between 2 interventions and control, method not described
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence not biochemically validated, but similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	Per-protocol analysis, 33% lost to follow-up. Distribution of baseline 550 participants among the 3 groups not reported. "There were no significant differences between treatment groups with respect to loss to follow-up."

Bovet 2002

Methods	**Setting:** Seychelles Heart Study II **Recruitment:** age- and sex-stratified sample drawn from general population of Mahé, invited by letter to a cardiovascular risk factor survey **Selected:** last 155 participants to the Seychelles Heart Study II who reported smoking
Participants	155 smokers (defined as >= 1 cpd during previous week); mean age 46 years, 15% female, mean cpd: 11.9 **Therapist:** physician
Interventions	**Intervention:** ultrasonography of carotid and femoral arteries + quit-smoking counselling. Smokers with >= 1 plaque given 2 photographs of their plaque plus explanation. **Control:** quit-smoking counselling
Outcomes	Definition of abstinence: 7-day abstinence Duration of follow-up: 6 months Biochemical validation of non-smokers: none (assessor blinded)
Identification	
Notes	**Source of funding:** This study was supported by the Ministry of Health of Seychelles, the University Institute of Social and Preventive Medicine of Lausanne (Switzerland), and the Division of Cardiology of the University Hospital of Lausanne P Bovet benefited from a grant from the Swiss National Science Foundation (No. 3233-038792.93). F Paccaud benefited from a grant from the Swiss National Science Foundation (No. 3233-038792.93). F Paccaud benefited from grants from the "Fondation Vaudoise de Cardiologie" and the "Fondation Emma Muschamp" (Switzerland) Sonotron Ltd (Switzer-products) provided the echographic system for the study, and Air Seychelles transported this equipment free of charge

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Pre-established random sequences of numbers matched to rank of arrival
Allocation concealment (selection bias)	Unclear risk	Unclear whether allocation was concealed or not
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No biochemical validation, but follow-up assessors blinded to allocation group
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 participants lost to follow-up, not included for analysis

Brunette 2013

Methods	**Setting:** large mental health treatment organisation, Chicago, USA **Study design:** randomised controlled trial **Study grouping:** parallel group **Screened participants:** 279 referred participants **Included participants:** 124 **Intention-to-treat analyses:** not specified
Participants	**Inclusion criteria:** adult, English-speaking, daily smoker, in treatment for severe mental illness (defined as mood or psychotic disorder with persisting functional disability) at the mental health program **Exclusion criteria:** current other substance dependence; used smoking cessation treatment to try to quit in the past month **Baseline characteristics:** mean age 46.5 years, 28.2% female, 48.4% African-American, 15.0 mean number of cigarettes per day
Interventions	**Intervention characteristics** Intervention: Decision support system (DSS) with CO • *Description of intervention*: multicomponent web-based DSS with CO feedback • *How was the intervention performed*: information about CO, reading of the level, and brief interpretation of the reading Control: DSS without CO • *Description of intervention*: multicomponent web-based DSS without CO feedback
Outcomes	*Smoking cessation: 7-day point-prevalence abstinence at 2 and 6 months, self-reported*
Identification	**Country:** USA **Setting:** Thresholds, a large mental health treatment organisation in Chicago **Author's name:** Mary F Brunette, MD **Institution:** Geisel School of Medicine at Dartmouth and Dartmouth Psychiatric Research Center, Concord, NH 03301, USA **Email:** Mary.F.Brunette@Dartmouth.Edu **Address:** Geisel School of Medicine at Dartmouth College, 46 Centerra Parkway, Ever-Green Center, Suite 315, Lebanon, NH 03766, USA
Notes	6-month outcome data by arm obtained directly from main author **Source of funding:** This research is funded in part by the US Department of Education, National Institute on Disability and Rehabilitation Research and the Substance Abuse and Mental Health Services Administration, Center for Mental Health Services and Consumer Affairs Program, under Cooperative Agreement No. H133B100028 This research was also supported by the Bristol-Myers Squibb Foundation The views expressed in this manuscript do not reflect the policy or position of any federal agency. **Declaration of interest:** The authors do not have any competing interests to report.

Risk of bias

Bias	Authors' judgement	Support for judgement

Brunette 2013 (*Continued*)

Random sequence generation (selection bias)	Low risk	Computer-based randomisation program (using blocks of 10) assigned participants to use the multicomponent decision support system with or without the CO feedback
Allocation concealment (selection bias)	Low risk	Computer based. Research assistant adherence to the decision support system study visit protocol was assessed with a 10-item checklist. Adherence to the visit protocol was high (mean score 9.6 out of 10) and did not differ between treatment groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence not biochemically validated, but similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	High risk	3 participants did not complete the 2-month assessment. Numbers not completing 6-month assessment not given
Other bias	Low risk	6-month outcome not reported by allocation arm, but information was retrieved directly after contacting the authors

Buffels 2006

Methods	**Setting**: 14 general practices, Belgium **Recruitment**: screening of all attending patients above 15 years of age **Selected**: smokers in the motivation or action stage
Participants	215 randomised out of 1206 screened smokers. 182 analysed. Smoker definition not given. Mean age: 47.0, 47.3% female, mean pack-years: 24.6 **Therapist**: physicians
Interventions	**Intervention**: spirometry plus control intervention **Control**: minimal intervention based on the 5A model: ask, advise, assess, assist, arrange plus quit date plus NRT or bupropion plus follow-up contact
Outcomes	**Definition of abstinence**: continuous abstinence from quit date **Duration of follow-up**: 12 months (24-month data not used in analysis because of increasing loss to follow-up) **Biochemical validation of non-smokers**: none at the 12-month follow-up. Very partial at 24 months
Identification	

Buffels 2006 (*Continued*)

Notes	Additional data provided by author. **Source of funding:** This study was realised with an unconditional grant by Voorzorgskas voor Geneesheren, Brussels, Belgium

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation by coin toss
Allocation concealment (selection bias)	Unclear risk	No statement that random sequence generated by coin toss was concealed at time of enrolment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Biochemical validation of abstinence requested, but few completed. Similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	13 (13%) intervention, 20 (18%) control lost before 6 months, all losses included as smokers

Drummond 2014

Methods	**Setting:** AIDS Linked to the Intravenous Experience (ALIVE) study, a prospective, longitudinal cohort of people with a history of injecting drugs, Baltimore, USA **Study design:** randomised controlled trial **Study grouping:** parallel group **Comment:** factorial design **Duration of inclusion:** from 16 March 2011 to 3 February 2012 = 1 year **How sample size is determined:** not specified **Duration of follow-up:** 6 months **Intention-to-treat analyses:** yes **Number of participants screened for eligibility:** 265 **Number of participants included:** 100
Participants	**Inclusion criteria:** injection drug users (current and former) from ALIVE cohort; smoking at least 100 cigarettes in their lifetime as well as reporting any cigarette smoking in the last month; interested in involvement in a smoking cessation trial; ability to perform spirometry **Exclusion criteria:** current involvement in a smoking cessation programme; current use of nicotine replacement therapy or other smoking cessation pharmacological treatments (bupropion, varenicline) **Definition of smokers:** history of smoking at least 100 cigarettes in their lifetime and reporting any cigarette smoking in the last month **Study population:** residents of Baltimore with a history of injecting drugs

Drummond 2014 (*Continued*)

	Baseline characteristics (range of medians or proportions across arms) • *Mean age*: 46.1 (8.9) to 51.2 (7.5) • *% women*: 42% to 65% • *% African-American*: 75% to 100% • %*IDU:* 12% to 33% • *Pack-years, median*: 17.8 to 20.3 • *Fagerström score, median*: 3.5 to 4 • *Age at smoking initiation, mean*: 14.9 to 17.1 • *Predicted FEV1, %*: 84.1 to 93.7 • *FEV1/FVC, %*: 0.72 to 0.76
Interventions	**Intervention characteristics** Experimental intervention A: lung age • *Detailed description of the intervention*: spirometric results reviewed in the context of lung age vs chronological age Experimental intervention B: contingency management • *Detailed description of the intervention*: USD 25 to 50 for each eCO < 7 ppm Experimental intervention C: lung age plus contingency management • *Detailed description of the intervention*: lung age and contingency management Control intervention: usual care • *Detailed description of the intervention*: review of baseline spirometry results of their lung function reported as a % of predicted values communicated in a standardised written format
Outcomes	*Smoking cessation: 7-day point-prevalence abstinence, validated* • **Notes**: 7-day point-prevalence abstinence at 6 months, validated with exhaled CO 7 ppm and salivary cotinine 6 ng/mL *Smoking cessation: 7-day point-prevalence abstinence self-reported*
Identification	**Country:** USA **Setting:** AIDS Linked to the Intravenous Experience (ALIVE) study, a prospective, longitudinal cohort of people with a history of injecting drugs followed in Baltimore, Maryland since 1988 **Author's name:** Michael B Drummond **Institution:** Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD, USA **Email:** mdrummo3@jhmi.edu **Address:** Johns Hopkins University, Baltimore, MD, USA
Notes	**Source of funding:** This study was funded primarily by a Tobacco Dependence Research Fund from the American Thoracic Society (Principal Investigator: Drummond). This work was also supported in part by the National Institutes of Health (grants R01-HL-90483, R01-DA-04334, and R01-DA-12568). The funding sources had no role in study design, collection, analysis, or interpretation of data, writing the manuscript, or decision to submit for publication **Declaration of interest:** All authors have no financial conflict of interest to disclose
Risk of bias	

Drummond 2014 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation sequence was computer generated using a block randomisation approach with randomly ordered 4 and 8 sample blocks
Allocation concealment (selection bias)	Low risk	120 sequentially numbered, opaque, sealed envelopes that included random assignment to 1 of 4 interventions were externally prepared. Study staff were provided the next sequential envelope which assigned the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not clear

Hishida 2010

Methods	**Setting**: a bank in Japan **Recruitment/selection**: employees who indicated they were smokers on a questionnaire used at an annual workplace health checkup
Participants	All 562 eligible participants were included. No inclusion or exclusion criteria apart from being an employee of the bank and identifying as a smoker in the questionnaire Smoker definition not given. 6.2% female. Stage of quitting smoking at initiation: "no concern" 20.3% in intervention group vs 17.0% in control group; "no intention" 73.4% vs 79.3%; "wish to quit" 5.9% vs 3.3%; "no answer" 0.3% vs 0.4% **Therapist**: public nurses
Interventions	All participants received a booklet on tobacco-related diseases, concept of tobacco carcinogen susceptible genotypes, and benefits of smoking cessation **Intervention group**: participants who agreed to genotype testing had a blood sample taken. The staff handed a report of the results with a written explanation to each of the participants at 3 months. In the reports, an explanation was attached that smoking elevates the risk of oesophageal cancer substantially among those with genotypes SS (OR = 8) and LS (OR = 7), while OR = 2 among those with LL genotype, and similar for lung cancer. The staff added general comments on the genotype for each participant, and provided specific comments when participants asked for details. 29 participants allocated to genotyping group refused genotype testing. They were later excluded from analysis **Control group**: no further intervention

Hishida 2010 (*Continued*)

Outcomes	Abstinence assessed by postal questionnaire (no validation). **Duration of follow-up**: 12 months No definition of abstinence provided.	
Identification		
Notes	New for 2012 update **Source of funding:** This study was supported in part by a Grant-in-Aid for Cancer Research from the Japanese Ministry of Health, Labour and Welfare **Declaration of interest:** The authors have no conflicts of interest to declare.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Pseudo-random allocation by month of attendance
Allocation concealment (selection bias)	High risk	Allocation known at time of enrolment may lead to selection bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Abstinence not biochemically validated, and difference in face-to-face contact between intervention arms
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up (no response to follow-up questionnaire) 16.1% in intervention group, 11.2% in control group
Other bias	Unclear risk	A law against smoking in the workplace was issued in August 2002 in Japan, which may be a confounding factor

