Smoking cessation treatment and its reimbursement

The costs and effects

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Smoking cessation treatment and its reimbursement

The costs and effects

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Chapter 1

Introduction

This thesis focuses on the effects and the cost-effectiveness of smoking cessation treatment (SCT) and its reimbursement. In this *first chapter*, the different studies are introduced and an outline of the research questions is given.

Smoking related diseases and its costs

Smoking is one of the most avoidable causes of death and disability in developed countries.¹ Worldwide, five million people die due to smoking related diseases each year.² In the Netherlands, the number of smoking-related deaths was over 20.000 in 2003.³ Smokers have an increased risk to develop cardiovascular disease, lung cancer and chronic obstructive pulmonary disease (COPD), but also more often have non-fatal diseases like osteoporosis, impotence, cataracts and gum disease.¹

Of the €36000 million that were spent on health care in the Netherlands in 1999, €509 million could be attributed directly to smoking (1.4%). When also including the indirectly attributed costs, smoking may account for up to 15% of the total annual health care costs in developed countries.⁴ As a result of the population distribution in developed countries, the smoking related health care costs and the health care costs themselves are expected to rise in the future. When stopping smoking, we expect that the smoking related costs of hospitalisation, contacts with health care providers, medication use and costs due to sick leave from work will reduce due to an improvement in health.

After a continuous decrease in the percentage of smokers since the 1950s and a stabilisation in the 1990s of one third of the population being a smoker, the percentage of smokers has now slowly decreased to 28% in the Netherlands.⁵ To further reduce the risk and costs of smoking related diseases and to increase life expectancy, smoking cessation strongly needs to be encouraged.^{1, 4}

Efficacy and effectiveness of SCT in healthy smokers and in smokers with COPD

Stopping smoking is not easy. The addictive effects of nicotine and the psychosocial aspects of smoking make it difficult to quit. Many studies have demonstrated that smokers who stop smoking are more successful when using nicotine replacement therapy (NRT), pharmacotherapy, like bupropion and nortriptyline, and behavioural interventions.⁶⁻¹⁰ The chance of being a successful quitter after one year increases from 3-5% for quitting cold turkey to 7-16% for behavioural interventions alone to 11-24% for pharmacological treatment plus behavioural support.¹¹

Most efficacy studies, however, are performed with well-motivated and healthy participants. In daily practice, smokers who seek assistance in their attempt to quit often have smoking related health complaints like COPD, are

more addictive and may be susceptible to depression.¹² As a result, we expect that the effectiveness of smoking cessation interventions in daily practice or patient populations is lower.

Earlier, Wagena et al. conducted a randomised controlled trial to study the effects of antidepressants for smoking cessation in patients at risk for or with existing COPD.¹³ The abstinence rate after 6 months was 28% in the bupropion group, 25% with nortriptyline and 15% in the placebo group, which are even higher success rates than presented in studies with healthy subjects at six months.^{9 14} However, results showed that after six months the estimated risk of relapse in participants with existing COPD was more than 30% higher compared with participants at risk for COPD.¹³

Cost-effectiveness of SCT in healthy smokers and in smokers with COPD

Comparisons of the costs and consequences of an existing intervention to a new intervention are important to demonstrate which is most optimal.¹⁵ In the Netherlands, a cut-off point of €18000 per quality adjusted life year (QALY) according to the societal perspective is used to indicate cost-effective health care interventions.¹⁶

Clear evidence exists that in healthy participants smoking cessation interventions show value for money. The National Institute for Clinical Excellence (NICE) estimated that the costs per quality adjusted life year (QALY) gained were €1080 to €2594 for advice and NRT, €689 to €1603 for advice plus bupropion, and €962 to €2128 for advice, combined with NRT and bupropion (€1=£0,69).⁴ In general, the cost-effectiveness ratios of smoking cessation interventions seem comparable to or even lower than those of other public health interventions like treating mild to moderate hypertension and lowering cholesterol levels.^{4 17 18}

However, less is known of the costs-effectiveness of smoking cessation interventions in specific patient populations like COPD. As indicated in the previous paragraph, we expect the efficacy of SCT to be lower in smokers with COPD, but we also expect that the health care costs are higher in these smokers because of airway related health problems. Since only little is known about the cost-effectiveness of SCT for patients with COPD, more information is needed in this area to be able to assist policy makers in their decisions.

Reimbursement for SCT

Despite the knowledge that using SCT increases the abstinence rate and is highly cost-effective, the use remains limited.¹⁹ Zhu et al. showed with data from the 1996 California Tobacco Survey, that in the general population only 20% of those who attempted to quit used one or more treatment methods.¹⁹ In

2000, 17% of a random sample of the Dutch population used SCT in their latest quit attempt.²⁰ As the cost of cessation treatments are considered an important barrier,¹⁹ reimbursing the costs of SCT might overcome this barrier.

In the United States, several insurance plans already offer full or partial coverage for using SCT, however not to the extent recommended by the updated smoking cessation guideline from the U.S Public Health Service.²¹ In Europe, the United Kingdom is the only country, in which the NHS offers reimbursement for SCT.²² In the Netherlands, SCTs are not reimbursed, but this might change in the future, since on the initiative of the Dutch Minister of Health, a randomised controlled trial was set up to assess the (cost)-effectiveness of a reimbursement system for SCT. The reimbursement system consisted of a full coverage of all proven effective SCTs available in the Netherlands plus information about these treatment methods. Not only a Dutch study, but also four studies in the United States²³⁻²⁶ and one study in the United Kingdom²⁷ have been performed. As each country has a different healthcare system, comparisons between studies have to be made to know if the findings are consistent. Assessing the cost-effectiveness of reimbursement for SCT is an important next step towards implementation and provides information on the financial consequences of introducing a system.

Research questions

In this thesis we answered the following research questions:

- Which smoking cessation intervention; bupropion, nortriptyline compared to placebo is most cost-effective combined with a behavioural intervention in facilitating smoking cessation and in increasing the number of for quality-adjusted life years (QALYs) in patients at risk for COPD or with existing COPD? (*Chapter 2*)
- Could a reimbursement system for SCT in the Netherlands increase the use of SCT and could it increase the abstinence rate after six months? (*Chapter 3*)
- Could a reimbursement system for SCT in the Netherlands increase the prolonged abstinence rate at 12 months and after two years? (*Chapter 4*)
- Can health care financing systems for smoking cessation interventions in general increase the use of SCT and the number of (successful) quitters? (*Chapter 5*)
- Is a reimbursement system for SCT in the Netherlands cost-effective in terms of incremental costs per quitter? And is it cost-effective if extrapolated to costs per quality adjusted life year (QALY) gained? (*Chapter 6*)

In Chapter 7, the results and implications of the different studies described in this thesis will be discussed. At the end of this chapter, we consider the possibilities of reimbursing SCT in the future and ways to further increase the use of SCT and the number of successful quitters.

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Chapter 2

The cost-effectiveness of antidepressants for
smoking cessation in COPD patients

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Abstract

Introduction

From a societal and health care perspective, we assessed which intervention, bupropion or nortriptyline, was most cost-effective after 1 year compared with placebo among smokers at risk or with existing COPD in stopping smoking and increasing the number of for quality-adjusted life years saved (QALYs).

Methods

255 participants, aged 30-70 years, were assigned bupropion SR, nortriptyline or placebo for 12 weeks and received smoking cessation counselling. Prolonged abstinence from smoking was defined as a participant's report of 0 cigarettes from week 4 to week 52, validated by urinary cotinine. Changes in utility (QALYs) were calculated using the EuroQol-5d.

Results

The prolonged abstinent rate was 20.9% with bupropion, 20.0% with nortriptyline and 13.5% with placebo. The mean utility change was 0.04 with bupropion, 0.02 for nortriptyline and -0.004 for placebo. According the societal and health care perspective respectively, the costs were €1368 and €562 with bupropion, €1906 and €616 with nortriptyline and €1212 and €383 with placebo. If willing to pay more than €2000 for a quitter or over €4000 for a QALY, bupropion was most cost-effective.

Conclusion

Bupropion seems to be more cost-effective when compared to placebo and nortriptyline. However, future studies are needed to replicate these findings.

Introduction

Smoking and COPD go hand in hand. Smoking is the main risk factor for developing this respiratory disease,¹ and stopping smoking is the most effective treatment and preventive intervention in the battle against it.^{2,3} For that reason, stopping smoking needs to be encouraged strongly in smokers at risk for COPD and smokers with existing COPD. However, stopping smoking is hampered by psychological, social and physiological factors. As nicotine withdraw can cause feelings of depression and anxiety,⁴ the use of antidepressant drugs like nortriptyline and bupropion for smoking cessation seems warranted.

Nortriptyline is a generic drug and bupropion is registered as a specific stop-smoking medication. In healthy smokers, both bupropion and nortriptyline can double the odds of cessation and increase the number of quitters after 6 months by 10% compared with placebo to 17-20%.⁵ For a 12-week treatment, the costs of nortriptyline are about €50,00 and for bupropion SR about €210,00, respectively. Because of its four times lower costs and comparable efficacy in healthy smokers nortriptyline seems favourable as an aid for smoking cessation.

Wagena et al. conducted a randomised, double-blind placebo-controlled trial to assess the efficacy of bupropion and nortriptyline, compared with placebo for smoking cessation among smokers at risk for COPD and smokers with COPD.⁶ Alongside this trial, an economic evaluation was performed from both a societal and health care perspective. The primary objective of this paper is to demonstrate which intervention, bupropion, nortriptyline or placebo, in combination with a behavioural intervention, is most cost-effective in facilitating smoking cessation in patients at risk for COPD or with existing COPD. Secondary, we assessed which intervention was most cost-effective in increasing the number of for quality-adjusted life years (QALYs). Wagena et al. found that after six months the estimated risk of relapse in participants with existing COPD was more than 30% higher compared with participants at risk for COPD.⁶ Since we also expected higher costs in participants with COPD than in participants at risk for COPD, we assessed the cost-effectiveness for these subgroups in terms of both smoking cessation and QALYs gained.

Methods

Participants

We included participants between 30 and 70 years of age, at risk for or with mild to moderately severe COPD, who smoked at least 10 cigarettes per day and were motivated to quit.⁶ At risk for COPD was defined as FEV₁/FVC from 0.7 to 1.0, combined with the presence of cough, sputum production or dyspnoea. Mild to moderately severe COPD was defined as FEV₁/FVC <0.7 and FEV₁ between 30 to 80%.¹ After screening, 255 eligible participants were randomly assigned bupropion SR (150 mg/day), nortriptyline (75 mg/day) or matching placebo for 12 weeks. The baseline characteristics of these participants are described in the efficacy study.⁶ All patients received individual face-to-face smoking cessation counselling (3x20 minutes) and telephone calls (6x5 minutes).

Efficacy outcome

The efficacy outcomes for this study were prolonged abstinence from smoking and change in utility, presented in QALYs. Prolonged abstinence from smoking was defined as a participant's report of 0 cigarettes per day (not even a puff) from week 4 to week 52 after the target quit date, confirmed by urinary cotinine values (cut-off point 60 ng/ml). The QALY score was calculated using the relative change in score at the EuroQol-5d⁷ between baseline and 12 months. The score of the EuroQol-5d can range from 0 (state of dead) to 1 (perfect health). We expected that the score would have stayed unchanged without intervention.