Hollands 2012

Methods	**Setting:** family clusters of relatives of people with Crohn's disease **Study design:** cluster-randomised controlled trial **Study grouping:** parallel group **Duration of follow-up:** 6 months **Duration of inclusion:** April 2007 to September 2010 **How sample size is determined:** the sample size was originally set at 540 participants (270 per arm) with an anticipated follow-up of 430 participants (projected 80% follow-up rate). We allowed for clustering of participants in families by assuming an intracluster correlation no greater than 0.6 and a mean cluster size of 1.13 derived from a pilot study **Intention-to-treat analyses:** yes **Type of recruitment:** • Approaching probands receiving care through hospital services • Obtaining addresses of probands through Crohn's disease databases at 42 participating hospitals • Advertising in the newsletters of the National Association for Colitis and Crohn's Disease and the charity Ostomy Lifestyle **Consecutive recruitment:** no **Number of participants screened for eligibility:** 1890 **Number of participants included:** 497
Participants	**Inclusion criteria:** • First-degree relatives of probands with Crohn's disease • > 18 years old smokers • Smoked 5 or more cigarettes daily **Exclusion criteria:** having a diagnosis of Crohn's disease or ulcerative colitis **Definition of smokers:** smoking 5 or more cigarettes daily **Baseline characteristics** Intervention: • *Mean age*: 42 (14.0) • *% women*: 145 (58) • *% white*: 240 (96) • %*least deprived*: 133 (53) • *Number of participants*: 251 Control • *Mean age*: 43 (14.8) • *% women*: 150 (61) • *% white*: 241 (98*)* • *% least deprived*: 137 (56) • *Number of participants*: 246
Interventions	**Intervention characteristics** Intervention: DNA arm • *Detailed intervention*: communication of risk assessment for Crohn's disease by postal booklet based on family history of the disease, smoking status, and additional DNA analysis for the NOD2 genotype --> followed by telephone by an NHS stop smoking counsellor to review the booklet and deliver brief standard smoking cessation intervention Control: non-DNA arm • *Detailed intervention*: communication of risk assessment for Crohn's disease by postal booklet based on family history of the disease and smoking status alone -->

	followed by telephone by an NHS stop smoking counsellor to review the booklet and deliver brief standard smoking cessation intervention
Outcomes	*Smoking cessation: 7-day point-prevalence abstinence validated* • **Notes**: reporting smoking no more than 5 cigarettes in the previous 7 days, validated by saliva cotinine (< 15 ng/mL) *Smoking cessation: 7-day point-prevalence abstinence self-reported*
Identification	**Country:** UK **Setting:** First-degree relatives of probands with Crohn's disease **Comments:** NA **Author's name:** Theresa M Marteau **Institution:** Department of Psychology (at Guy's), Section of Health Psychology **Email:** theresa.marteau@kcl.ac.uk **Address:** King's College London, London SE1 9RT, UK
Notes	**Source of funding:** This study was funded as part of a grant from the Medical Research Council, UK (Risk communication in preventive medicine: optimising the impact of DNA risk information; G0500274). NJP and CGM are supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at St Guy's and St Thomas' NHS Foundation Trust in partnership with King's College London. AF is supported by NIHR through the Comprehensive Biomedical Research Centre at UCLH/UCL. The trial protocol was peer reviewed by the Council. Other than as indicated, the funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. **Declaration of interest:** All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The trial statistician prepared the randomisation sequence using randomly selected block sizes of 6, 8, and 10 with randomly permuted allocations within each block, and with an equal allocation ratio. Participants were randomised by family cluster. Each participant was allocated by using the next assignment in the sequence, with clusters of participants required to be allocated to the same arm along the sequence

Hollands 2012 (*Continued*)

Allocation concealment (selection bias)	Low risk	The randomisation sequence was concealed from the trial co-ordination team and research counsellor, and the statistical team was only given study data needed for randomisation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Completed primary outcome measure: 209/251 (83%) for the DNA risk assessment group and 217/246 (88%) for the non-DNA risk assessment group
Other bias	Unclear risk	Table 3 reports a total number of participants in the DNA arm of n = 232, whereas only n = 226 received the intervention according to Figure 2

Irizar Aramburu 2013

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel group **Comment:** sample size not reached; clustering by practice not taken into account in analysis **Duration of follow-up:** 1 year **Duration of inclusion:** not specified **How sample size is determined:** based on assuming a level of significance of 5%, a quit rate after brief antismoking intervention only (control group) of 5%, an expected quit rate in the experimental group of 14%, and a 1:1 ratio of control to experimental participants. Given these premises, to obtain a power of 80% to detect differences in the test of the null hypothesis Ho: p1 = p2 using a 2-tailed Chi^2 test for 2 independent samples, it would be necessary to include 166 experimental units in the reference group and a further 166 in the experimental group, making a total of 332 units for the study. Assuming a loss to follow-up of 25%, it would be necessary to recruit 222 participants for the reference group and a further 222 for the experimental group, summing to the aforementioned total of 444 participants for the study **Intention-to-treat analyses:** yes **Number of participants included:** 335 **Number of participants screened for eligibility:** 1775
Participants	**Baseline characteristics** Overall • *Mean age*: 53.6 (SD 8.1) • *% women*: 51.6% • *Number of participants:* 335 **Inclusion criteria:** active smokers; older than 40 years of age; more than 10 pack-year

	history of smoking; have not been diagnosed with COPD **Exclusion criteria:** older than 80 years of age or institutionalised or having a life expectancy of less than 1 year; having undergone spirometry testing within the previous 2 years; previously diagnosed with respiratory diseases (asthma, interstitial lung diseases, or COPD) that cause pattern changes in spirometry tests; having contraindications for spirometry testing **Pretreatment:** no full text available **Definition of smokers:** > 10 pack-years **Study population:** primary care active smokers > 40 years without COPD
Interventions	**Intervention characteristics** Experimental intervention • *Detailed intervention*: the intervention consists of the nurse collecting data, performing a spirometry test, and then giving the participant an appointment with their general practitioner (GP) within 10 days. At this appointment, the doctor will deliver a brief antismoking intervention and provide the participant with a short explanation of the spirometry results. Both the delivery of the advice and the spirometry report will be carried out in a standardised way (in accordance with the guidelines) --> *follow-up:* contact by telephone 1 and 3 months after the intervention to determine whether they have stopped smoking and, if they have not, how many cigarettes they are smoking per day at the time. Control intervention • *Detailed intervention*: the nurse will only interview the participant to collect data on the study variables and make them an appointment with their GP within 10 days. The doctor will just perform the brief antismoking intervention in the same standardised way as for the intervention group. These participants will not undergo spirometry during the study period of 1 year --> *follow-up:* contact by telephone 1 and 3 months after the intervention to determine whether they have stopped smoking and, if they have not, how many cigarettes they are smoking per day at the time.
Outcomes	*Smoking cessation: 7-day point-prevalence abstinence validated by exhaled CO < 10 ppm*
Identification	**Sponsorship source:** International Centre of Research Excellence in Chronicity, Kronikgune, and the Department of Health of the Basque Government **Country:** Spain **Setting:** primary care (general practitioners from health centres) **Comments:** 39 health professionals work in 22 health centres **Author's name:** María Isabel Irizar-Aramburu **Institution:** Idiazabal Primary Care Medical Centre, Idiazabal, Gipuzkoa, Spain **Email:** MARIAISABEL.IRIZARARAMBURU@osakidetza.net **Address:** Idiazabal Primary Care Medical Centre, Idiazabal, Gipuzkoa, Spain
Notes	Results provided by authors upon request. **Source of funding:** We would also like to thank the International Centre of Research Excellence in Chronicity, Kronikgune and the Department of Health of the Basque Government's decision to fund this project **Declaration of interest:** The authors declare that they have no competing interests.
Risk of bias	

Irizar Aramburu 2013 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Doctors will send data on the patients recruited to the Primary Care Research Unit of the Gipuzkoa Health Region where the patients will be randomly assigned to the intervention or control group. The randomization sequence will be generated by computer and kept in the research unit. The list of patients assigned to each group will be sent to the nurses in charge of the first appointment. At this appointment, once written informed consent has been given, the interventions detailed below will be performed for each group."
Allocation concealment (selection bias)	High risk	Nurse in charge of organising appointment aware of allocation before confirming consent. Imbalance between size of groups (159 vs 176)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated. Assessment of outcome made by health professionals blinded to the group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 lost to follow-up out of 335 individuals.

Ito 2006

Methods	**Setting**: first visit at Aichi Cancer Center Hospital (ACCH), Japan **Recruitment**: screening of first-visit outpatients (whether consecutive or not is unknown)
Participants	697 included out of 859 eligible smokers. Smoker defined as smoking at least 1 cigarette on the previous day. Mean age 46.5, 40.5% female, mean cpd: 22.2, pre-contemplator/contemplator: 70% **Therapist**: trained interviewer
Interventions	**Intervention**: information at baseline on the effect of L-myc polymorphism on modulating the risk of cancer due to smoking (5 to 10 minutes). Sent genotype report at 3 months, with same information about effect of polymorphism (65% got genotype information) **Control**: just followed-up for smoking status
Outcomes	**Definition of abstinence**: point prevalence at 9 months (continuous abstinence, not smoking at both the 3- and 9-month follow-ups also reported, but genotype only provided after 3 months follow-up) **Duration of follow-up**: 9 months

Ito 2006 (*Continued*)

	Biochemical validation of non-smokers: none (attempt made but none agreed to return for CO measurement)
Identification	
Notes	Not given genotype until 3 months. Most participants in both groups had already quit at 3 months, small proportion of new quitters after 3 months **Source of funding:** This work was supported in part by a Grant-in-Aid for Cancer Research from the Japanese Ministry of Health, Labor and Welfare (17-1)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Pseudo-random allocation by week of attendance
Allocation concealment (selection bias)	High risk	Allocation known at time of enrolment, so potential for selection bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessed by postal questionnaire, biochemical validation attempted but refused. Similar amount of contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete data for 52.9% (369), did not differ significantly between groups

Jamrozik 1984

Methods	**Setting**: 6 general practices, the UK **Recruitment**: clinic, first visit **Selected**: outpatients
Participants	2110 smokers (defined as a person admitting to smoking cigarettes) out of 6052 screened. 1040 in relevant arms 61% female, no detailed patient characteristics given. Significant difference of social classes between groups **Therapist**: physician
Interventions	**Intervention**: demonstration of participant exhaled CO plus verbal advice plus booklet **Control**: verbal advice plus booklet 2 study arms were not relevant to this review
Outcomes	**Definition of abstinence**: point prevalence **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: urinary cotinine in a sample (41%) of self-reported non-smokers

Jamrozik 1984 (*Continued*)

Identification	
Notes	Outcome based on unvalidated data. Between 24% and 40% may have misrepresented smoking status, but no evidence of differential misreporting between groups **Sources of funding:** Nuffield Dominions Trust and the Health Education Council. National Institute on Drug Abuse, DA 2507, D A0007 for cotinine assays. Helen Van Vunakis is the recipient of a US Public Health Service Career Award 5K6/A 12372

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Randomised according to day of attendance, balanced over 4 weeks
Allocation concealment (selection bias)	High risk	Allocation known at enrolment, possibility of selection bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome based on unvalidated data. Between 24% and 40% may have misrepresented smoking status, but no evidence of differential misreporting between groups
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	28% lost to follow-up across all 4 arms, treated as smokers. No information on differential loss

McClure 2009

Methods	**Setting**: Group Health Center for Health Studies, Seattle, Washington, USA (research institution) Recruitment: health plan records, data from the Washington State Quitline, purchased mailing list of smokers, ads in local media, public clinics, and other local venues
Participants	536 smokers (with elevated expired CO levels >= 10 ppm and a mean of 15 cpd for the past year or smoked >= 10 cpd but had smoked for >= 10 years), mean age 50.8 years, 53.2% female, 24.8% pre-contemplation, 50.8% contemplation, 24.2% preparation, mean cpd: 20.7 Therapists: health educators
Interventions	**Intervention**: brief (20 minutes), personally tailored counselling sessions based on lung functioning (spirometry), CO exposure, and smoking-related health conditions **Control**: generic smoking risk information and personalised counselling about diet, body mass index, and physical activity All were advised to quit smoking and were offered access to a free phone-counselling programme