Cost estimates

Cost analyses were performed from both a societal and health care perspective, including costs related to COPD and the intervention offered (Table 2.1).⁸ The costs related to COPD were registered in cost diaries. In total, nine booklets were handed out to every participant, covering four weeks each. In order to give an estimate of the total costs made during the 12 months, we extrapolated the costs made in the registered weeks to the weeks in which participants did not have to fill in a cost diary.

Table 2.1 The costs included in the societal and health care perspective.

Societal perspective

Prescription medication, which were calculated using the pharmacotherapy manual of the Health Care Insurance Board (www.cvzkompassen.nl). In this manual, the costs of the use of medication are presented, often per month. The price year of the manual used was 2004. For the years 2002 and 2003, prices were adjusted using the consumer price index

Medication without prescription, which were specified by the participants themselves.

Visits to health care providers, which had a fixed price based on the Dutch guidelines for economic evaluation in health care.⁸

Paid and unpaid home care

Absenteeism from work, which was measured in lost working hours. The costs associated with being abstinent were calculated using the friction cost method, which assumes that organizations need a certain time, the friction period, to restore the initial production level when an employee is absent from work. The productivity costs per hour varied between €20 and €47 depending on age group and gender. The total productivity costs were multiplied by a correction factor of 0.8, which represents the elasticity regarding lost work time and productivity.⁸

The use of bupropion and nortriptyline. The costs were calculated conservatively. If the amount of bupropion or nortriptyline used was unclear or over 80%, than 100% of the total treatment costs were calculated, i.e. for bupropion SR €208,98 and for nortriptyline €50,82. If the compliance was less than 80% but over 50%, than 80% of the treatment costs were calculated. If the less than 50% of the medication was used, than 50% of the treatment costs were calculated.

Counseling sessions of which the costs of contacts with a pulmonary nurse were calculated and set at €23,00 per face-to-face counseling session and €5,75 per telephone session.

Travel cost were calculated per face-to-face counseling session and for visits to health care providers, for both a fixed price was calculated, based on the Dutch guidelines for economic evaluation in health care.⁸

Health care perspective

Included the costs of prescription medication, visits to health care providers, paid home care, the use of bupropion and nortriptyline and the costs of counseling sessions; calculated similar as in the societal perspective.

Incremental cost-effectiveness analyses

Intention-to-treat analyses were performed for the following combinations:

Patients	Treatment	Outcome	Perspective
- At risk for COPD	- Bupropion	- Quitters	- Society
- COPD	- Nortriptyline	- QALY's	- Health care
	- Placebo		

All dropouts were considered to be smokers. If scores on the EQ-5d were missing, we assumed that the change in utility outcome was equal to zero. For the costs of the weeks that were missing at random, maximal three booklets per participant were imputed by carrying forward available data of the subject

(LOCF). If four or more booklets were missing, the costs of these missing costs diaries of dropouts were imputed by the mean costs of all participants who missed maximum three booklets.

The incremental cost-effectiveness ratio (ICER) was defined as the difference in average costs for the intervention group minus the control group divided by the average difference in health outcome (quitters or QALYs). The ICER gives the cost per additional unit of health outcome gained from the intervention relative to the control approach. An intervention is considered to be cost-effective if the intervention leads to an improvement in outcome, even if the costs are more than usual care, but the incremental cost is not more than the amount that society is willing to pay.

The uncertainty of the ICERs was estimated using non-parametric bootstrapping.⁹ A specified number of samples (in this case 1000) of the same sample size as the original data set are drawn with replacement. The distribution of the 1000 observations provides an estimate of the sampling distribution of the ICER. (Figure 2.1) From this distribution acceptability curves are generated representing the probability that an intervention is most cost-effective over a range of cost-effectiveness thresholds. The costs are not discounted, as the time horizon of the trial was one year. With sensitivity analyses, we assessed whether the results are robust to changes in imputation method of the cost diaries.

Figure 2.1 Definition of quadrants in cost-effectiveness plane.

North east = replicates in this quadrant indicate the probability that the intervention was more effective, but generates more costs compared with its control group.

South east = replicates in this quadrant represent a higher effect and fewer costs.

North west = replicates in this quadrant represent less effect and more costs.

South west = replicates in this quadrant represent less effect and less costs.

Results

Abstinence from smoking and QALYs changed

After 12 months, 18 of the 86 participants (20.9%) in the bupropion group, 16 of the 80 participants (20.0%) in the nortriptyline group and 12 of the 89 participants (13.5%) in the placebo group were prolonged abstinent. After 12 months, participants using bupropion gained on average 0.04 QALYs (0.15 standard deviation (sd)). With nortriptyline, 0.02 QALYs were gained (0.14 sd) and in the placebo group participants lost on average 0.004 QALYs (0.16 sd).

Costs

The number of participants that filled in all cost diaries was low. Only 53.7% of the participants returned all cost diaries or at least 6 of the 9 booklets they received. Eighteen percent of the participants returned no booklet at all. Table 2.2 presents the data of the cost diaries, the intervention costs per group, the mean imputed costs of the cost diaries, the intervention costs and total costs for both the societal and health care perspective.

Table 2.2 Mean reported volume and costs (in €).

Item	Bupropion (n=86)		Nortriptyline n=80		Placebo n=89	
	Volume	Cost	Volume	Cost	Volume	Cost
Use of prescribed medication per week	0.16	2.13	0.18	2.18	0.28	3.39
Use of medication without prescription per week	0.07	1.45	0.05	0.69	0.04	0.02
Visits to health care providers per week	0.06	1.63	0.20	5.54	0.07	2.04
Travel cost visit health care provider per week	0.06 ²	0.24	0.20 ²	1.16	0.07 ²	0.29
(Un)paid home care per week in hrs.	0.02	0.23	0.24	1.96	0.19	1.53
Absenteeism per week in hrs.	0.35	9.42	0.67	22.53	0.26	8.45
Study medication	62% ¹	173.50	55% ¹	39.73	65% ¹	0
Counseling sessions	7.3	87.24	7.3	86.46	7.5	88.13
Travel cost face to face counseling sessions	2.7 ³	6.00	2.7 ³	5.93	2.7 ³	6.00
Societal perspective	Cost	2.5 th -97.5 th	Cost	2.5 th -97.5 th	Cost	2.5 th -97.5 th
Mean imputed costs of diaries	1102	0-4988	1774	0-17602	1118	0-6500
Mean intervention costs	267	150-316	132	56-159	94	33-109
Mean total costs	1368	193-5260	1906	120-17761	1212	96-6602
Health care perspective	Cost	2.5 th -97.5 th	Cost	2.5 th -97.5 th	Cost	2.5 th -97.5 th
Mean imputed costs of diaries	301	0-1532	490	0-6271	295	0-1835
Mean intervention costs	261	147-319	126	54-153	88	31-102
Mean total costs	562	187-1833	616	114-6423	383	89-1929

¹ Percentage of the cases in which the use of medication was over 80% or unclear; ² number of visits; ³ number of sessions.

Results indicated that the costs in the nortriptyline group were higher than in the bupropion and placebo group. In particular, the costs for visits to health care providers and absenteeism from work were higher. Table 2.2 shows that the deviation (2.5th percentile to 97.5th percentile) around the mean is large in the nortriptyline group. Data showed that in the nortriptyline group there were three participants that had costs higher than 3 standard deviations above the mean (cut off point €9683), in the bupropion group and placebo group, this was one and zero participants, respectively. The costs according to the health care perspective were lower than the costs for society, since for example no costs from absenteeism from work were included.

Cost per quitter

Both bupropion and nortriptyline were more effective in increasing the abstinence rate than placebo, but the costs according the societal perspective were lower in the placebo group. The incremental costs per quitter presented in Table 2.3 demonstrate that money has to be invested to gain one additional quitter, if comparing bupropion and nortriptyline with placebo. If comparing bupropion with nortriptyline, than less money needs to be spend to gain one quitter using bupropion instead of nortriptyline.

Table 2.3 Costs per quitter and QALY for the different comparisons according the societal and health care perspective.

Comparison	bupropion vs. placebo	nortriptyline vs. placebo	bupropion vs. nortriptyline
Δ quitter	0,07	0,07	0,01
Δ QALY	0,05	0,02	0,02
Δ costs societal perspective	156	693	-537
Δ costs health care perspective	179	232	-54
Incremental costs for society per quitter	2097	10640	-57753
Quadrant distribution	9% 62%	13% 81%	8% 8%
Incremental costs for health care per quitter	2400	3566	-5766
Quadrant distribution	9% 91%	14% 84%	19% 19%
Incremental costs for society per QALY	3349	30335	-22607
Quadrant distribution	1% 66%	15% 79%	1% 14%
Incremental costs for health care per QALY	3834	10166	-2257
Quadrant distribution	1% 99%	18% 81%	4% 32%
	0% 0%	0% 1%	9% 55%

In Table 2.3, the 1000 bootstrap replicates are presented as quadrant distribution like in Figure 2.1. Of the replicates, 45% indicates that bupropion increases the effect and reduces the cost compared to nortriptyline. 39% of the replicates are in the quadrant indicating more effect, but also more costs in the nortriptyline group. From the quadrant distribution in Table 2.3, acceptability curves were generated. These curves are presented in Figures 2.2 and 2.3 and demonstrate the probability that for a certain amount of money (λ) an intervention is most cost-effective. Figure 2.2 shows that the placebo intervention is most cost-effective, if willing to pay zero (additional effectiveness is regarded to be worthless in this situation) or less than €2000 for a quitter. Bupropion is most cost-effective if society is willing to pay over €2000 (crossing lines placebo and bupropion).

From a health care perspective, the effects are equal to the outcomes from the societal perspective, but the costs are different (Table 2.3). The costs decreased in all groups, nevertheless the costs in the nortriptyline group are still higher compared with the other groups. Figure 2.2 shows that if willing to pay less than about €3000, the placebo condition is the optimal strategy. If in health care one is willing to pay over €3000, then bupropion is the most cost-effective intervention, however the probability that this intervention is most cost-effective is maximum 54%.

Figure 2.2 Probability that an intervention is most cost-effective in terms of cost per quitter according the societal perspective (left) and health care perspective (right).

Costs per QALY

Table 2.3 demonstrates that bupropion and nortriptyline were more effective in increasing the number of QALYs in comparison with the placebo condition. The costs according to the societal perspective in the placebo group were however lower than in the bupropion and nortriptyline group and the costs in the nortriptyline group were higher than in the bupropion group. Figure 2.3 shows that if willing to pay over €3000, bupropion will be the most cost-

effective intervention. The placebo condition is only optimal if willing to pay less than €3000 per QALY. According society, a Dutch cut-off point for cost-effectiveness is €18000 per QALY.¹⁰ At a threshold of €18000, the probability that bupropion is the optimal intervention is 89%.

According to the health care perspective, if willing to pay over €4000, then bupropion will be the most cost-effective intervention. If only less than €4000 per QALY can be spend, then the placebo condition will be the most cost-effective strategy according to the outcomes of the current study. Due to its small effect and high costs, nortriptyline appeared least cost-effective (Figure 2.3).

Figure 2.3 Probability that an intervention is most cost-effective in terms of cost per QALY according the societal perspective (left) and the health care perspective (right)

Subgroup analyses for participants at risk for COPD and with existing COPD

Subgroup analyses showed that overall the effects in terms of smoking cessation and QALYs gained were higher and the costs were lower in participants at risk for COPD when compared to participants with existing COPD. Table 2.4 shows the mean costs per additional quitter and QALY according the societal and health care perspective and also the incremental costs for the different comparisons. If comparing bupropion, nortriptyline and placebo for participants at risk for COPD, then the placebo condition is most effective in increasing the abstinence rate and less costly, followed by bupropion for both perspectives. In participants with COPD, bupropion was most cost-effective, followed by the nortriptyline group. The placebo was least cost-effective, since the abstinence rate was only 6% in this subgroup. The mean costs per QALY gained were lowest with bupropion, followed by placebo in the group at risk for COPD and followed by the nortriptyline group in the group with existing COPD.

Table 2.4 Mean costs per quitter and QALY according the societal and health care perspective.

	Bupropion		Nortriptyline		Placebo	
	At risk	COPD	At risk	COPD	At risk	COPD
% of quitter	21.4	20.4	21.4	19.2	22.0	6.3
Mean change in QALY	0.063	0.024	0.014	0.022	0.023	-0.026
Mean costs society	1480	1262	1859	1931	908	1473
Mean costs health care	480	641	548	653	269	481
Incremental costs for:	Bupropion vs. placebo		Nortriptyline vs. placebo		Bupropion vs. nortriptyline	
	At risk	COPD	At risk	COPD	At risk	COPD
Society per quitter	-109597 ¹	1485 ²	-182063 ¹	3530	-379 ³	-54679 ²
Health care per quitter	-40315 ¹	1125	-53339 ¹	1319	-68 ³	-936 ²
Society per QALY	14262	-4210 ²	-99127 ¹	9399	-7611 ²	-490705 ²
Health care per QALY	5246	3188	-29041 ¹	3512	-1368 ²	-8396 ²

¹ more cost, less effect; ² less cost, more effect; ³ no incremental costs per quitter could be calculated because equal effectiveness, difference in cost is presented.

Discussion

The objective of this paper was to study which intervention, bupropion, nortriptyline or placebo, in combination with a behavioural intervention, was most cost-effective in facilitating smoking cessation and increasing the number of QALYs in patients at risk for COPD or with existing COPD.

Results indicated that the effect after one year on smoking cessation was almost equal for bupropion (20.9%) and nortriptyline (20.0%). The effect in the placebo group was lower (13.5%). We did not estimate the lifetime effect of the intervention on for quality adjusted life expectancy, but measured the change in QALYs after one year. With both bupropion and nortriptyline, respectively 0.04 and 0.02 QALYs were gained compared to baseline. In the placebo group there was a slight mean reduction in QALYs of 0.004.

According the societal and health care perspective, the costs in the placebo group (€1212 and € 383, respectively) were lower than the costs made in the bupropion group (€1368 and €562, respectively) and lower than in the nortriptyline group (€1906 and €616, respectively). If willing to pay more than €2000 for a quitter or more than €4000 for a QALY, bupropion was the most cost-effective intervention according to both perspectives.

Overall, the effects in terms of smoking cessation and QALYs gained were higher and the costs were lower in participants at risk for COPD when compared to participants with existing COPD. The conclusion per subgroup differed from the conclusion of the total group due to the fact that the effect of the participants at risk in the placebo condition was much larger than in the participants with existing COPD. Since the subgroups were only small, we only present the outcomes and do not interpret the findings.

In contrast to our expectations, nortriptyline was in none of the comparisons the most cost-effective intervention due to slightly smaller effect compared with bupropion and very high costs registered in the cost diaries for visits to health care professionals and sick leave from work by only three participants in this group. These outliers increased the mean value by which the missing cost diaries were imputed. However, as it is reality that only few people are responsible for high health care costs, it is not valid to exclude these participants from the analyses. One explanation for the higher costs in the nortriptyline group could be that these participants had poorer health at baseline and as a result a higher medical consumption. The nortriptyline group consisted of relatively more participants with existing COPD (65%) compared with bupropion (51%) and placebo (54%). As we had not made a registration of health care costs before baseline, we cannot exclude a difference in health care

consumption in advance. A second possible reason for the high costs in the nortriptyline group could be that participants using nortriptyline experienced more side effects of the treatment. Wagena et al. reported that significantly more participants using nortriptyline reported to have a dry mouth, diarrhoea or constipation and fatigue.⁶ More side effects corresponded with higher costs in all three groups. Having stopped earlier with the study medication was associated with higher costs only in the nortriptyline group. More studies are needed to find out whether the use of nortriptyline is related to a higher medical consumption and whether the findings of this study can be replicated.

The cost analyses concern some uncertainties and several assumptions had to be made. The cost diary used was based on a diary of which the validity to obtain data on health care consumption was assessed previously.¹¹ Nonetheless, as the percentage of participants that missed maximum three was only 53.7%, the costs were imputed and bias could have occurred. This bias might have caused an overestimation of the costs, as people who have not filled in a diary possibly made no costs. However, there were no differences between the groups in percentage of missed cost diaries and sensitivity analyses showed that when varying from intention to treat analyses to analyses with participants who missed maximum three cost diaries, the conclusions of the study remained the same. Sensitivity analyses also demonstrated that varying the intervention costs between minimal and maximum did not change the conclusions.

Only one other randomised trial has evaluated the efficacy of bupropion in patients with COPD, but did not perform cost analyses.¹² Cost-effectiveness analyses of bupropion for smoking cessation in healthy subjects showed that the incremental cost per life-year saved is about €940 to €2210.¹³ A dynamic population model of disease progression in COPD showed that if in one year 25% of the patients receive bupropion plus intensive counselling than the costs per QALY were €7300.¹⁴ The results of both studies are in the same magnitude as the results found in the current study. Recently, Hall et al. published a study, which demonstrated that in healthy subjects nortriptyline was more cost-effective than bupropion if only intervention costs were included.¹⁵ This is not surprising, as in the current study, the intervention costs for nortriptyline were also lower than for bupropion, and the efficacy in both groups was about the same. Unfortunately, Hall et al. did not present the cost of medical consumption, which was in the current study much higher in the nortriptyline group.

In conclusion, if willing to pay more than €2000 for a quitter or more than €4000 for a QALY, bupropion in combination with a behavioural intervention

seems the most cost-effective compared to nortriptyline and placebo in patients at risk for COPD or with existing COPD. Since the Dutch cut-off point for cost-effectiveness is about €18000 per QALY, these costs are quite low. However, as the analyses concern some uncertainties and assumptions had to be made, the results have to be interpreted with care and future studies are needed to replicate the findings.

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Chapter 3

Reimbursement for smoking cessation treatment
may double the abstinence rate:
results of a randomised trial

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Abstract

Introduction

Few smokers who try to quit smoking use smoking cessation treatment (SCT) and cost could be one factor. To increase the number of successful quitters, we assessed whether financial reimbursement for SCT would encourage the use of SCT and would as a result increase the 6-month point abstinence rate.

Methods

We recruited smokers aged over 18 years from a random sample of Dutch inhabitants insured by one health insurance company.

The smokers were randomly assigned to the intervention group (n=632) or control group (n=634). Respondents in the intervention group received an offer of reimbursement for nicotine replacement therapy, bupropion, and behavioural counselling. No reimbursement was offered to the control group. To preclude a change of behaviour due to disappointment in the control group, we used a randomised consent design.

Results

During the reimbursement period, 10.8% smokers in the intervention group reported having used SCT compared with 4.1% in the control group (OR=2.9; 95% CI 1.8-4.7). In the intervention group, 23.4% smokers tried to stop compared with 20.8% in the control group (OR=1.2; 95% CI 0.9-2.4). After six months, the biochemically validated 7-day point prevalence abstinence rate was 5.5% in the intervention group and 2.8% in the control group (OR=2.3; 95% CI 1.2-4.1).

Conclusion

Reimbursement for SCT seems efficacious in increasing the use of SCT and may double the number of successful quitters.

Introduction

There are a number of treatment methods available to help people stop smoking, for example, counselling, nicotine replacement therapy (NRT), and non-nicotine pharmacotherapy. Numerous studies have examined the efficacy of smoking cessation treatment (SCT). Research indicates that using SCT increases short and long term abstinence rates compared with placebo.¹⁻⁵ Despite this evidence, few smokers who attempt to quit, use SCT.^{6,7} Cost could be a limiting factor in the use of SCT. One way of overcoming this limitation is to offer financial reimbursement for SCT as happens in the UK and some other jurisdictions.^{8,9}

Three randomised controlled trials¹⁰⁻¹² and two controlled trials^{13,14} have already assessed the effects of reimbursements for smokers on the use of SCT and smoking cessation. These studies and their results are described in a Cochrane review assessing the effects of healthcare financing systems for increasing the utilization of smoking cessation treatment.¹⁵ However, these studies had one or two important restrictions. First, to reach as many smokers as possible, we consider it important to offer reimbursement for all available and efficacious smoking cessation methods. In the studies mentioned above, the effects of reimbursement were only examined for one or two smoking cessation methods. Two studies examined the effects of reimbursement for NRT,^{10, 11} one study offered reimbursement for NRT and bupropion¹³ and two studies offered reimbursement for NRT and behavioural counselling.^{12,14} Second, to examine the overall effects of reimbursement, the study population should include a general sample of smokers. However, one study included only smokers willing to quit smoking,¹⁰ and another study included smokers who were interested in receiving a financial benefit.¹¹ These studies may overestimate the effect of reimbursement when the results are extrapolated to a general population of smokers.

We conducted a randomised trial in a general sample of smokers to examine the effects of financial reimbursement for all SCT that have been shown to be efficacious and are available in the Netherlands. We hypothesized that reimbursement for SCT would increase the use of SCT, the number of smokers who attempt to quit, and the abstinence rate. In addition, we assessed whether social economic status, tobacco consumption at baseline, attempts to quit in the past and the use of SCT in the past would modify the effects of reimbursement. We hypothesized that reimbursement would be most effective in increasing the use of SCT and the number of quit attempts in the low-income group. Furthermore, research has shown that a lower daily tobacco consumption is a predictor of successful smoking cessation.¹⁶

Finally, we were interested to know whether more quit attempts in the past, and having used SCT in the past would increase the effectiveness of reimbursement. In the literature, however, no evidence was found to support firm hypotheses.

Figure 3.1 Study design and assessments.

Methods

Setting and recruitment

In the Netherlands, no reimbursement for smoking cessation treatment is available. NRT is provided over the counter and bupropion can be obtained through a general practitioner. When planning the study, a difference in the 6-month abstinence rate of 12% in the group that is offered reimbursement and 6% in the group without reimbursement was judged clinically relevant. To establish this difference statistically, a target sample size of 525 smokers per group was needed when assuming a type 1 error of 0.05 (two-tailed) and a power of 90%. This number accounts for a lost to follow-up of 10%. The study participants had to be insured by health insurance company 'De Friesland Zorgverzekeraar'. The smokers recruited did not have to be motivated to quit smoking, but had to be at least 18 years old. Only one smoker per household was allowed to participate.

A random sample was taken of 12000 Dutch inhabitants of a northern province (Friesland). The Dutch Institute for Public Opinion and Market Research ('TNS NIPO') was able to contact 5651 inhabitants by telephone and asked if they wanted to participate in a study about smoking, cessation and the use of SCT. No further information was provided regarding the study. 2568 persons refused to speak to the employee of TNS NIPO, and 681 could not be reached. No telephone number was available for the remaining people. As not enough eligible smokers were recruited from the first random sample, a second random sample was taken of 30000 inhabitants. From this second sample, two smaller samples were taken of 6000 and 3000 inhabitants respectively, of which respectively 2318 and 747 inhabitants were contacted.