McClure 2009 (*Continued*)

Outcomes	**Definition of abstinence**: 7-day point-prevalence abstinence **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: none
Identification	
Notes	New for 2012 update **Source of funding:** This study was supported by the National Cancer Institute (R01 CA100341) and the Group Health Center for Health Studies in Seattle. We thank Amy Mohelnitzky, Richard Hert, MD, Ralph Stumbo, RRT, CPFT, Rick Bloss, Zoe Bermet, Mary Shea, Lisa Shulman, Emily Westbrook, Mona Deprey, Free & Clear Inc. , the Washington State Quitline, and the staff of the Center for Health Studies' Survey Research Programme for their help with this research **Declaration of interest:** No financial disclosures were reported by the authors of this paper

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Eligible smokers were randomised to treatment using an automated randomisation algorithm
Allocation concealment (selection bias)	Unclear risk	Concealment not mentioned.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence not biochemically validated, but similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data missing for 13% of participants in each group at 12 months

Nichols 2014

Methods	**Setting:** large general practice, Surrey, UK **Study design:** randomised controlled trial **Study grouping:** parallel group **Comment:** sample size based on previous research = 602 **Quasi-randomisation:** clinics were run in parallel at the same venue but on different weekdays for the tests and control groups **Study period:** 2011 to 2013 **Number of participants screened:** 1775 **Number of participants included:** 109
Participants	**Included criteria:** aged 20 to 70 years; smoking more than 10 cigarettes daily **Excluded criteria:** history of major depression and other psychiatric conditions, dementias, and serious or terminal illness (cancers, etc.). Individuals on warfarin. Individuals

	who do not wish to have a genetic test or do not wish to take part in a research study **Recruitment setting:** primary care premises of a group general practitioner practice in an English suburb southwest of London **Baseline characteristics** Test group (genetic test and risk score) • *N*: 36 • *% female*: 55.6% • *mean age*: 49. • *mean pack years*: 32.0 • *mean cigarettes/day*: 18.1 • *mean Fagerström score*: 5.3 • *mean salivary cotinine score*: 2.5 Control group • *N*: 31 • *% female*: 53.3% • *mean age*: 49.0 • *years in education*: 26.2 • *mean pack years*: 28.9 • *mean cigarettes/day*: 18.1 • *mean Fagerström score*: 4.5 • *mean salivary cotinine score*: 2.3
Interventions	**Intervention characteristics** Intervention: genetic test and risk score (Respiragene) • *Biofeedback*: buccal swab was taken for the 20-gene test on the first or second attendance. The gene-based test report included the risk score with an explanation of how the scores relate to the 3 different risk categories: moderate, high, and very high. Both groups: • *Counselling intervention*: 8 weekly smoking cessation sessions including group counselling and advice on smoking cessation pharmacotherapy (varenicline or range of NRTs)
Outcomes	*Smoking cessation at 6 months, validated (CO breath test and salivary cotinine)*
Identification	**Country:** UK **Setting:** United Kingdom National Health Services (NHS) smoking cessation clinic **Comments:** NA **Authors name:** John A A Nichols **Institution:** Department of Clinical and Experimental Medicine, University of Surrey, Guildford **Email:** drjaan@ntlworld.com **Address:** 60 Manor Way, Onslow Village, Guildford, Surrey GU2 7RR, UK
Notes	**Source of funding:** Lab 21, Cambridge, UK; Synergenz BioScience Ltd, Evanston, IL, USA **Declaration of interest:** JN and PG are in receipt of research grants from Lab 21, Cambridge, who are marketing the Respiragene test in the UK, and Synergenz BioScience Ltd, who financed the development of the test from its origins in New Zealand. We initially purchased SmokeScreen kits (for salivary cotinine estimation) from GFC Diag-

Nichols 2014 (*Continued*)

	nostics Ltd, but they subsequently supplied 30 kits free of charge

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	2 clinics were run in parallel at the same venue but on different weekdays for test and control groups. Participants who replied stating that they wished to stop smoking by attending our clinic were randomised by the principal investigator
Allocation concealment (selection bias)	High risk	Participants were allocated by the principal investigator.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated
Incomplete outcome data (attrition bias) All outcomes	High risk	Analyses are not intention-to-treat, and lost to follow-up excluded from analyses
Other bias	Unclear risk	Selective reporting = unclear: Initially defined secondary endpoints (intention to stop smoking, cigarette consumption, uptake of invitation to cessation, adherence to cessation course, and self-reported smoking cessation) not all reported. Self-reported cessation also considered as primary endpoint in final analysis

Parkes 2008

Methods	**Setting**: primary care (5 general practices, UK) **Recruitment**: by letter to registered patients **Selection**: not selected by motivation
Participants	561 current smokers (not defined) aged > 35, 54% female, average age 53, mean cpd: 17, 29% pre-contemplative, 32% contemplative, 17% preparation, 21% action **Therapists**: study staff member
Interventions	All participants had lung function assessed by spirometry before randomisation. Strongly encouraged to give up and given written contact details of National Health Service (NHS) smoking cessation services. If evidence of asthma or restrictive lung disease, advised to see GP. Told they would be re-tested at 12 months. **Intervention 1**: immediate verbal feedback of lung age with explanation. Described as normal if lung age less than or equal to chronological age.

Parkes 2008 (*Continued*)

	Intervention 2: letter giving test results without lung age
Outcomes	**Definition of abstinence**: unspecified **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: exhaled CO, cotinine < 14.2 ng/mL
Identification	
Notes	**Source of funding:** Leading Practice Through Research award from the Health Foundation **Declaration of interest:** None declared.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"A clerk (who then took no further part in the study) prepared 600 sequentially numbered opaque sealed envelopes, each containing a card with allocation group determined by computer generated random number (odd = intervention)"
Allocation concealment (selection bias)	Low risk	"If the participant met the inclusion criteria and gave consent, he or she was entered into the study and underwent baseline spirometry. The next numbered envelope in the series was then opened to determine allocation group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Follow-up assessors blind to allocation group, biochemical validation used
Incomplete outcome data (attrition bias) All outcomes	Low risk	11% lost to follow-up in each arm, included as smokers.

Risser 1990

Methods	**Setting**: US Veterans Administration Demonstration Project **Recruitment**: veterans attending a health promotion clinic **Selected**: responding to mailed invitations for health promotion. Some recruited at second visit
Participants	90 smokers (not defined); mean age 53.7 years (55.5 vs 51.7), 4% female, mean cpd: 23.5, mean pack-year: 60.4 Initial cessation intent: 51% vs 44% **Therapist**: nurse-practitioner

Risser 1990 (*Continued*)

Interventions	**Intervention**: spirometry, exhaled CO, discussion of pulmonary symptoms + control intervention **Control**: 50-minute educational intervention, review of self-help manual, invitation to a 9-session 1-to-1 counselling programme
Outcomes	**Definition of abstinence**: point prevalence **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: exhaled CO <= 10 ppm
Identification	
Notes	**Funding source:** supported by VA Health Services Research and Development Funds

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised, method not stated
Allocation concealment (selection bias)	Unclear risk	No details given.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Follow-up assessors blind to allocation group, biochemical validation used
Incomplete outcome data (attrition bias) All outcomes	Low risk	13 (29%) intervention, 6 (13%) control lost to follow-up at 12 months, included as smokers

Rodondi 2012

Methods	**Setting**: Department of Ambulatory Care and Community Medicine, University of Lausanne **Recruitment**: newspaper advertisement (lay press) in the French-speaking part of Switzerland **Selected**: smokers from the general population
Participants	536 smokers randomised (267 in the intervention group and 269 in the control group) out of 1036 participants screened for eligibility; 265 and 267 analysed in the intervention group and control groups, respectively; smokers defined as more than 10 cpd with no period of smoking abstinence of at least 3 months in the past year Mean age: 51.1 years; 43.5% female; median cpd: 20; 17 years age at initiation (median) ; 5.2 Fagerström score (mean); 2 previous quit attempts (median) **Therapist**: nurse

Rodondi 2012 (*Continued*)

Interventions	**Intervention**: carotid plaque screening (ultrasound) + control intervention (smokers with at least 1 carotid plaque received a 7-minute standardised brief explanation on the significance of atherosclerotic plaques) **Control**: brief advice for smoking cessation; 7-minute explanation on the risks associated with tobacco smoking; 6 individual counselling sessions, 1 telephone call at 6 months, NRT patches tailored to individual needs; brochures on smoking cessation
Outcomes	**Definition of abstinence**: 1-week smoking abstinence (point prevalence) **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: exhaled CO < 10 ppm and serum cotinine level < 25 ng/mL
Identification	
Notes	New for 2012 update **Source of funding:** This study was supported by research grant 3200B0-116097 from the Swiss National Science Foundation, by the Swiss Heart Foundation, by the Lausanne University Hospital Strategic Plan, and by grant FPT 08.002282 from the Swiss Tobacco Prevention Funds, Federal Office of Public Health **Declaration of interest:** None declared.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random assignment to 1 of the 2 groups using a computer-generated randomisation scheme in a 1:1 ratio
Allocation concealment (selection bias)	Low risk	Sealed, opaque, sequentially numbered envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated
Incomplete outcome data (attrition bias) All outcomes	Low risk	14 participants were lost to follow-up; 7 who withdrew their participation were classified as current smokers

Sanders 1989

Methods	**Setting**: 11 UK general practices **Recruitment**: screening of all outpatients **Selected**: outpatients plus made appointment for health check

Sanders 1989 (*Continued*)

Participants	751 participants out of 4330 identified smokers (self-defined) Mean age 38.5 years. Other characteristics not mentioned. **Therapist**: practice nurse
Interventions	**Intervention**: exhaled CO measure plus discussion of significance plus control intervention **Control**: counselling by practice nurse plus written material given plus offer of a follow-up appointment
Outcomes	**Definition of abstinence**: point prevalence **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: urinary cotinine for sample, cut-off not reported Outcomes used are self-report
Identification	
Notes	**Sources of funding:** We are grateful to the doctors, nurses, receptionists and others in the practices participating in this study, to Elaine Fullard for her advice, to Valerie Stone for clerical assistance, and to the department of preventive medicine at St Bartholomews Hospital for performing the cotinine assays. We also thank the British Heart Foundation and Health Education Authority for financial support. David Mant and Lesley Jones are supported by the Imperial Cancer Research Fund

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Randomised by day of attendance on a 1: 2 basis. Desktop card reminding doctors of right allocation. 120 wrongly allocated participants, excluded from further analysis. Second step randomised health check attenders for the CO intervention, method not described
Allocation concealment (selection bias)	High risk	First-stage randomisation had potential for selection bias; only attenders eligible for second stage, no information on concealment at this stage
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Biochemical validation used only for a sample, results used in analysis not validated, but similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	63.8% followed up, but percentage by group not provided; unclear if differential attrition present. Non-responders included

		as smokers

Segnan 1991

Methods	**Setting**: 44 general practices, Italy **Recruitment**: screening of outpatients on specific days **Selected**: outpatients
Participants	923 included out of 1009 screened. Smoker definition not given. Age: 20.1% < 31 years; 28.0% 31 to 40 years; 26.8% 41 to 50 years; 25.0% > 50 years. 38% female, cpd: 16. 7% <= 10 cpd; 55.2% 11 to 20 cpd; 28.1% > 20 cpd. 51% reporting symptoms. **Therapist**: physician
Interventions	**Intervention**: spirometry prescription plus control intervention **Control**: repeated counselling with reinforcement sessions (2 other groups not used in our comparison: minimal intervention and repeated counselling plus nicotine gum)
Outcomes	**Definition of abstinence**: 7 days abstinence **Duration of follow-up**: 12 months **Biochemical validation of non-smokers**: urinary cotinine < 100 ng/mg
Identification	
Notes	In the intervention group, 124 participants out of 292 reported having a spirometry test **Funding sources/declaration of interest:** Serono SPA provided the nicotine gum used in the study. The Anti-Smoking Committee of the Municipality, Torino, and ACI (Automobile Club Italiano) also helped in various ways