Study design

All smokers who gave oral consent for participating in the study were randomly assigned to the intervention or control group. The authors performed the randomisation using a list of computer-generated randomisation codes. These codes were pre-stratified by postal codes to avoid differences between the groups in demographic characteristics. Since employees from TNS NIPO contacted the smokers, the authors did not know the participants when performing the randomisation. Only smokers in the intervention group were offered reimbursement. As reimbursement was expected to be a popular intervention, smokers in the control group could have been disappointed if they knew that they were not being offered this benefit. Disappointment could have led to selective dropout or unwanted changes in behaviour. To avoid this, we used a randomised consent design¹⁷ in which the control group was blinded with regard to the existence of the intervention group (see Figure 3.1 for the design of the study). The blinding of the control

group was checked at the end of the study by the first author (JK) by way of telephone interviews. Before randomisation, we told all the smokers that the aim of the study was to assess attitudes towards smoking, smoking cessation and the use of SCT. After randomisation, only smokers in the intervention group were told that they participated in a study that assessed the effects of reimbursement for SCT. Together with the baseline assessment, smokers in both the intervention and control group gave written informed consent for participation in the study. The study was approved by the Medical Ethics Committee of the Trimbos Institute in Utrecht, The Netherlands.

Figure 3.2 Participants flow chart and reasons for dropout
¹ intention to treat population; ² per protocol population

Intervention

For a period of six months, smokers in the intervention group had the opportunity to apply for reimbursement for SCT. They received a leaflet with a description of the SCTs for which reimbursement was available, and information on how to receive the reimbursement. Smokers in the intervention group could receive full reimbursement for pharmacological treatment (bupropion and NRT (chewing gum, patch, tablet, sublingual tablet and inhaler)), behavioural counselling (written advice, telephone or face to face counselling) or a combination. To receive reimbursement, they had to send the receipt and two statements of personal contact with a health care professional (general practitioner, general practice nurse, physician, psychologist or health community worker) to the health insurance company. Before the study started, all the health care professionals in the study region were informed about the study objective and the procedure by which the intervention group could receive reimbursement. No limit was set on the number of applications for reimbursement.

Assessments

Figure 3.1 shows the timing of the questionnaires, the written reminders and telephone reminders. We collected information by means of the baseline questionnaire on the following demographic variables and smoking characteristics: age, gender, educational level, annual income, type of health care insurance, the number of daily smokers, tobacco consumption at baseline, mean age at onset of smoking and the level of nicotine dependence, the number of quit attempts and the use of SCT in the past. The educational level of participants was classified as low (primary and lower vocational education), middle (lower secondary and intermediate vocational education) or high (secondary school, higher professional school and university). A gross annual income of less than €20000 was defined as low, between €20000 and €30000 was defined as middle and more than €30000 was considered to be a high income. The level of nicotine dependence was measured by the Fagerström Test for Nicotine Dependence (FTND).¹⁸

The effects of reimbursement on the outcome measurements were assessed with data collected by the 6-month assessment. The 6-month questionnaire included questions on the number of respondents using SCT, the number of respondents attempting to quit and the self-reported abstinence rates. The use of SCT was defined as the self-reported use of SCT. Participants were defined as having made a quit attempt when they reported not having smoked for at least 24 hours since the start of the study because they were trying to quit and not for some other reason. Self-reported abstinence was defined as not having

smoked for at least seven days preceding the questionnaire and was biochemically confirmed by an expired air carbon monoxide level lower than seven parts per million (ppm).¹⁹

Statistical analysis

An analysis plan was prepared in advance. The investigators were not blinded for the treatment condition. Both intention-to-treat (ITT) and per protocol (PP) analysis were performed. Participants who were considered ineligible after randomisation were excluded from the analysis. In the ITT analysis, non-respondents, participants lost to follow-up and dropouts were considered to be smokers who had not used SCT and had not quit smoking. In the PP analysis, only respondents who returned the 6-month questionnaire were included.

Risk differences (RD) and odds ratios (OR) with corresponding 95% confidence intervals (CI) were calculated to compare both study groups on primary and secondary outcomes. Odds ratios were adjusted for age and gender. Multivariate logistic regression analyses were performed to test whether educational level, tobacco consumption at baseline, the number of quit attempts in the past and the use of SCT in the past modified the association between reimbursement on the one hand and the use of SCT and the number of smokers who tried to quit on the other. A variable was considered an effect-modifier when the Wald-test on the interaction term was significant. The level of significance was set at $\alpha < 0.05$ (two-tailed). Stratum specific RDs were calculated for effect modifiers only. The Z-test was used to assess whether the stratum specific RDs differed significantly. We performed PP analyses, as information from both the baseline and the 6-months questionnaire was required to determine effect modification. This information was missing for most dropouts. Because only 64.3% of the smokers provided information concerning their income, educational level was used as a proxy measure.

Results

Participant characteristics

Figure 3.2 shows that overall 8716 inhabitants were contacted. Of these inhabitants, 2018 smokers cooperated with the telephone interview of which 1320 smokers gave oral consent for participation in the study. These 1320 smokers were randomly assigned to the intervention (n=658) and control group (n=662).

Twenty-six of the participants from the intervention group and 28 from the control group turned out to be ineligible after randomisation, leaving respectively 632 and 634 participants for the ITT analyses. The baseline characteristics of the participants are presented in Table 3.1. The mean age of the participants was 39.7 (sd 12.8), 55.3% were male and 80.0% had a Sickness Fund insurance.

Table 3.1 Baseline demographics and smoking characteristics.

	Control group (n=634)	Intervention group (n=632)
Age in years, mean (sd)	39.9 (12.8)	39.5 (12.9)
Males, n (%)	338 (53.3)	362 (57.3)
Educational level, n (%)		
low	169 (26.7)	180 (28.5)
middle	299 (47.2)	268 (42.4)
high	125 (19.7)	115 (18.2)
missing	41 (6.5)	69 (10.9)
Annual income, n (%)		
low	172 (27.1)	153 (24.2)
middle	138 (21.8)	113 (17.9)
high	129 (20.3)	109 (17.2)
missing	195 (30.8)	257 (40.7)
Health care insurance, n (%)		
private insurance	125 (19.7)	102 (16.1)
Sickness Fund insurance	496 (78.2)	517 (81.8)
missing	13 (2.1)	13 (2.1)
Smoking characteristics		
daily smoker, n (%)	570 (89.9)	531 (84.0)
Fagerström Test of Nicotine Dependence, mean (sd)	3.3 (2.0)	3.5 (2.1)
age of onset of smoking in years, mean (sd)	16.1 (4.3)	16.2 (3.7)
daily tobacco consumption, mean (sd)	13.6 (9.0)	13.7 (9.6)
Tobacco products, n (%)		
smoking cigarettes	169 (26.7)	144 (22.8)
smoking hand-rolled cigarettes	312 (49.2)	318 (50.3)
smoking cigars/ cigarillo's/pipe	24 (3.9)	16 (2.5)
smoking different tobacco products	75 (11.8)	58 (9.2)
missing	54 (8.5)	96 (15.2)
Attempts to quit in the past, n (%)		
none	154 (24.3)	140 (22.2)
1	136 (21.5)	138 (21.8)
2	121 (19.1)	119 (18.8)
3	76 (12.0)	66 (10.4)
more than 4	105 (16.6)	100 (15.8)
missing	42 (6.6)	69 (10.9)
Use of SCT in past, n (%)	139 (21.9)	109 (17.2)

Figure 3.2 demonstrates that the dropout rate in the intervention group was higher compared with the control group for both baseline and 6-month questionnaire. The mean age of the dropouts was 37.7 (sd 13.3), 54.2% were male and 78.4% had a basic health care insurance. We tested whether respondents differed from dropouts on the baseline characteristics. The dropouts were significantly younger than the respondents ($t=2.8$, $df=1190$ $p<0.05$). No differences were found for gender and type of health care insurance. Only a few dropouts had answered questions about education and income. One year after the study had started, we collected data on the smoking behaviour and the use of SCT of 89 dropouts (11 of the 89 contacted dropouts refused (12.4%)) through telephone interviews. These interviews revealed that 18.8% of the dropouts in the intervention group and 13.3% of the dropouts in the control group had quit smoking.

Use of smoking cessation treatment

Table 3.2 shows that 68 participants in the intervention group (10.8%) and 26 participants in the control group (4.1%) used SCT during the reimbursement period. The number of respondents using SCT was significantly higher in the intervention group compared with the control group (ITT: RD=6.7; 95% CI 3.8-9.5; OR=2.9; 95% CI 1.8-4.7 and PP: RD=10.2; 95% CI 6.3-14.0; OR=3.4; 95% CI 2.1-5.5). None of the possible effect-modifiers modified the effect of reimbursement on the use of SCT.

Table 3.2 Effects of reimbursement on the number of respondents who used SCT, who tried to quit and the number of self-reported and biochemically validated quitters.

	Control group n (%)	Intervention group n (%)	RD (95% CI)	OR ¹ (95% CI)
Intention to treat analysis	634	632		
Using SCT	26 (4.1)	68 (10.8)	6.7(3.8-9.5)	2.9 (1.8-4.7)
NRT	6 (0.9)	23 (3.6)	2.7 (1.0-4.3)	4.0 (1.6-9.9)
bupropion	6 (0.9)	27 (4.3)	3.3 (1.6-5.1)	5.0 (2.0-12.2)
behavioural counselling	7 (1.1)	32 (5.1)	4.0 (2.1-5.8)	5.1 (2.2-11.6)
Attempted to quit	132 (20.8)	148 (23.4)	2.6 (-2.0-7.2)	1.2 (0.9-1.6)
Self-reported abstinence	35 (5.5)	49 (7.8)	2.2 (-0.5-5.0)	1.5 (0.9-2.4)
Bioch. validated abstinence	18 (2.8)	35 (5.5)	2.7 (0.5-4.9)	2.3 (1.2-4.1)
Per protocol analysis	503	444		
Using SCT	26 (5.2)	68 (15.3)	10.2 (6.3-14.0)	3.4 (2.1-5.5)
NRT	6 (1.2)	23 (5.2)	4.0 (1.7-6.2)	4.5 (1.8-11.2)
bupropion	6 (1.2)	27 (6.1)	4.9 (2.5-7.3)	5.7 (2.3-14.0)
behavioural counselling	7 (1.4)	32 (7.2)	5.8 (3.2-8.4)	5.8 (2.5-13.4)
Attempted to quit	132 (26.2)	148 (33.3)	7.1 (1.3-12.9)	1.4 (1.1-1.9)
Self-reported abstinence	35 (7.0)	49 (11.0)	4.1 (0.4-7.7)	1.7 (1.1-2.7)
Bioch. validated abstinence	18 (3.6)	35 (7.9)	4.3 (1.3-7.3)	2.6 (1.4-4.7)

¹ corrected for age and gender

In the intervention group and the control group the use of NRT was 3.6% and 0.9% respectively. The use of bupropion was 4.3% in the intervention group and 0.9% in the control group. The percentage of participants that consulted a health care provider for behavioural counselling was 5.1% in the intervention group and 1.1% in the control group. Table 3.2 shows that significantly more participants in the intervention group used NRT, bupropion and behavioural counselling when compared with the control group.

Number of respondents who attempted to quit

During the reimbursement period, 148 participants (23.4%) in the intervention group and 132 (20.8%) in the control group tried to quit smoking at least once (Table 3.2). ITT analysis showed no significant difference between the groups (RD=2.6; 95% CI -2.0-7.2; OR=1.2; 95% CI 0.9-1.6)), but PP analysis did (RD=7.1; 95% CI 1.3-12.9; OR=1.4; 95% CI 1.1-1.9)).

The use of SCT in the past modified the effect of reimbursement on the number of respondents who tried to quit. Stratified analysis showed that if smokers had used SCT in the past, significantly more smokers in the intervention group (52.7%) had tried to quit smoking compared with the control group (29.0%) (RD=23.7; 95% CI 10.7-36.7). If smokers had not used SCT before, 27.9% of the smokers from the intervention group tried to quit compared with 25.3% in the control group (RD=2.6; 95%CI -3.8-9.1). The difference between the two strata was statistically significant ($Z=2.8$, $df=2$, $p<0.01$). Multivariate logistic regression analyses showed that smokers with a middle educational level were less likely to try to quit when reimbursement was offered compared with smokers of a low educational level. However, stratified analysis showed that the difference between the intervention group and control group for smokers with a middle education level (RD=1.3; 95% CI -7.1-9.7) was not significantly smaller in comparison with smokers of a low educational level (RD=14.8; 95% CI 4.1-25.5) ($Z=1.94$, $df=2$, $p=0.052$). When reimbursement was offered, participants smoking less than 10 cigarettes at baseline tended to try to quit less often than respondents smoking 11 to 20 or 21 to 30 cigarettes per day. Stratified analysis showed that the difference between the intervention group and control group for participants smoking less than 10 cigarettes per day (RD=-1.1; 95% CI -10.4-8.1) was not significantly smaller if compared with participants smoking 11 to 20 cigarettes (RD=11.9; 95% CI 2.7-21.2; $Z=1.96$, $df=2$, $p=0.051$) or compared with participants smoking 21 to 30 cigarettes a day (RD=15.4; 95% CI -1.4-32.1; $Z=1.69$, $df=2$, $p=0.091$).

Number of quitters

Table 3.2 shows that after six months, 49 respondents in the intervention group (7.8%) reported to have quit smoking for at least seven days compared with 35

respondents (5.5%) in the control group. This difference was not significant in the intention to treat analysis (RD=2.2; 95% CI -0.5-5.0; OR=1.5; 95% CI 0.9-2.4), but was significant in the per protocol analysis (RD=4.1; 95% CI 0.4-7.7; OR=1.7; 95% CI 1.1-2.7).

We tried to biochemically verify the smoking status of all self-reported quitters. We were unable to make an appointment with 11 self-reported quitters in the control group (31.4%) and six quitters in the intervention group (12.2%). There was no clear reason for this difference. In the control group three quitters had started smoking (8.6%) and three refused to participate (8.6%). In the intervention group, also three quitters had smoked again (6.1%) and four did not want to cooperate with the biochemical validation (8.2%). Expired air CO samples could be taken from 18 of the 35 self-reported quitters in the control group (51.4%) and 36 of the 49 self-reported quitters in the intervention group (73.5%). One biochemically validated quitter in the intervention group had a CO level higher than 7 ppm and was considered to be a smoker. The difference in biochemically verified point prevalence abstinence rates was 2.7 (95% CI 0.5-4.9) according to ITT analysis (OR=2.3; 95% CI 1.2-4.1), and 4.3 (95% CI 1.3-7.3) according to PP analysis (OR=2.6; 95% CI 1.4-4.7) (Table 3.2).

Blinding of the control group

At the end of the study, a random sample of 50 respondents in the control group were asked whether they knew about the intervention group or a study about reimbursement for SCT during the study. Three respondents could not be reached (6.0%) and four refused to participate (8.0%). None of the 43 interviewed respondents (86.0%) knew about the reimbursement offered in the intervention group. Forty respondents (80.0%) did not know about a reimbursement study for SCT either. Two respondents (1.0%) were not sure and one participant (0.5%) knew about a reimbursement study, but did not know that he had participated in this study.

Discussion

Results showed that participants from the intervention group had a 2.9 times higher chance of using smoking cessation treatment during the 6-month period compared with participants from the control group and were 1.4 times more likely to have quit smoking. However, the difference in quit attempts was only significant when per protocol analyses were performed. A 1.7 times higher point prevalent self-reported abstinence rate was found in the intervention group compared with the control group. This difference was also only significant when per protocol analyses were performed. The difference in biochemically verified abstinence rate was significant in both intention to treat and per protocol analysis. CO assessments showed that the chance of being abstinent at 6 months was 2.3 times higher in the intervention group than in the control group.

After six months, only having used SCT in the past appeared to be an effect modifier and increased the number of respondents who tried to quit during the reimbursement period. If smokers had used SCT in the past, the difference in use of SCT between the intervention group and the control group was larger than if smokers had not used SCT before. We suppose that smokers, who have used SCT in the past, are more experienced with smoking cessation and the use of SCT. When reimbursement for SCT was offered, it might have been easier for these smokers to make another quit attempt and use SCT compared with smokers who had not used SCT before.

The results of this study showed that reimbursement is effective in increasing the use of SCT. However, the percentage of smokers who used SCT when reimbursement was offered seems low. Nonetheless, when calculated for only smokers who tried to quit, the percentage of smokers who used SCT was about 45%. Compared with the studies carried out by Fiore et al.¹ and Zhu et al.,⁷ in which correspondingly 8% and 20% of the smokers trying to quit without intervention used SCT, the percentage of quitters using SCT more than doubled when reimbursement was offered. The effect of reimbursement on the abstinence rate was smaller than the effect of reimbursement on the use of SCT. This can be explained by the fact that the effect on the number of quitters is dependent on the number of smokers trying to quit and the effectiveness of the used SCT. Because the maximum long-term effectiveness of SCT is currently around 24%,²⁻⁵ the effect of reimbursement on the abstinence rate will always be limited.

As presented in the result section, the percentage of self-reported quitters that could be biochemically validated was 22.1% higher in the intervention group. The difference between the two groups was mainly caused by the inability to

make appointments with the self-reported quitters in the control group. Less involvement and as a result less commitment of participants in the control group could be an explanation for the difference in scheduling problems. Because of this difference, the results of the biochemical validation should be interpreted with care. However, we expect that not many quitters would have lied about their smoking status and that the bias in the self-reported abstinence rate is only small. The study was not a stop-smoking study; i.e. participants did not have to quit smoking and no reward or penalty was linked to the smoking status.

A consequence of using a randomised consent design was an increased likelihood that participants in the intervention group would drop out after the start of the study.²⁰ The response to the baseline questionnaire in the intervention group was indeed lower compared with the response rate in the control group. This can be explained by the fact that only after randomisation the participants of the intervention group were informed about the intervention. As the study was more demanding for the intervention group than for the control group, it is not surprising that at baseline and even at the 6-month assessment more participants in the intervention group dropped out. In the intervention group, for example, the general practitioner and health insurance company were involved, the amount of study information was substantially larger, and to receive reimbursement, two personal contacts with a health care professional were required. As selective dropout is a threat to the internal validity of the study, we investigated whether the smoking behaviour of dropouts was different from the smoking behaviour of the respondents. We expected that dropouts were less likely to quit smoking than respondents but telephone interviews revealed that the quit rate among dropouts was higher. Some quitters stated that participating in the study was no longer important, as they had quit smoking. Because there was a high percentage of quitters among the dropouts, it is likely that selective dropout caused the effect of reimbursement on the number of quitters to be underestimated, rather than overestimated.

Although, many persons had to be approached to achieve the final sample size, there are three reasons to consider it unlikely for selection bias to have occurred during the recruitment. First, only random samples or the available databases were taken. Secondly, none of the contacted inhabitants knew about the purpose of the study and lastly, TNS NIPO, which contacted the inhabitants for the inclusion, was not involved in the study.

As all participants were inhabitants of one province, we compared the baseline and smoking characteristics of the study participants with a random sample of smokers of the national population, which is collected annually by STIVORO.²¹ The participants in the study seem comparable with the general population of

smokers with regard to age, gender, daily tobacco use, the use of smoking cessation treatment in earlier attempts and the percentage of subjects not motivated to quit smoking.

In conclusion, we may say that financial reimbursement for SCT can increase the use of SCT and might be able to double the number of (successful) quitters. Although aware of these results, the Dutch government decided not to offer reimbursement for SCT. As other treatments are currently being removed from the health insurance package for financial reasons, the government could not justify the introduction of SCT into the package. In the UK and several insurance plans in the USA reimbursement for SCT is already available, although not to the extent recommended by the updated smoking cessation guideline from the U.S Public Health service.^{1,22,23} To further decrease the percentage of smokers, the importance of reimbursement for SCT should be emphasized.

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Chapter 4

A randomised controlled trial to assess the effects of reimbursing the costs of smoking cessation therapy on sustained abstinence

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Addiction, in press

Abstract

Introduction

We studied whether reimbursement for smoking cessation treatment (SCT) can increase prolonged abstinence from smoking up to two years.

Methods

From the general population, we recruited smokers and randomly assigned them to a control group (n=634) or an intervention group (n=632). For six months, participants in the intervention group could apply for reimbursement and received information regarding the reimbursed SCT. Participants in the control group received no reimbursement or information.

In this follow-up study, prolonged abstinence from smoking was defined as reported being abstinent from at least seven days before the end of reimbursement until the follow-up assessment six months or two years later

Results

At six months after the end of reimbursement, 18 participants in the control group (2.8%) and 35 participants (5.5%) in the intervention group were reported sustained abstinence for at least six months (OR=2.0; 95% confidence interval (CI) 1.1-3.6). Two years after the reimbursement period, still 10 participants in the control group (1.6%) and 27 participants in the intervention group (4.3%) reported sustained abstinence (OR=4.1; 95% CI 1.7-10.2). The overall effectiveness of SCT increased with reimbursement and was 22% in the intervention group and 8% in the control group after two years.

Conclusion

Reimbursement may be an effective strategy to increase the prolonged abstinence rate even after two years.

Introduction

Smoking is the main risk factor for developing respiratory and cardiovascular diseases.¹ Stopping smoking is most essential for treatment and prevention, however, success rates of smoking cessation interventions are rather low.^{2,3}

From the literature, it is known that smokers who use smoking cessation treatment (SCT) have a higher probability of being a successful quitter after one year.^{4,5} Despite this knowledge, few quitters use these treatment methods.⁶ An opportunity to promote the use of SCT and to increase the success rate of a quit attempt is to offer reimbursement for all proven effective treatment methods.

In the Netherlands, currently no reimbursement for SCT is offered. Nicotine replacement therapy is available over the counter, and bupropion is available at pharmacies and can be obtained with a prescription of a health care provider. Also smoking cessation interventions offered by health care community centres or health care providers have to be paid for by the smokers themselves. Only if a smoker already has a smoking related disease, then smoking cessation interventions given by health care providers are often reimbursed. Some health insurance companies privately offer reimbursement for smoking cessation group interventions and alternative treatment methods like acupuncture and laser therapy.