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised; "blocked treatment allocation was based on a sequence of random numbers"
Allocation concealment (selection bias)	Low risk	"Closed, numbered envelopes"; "The envelopes were indistinguishable from the outside"; "The research staff checked physicians' compliance with the procedure for assignment by comparing envelope numbers and dates of recruitment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated

Incomplete outcome data (attrition bias) All outcomes	Low risk	13% lost to follow-up at 12 months, included as smokers

Shahab 2011

Methods	**Setting**: Laboratory at University College London (research institution) **Recruitment**: smokers were recruited from the general population through advertisements in local newspapers, flyers, e-mails, posters on public bulletin boards at and around University College London **Selected**: smokers who responded to the advertisements
Participants	160 smokers (> 5 cpd for the past year) aged between 18 and 35 years, 43.7% female, average age 31.7 years, mean cpd: 13.8 **Therapists**: postdoctoral researchers
Interventions	**Intervention**: expired air CO level + generic leaflet about lung disease + brief targeted feedback about their CO levels in relation to the development of cardiovascular and respiratory diseases **Control**: expired air CO measurement (results not shown) + generic leaflet about lung disease + standardised brief advice to quit smoking
Outcomes	**Definition of abstinence**: 7-day point-prevalence abstinence **Duration of follow-up**: 6 months **Biochemical validation of non-smokers**: none
Identification	
Notes	New for 2012 update. Participants received an incentive of GBP 50 for their time **Source of funding:** This study was funded by the Department of Health and the charity Cancer Research United Kingdom. These bodies bear no responsibility for the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. We thank Erdem Pulcu and Onupama Roy for their help with collecting data for this study **Declaration of interest:** Lion Shahab has received an honorarium for a talk and travel expenses from Pfizer. Robert West undertakes research and consultancy for the following developers and manufacturers of smoking cessation treatments; Pfizer, J7J, McNeil, GSK, Nabi, Novartis and Sanofi-Aventis. Robert West also has a share in the patent of a novel nicotine delivery device

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Random number-generated group allocation. No description about the random sequence generation

Shahab 2011 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Sealed envelope containing the random number-generated group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence not biochemically validated. Participants were contacted by a researcher blinded to group allocation to complete the follow-up. Similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	Similar numbers lost to follow-up in both groups (23/79 control, 28/81 intervention - reason given for all: "could not be contacted"). All lost to follow-up included as smokers in analysis

Sippel 1999

Methods	**Setting**: 2 primary care clinics, USA **Recruitment**: all smokers among outpatients **Selected**: outpatients
Participants	205 included out of 360 smokers (self-defined); mean age 38.5 years, 62.5% female, mean cpd: 20.0, mean pack-years: 28.9. Stage of change: 36% in preparation stage **Therapist**: study staff
Interventions	**Intervention**: spirometry and exhaled CO + control intervention **Control**: counselling according to transtheoretical model stage + written material + NRT encouraged if prepared to stop
Outcomes	**Definition of abstinence**: sustained quitting rate **Duration of follow-up**: 9 months **Biochemical validation of non-smokers**: none
Identification	
Notes	**Source of funding:** This project was funded by the American Lung Association of Oregon and the American Academy of Family Practice

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Pseudo-randomised; questionnaires numbered consecutively, and participants enrolled in chronological order based on time of check-in. Odd numbered = intervention

Sippel 1999 (*Continued*)

Allocation concealment (selection bias)	High risk	Not concealed, potential selection bias, although nurses performing participant check-in were blinded to the questionnaire numbers. "As 4 to 6 nurses conducted patient check-in independently and simultaneously at each clinic, it is unlikely that any given patient would be preferentially enrolled into either study arm."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Follow-up assessors blind to allocation group. No biochemical validation used, but similar amounts of face-to-face contact between groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	18.6% intervention and 12.6% control lost to follow-up, included as smokers

Walker 1985

Methods	**Setting**: "stop-smoking clinic", USA **Recruitment**: public service announcement + media advertising **Selected**: those responding to advertising, paying USD 45
Participants	64 out of 141 eligible (self-defined smokers) Mean age: 35.5 years, 59% female, mean cpd: 29.2, mean 3.4 previous quit attempts **Therapist**: first author
Interventions	**Intervention**: exhaled CO and spirometry feedback plus Taste Satiation (TS) (in 50%) or Focused Smoking (FS) (in 50%) and booster sessions for half of each subgroup **Control**: 50% TS sessions or 50% FS sessions, booster sessions for half of each subgroup
Outcomes	**Definition of abstinence**: 10 days abstinence **Duration of follow-up**: 6 months **Biochemical validation of non-smokers**: exhaled CO < 8 ppm
Identification	
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised in 2x2x2 factorial design, method not described
Allocation concealment (selection bias)	Unclear risk	No details given.

Walker 1985 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Abstinence biochemically validated
Incomplete outcome data (attrition bias) All outcomes	High risk	Only participants reached at 6 months included in analysis. "Five subjects dropped out of treatment and 3 additional subjects were randomly eliminated to facilitate data analysis."

CO: carbon monoxide
COPD: Chronic Obstructive Pulmonary Disease
cpd: cigarettes per day
FEV1: forced expiratory volume in one second
FVC: forced vital capacity
ICMJE: International Committee of Medical Journal Editors
IDU: injecting drug user
NRT: nicotine replacement therapy
ppm: parts per million

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Anthonisen 1994	Effect of spirometry cannot be isolated. Spirometry performed in all participants. Randomisation to 3 groups: smoking intervention (12-session programme) + bronchodilatator, smoking intervention + placebo, no intervention
Ashraf 2014	Cannot isolate effect of biofeedback
Barnfather 2005	Only 8 weeks follow-up. Intervention was immediate feedback from a point-of-care test for salivary nicotine metabolites
Borrelli 2002	Effect of CO cannot be isolated. No results available. Intervention: Precaution Adoption Model: CO feedback + environmental tobacco smoke to the child feedback + motivational counselling Control: Behavioral Action Model: self efficacy-enhancing counselling
Borrelli 2005	Effect of CO cannot be isolated. Intervention: motivational interviewing and CO feedback Control: standard care
Borrelli 2010	Feedback about secondhand CO in asthmatic children of the participants. Too-short follow-up (3 months)

(*Continued*)

ChiCTR-TRC-13003255	Trial not completed.
Cope 2003	Not a true randomised trial
Cox 2003	No control group. All participants received chest CT scan screening for lung carcinoma
Ferketich 2012	Effect of CT scan on the motivation to quit cannot be isolated
Foulds 2015	No measure of smoking cessation at 6 months
Frank 1999	Full text not available. Intervention: urinary cotinine feedback to prenatal patients
Gulliver 2008	Spirometry was not used to give feedback on lung function.
Hajek 2001	Effect of CO cannot be isolated. Intervention: counselling, written materials, CO Control: standard antismoking leaflets
Hajek 2002	Effect of CO cannot be isolated. Intervention: CO feedback, booklet, quiz, "buddy", declaration of commitment to give up, sticker in patient's notes Control: verbal advice + different booklet
Humerfelt 1998	Effect of spirometry cannot be isolated. Intervention: spirometry + written counselling + pamphlet Control: spirometry
Kaminsky 2011	Follow-up at 1 month only
Kanner 1996	Effect of spirometry cannot be isolated. Spirometry performed in all participants. Randomisation to 3 groups: smoking intervention (12-session programme) + bronchodilatator, smoking intervention + placebo, no intervention
Kanner 1999	Effect of spirometry cannot be isolated. Spirometry performed in all participants. Randomisation to 3 groups: smoking intervention (12-session programme) + bronchodilatator, smoking intervention + placebo, no intervention
Kotz 2009	Effect of spirometry feedback cannot be isolated. Intervention group received spirometry/COPD feedback but also an intervention to challenge irrational beliefs about smoking. They were further instructed to use a smoking cessation diary to monitor smoking behaviour and beliefs about smoking. The latter interventions were not offered to the control group
Lipkus 2007	Outcomes were perceived smoking-related health risks, worries, and desire to quit, not smoking cessation
Marteau 2012	Study of behavioural impact of pharmacogenomics. Outcome was adherence to smoking cessation medication. Measures effect of informing smokers of genetic test results on responsiveness to smoking cessation medication

(*Continued*)

Martucci 2010	Effect of bronchoscopy results on smoking cessation cannot be isolated
McBride 2002	Effect of genetic biomarker feedback cannot be isolated. Intervention: feedback on glutathione-S-transferase M1 (*GSTM1*) + 4 phone calls + control intervention Control: self help manual +/- NRT. No phone calls
McClure 2013	No measure of smoking cessation at 6 months
McIntosh 1994	Smoking cessation is not considered as an outcome.
Mols 2015	Cannot isolate effect of biofeedback
NCT00862368	Cannot isolate effect of biofeedback
NCT00991081	No measure of smoking cessation at 6 months
NCT01145729	No measure of smoking cessation at 6 months
NCT02206971	No measure of smoking cessation at 6 months
NCT02837809	Wrong intervention
NCT02922790	No measure of smoking cessation at 6 months
Nuesslein 2006	Only 6 weeks' follow-up Intervention: notification of urine cotinine levels + control Control: written advice to quit from a paediatrician
Ojedokun 2013	No measure of smoking cessation at 6 months
Paek 2014	Wrong intervention
Pistelli 2007	Conference abstract. Post hoc analysis Intervention: participation in a lung cancer screening + control Control: biofeedback (lung CT) + smoking cessation programme
Powers 2011	Only 3 months' follow-up. Coronary heart disease risk communication. Participants were smokers and non-smokers (being a smoker was not a criterion for inclusion)
Prokhorov 2008	Effect of the health feedback (expired CO) cannot be isolated. The aim of the study was to compare standard care with computer-assisted care
Rennie 2012	Participants assigned to hypothetical risk scenarios; outcome was motivation, not cessation
Richmond 1986	Effect of biomarker feedback cannot be isolated. Spirometry, blood CO, urinary cotinine in both groups. Intervention: 4 visits and discussion of manual

(*Continued*)

Rodriguez 2011	Effect of biomarker feedback cannot be isolated. "Both arms will receive brief structured advice and a detailed discussion of the spirometry results at visit 0. The control group will only be given brief structured advice about giving up smoking on the follow up"
Sanderson 2005	Short-term study of effect of genetic testing for lung cancer susceptibility. Follow-up at 10 weeks. Main outcomes were motivation to quit, perceived risk, depression and anxiety
Sanderson 2007	Hypothetical scenario tested (not real life)
Sanderson 2008	Follow-up too short (2 months)
Sejourne 2010	No measure of smoking abstinence at 6 months or later after the start of the intervention
Shahab 2007	Pilot study of visual personalised biomarker feedback with follow-up at 4 weeks. Main outcomes were perception of susceptibility, engagement in cessation behaviours, and intentions to stop
Shi 2013	Wrong intervention
Shoptaw 2002	Effect of CO feedback cannot be isolated. CO feedback given to all groups. 2x2 design: 1. relapse-prevention counselling + NRT 2. contingency management: vouchers given for validated abstinence + NRT Control: NRT
Stotts 2009	Assessments at baseline (16 to 26 weeks of gestation) and at the end of pregnancy. Too-short follow-up
Stratelis 2006	Not a true randomised trial, no control without biomedical risk assessment. Smokers with normal lung function at baseline received different frequencies of spirometry (annually or in 3 years)
Tammemagi 2014	Wrong study design
Taylor 2007	No control group. Study of impact of screening on smoking cessation and readiness to stop smoking among participants in trials of lung screening
Terazawa 2001	Effect of biomarker feedback (CO and urinary cotinine) cannot be isolated, combined with 1 counselling session and 4 follow-up calls
Townsend 2005	No control group. Longitudinal study of smoking behaviour in people receiving lung cancer screening
van der Aalst 2011	Post hoc analysis. Current and former smokers. Screening of lung cancer by low-dose thoracic CT in intervention arm. Only positive or indeterminate test results (lung nodules) were managed according to a protocol (feedback was not standardised, and not about smoking cessation but lung cancer)
Wakefield 2002	Biomarker feedback given on the health of the participant's child, not on the participant's own health. The motivational component here differs from the approach in the other included studies