To evaluate the potential effects of a reimbursement system in the general Dutch population, we previously conducted a randomised controlled trial.⁷ In this trial, for a period of six months, participants in the intervention group were offered full reimbursement for all proven effective and currently available treatments in the Netherlands, i.e. nicotine replacement therapy (NRT), bupropion, behavioural counselling, including smoking cessation interventions given by health care providers, or any combination of these interventions. The control group received care as usual and was not offered reimbursement for SCT. The results showed that at the end of a 6-month period of financial reimbursement, the use of smoking cessation treatment increased from 4.1% to 10.8% and the 7-day point prevalence abstinence rate increased from 2.8 to 5.5%.⁷

In the follow-up study that is presented in this paper, we primarily examined the effects of reimbursement for SCT on prolonged abstinence from at least seven days before the end of reimbursement until six months and two years later.

Furthermore, the concern was that if SCT is available for free that the effectiveness of the treatment methods would decline, i.e. smokers could be less motivated to quit. To evaluate this assumption, we related the cessation methods that were used during the reimbursement period to the self-reported prolonged abstinence outcomes at 6-month and 2-year follow-up.

Methods

Settings, participants and design

The setting, the recruitment of participants, the study design and the intervention have been described previously.⁷ To summarize, a general sample of 1320 smokers, who were insured at the same regional health insurance company, gave oral consent for participation in a study concerning smoking, smoking cessation and the use of SCT and were randomised to the intervention or control group. Participants did not have to be motivated to quit smoking. After randomisation, 54 participants were excluded as they appeared ineligible.⁷

Only smokers in the intervention group were told that they participated in a study that assessed the effects of reimbursement for SCT. Participants were not encouraged to stop smoking. Participants in the intervention group received by mail a letter about the offered reimbursement as well as a leaflet describing for which SCT reimbursement was available and how they could be reimbursed. No reimbursement or information was offered to participants in the control group. For example, twelve weeks treatment with bupropion including two visits to a general practitioner would cost €0 in the intervention group and €250 in the control group.

As we expected that participants in the control group might change their behaviour because they were disappointed, we used a double randomised consent design in order to blind them for the intervention group. The study was approved by the Medical Ethics Committee of the Dutch Trimbos Institute.

Assessments

To evaluate the long-term effects of the intervention, data were collected after the 6-month period of reimbursement and followed up at six months and at two years after the reimbursement period had ended. The smoking status at the end of the reimbursement period and at 6-month follow-up was assessed by self-report and validated by carbon monoxide breath tests two months later. Two years later, we tried to contact all respondents who reported being prolonged abstinent from smoking until 6-month follow-up and asked them about their smoking behaviour between the follow-up assessment at six months and at two years.

Outcomes

At baseline we collected data concerning age, gender, nicotine dependence, education and airway complaints. The level of nicotine dependence was measured by the six-item Fagerström Test for Nicotine Dependence (FTND), with scores ranging from 0-10 points.⁸ A score higher than 5 corresponds to a high level of nicotine dependence. The educational level was defined low for primary and lower vocational school, middle for lower secondary and intermediate vocational school and high for secondary and higher vocational school or university.

The primary outcome measure was prolonged abstinence from smoking. At 6-month follow-up, prolonged self-reported abstinence was defined as reported being abstinent for at least seven days preceding the end of the reimbursement period and not having smoked until the questionnaire six months later. Prolonged biochemical validated abstinence was defined as prolonged self-reported abstinence combined with an expired air carbon monoxide level lower than seven parts per million (ppm) at both the end of the reimbursement period and 6-month follow-up.⁹ Prolonged abstinence at two years was defined as self-reported abstinence since seven days preceding the end of the reimbursement period and reported not having smoked until the follow-up assessment two years later.

As smokers could be less motivated to quit if SCT is available for free, we examined the possibility that with reimbursement the effectiveness of SCT would decline. For that reason, we linked the cessation methods that participants had used during the reimbursement period to the self-reported prolonged abstinence outcomes at 6-month and 2-year follow-up. The used cessation methods were registered by questionnaire at the end of the reimbursement period. We did not assess the compliance of using SCT.

Statistical analysis

All eligible and randomised participants were included in the intention to treat (ITT) analyses, in which non-responders or dropouts were considered smokers. For the demographic variables and smoking characteristics, descriptive statistics were presented and χ^2 -tests and t-tests were performed. Risk differences (RD), (i.e. absolute change in risk attributable to intervention) and odds ratios (OR) with corresponding 95% confidence intervals (CI) were calculated to determine the difference between the control and intervention group on abstinence from smoking. The level of significance was set at $\alpha < 0.05$ (two-tailed).

Results

Participants

Of the 1266 included smokers, the mean age was 39.7% (12.8 standard deviation (sd)) and 55.3% was male. Of the participants, 25.7% had a low education level, 19.8% a middle education level and 18.8% a high level of education (35.7% was missing). The mean score on the FTND was 3.4 (2.1 sd) and on average people smoked 13.7 cigarettes (9.3 sd). At 6-month follow-up, questionnaires were completed and returned by 400 participants from the intervention group (63%) and 438 participants from the control group (69%) (Figure 4.1). Non-responders and dropouts were compared with those who returned the questionnaire. There were no significant differences, except for age. The non-responders and dropouts had a mean age of 38.0 years (13.6 sd) and the responders were 40.4 years (12.5 sd) old ($t=3.1$, $df=1190$, $p<0.01$). Of the participants that were still abstinent at 2-year follow-up, the mean age was 41.7 years (14.7 sd), 62.2% was male, the education level of 32.4% was low, 54.1% had a middle educational level and 13.5% had a high educational level. At baseline, the mean score of the FTND was 2.9 (2.0 sd) and smoked on average 12.9 cigarettes (6.9 sd).

Figure 4.1 Recruitment, study design, assessments and participants' flow chart.

Prolonged abstinence for six months

Six months after the reimbursement period, 18 participants in the control group (2.8%) and 35 participants in the intervention group (5.5%) reported abstinence for at least six months. Table 4.1 shows that significantly more quitters were abstinent in the intervention group (OR=2.0; 95% CI 1.1-3.6).

The smoking status of 6 of the 18 self-reported quitters in the control group (33.3%) and 24 of the 35 self-reported quitters in the intervention group (68.6%) was biochemically validated at both the end of the reimbursement period and 6-month follow-up. Table 4.1 shows that the biochemically validated 7-day point prevalence at 6-month follow-up and the 6-month sustained abstinence rate was significantly higher in the intervention group when compared with the control group.

Five smokers in the control group and three smokers in the intervention group, who reported abstinence at the end of the reimbursement period or at 6-month follow-up, appeared to be a smoker by biochemical validation. These smokers were not counted as self-reported quitters. No one who claimed prolonged abstinence was proven to be smoking by exhaled CO. No appointment for biochemical validation at both the end of the reimbursement period and 6-month follow-up could be made with nine of the 18 self-reported quitters (50.0%) of the control group, one other participant (5.6%) was in hospital and two participants (11.1%) refused to participate. Of the 35 self-reported quitters in the intervention group, no appointment could be made, at one or both occasions, with six self-reported quitters (17.1%) and five participants refused to participate (14.3%). Defining the participants who refused to participate to the biochemical validation as smokers, than the OR for 6-month sustained abstinence was 1.9 (95% CI 0.98-3.7) in favour of the intervention group.

Table 4.1 Effects of reimbursement on abstinence from smoking at 6-month and 2-year follow-up.

	Control group n (%)	Intervention group n (%)	RD (95% CI)	OR ¹ (95% CI)
Point prevalent abstinence				
6-month self-reported	44 (6.9)	62 (9.8)	2.9 (-0.1-5.9)	1.5 (1.0-2.3)
6-month biochemically validated	18 (2.8)	34 (5.4)	2.5 (0.3-4.7)	1.9 (1.1-3.5)
Prolonged abstinence				
6-month self-reported	18 (2.8)	35 (5.5)	2.7 (0.5-4.9)	2.0 (1.1-3.6)
6-month biochemically validated	6 (0.9)	24 (3.8)	2.9 (1.2-4.5)	2.8 (1.3-5.8)
2-year self-reported	10 (1.6)	27 (4.3)	2.7 (0.8-4.5)	4.1 (1.7-10.2)

¹corrected for age and gender

Prolonged abstinence for two years

Of the 53 self-reported quitters, 48 could be contacted for the 2-year follow-up measurement. Two quitters in the intervention group (5.7%) and three quitters in the control group (5.6%) could not be reached (Figure 4.1). Ten participants in the control group (1.6%) and 27 participants in the intervention group (4.3%) reported abstinence for at least two years (OR=4.1, 95% CI 1.7-10.2) (Table 4.1). The mean time of abstinence was 26.7 months (1.9 sd) in the control group and 28.2 months (1.9 sd) in the intervention group ($t=2.0$, $df=35$, $p<0.05$). The relapse rate after the 6-month follow-up assessment was 44% in the control group and

23% in the intervention group. This difference in relapse rate was not statistically significant ($\chi^2(1)=2.6, p=0.1$).

The effectiveness of SCT

Of the 68 participants that used SCT during the reimbursement period in the intervention group, 42 (61.8%) combined behavioural support and pharmacological treatment. In the control group, 10 (38.5%) of the 26 participants used both treatment methods. As the treatment methods were not mutually exclusive, we did not present the effectiveness per treatment method. At 6-month follow-up, the overall effectiveness of SCT in the intervention group was 25%, i.e. 17 participants of the 68 participants who had used SCT were abstinent (Table 4.2). Two years after the reimbursement period, the overall effectiveness was 22%. Without reimbursement, i.e. in the control group, the overall effectiveness of SCT was 15% at 6-month and 8% at 2-year follow-up.

Of the users of SCT in the intervention group, only 45 participants (66.2%) applied for reimbursement. Thirty-eight participants received reimbursement for pharmacotherapy (combined with visits to the general practitioner in 40% of the cases) and seven participants applied for reimbursement of health care providers only. Eighty percent of the applications were send in the first three months of the reimbursement period. Participants who applied for reimbursement were older (47.9 years, 10.5 sd) and 44.4% had a low educational level. Both were not significantly different from the intervention group.

Table 4.2 Use and effectiveness on self-reported prolonged abstinence of SCT in the control and intervention group.