(*Continued*)

Warner 2012	Long-term abstinence not an outcome. CO levels were measured preoperatively
Wilt 2007	Review
Wright 2006	Outcome was motivation to quit based on hypothetical risk information
Zullig 2014	No measure of smoking cessation at 6 months

CO: carbon monoxide
COPD: chronic obstructive pulmonary disease
CT: computed tomography
NRT: nicotine replacement therapy

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT02351167

Methods	Randomised controlled trial with parallel assignment (triple-blinded)
Participants	822 participants aged 21 years and older Inclusion criteria: 1. Adult (>= 21 years of age), seeking treatment for smoking cessation 2. Able to speak English 3. Active smoking (cigarettes per day >= 5) and exhaled carbon monoxide >= 8 ppm 4. Agree to participate in this randomised smoking cessation trial with follow-up assessments up to 12 months Exclusion criteria: 1. Pregnancy or breastfeeding 2. Active use or recent use (< or equal to 1 month) of medication or e-cigarettes for nicotine dependence/ smoking cessation, or use of e-cigarettes for more than 9 days in the prior month 3. Allergy to nicotine patch, lozenge, or varenicline 4. Unwillingness to prevent pregnancy during the medication phase and 1 month afterwards (women only) 5. Significant cardiac conditions (myocardial infarction, unstable angina, coronary angioplasty, cardiac bypass) or serious arrhythmia in past 6 months 6. Current heavy alcohol consumption (>= 6 drinks/day, 6 days/week) 7. Active psychosis or poorly controlled depression within the past 6 months 8. Any prior suicide attempt or suicidal ideation within the past 6 months 9. End-stage renal disease with haemodialysis
Interventions	The investigators propose a prospective, genotype-based stratified randomisation trial to compare 2 smoking cessation medications (combination NRT (patch and lozenge), varenicline vs placebo) for 3 months in 720 smokers with known genotypes
Outcomes	Primary outcome measures 1. 7-day point-prevalence quit rate (Time Frame: Week 12). The definition of this measure requires: i) no self-reported smoking (not even a puff of a cigarette) for at least the 7 days prior to the assessment; and

NCT02351167 (*Continued*)

	ii) biochemical verification of abstinence. Secondary outcome measures 1. Continuous abstinence (Time Frame: 12 weeks (with first week initial grace period)). The definition of this measure requires: not taking even 1 cigarette puff from target quit date to end of treatment. 2. 7-day point-prevalence quit rate (Time Frame: Week 24). The definition of this measure requires: i) no self-reported smoking (not even a puff of a cigarette) for at least the 7 days prior to the assessment; and ii) biochemical verification of abstinence.
Notes	7-day point-prevalence abstinence at 6 months should be available. Genotype-based randomisation, but apparently no biofeedback

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12618000291280

Trial name or title	Effectiveness of quit smoking motivation with carbon monoxide feedback module (COQUIT) among college smoker in Selangor
Methods	Single-blinded cluster-randomised controlled trial at 10 tertiary colleges
Participants	160 students at Community College in Selangor, Malaysia
Interventions	Standard brief 5R motivational strategy and an additional CO motivational feedback module. Expired carbon monoxide is measured by the principal investigator on a 1-to-1 basis. The CO reading is recorded directly into the iPad (using a mobile phone application) together with explained feedback about the result and interpretation. The result of the CO is then e-mailed to the participants Participants in the control group only receive the standard brief 5R motivational strategy
Outcomes	Primary: stage of changes based on the Transtheoretical Model that will be measured using validated questionnaire at 1, 3, and 6 months postintervention Secondary: any quit attempt defined as 24 hours of not smoking, number of cigarettes smoked per day, and smoking habit at 1, 3, and 6 months
Starting date	Anticipated 16 April 2018
Contact information	Dr Muhammad Adil Zainal Abidin adilzainal@gmail.com
Notes	

IRCT2017080435257N1

Trial name or title	Effectiveness of spirometry as a motivational tool for smoking cessation based on health belief model
Methods	Single-blinded, parallel-group randomised controlled trial
Participants	160 participants Inclusion criteria: patient satisfaction; smoking history at least 10 pack/year; lack of non-cigarette related pulmonary disease; new spirometry test; ages between 20 and 90 Exclusion criteria: patient dissatisfaction
Interventions	Intervention group: participants will attend a speech meeting to increase information about cigarettes and make them susceptible to smoking cessation. At this meeting, educational pamphlets will be distributed on health, economic, and social disadvantages. Then an individual motivational educational counselling exercise will be carried out for each participant, with an emphasis on testing the spirometry of the participant and comparing it with spirometry of a healthy person of the same age and sex, and providing relevant statistics. In the next step, the intervention group will be divided into groups of 10, discussing the benefits and barriers to smoking cessation in the group discussion. Then the questionnaire will be filled by self-reporting to determine the perceived sensitivity, perceived severity, perceived benefits, and perceived barriers. At intervals at the end of the second week, 3 and 6 months, information about the rate of smoking cessation will be collected using the follow-up questionnaire
Outcomes	"Action to smoking cessation"? at 2 weeks, 3 months and 6 months "keep smoking cessation"? at 2 weeks, 3 months and 6 months
Starting date	20 March 2016
Contact information	Saeid Ghasemian ghasemian@shmu.ac.ir
Notes	

Martin Lujan 2011

Trial name or title	Effectiveness of Smoking Cessation Advice Combined With Spirometric Results in Adult Smokers (ESPITAP)
Methods	Randomised controlled trial, parallel assignment, single-blinded (participants)
Participants	596 participants Inclusion criteria: • Adult smokers aged between 35 and 70 years Exclusion criteria: • Antecedents of any respiratory disease • Suffering from any chronic or terminal disorder • Counterindication to undertake spirometry or that may hinder the performance of the spirometry test
Interventions	Intervention arm: spirometry and smoking cessation advice. Participants will be given a brief but structured smoking cessation advice (according to the standards of the Tobacco Study Group of the Catalan Society of Family Medicine) together with a detailed and structured discussion of the spirometric results Control arm: smoking cessation advice. Brief but structured smoking cessation advice (according to the standards of the Tobacco Study Group of the Catalan Society of Family Medicine)

Martin Lujan 2011 (*Continued*)

Outcomes	Smoking abstinence: self-reported abstinence (12 or more months). Time Frame: 12 months Smoking abstinence confirmed by an expired air carbon monoxide
Starting date	June 2008
Contact information	Principal Investigator: Francisco Martín-Luján, MD, Catalan Institute of Health
Notes	Last update posted on ClinicalTrials.gov: 7 April 2011 Authors contacted but no answer received.

Martin Lujan 2016

Trial name or title	Multicentric Randomized Clinical Trial to Evaluate the Long-term Effectiveness of a Motivational Intervention Against Smoking, Based on the Information Obtained From Spirometry in Primary Care. (RESET-ESPITAP2)
Methods	Randomised controlled trial, parallel assignment, open-label
Participants	1100 participants Inclusion criteria: • Active smokers (consumption > 10 packs/year) Exclusion criteria: • Active respiratory disease • Practice of a spirometry during prior 12 months • Suffering from any chronic or terminal disorder • Counterindication to undertake spirometry or that may hinder the performance of the spirometry test
Interventions	Intervention arm: spirometry. Will be given brief but structured smoking cessation advice (according to the standards of the Tobacco Study Group of the Catalan Society of Family Medicine) together with a detailed and structured 20-minute visit with details of the spirometry data (values of respiratory capacity and volumes referring on the theoretical) Control arm: brief smoking cessation advice. Will be given brief but structured smoking cessation advice (according to the standards of the Tobacco Study Group of the Catalan Society of Family Medicine)
Outcomes	Cessation of tobacco consumption at 12 months. Time Frame: 12 months
Starting date	November 2011 (estimated study completion date: November 2014)
Contact information	Principal Investigator: Antoni Santigosa-Ayala, MD, Catalan Institute of Health
Notes	Last update posted on ClinicalTrials.gov: 2 June 2014 Authors contacted but no answer received. Protocol published in 2016, but no results published

Muhammad 2015

Trial name or title	A pilot randomized controlled trial on the effectiveness of a 'lung age' intervention on smoking cessation Effectiveness of a 'lung age' intervention on smoking cessation rate in a Singaporean community
Methods	Pilot randomised controlled trial
Participants	108 participants (convenience sample) recruited from population health screenings in Singapore Inclusion criteria: • Currently smoking • Aged 35 years and above • Able to read and/or speak in English and/or Mandarin Exclusion criteria: • Known history of major psychiatric illness • History of respiratory-related diseases: COPD, asthma, bronchiectasis • Ejection fraction < 4%, or diagnosed with congestive cardiac failure • Diagnosed with acute myocardial infarction within 1 month • Diagnosed with fluid overload/acute pulmonary oedema • Receiving oxygen therapy • Recent eye/thoracic/abdominal surgery • Chest/abdominal/oral and facial pain • Hyperventilation syndrome
Interventions	Intervention arm: lung age intervention A spirometry test will be conducted to determine the lung age of participants in the intervention group. These participants will then receive an educational intervention on their lung age in addition to standard smoking cessation counselling Control arm: usual smoking education
Outcomes	Smoking cessation rates at 3 and 6 months
Starting date	4 September 2014 (end date 3 September 2015)
Contact information	Wenru Wang, PhD, RN nurww@nus.edu.sg
Notes	Study completed but data not published. Author contacted but no answer received.

NCT01186016

Trial name or title	Developing genetic education for smoking cessation
Methods	Randomised controlled trial with parallel assignment, open-label
Participants	103 participants. Inclusion criteria: • Current smoker • Smoking 10 or more cigarettes per day • 19 years of age or older • Intention of quitting smoking in the next month

NCT01186016 (*Continued*)

	• Agree to use 2 forms of acceptable birth control while using the nicotine replacement patch Exclusion criteria: • Not currently seeking treatment for a mental disorder with psychotic symptoms • Not currently pregnant or nursing • Not been recently diagnosed or currently affected with cancer or any other life-threatening illness • No recent heart attack • No history of high blood pressure or not currently receiving treatment to manage high blood pressure • No history of an irregular heartbeat • Not currently taking medications to help quit smoking (i.e. varenicline (Chantix), bupropion (Zyban, Wellbutrin), NRT) • No history of adverse effects from using nicotine replacement patches • Not currently experiencing serious pain or discomfort due to heart disease
Interventions	Experimental: Genetic Education Session (GES) The intervention includes receiving education about genetics and smoking. The content is basic genetics and education about the multifactorial nature of smoking; research findings about genetic contributions to smoking, potential applications of this research for cessation treatment, and legal, ethical, and social implications of future use of genotyping for cessation. All participants also receive a 5-week standard cognitive-behavioural smoking cessation intervention with 6 weeks of over-the-counter transdermal nicotine replacement therapy Active comparator: Nutrition Education Session (NES) To control for an attention placebo effect, the control group will receive information about nutritional guidelines as established by the US Department of Agriculture (USDA) and the US Food and Drug Administration. The attention control group will be referred to as the Nutritional Education Session (NES) group. The content of NES sessions 1 and 2 are use of the USDA (MyPyramid) dietary and food safety guidelines. All participants also receive a 5-week standard cognitive-behavioural smoking cessation intervention with 6 weeks of over-the-counter transdermal nicotine replacement therapy
Outcomes	Smoking-related behaviour when experimental and attention control groups are compared. Time Frame: 6 months after the end of the Smoking Cessation Intervention Use of cessation strategies, abstinence, and interest in genotyping
Starting date	February 2010
Contact information	Professor Julia Houfek, PhD, APRN-CNS, University of Nebraska
Notes	Last update posted on ClinicalTrials.gov: 21 January 2013 Authors contacted but no answer received.