Group	Follow-up	Smoking status	Total use, n (%)	Effectiveness, %
Control group	6 years	smokers (n=616)	22 (4)	15
		quitters (n=18)	4 (22)	
	2 years	smokers (n=624)	24 (4)	8
		quitters (n=10)	2 (20)	
Intervention group	6 months	smokers (n=597)	51 (9)	25
		quitters (n=35)	17 (49)	
	2 years	smokers (n=605)	53 (9)	22
		quitters (n=27)	15 (56)	

Discussion

Sustained abstinence

In this follow-up study, we primarily assessed the effects of reimbursement for SCT on sustained abstinence. Results showed that with reimbursement significantly more participants were abstinent six months and two years after the reimbursement period had ended. The adjusted odds of being abstinent, controlling for age and gender, was two to four times higher when reimbursement was offered compared to no financial compensation. Only one other study reported the effects of reimbursement on prolonged abstinence, but in this study of Boyle et al.¹⁰ no effect was found. In contrast to our study, participants in the study of Boyle et al.¹⁰ were not explicitly informed about the offered reimbursement and accordingly only 30% of the smokers in the benefit group were aware of the reimbursement. The suggestion that reimbursement for SCT is more effective when smokers are informed and aware of the coverage seems supported by US data.¹¹⁻¹³

The effects of full reimbursement versus no reimbursement for SCT on self-reported point prevalence abstinence after six months were studied by two controlled trials of Hughes et al.¹⁴ and of Schauffler et al.¹⁵ In a Cochrane review, the point prevalence abstinence data^{14,15} and the prolonged abstinence data¹⁰ were pooled, which resulted in an odds of 1.48 (95% CI 1.17-1.88) in favour of offering reimbursement for SCT.¹⁶ In addition, if comparing full with partial coverage, studies of Curry et al.¹⁷ and Hughes et al.¹⁴ demonstrate that more participants quit smoking at six months in the full coverage group (OR=2.49; 95% CI 1.59-3.90).¹⁶

Effectiveness of reimbursed SCT

Furthermore, we examined the effectiveness of reimbursed SCT. At 6-month follow-up, the overall effectiveness of SCT was 10% higher with than without reimbursement and two years after the reimbursement period the difference was 14% in favour of the reimbursement group. The concern that the effectiveness of the treatment methods would decline if SCT was available for free, is not supported by our results. An explanation for an increased effectiveness with reimbursement might be that participants had to contact their health care provider before they could obtain coverage. From the literature, it is known that personal contact with a health care provider increases the abstinence rate.^{4,18} Second, reimbursed participants may have used SCT for longer periods, which can also increase the success rate of a quit attempt.

The effectiveness of SCT on prolonged abstinence from smoking after two years in the intervention group (22%) is relatively high. Data from Cochrane Reviews show that the 12-month effectiveness in clinical studies was between 13 and 20% for the diverse treatment methods.¹⁹⁻²¹ Since, in this study only a small number of participants used SCT, it may give an indication that with reimbursement the real-life effectiveness is not lower than in clinical studies, but no hard conclusions can be drawn.

Limitations

A limitation of this study concerns the validation of self-reported quitters. We measured expired air carbon monoxide, which is non-invasive and easy to use, but has a restricted time period and low sensitivity if smoking less than 10 cigarettes a day. Not all self-reported quitters could be biochemically validated and the number of participants with whom no appointment could be made was higher in the control group. Only 33% of the self-reported quitters in the control group could be biochemically validated at the end of the reimbursement period and 6-month follow-up and in the intervention group this was 69%. Less involvement in the study and less compliance could be an explanation for the difficulties that were present when making appointments for biochemical validation with participants in the control group. Because of this difference between the groups, the results of the biochemical validation should be interpreted with care. However, one should keep in mind that in the current study no reward or penalty was linked to smoking status. Still, quitters could have lied about their smoking status. The same is true for the quitters at 2-year follow-up, i.e. no biochemical validation was performed with this assessment.

Concluding remarks

Taken into account the limitations, we cautiously conclude that reimbursement for SCT in combination with information may be effective in increasing prolonged abstinence rates, even after two years and that reimbursement might increase the success rates of evidence based SCT.

The impact of this study on the Netherlands and on other countries depends on the generalizability of the study results. Despite the fact that the study was done in one region with one local health insurance company, there is no reason to assume that the results are not generalizable to the general population. Moreover, since we explicitly tried to fit the real-life situation, the examined reimbursement system could almost be directly implemented into the Dutch health care system. This study showed that reimbursement for SCT may increase the number of quitters by 2.7%. In the Netherlands, 28% of the population smokes. If implemented in the Netherlands, reimbursement could help 120.000 people to stop smoking for at least two years. The generalizability of the results of this study to other countries is depended on the differences in

health care system between the countries, which is not easily to evaluate (see chapter 5).

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Chapter 5

Health care financing systems for increasing the
utilisation of smoking cessation treatment

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The Cochrane Library, Issue 1. Oxford: Update Software, 2005. (Shortened version)

Abstract

Introduction

Smoking cessation treatment increases the number of successful quitters compared with unaided attempts to quit. However, only a small proportion of smokers take up treatment. The primary objective was to assess whether financial support through healthcare financing interventions for smoking cessation treatment increase abstinence from smoking. Secondary, the effects of healthcare financing interventions on the utilization and/or prescription of smoking cessation treatment and the number of smokers trying to quit were evaluated.

Methods

Eligible studies were identified by a computer-aided search of the Cochrane Central Register of Controlled Trials (CENTRAL), Issue 3, 2003, MEDLINE and EMBASE, screening references, and contacting experts in the field. We included randomised controlled trials, controlled trials and interrupted time series in which the study population consisted of smokers or healthcare providers.

We performed meta-analysis using a random effects model to estimate the general effect of the financial intervention. We included economic evaluations when a study presented the costs and effects of two or more alternatives.

Results

Six studies were included. The four studies that compared full coverage with no coverage all showed an increase in: abstinence rate (odds ratio (OR)=1.48; 95% confidence interval (CI) 1.17 to 1.88; risk difference (RD)=0.02; 95% CI 0.00-0.05), in number of participants with at least one quit attempt (OR=1.32; 95% CI 1.18 to 1.49; RD=0.05; 95% CI 0.03-0.08) and in the use of smoking cessation treatment (OR=2.12; 95% CI 1.50-3.00; RD=0.04; 95% CI 0.01-0.06). When full coverage was compared with partial coverage, the abstinence rate, the number of participants making a quit attempt and the use of smoking cessation treatment were higher with full coverage in all three studies that examined this comparison, but the increase was not always significantly higher. One study compared partial coverage with no coverage and found no significant differences. When full coverage was compared with partial or no coverage, the costs per user who quit varied between \$260 and \$2330.

Conclusions

Healthcare financing systems, which offer full coverage, can increase the use of smoking cessation treatment, the number of participants making a quit attempt and can increase the prolonged abstinence rates at relatively low costs when compared with partial or no coverage.

Introduction

A number of interventions, including counselling and pharmacotherapy, can help individuals to quit smoking. Although the absolute number of people who make a successful quit attempt is low, quit rates are higher with the use of smoking cessation treatment than without.¹⁻⁴ Without the use of smoking cessation treatment, only about 3% remain abstinent after one year.⁴ Despite this evidence, the use of smoking cessation treatment is still limited.⁵ Costs are a significant barrier to the use of smoking cessation treatment. Healthcare providers may be deterred from offering treatment if they do not receive reimbursement, and patients may be deterred if they must pay for treatment costs. We hypothesized that provision of financial support to providers and/or patients would increase the use of smoking cessation treatment with a corresponding increase in the number of smokers undertaking a successful quit attempt.¹⁻⁴

As healthcare costs increase and resources are limited, it is important to determine whether financial support for smoking cessation treatment is cost effective.⁶ In general, smoking cessation treatments are highly cost effective when compared with other common preventive healthcare treatments like treating mild to moderate hypertension and lowering cholesterol levels.^{6,7} However, no previous review has evaluated the cost effectiveness of healthcare financing systems for increasing the utilization of smoking cessation treatment. We hypothesized that like other smoking cessation interventions healthcare financing interventions would also be cost effective.

The primary objective of this review was to assess, by pooling the results of individual studies, the effect of healthcare financing interventions for smoking cessation treatment on abstinence from smoking. As a secondary objective, we examined the effects of healthcare financing interventions on the use and/or prescription of smoking cessation treatment and on the number of smokers trying to quit. We also aimed to assess the cost effectiveness of healthcare financing interventions. We examined the costs per additional quitter, per life year gained or per quality-adjusted life year gained.

Methods

Study selection

Types of study design, population and interventions

We included randomised controlled trials, controlled trials and interrupted time series. The study population consisted of smokers or healthcare providers, as the primary and secondary objectives were assessed from either a smoker's or a healthcare provider's perspective. For smokers, the aim of the healthcare financing interventions had to be to encourage the use of smoking cessation treatment. When the intervention was directed towards healthcare providers, then the intervention had to affect the prescription of treatment methods or the smoking behaviour of the patients. (Table 5.1)

Table 5.1 Definitions of healthcare financing interventions.

Directed at patients	Directed at healthcare providers
Premium or user fees (= amount of money paid by a patient in exchange for insurance coverage)	Salary (= payment for a number of working hours or sessions per time unit)
Coverage or financial incentives (= amount of money paid by the insurance company for medical expenses of patient)	Capitation (= set amount of payment per patient for providing specific care)
Co-payment or out-of-pocket payment (= patient's payment for medical costs in addition to coverage provided by the third party payer)	Fee-for-service (= payment for every unit of care provided)
	Target payment (= payment made in respect of achieving an agreed target)
	Fund holding and organization level payment (= improve working conditions within an organization and can indirectly influence the salary of a healthcare provider)

We differentiated between full, partial and no financial coverage. There were no restrictions on the type of smoking cessation treatment for which the financial benefit could be offered. This could include pharmacotherapy, e.g. nicotine replacement therapy and bupropion, and/or behavioural counselling. When the financial intervention of a study was aimed at more than one type of smoking cessation treatment, the effect of the financial intervention could be spread out over the different types of products. Studies of financial interventions that are aimed at more than one type of smoking cessation treatment, therefore, cannot formally be compared with studies that offer coverage for only one product. As a smoker could use more than one type of product, summing the use of the different types of smoking cessation treatment could overestimate the number of smokers who used smoking cessation

treatment. For clarity, and if the data allowed, we summarized the effects for each type of smoking cessation treatment.

Types of outcome measures

We included studies when at least one of the following outcome measures was used to describe the effects of the intervention.

- Abstinence from smoking was the primary outcome measure of this review. We included studies reporting abstinence from smoking at least six months after the start of the intervention, and we used the longest available follow up as the preferred outcome measure.^{8,9} Biochemically validated abstinence was preferred to self-reported abstinence, and continuous or prolonged abstinence was preferred to point prevalence abstinence.
- Number of participants making a quit attempt, defined as the number of participants that attempted to quit at least once. A quit attempt is defined as not having smoked for at least 24 hours.
- Use of smoking cessation treatment, defined as the number of participants reported to have used smoking cessation treatment or registered by healthcare providers or medical insurance organizations to have used smoking cessation treatment.

To evaluate the cost effectiveness of financial interventions for smoking cessation treatment, we considered data from studies that examined both cost and effects and compared two or more alternatives. The primary outcome measure of the economic evaluation was costs per additional quitter. The secondary outcome measures were costs per life year saved (LYS), and costs per quality-adjusted life year saved (QALY).

Search strategy

There was no limitation on language. Eligible studies were identified by:

- A computer-aided search of the Cochrane Central Register of Controlled trials (CENTRAL), Issue 3, 2003, MEDLINE (from January 1966 to August 2003) and EMBASE (from January 1989 to October 2003). This search was performed by the trials search co-ordinator of the Tobacco Addiction review group. The following search terms, MeSH subheadings and free text words from the Effective Practice and Organisation of Care review group and the Tobacco Addiction review group were used (* indicates wild card symbol): randomised controlled trial, controlled clinical trial, random*, research design, experiment, intervention studies, comparative studies, evaluation studies, time adj series, tobacco*, nicotine*, smok*, smoking, smoking-cessation, quit*, stop*, abstin*, abstain*, cessat*, ceas*, control*, coverage*, reimburse*, target*, payment*, remunerat*, incentive*, financ*, salar*, fee*, deductibles*, coinsurance*, co-payment*, capita*, cost

next shar, prospective payment*, fund hold, prepay, prepaid, health care costs, health insurance, health care organization, health maintenance organization or health care system.