NCT02431611

Trial name or title	Biomarker Feedback to Motivate Tobacco Cessation in Pregnant Alaska Native Women (MAW) - Phase 3 Pilot Clinical Trial
Methods	Randomised controlled trial, parallel assignments, open-label
Participants	60 participants Inclusion criteria: • Alaska Native

NCT02431611 (*Continued*)

	• 18 years of age or older • Provide written informed consent • Be currently pregnant and at < 24 weeks gestation • Reside in Anchorage and plan to deliver at the ANMC • Current tobacco user defined as any use of iqmik, commercial smokeless tobacco, and/or cigarettes during the past 7 days Exclusion criteria: • Use of nicotine replacement therapy or medications for tobacco cessation or participation in a behavioural cessation programme within the past 30 days • Another woman from the same household has enrolled
Interventions	Experimental: biomarker feedback intervention (phone-based smoking cessation counselling). Feedback on maternal cotinine and likely infant NNAL. Phone-based behavioural smoking cessation counselling Active comparator: control condition (phone-based smoking cessation counselling) Phone-based behavioural smoking cessation counselling
Outcomes	Smoking abstinence in late pregnancy (self-reported abstinence verified with cotinine). Time Frame: at week 36 gestation or greater up to the time of delivery Self-reported abstinence verified with cotinine.
Starting date	March 2015 (study completion date 2017)
Contact information	Christi A Patten, PhD, Mayo clinic
Notes	Last update posted: 19 December 2017 No data published, author contacted but no answer received.

NCT02658032

Trial name or title	Personalized Intervention Program: Tobacco Treatment for Patients at Risk for Lung Cancer (PIP)
Methods	Single-blind (participants) randomised trial with factorial assignment (2 interventions)
Participants	276 adults 50 years of age and older Inclusion criteria: • Current smoker • 20 pack/year smoking history • Eligible for the Smilow treatment programme • Willing to enrol in smoking cessation programme • Willing to be randomised in smoking cessation study • English speaking Exclusion criteria: • Dementia or current serious psychiatric or unstable medical illness • Pregnancy or breastfeeding • Known fat malabsorption diseases that may affect skin carotenoid status

NCT02658032 (*Continued*)

Interventions	The purpose of this study is to test the efficacy of 2 separate, sequential interventions to promote tobacco cessation/reduction in individuals who are screened for lung cancer or who are eligible for lung cancer screening. Each intervention will be compared to standard of care. The first intervention will be a personalised-message intervention; the second intervention will consist of a biofeedback-based intervention The aim of the second intervention is to evaluate the efficacy of a novel, biofeedback-based intervention that provides personalised individual-level feedback on biomarkers of lung cancer risk and how they improve in response to cessation, delivered in a gain-framed way. The biomarkers include skin carotenoid status, spirometry, and plasma bilirubin, all of which improve with cessation. The study team will examine whether the biofeedback prevents relapse in those who quit and leads to reductions in smoking in lung nodule patients who failed to quit
Outcomes	Primary outcome: 1. Smoking cessation (Time Frame: 8 weeks). Smoking cessation will be measured by self-report and validated by the study team using CO levels. CO will be measured. 2. Number of cigarettes smoked (Time Frame: 6 months). Number of cigarettes smoked will be assessed by self-report. Smoking cessation will be measured by self-report and validated by the study team using CO levels. CO will be measured. Secondary outcomes 1. Smoking cessation (Time Frame: baseline, 4 weeks, 3 months). Smoking cessation will be measured by self-report and validated by the study team using CO levels. CO will be measured.
Starting date	January 2016
Contact information	Brenda Cartmel, PhD brenda.cartmel@yale.edu
Notes	Unclear whether 6-month smoking cessation outcome will be available

NCT02840513

Trial name or title	Smartphone App and CO Self-monitoring for Smoking Cessation (SMART-CO)
Methods	Parallel-group, open-label randomised controlled trial
Participants	510 participants, 16 years of age and older Inclusion criteria: • HIV-infected smokers 16 years and older smoking 3 cigarettes per day enrolled into the Swiss HIV Cohort Study • Willingness to quit smoking • Speaking 1 or more of official Swiss national languages or English users of smartphone (specifically iPhone 5, 5c, 5s, 6, 6+ running iOS version 8.0+; smartphones with resolution of at least 800 x 400 pixels running Android version 5.0+; and Android smartwatches) • Informed consent Exclusion criteria: • Limitations in hearing, comprehension, or vision problems that preclude full study participation • Participants with a life expectancy of less than 12 months due to any serious medical condition

NCT02840513 (*Continued*)

Interventions	The app offers a coaching function where users receive personalised messages to encourage smoking cessation and advice for behavioural changes. For the first 4 weeks of the intervention, individuals will also be asked to blow daily into a breath carbon monoxide monitor before going to sleep. Depending on the results of the breath test, individualised messages will be delivered by the Smokelyzer feedback app to either enhance maintenance of abstinence or to increase the motivation to quit. After the first 4 weeks, participants will use the breath carbon monoxide monitor at least twice a week until the end of the 6-month study. The app will react with positive feedback in individuals doing well with smoking cessation and messages to encourage individuals with difficulties quitting smoking
Outcomes	Primary outcome measures: Self-reported abstinence biochemically verified by a carbon monoxide test in-person. (Time Frame: 6 months) Secondary outcome measures: Differences in the number of daily cigarettes smoked from baseline to 6-month follow-up and point prevalence of abstinence (i.e. no smoking in the past 7 days) at 6-month follow-up. (Time Frame: 6 months)
Starting date	1 June 2017
Contact information	Dmitry Gryaznov dmitry.gryaznov@usb.ch
Notes	Estimated study completion date: 1 July 2019

NCT02991781

Trial name or title	Combined bio- and neuro- feedback vs. varenicline use for smoking cessation
Methods	Randomised, parallel-group, open-label trial
Participants	140 participants: Inclusion criteria: • Being continuous tobacco smokers (> 10 cigarettes per day) for at least 6 months • Being unemployed for at least 3 months • Being diagnosed with asthma • Being diagnosed with COPD • Age < 35, for the group of young unemployed • Age > 35 years, for the groups of asthma and COPD patients Exclusion criteria: • Diagnosed neurological, mental, or psychiatric illness • Drug-resistant epilepsy
Interventions	This study will develop and experimentally test the efficiency of a neurofeedback (NF) training protocol for smoking cessation. As non-pharmacological, non-invasive, and painless brainwave technique, NF contributes to teach individuals how they can take control of their mind through operant conditioning. NF regulates brain function in a natural way. The protocol will consist of 5 sessions of skin temperature biofeedback and 20 sessions of a neurofeedback training protocol that will consist of Alpha-Theta ratio up-training. The aim of the training is to reach a cross-over state, were initially Alpha activity will increase and then in a deeper state,

NCT02991781 (*Continued*)

	the Theta activity will take over. This state is associated with a reverie and disidentification with problems, stress, or traumatic experiences. Participants will therefore will learn how to increase their Theta/Alpha ratio The neurofeedback intervention will be compared with a different group of participants receiving an intervention based on varenicline use for approximately 3 months. The electrophysiological evaluation of the efficacy of the intervention will include EEG resting state and a sleep polysomnography measurement. Questionnaires and clinical evaluation include the same measurements as the neurofeedback intervention but only at 3 time points: prior, during, after the completion of the study
Outcomes	Standardised percentage of participants that give up smoking (Time Frame 2 years)
Starting date	January 2017
Contact information	Professor Panos Bamidis bamidis@auth.gr
Notes	Not sure if it will be possible to isolate the effect of biofeedback

NCT03377738

Trial name or title	Effectiveness of the spirometry test as a motivational tool for quitting tobacco in primary care
Methods	Randomised controlled trial, parallel assignment, open-label
Participants	90 participants Inclusion criteria: • An active smoker • Aged between 40 and 75 years • No diagnosis of acute or chronic respiratory disease Exclusion criteria: • Serious or terminal diseases • Limiting osteoarticular diseases • Serious mental diseases: psychosis • Serious depressive disorder • Neurosis • Addiction to drugs/alcohol • Displaced patients (not habitual residents) • Pregnancy • Spirometry carried out for any reason in the year prior to inclusion in the study
Interventions	Intervention: diagnostic test: spirometry All participants will be given an intervention for tobacco cessation that will depend on the individual's cessation phase and will be given a spirometry test as a motivational element for dishabituation Control: no intervention: antismoking therapy All participants will be given only an intervention for tobacco cessation that will depend on the individual's cessation phase
Outcomes	1. Number of cessations of the tobacco habit (%) (Time Frame: 2 to 3 weeks, 3 months and 6 months) 2. Cessation phase of the tobacco habit (%) (Time Frame: 2 to 3 weeks, 3 months and 6 months)

NCT03377738 (*Continued*)

Starting date	May 2011
Contact information	A Lopez-santiago, MD
Notes	Last update posted on ClinicalTrials.gov: 17 December 2017 Authors contacted but no answer received.

NCT03521141

Trial name or title	PRecision Interventions for SMoking in the SCCS (PRISM-SCCS)
Methods	Single-blinded randomised trial with parallel groups
Participants	68 participants Inclusion criteria: • Daily smoker of >= 5 cigarettes per day • Enrolled participant of the Southern Community Cohort Study (SCCS) who completed a prior survey indicating they were willing to be contacted regarding a smoking cessation clinical trial • Residence in Tennessee or Mississippi • Has stored blood sample with the SCCS • Has established primary care provider • Medically eligible and willing to take varenicline and NRT Exclusion criteria: • Currently taking medication to quit smoking • Enrolled or planning to be enrolled in another smoking cessation programme • Inability to give informed consent or participate due to cognitive disorder (e.g. dementia, severe intellectual disability) • Unstable psychiatric illness (emergency room or hospitalised for psychiatric condition in past 6 months, change in psychiatric medications in past 3 months, or suicidal ideation in past 6 months) • Not able to send or receive mail • No access to a telephone or inability to communicate by telephone • Unable to speak and read English • History of seizures or Buerger's disease • Currently pregnant or breastfeeding
Interventions	3 intervention arms (only arm 3 (group 2) is provided with biofeedback) 1. Guideline-based care (GBC) GBC participants are 1) referred to the state quitline, 2) provided the National Cancer Institute Clearing the Air smoking cessation programme, and 3) asked to talk to their healthcare provider about potential lung cancer screening. Medication assignment is guided by standard guidelines and a conversation between the study tobacco counsellor and the participant. Groups 1 and 2 also receive GBC counselling 2. Active comparator: Nicotine metabolite ratio (PC-NMR) Group 1, nicotine metabolism. Medication is guided by nicotine metabolism 3. Active comparator: Respiragene (PC-Respiragene) Group 2, genetically informed lung cancer risk score. Medication assignment is guided by standard guidelines and a conversation between the study nurse and the participant

NCT03521141 (*Continued*)

Outcomes	Primary outcome measures: Intervention Feasibility: ability to retain participants. Time Frame: 6 months. Feasibility of delivering precision care interventions in the SCCS, as evidenced by ability to recruit, engage, and retain participants through the end of the study. Secondary outcome measures: Cessation History - Quit attempts (Time Frame: 6 months) Quit attempt (yes/no) Cessation History - Medication use (Time Frame: 6 months) Medication use (duration of use) Cessation History - Quitline (Time Frame: 6 months) Self-reported quitline utilisation Cessation History - Self-reported abstinence (Time Frame: 6 months) Self-reported abstinence Cessation History - Validated abstinence (Time Frame: 6 months) Biochemically verified (salivary cotinine, >= 10 ng/mL) abstinence
Starting date	18 May 2018
Contact information	Hilary Tindle, Associate Professor of Medicine, Vanderbilt University Medical Center
Notes	

NCT03583203

Trial name or title	Tobacco intensive motivational and estimate risk
Methods	Randomised, open-label, prospective study
Participants	204 participants, aged 40 to 70 years old Inclusion criteria: • Individuals aged between 40 and 70 years • Confirmed diagnosis of bipolar disorder or schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorder IV (DSM-IV-TR) • Active smokers who currently consume at least 10 cigarettes a day, with a cumulative consumption of 10 packets/year or more Exclusion criteria: • Previous respiratory diagnosis of asthma, cystic fibrosis, tuberculosis, simple chronic bronchitis, restrictive pulmonary disease, or bronchiectasis • Acute respiratory symptoms • Heart disease or advanced oncological processes • Existence of a pathology that makes it advisable not to perform spirometry (recent pneumothorax, recent thoracic or abdominal surgery, aortic aneurysm, unstable angulation, retinal detachment, facial hemiparesis, or oral/dental problems) • Individuals who, due to their intellectual disability or mental pathology, do not understand or cannot be forced to perform spirometry • Clinical instability with results of over 14 points on the Hamilton Depression Rating Scale, a Young Mania Rating Scale of over 6, or a Positive and Negative Syndrome Scale of over 70
Interventions	The primary objective evaluates the effectiveness of an intensive antismoking programme that informs participants of their individual risk of lung damage and the possibilities of prevention. The intervention group will undergo spirometry, and the presence and degree of respiratory obstruction will be assessed. Participants

NCT03583203 (*Continued*)

	will be given individual information to generate a motivational message about the possibilities of prevention, and the information will be maintained for 3 months by sending text messages (SMS) to their mobile phones. This group will include personalised information about lung damage. After evaluating their COPD, participants will be informed about its existence and staging. Depending on the damage found, the generation of motivation will focus on the different prevention methods. Likewise, after the motivation level is set, participants will be offered the option of treatment and regular follow-up. The intervention will be strengthened by motivational messages, half of which are linked to the possibilities of preventing respiratory damage, sent to the participant's mobile phone via SMS during the 3 months after the face-to-face intervention. Participants without mobile phones will receive a call on their phone to convey the same messages The control intervention lasts 30 minutes and will be structured around the 5 A's technique (Ask, Advice, Assess, Assist and Arrange)
Outcomes	Primary outcome measures: smoking cessation (Time Frame: 12 months) self-reported abstinence over the previous 7 days, confirmed by co-oximetry with expired CO < 10 ppm
Starting date	12 July 2018
Contact information	Fernando Sarramea Crespo fscferro69@gmail.com
Notes	

Pita Fernandez 2015

Trial name or title	Effectiveness of co-oximetry and minimum advice for smoking cessation in kidney transplant recipients
Methods	Randomised controlled trial (open, with blinded evaluation)
Participants	122 participants Smoking kidney transplant recipients, in preparation stage, pre-contemplation, and contemplation stage of change, who consent to participate
Interventions	Intervention group: brief advice + exhaled CO measurement Control group: brief advice for smoking cessation
Outcomes	Smoking cessation at 6 and 12 months confirmed by nicotine test
Starting date	1 December 2012 (end date 31 December 2015)
Contact information	Dr Salvador Pita-Fernández
Notes	Study completed but data not published. Author contacted but no answer received.

Ripoll 2012

Trial name or title	Clinical trial on the efficacy of exhaled carbon monoxide measurement in smoking cessation in primary health care
Methods	Parallel randomised controlled trial with blind evaluation (single)
Participants	942 participants Inclusion criteria: • Smokers >= 18 years of age attended for any reason • Smokers in contemplation or pre-contemplation phase
Interventions	Intervention group: brief advice plus exhaled CO measure Control group: brief face-to-face antismoking advice from the physician during patient consultation
Outcomes	Sustained abstinence (at 6 and 12 months) validated by urine cotinine test
Starting date	15 October 2010 (end date 15 October 2012)
Contact information	Miss Joana Ripoll jripoll@ibsalut.caib.es
Notes	Study no longer recruiting, no data published. Author contacted but no answer received.

CO: carbon monoxide
COPD: chronic obstructive pulmonary disease
EEG: electroencephalogram
NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
NRT: nicotine replacement therapy

DATA AND ANALYSES

Comparison 1. All interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Smoking cessation - feedback on smoking exposure	5	2368	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.83, 1.21]
2 Smoking cessation - feedback on smoking-related disease risk	5	2064	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.63, 1.01]
2.1 Genetic marker for cancer risk	3	1297	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.65, 1.10]
2.2 Genetic marker + CO	1	270	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.34, 1.17]
2.3 Genetic marker for risk of Crohn's disease	1	497	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.32, 1.71]
3 Smoking cessation - feedback on smoking-related harm	11	3314	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.99, 1.61]
3.1 Spirometry with or without lung age	5	1728	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.83, 1.84]
3.2 CO and spirometry feedback	4	895	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.74, 2.18]
3.3 Carotid ultrasound	2	691	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.67, 3.66]

Comparison 2. Multiple versus single measurement

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Smoking cessation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Genetic marker + CO vs CO only	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 3. All interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Spirometry and/or lung age	5	1728	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.83, 1.84]
1.1 Spirometry with lung age	2	611	Risk Ratio (M-H, Random, 95% CI)	1.77 [0.62, 5.05]
1.2 Spirometry without lung age	3	1117	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.73, 1.48]

Analysis 1.1. Comparison 1 All interventions, Outcome 1 Smoking cessation - feedback on smoking exposure.

Review: Biomedical risk assessment as an aid for smoking cessation

Comparison: 1 All interventions

Outcome: 1 Smoking cessation - feedback on smoking exposure

Study or subgroup	Intervention n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Audrain 1997	20/156	23/137		11.7 %	0.76 [0.44, 1.33]
Brunette 2013	15/58	21/66		11.4 %	0.81 [0.46, 1.42]
Jamrozik 1984	91/528	77/512		46.2 %	1.15 [0.87, 1.51]
Sanders 1989	52/376	55/375		29.0 %	0.94 [0.66, 1.34]
Shahab 2011	5/81	3/79		1.8 %	1.63 [0.40, 6.57]
Total (95% CI)	**1199**	**1169**		**100.0 %**	**1.00 [0.83, 1.21]**

Total events: 183 (Intervention), 179 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.93$, df = 4 (P = 0.57); $I^2 = 0.0\%$

Test for overall effect: Z = 0.00 (P = 1.0)

Test for subgroup differences: Not applicable

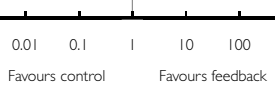
Analysis 1.2. Comparison 1 All interventions, Outcome 2 Smoking cessation - feedback on smoking-related disease risk.

Review: Biomedical risk assessment as an aid for smoking cessation

Comparison: 1 All interventions

Outcome: 2 Smoking cessation - feedback on smoking-related disease risk

Study or subgroup	Intervention n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Genetic marker for cancer risk					
Hishida 2010	15/257	22/276		13.5 %	0.73 [0.39, 1.38]
Ito 2006	58/341	67/356		53.4 %	0.90 [0.66, 1.24]
Nichols 2014	10/36	12/31		11.4 %	0.72 [0.36, 1.43]
Subtotal (95% CI)	**634**	**663**		**78.3 %**	**0.84 [0.65, 1.10]**
Total events: 83 (Intervention), 101 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.58$, df = 2 (P = 0.75); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.28 (P = 0.20)					
2 Genetic marker + CO					
Audrain 1997	14/133	23/137		14.1 %	0.63 [0.34, 1.17]
Subtotal (95% CI)	**133**	**137**		**14.1 %**	**0.63 [0.34, 1.17]**
Total events: 14 (Intervention), 23 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.48 (P = 0.14)					
3 Genetic marker for risk of Crohn's disease					
Hollands 2012	9/251	12/246		7.6 %	0.74 [0.32, 1.71]
Subtotal (95% CI)	**251**	**246**		**7.6 %**	**0.74 [0.32, 1.71]**
Total events: 9 (Intervention), 12 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.71 (P = 0.48)					
Total (95% CI)	**1018**	**1046**		**100.0 %**	**0.80 [0.63, 1.01]**
Total events: 106 (Intervention), 136 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.37$, df = 4 (P = 0.85); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.88 (P = 0.060)					
Test for subgroup differences: $Chi^2 = 0.78$, df = 2 (P = 0.68), $I^2 = 0.0\%$					

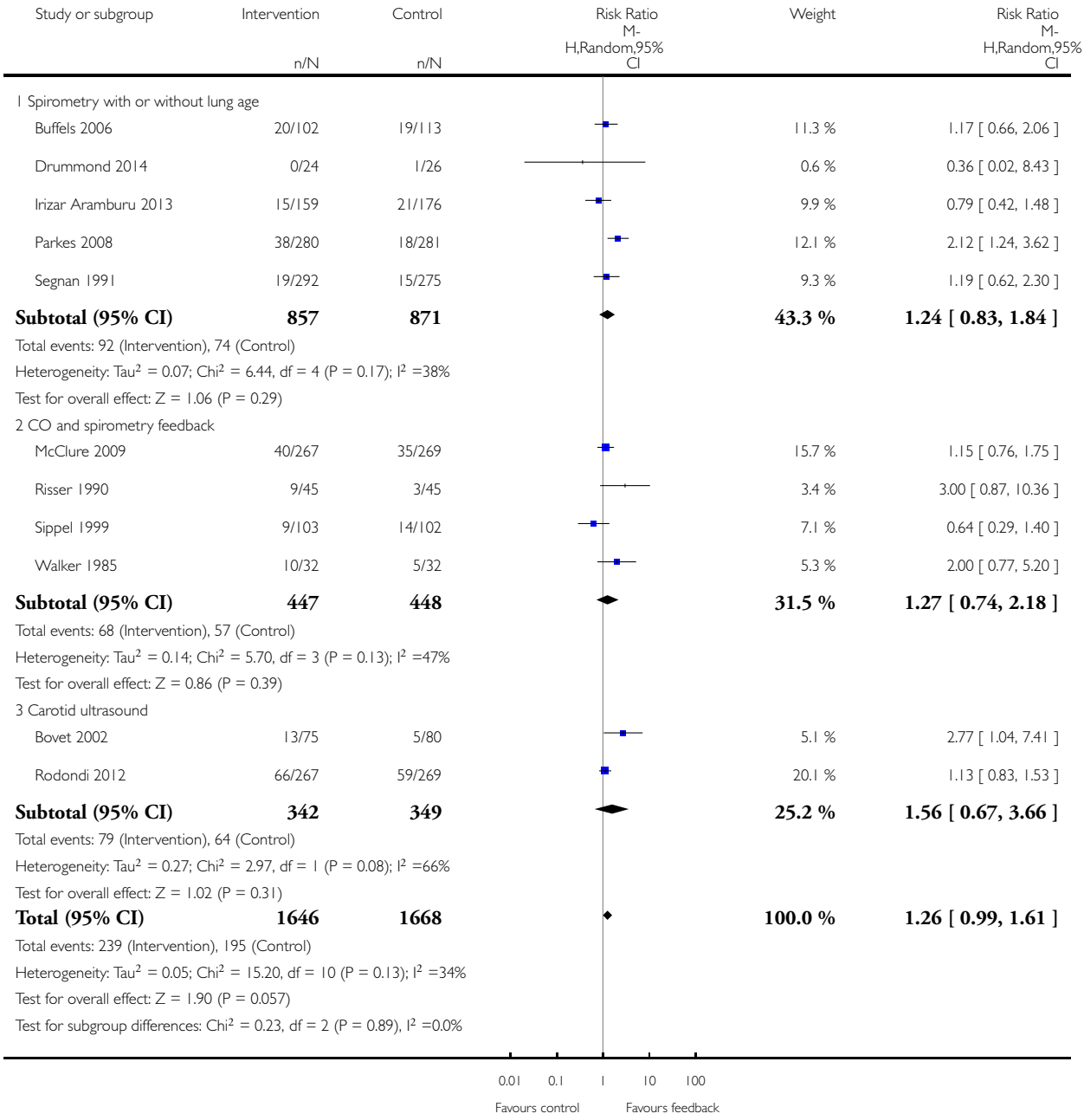


Analysis 1.3. Comparison 1 All interventions, Outcome 3 Smoking cessation - feedback on smoking-related harm.

Review: Biomedical risk assessment as an aid for smoking cessation

Comparison: 1 All interventions

Outcome: 3 Smoking cessation - feedback on smoking-related harm

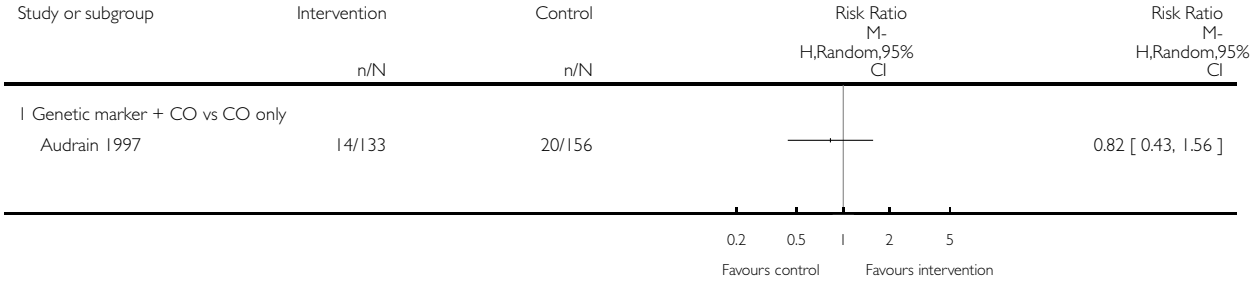


Analysis 2.1. Comparison 2 Multiple versus single measurement, Outcome 1 Smoking cessation.

Review: Biomedical risk assessment as an aid for smoking cessation

Comparison: 2 Multiple versus single measurement

Outcome: 1 Smoking cessation

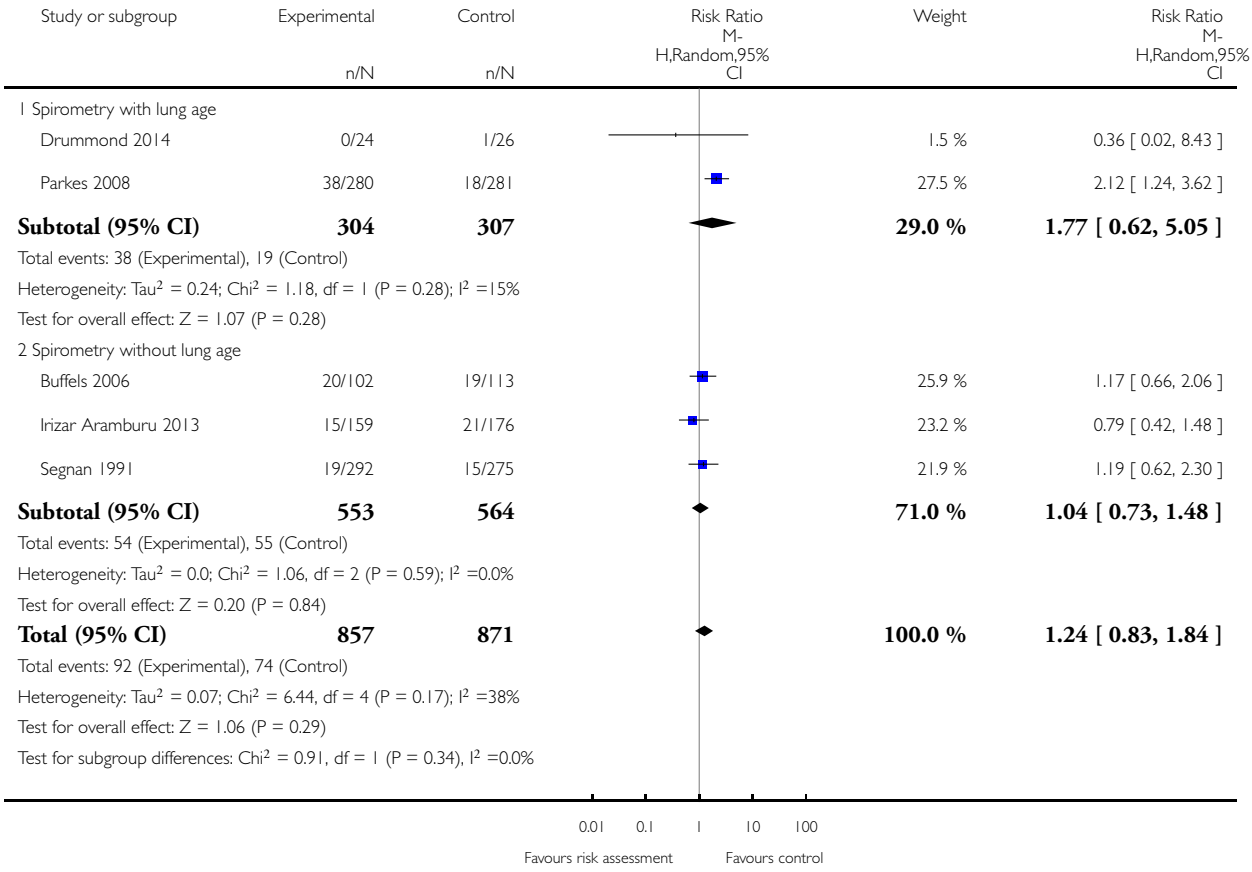


Analysis 3.1. Comparison 3 All interventions, Outcome 1 Spirometry and/or lung age.

Review: Biomedical risk assessment as an aid for smoking cessation

Comparison: 3 All interventions

Outcome: 1 Spirometry and/or lung age



APPENDICES

Appendix 1. Specialized Register search strategy

For Cochrane Register of Studies
#1 patient education:EMT,MH,KW,TI,AB
#2 patient compliance:EMT,MH,KW
#3 patient counsel?ing:EMT,MH,KW,TI,AB
#4 persuasive communication:EMT,MH,KW
#5 spirometry:EMT,MH,KW,TI,AB
#6 respiratory function:EMT,MH,KW
#7 bronchospirometry:EMT,MH,KW,TI,AB
#8 carbon monoxide:EMT,MH,KW,TI,AB
#9 (forced expiratory volume or forced expiratory flow):EMT,MH,KW,TI,AB
#10 FEV?:TI,AB
#11 obstructive lung disease*:EMT,MH,KW,TI,AB
#12 genetic testing:EMT,MH,KW
#13 genetic susceptibility:EMT,MH,KW
#14 genetic predisposition:EMT,MH,KW
#15 (genetic NEAR (test* OR risk*)):TI,AB
#16 biomarker*:EMT,MH,KW,TI,AB
#17 screening:TI,AB
#18 feedback:EMT,MH,KW,TI,AB
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

WHAT'S NEW

Date	Event	Description
16 November 2018	New citation required but conclusions have not changed	New searches run: 27 March 2018. Conclusions unchanged.
15 October 2018	New search has been performed	Updated, 5 new studies included (1 with incomplete data), conclusions unchanged

HISTORY

Protocol first published: Issue 2, 2004

Review first published: Issue 4, 2005

Date	Event	Description
20 August 2012	New citation required but conclusions have not changed	Updated with 4 new included studies, conclusions unchanged
20 August 2012	New search has been performed	Updated search run, 4 new studies included, text updated
28 January 2009	New citation required and conclusions have changed	1 new study shows a significant effect.
27 January 2009	New search has been performed	3 new studies identified in update for Issue 2, 2009.
21 April 2008	Amended	Converted to new review format
11 August 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

CC: (for 2019 update) screening search results, organising retrieval of papers, screening papers for inclusion, quality appraisal of papers, data extraction, data management, data entry into Review Manager 5, data analysis and interpretation, writing to authors of papers for additional information, update of the review.

YM: screening search results, organising retrieval of papers, screening papers for inclusion, quality appraisal of papers, data extraction, data management, data entry into Review Manager 5, data analysis and interpretation, writing the review, writing to authors of papers for additional information.

JLB: (for 2019 update) conducted the GRADE evaluation and added the 'Summary of findings' table, and contributed to the writing of the review.

BB: conception and design of the review, developing search strategy, screening papers for inclusion, quality appraisal of papers, interpretation of data, methodological perspective, general advice on the review, securing funding.

JYC: (for 2012 update) screening papers for inclusion, quality appraisal of papers, data extraction, data management, data entry into Review Manager 5, data analysis and interpretation, update of the review.

JC: conception and design of the review, developing search strategy, screening search results, screening papers for inclusion, quality appraisal of papers, interpretation of data, clinical and methodological perspective, general advice on the review.

MRW: (for 2012 update) screening papers for inclusion, quality appraisal of papers, data extraction, data management, data entry into Review Manager 5.

KS: (for 2019 update) screening papers for inclusion, quality appraisal of papers, data extraction.

RB : co-ordinating the review, conception and design of the review, data collection, developing search strategy and undertaking searches, screening search results, organising retrieval of papers, screening papers for inclusion, quality appraisal of papers, data extraction, data management, data entry into Review Manager 5, data analysis and interpretation, writing the review, writing to authors of papers for additional information, providing a clinical perspective.

DECLARATIONS OF INTEREST

CC: no interest to declare

YM: no interest to declare

JLB: no interest to declare

BB: no interest to declare

JYC: no interest to declare

JC: was the co-author of one of the studies included in the review. JC has also received funding from Cytos to conduct a clinical phase II trial testing the nicotine vaccine, NicQb. He attended two international scientific meetings to present the results of such a trial developed by this company, and travel costs were covered by Cytos.

MRW: no interest to declare

KS: no interest to declare

RB: no interest to declare

SOURCES OF SUPPORT

Internal sources

- Center for Primary Care and Public Health, University of Lausanne, Switzerland.

Core salaries of CC, YM, KS, and RB

- Nuffield Department of Primary Care Health Sciences, University of Oxford, UK.

External sources

- National Institute for Health Research (NIHR) Cochrane Programme Grant, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Following changes to the Cochrane Tobacco Addiction Group's recommended method of data analysis since this review was first prepared, we have changed the way in which we summarise the effects of treatment. From the 2009 update onwards, we use the risk ratio rather than the odds ratio for summarising individual trial outcomes and for estimates of pooled effect. Treatment effects will seem smaller when expressed as risk ratios than when expressed as odds ratios, unless the event rates are very low. For example, if 20 out of 100 participants have quit in the intervention group, and 10 out of 100 in the control group, the risk ratio is 2.0 ((20/100)/(10/100)), while the odds ratio is 2.25 ((20/80)/(10/90)). While there are circumstances in which odds ratios may be preferable, there is a danger that they will be interpreted as if they are risk ratios, making the treatment effect seem larger (Higgins 2011). We estimated a pooled weighted average of risk ratios using a Mantel-Haenszel random-effects method, with 95% confidence intervals.

From the 2019 update onwards, we decided to pool studies using similar biofeedback strategies even if they were performed in diverse settings. Given the fact that there were more studies included than in previous reviews, we considered that the clinical heterogeneity was acceptable even if the setting and staff were different.

From the 2019 update onwards, we changed the 'Risk of bias' assessment from assessing blinding of participants, study personnel, and outcome assessment (both performance and detection bias) to assessing outcome assessment (detection bias only) alone. This is because interventions of this type cannot be blinded, and is in accordance with Cochrane Tobacco Addiction Group guidance.

INDEX TERMS

Medical Subject Headings (MeSH)

Biofeedback, Psychology [*methods]; Breath Tests; Carbon Monoxide [analysis]; Genetic Predisposition to Disease; Randomized Controlled Trials as Topic; Risk Assessment [methods]; Smoking [*adverse effects; metabolism]; Smoking Cessation [methods; *psychology; statistics & numerical data]; Spirometry

MeSH check words

Humans