- Screening references of relevant reviews and identified studies.
- In order to retrieve unpublished studies, experts in the field were contacted via a standardized e-mail. Unpublished studies or abstracts were included only when sufficient data were available.

Based on title, keywords and abstract, one reviewer (JK) selected studies by applying the inclusion criteria to the studies identified by the literature search. When there was any doubt whether to select a study or not, a second reviewer (EJW) was consulted. Two reviewers (JK and EJW) assessed the full paper versions of the selected studies. Disagreements about inclusion were resolved by consensus, and a third reviewer (CPS) could be consulted if disagreements persisted.

Data extraction

Data from the included studies were extracted by two reviewers (JK and EJW). Any discrepancies between the two reviewers were resolved by discussion. The following data were extracted:

- Methods: setting (location of care, country, year of study) and study design;
- Participants and/or healthcare providers: method of recruitment, inclusion criteria, characteristics of study population (smoking status, age, gender and motivation to quit smoking);
- Interventions: description of the intervention for each group;
- Outcome measures and outcomes: definition for each study of continuous abstinence or point prevalence abstinence, number of participants making a quit attempt, prescription and use of tobacco dependence treatment.

Data concerning the economic evaluation were extracted by two reviewers (JK and JLS). Any discrepancies were resolved by discussion. The following data were extracted:

- Perspective and time horizon of the economic evaluation;
- Direct costs: volume and value of costs of the use of smoking cessation treatment, costs of consultations with healthcare providers and overhead costs;
- Indirect costs: volume and value of general medical care, lost productivity, time and travel costs spent by participants visiting healthcare providers;
- Discounting and sensitivity analyses;
- Results of the economic evaluations.

Quality assessment

The articles were not blinded for authors, institution or journal title. The methodological quality of the included studies was assessed by using the Delphi List,¹⁰ which also contains all items of the list developed by Jadad.¹¹ In addition to the Delphi List, we considered another six items to be important: evaluation of the success of the blinding of the outcome assessor, of the care provider and of the patient, comparability of co-interventions, specification of the primary outcome measures and a follow-up rate of over 80% (Table 5.2).

Table 5.2 Quality assessment based on Delphi list.

Item	Boyle ¹⁵	Curry ¹⁷	Dey ²⁰	Hughes ²⁴	Kaper ³⁸	Schauffler ³²
1 Was a method of randomisation performed?	no	no	yes	yes	yes	yes
2 Was the allocation concealed?	no	no	yes	yes	no	no
3 Blinding or naïve patient?	no	no	no	no	yes	yes
4 Blinding of patient evaluated and successful?	no	no	no	no	yes	no
5 Blinding or naïve health care provider?	no	yes	no	no	no	unclear
6 Blinding of health care provider evaluated and successful?	no	no	no	no	no	no
7 Blinding or naïve outcome assessor?	yes	yes	unclear	yes	no	unclear
8 Blinding of outcome assessor evaluated and successful?	no	no	no	no	no	no
9 Were both inclusion and exclusion criteria specified?	yes	yes	yes	yes	yes	yes
10 Were the groups similar at baseline regarding the most important prognostic indicators?	unclear	unclear	yes	yes	yes	yes
11 Was in one or more groups the percentage follow-up over 80%?	no	no	no	no	no	no
12 Were the co-interventions comparable between the groups? (no co-interventions = yes)	yes	yes	yes	yes	yes	yes
13 Did the analysis include an intention-to-treat analyses?	no	yes	no	yes	yes	no
14 Were the primary outcome measures specified?	yes	yes	yes	yes	yes	yes
15 Were point estimates and measures of variability presented for primary outcome measure(s)?	yes	yes	yes	yes	yes	yes
Total score	5	7	7	9	9	7

Two reviewers (JK and EJW) independently assigned a score for each of the 15 criteria. The items were scored as 'yes' (one point), 'unclear' or 'no' (both no points). A total score for each included study was calculated by summing the

number of positive criteria (range 0 to 15). High scores indicate a lower likelihood of bias. In a consensus meeting, disagreements between the two reviewers were discussed and resolved. If a study did not contain sufficient information on methodological criteria or the information was unclear, the authors were contacted for additional information.

The quality of the economic evaluations was assessed using the Consensus Health Economic Criteria (CHEC) list.¹² As with the development of the Delphi list, the CHEC list is based on expert consensus. The CHEC list consists of 19 items, which are described in Table 5.3. The quality of the economic evaluations was assessed by two reviewers (JK and JLS). Items scored as 'yes' received one point. Items scored as 'unclear' or 'no' received no points. A total score was calculated by summing the score of the 19 items (range 0 to 19).

Table 5.3 Quality assessment of economic evaluations (CHEC).

Item	Curry ¹⁷	Hughes ²⁴	Schauffler ³²
1. Is the study population clearly described?	no	yes	no
2. Are competing alternatives clearly described?	yes	yes	yes
3. Is a well-defined research question posed in answerable form?	yes	yes	yes
4. Is the economic study design appropriate to the stated objective?	yes	yes	yes
5. Is the chosen time horizon appropriate in order to include relevant costs and consequences?	yes	yes	yes
6. Is the actual perspective chosen appropriate?	yes	yes	no
7. Are all important and relevant costs for each alternative identified?	no	no	no
8. Are all costs measured appropriately in physical units?	no	no	no
9. Are costs valued appropriately?	no	no	no
10. Are all important and relevant outcomes for each alternative identified?	no	no	no
11. Are all outcomes measured appropriately?	no	yes	no
12. Are outcomes valued appropriately?	yes	yes	yes
13. Is an incremental analysis of costs and outcomes of alternatives done?	no	no	no
14. Are all future costs and outcomes discounted appropriately?	yes	yes	yes
15. Are important variables appropriately subjected to sensitivity analysis?	no	no	no
16. Do the conclusions follow from the data reported?	yes	no	yes
17. Does the study discuss the generalizability of the results to others settings/patients?	no	yes	yes
18. Does the article indicate that there is no potential conflict of interest of researchers and funders?	no	no	no
19. Are ethical and distributional issues discussed appropriately?	no	no	no
Total score	8	10	8

Data analyses

We used Review Manager 4.2 to estimate the odds ratio (OR), risk difference (RD) and the corresponding 95% confidence intervals (95% CI). Only intention-to-treat analyses were used. If no intention-to-treat analysis was presented than the published data were recalculated on an intention-to-treat basis, i.e. counting all dropouts and participants lost to follow up as continuing smokers with no quit attempt and not having used smoking cessation treatment. We pooled data when at least two trials assessed the effects of healthcare financing interventions and reported data on the same outcome measure. A formal test for statistical heterogeneity, the natural approximate chi squared test, assessed whether the observed variability in effect sizes is greater than would be expected to occur by chance.

The transferability of cost estimates of different economic evaluations is mostly restricted by differences in setting. These differences can be related to patient characteristics, incidence of smoking-related diseases, availability of health resources, variations in clinical practice, incentives to healthcare providers and relative prices or costs.¹³ Pooling of the different economic evaluations is only permissible when there is no interaction between the setting and the effect of the intervention on medical consumption.¹³ When pooling is allowed, the volumes of medical consumption, like the use of smoking cessation treatment, are pooled and multiplied with the pooled costs per unit consumption. The total costs were calculated in US dollars (US\$). When the cost estimates of the different economic evaluations were not transferable, we presented cost data of the individual studies. When no incremental ratios were presented, we calculated the incremental cost effectiveness ratios ourselves. First, we calculated the total costs per group. We then divided the difference in costs between the groups by the difference in number of quitters between the groups. The calculation was checked by the authors of the studies involved.

Results

Description of studies

Using the search strategy described above, we identified 2237 references. Twenty-one studies were selected based on title, keywords and abstract.¹⁴⁻³⁴ Three additional studies were found through experts in the field.³⁵⁻³⁷ One other study was conducted by the reviewers themselves.³⁸ We assessed the full reports of all 25 studies for eligibility.

Nineteen studies were excluded. Most studies were not (randomised) controlled trials or interrupted time series.^{14,16,19,21,23,25,27-29,31,33,34} Roski et al.³⁰ studied the effect of financial incentives on clinical practice and patient outcomes. The clinical practice outcomes were assessed with a before-and-after measurement, using cross-sectional patient exit surveys. For the patient outcomes, measurements were only performed after the intervention was introduced. There were also other reasons for exclusion. Lave et al.²⁶ compared two different financial systems in two different settings, and did not report data on the smoking status of the control group. The financial intervention in three studies^{18,22,36} was not directly related to the use of smoking cessation treatment. Hays et al.³⁵ was excluded, since it did not explicitly assess the effects of a financial intervention. Shaw et al.³⁷ assessed the effect of nicotine gum prices on the use of gum and abstinence rates, and has not yet reported the number of participants using smoking cessation treatment or the quit rate.

Six studies were included.^{15,17,20,24,32,38} Full details of the included studies are given in the Table 5.4. None of the included studies used an interrupted time series design and none of the included studies assessed the effects of financial interventions directed at healthcare providers. Three studies included a general population of smokers.^{17,32,38} One study included only smokers who were motivated to quit.²⁰ Half of the sample included in Boyle et al.¹⁵ were interested in quitting smoking. However, in the treatment group only 30.3% was aware of the pharmacy benefit. Participants in Hughes et al.²⁴ did not have to be motivated to quit to participate in the study, but were allowed to withdraw from the study after they were told that they would be randomly assigned to different price groups. Coverage was offered for three different types of smoking cessation treatment: NRT, bupropion and behavioural interventions. The treatment periods ranged from 12 weeks to one year and also varied in the extent of coverage and the comparisons made.

Three of the six included studies presented data on the costs of the intervention, and compared the costs and effects of the intervention with one or two alternatives.^{17,24,32} All three studies used a time horizon equal to the duration of the intervention, and all used a third party payer perspective in which only the direct costs of the intervention were presented.

Curry et al.¹⁷ also presented a users' perspective. The cost effectiveness ratio was presented in terms of costs per user who quit smoking or costs per subject enrolled.

Methodological quality of included studies

Table 5.2 shows the results of the methodological quality assessment. The scores of the six included studies varied between 5 and 9. Four studies randomly assigned their participants.^{20,24,32,38} The allocation was concealed in two studies^{20,24} and was unclear in Schauffler et al.³² Two studies were controlled trials.^{15,17} Only Kaper et al.³⁸ and Schauffler et al.³² blinded the participants in the control group to the treatment available to the experimental group, with Kaper et al.³⁸ also evaluating the success of the blinding. Only Curry et al.¹⁷ blinded the healthcare provider. The outcome assessor was blinded in three studies.^{15,17,24} The follow-up rate was less than 80% for all the included studies.

The methodological quality assessment regarding the economic evaluations is presented in Table 5.3. The score of the three studies varied between 8 and 10.^{17,24,32} In none of these studies were all relevant costs identified, and the identified costs were not measured and valued appropriately. For example, costs of visits to healthcare providers were not measured, no contact times were presented, the volumes of the use of smoking cessation treatment were incomplete and the sources of cost valuation were not described. The preferred effect outcome, e.g. biochemically validated abstinence, was not measured. Incremental analyses and sensitivity analyses were not performed. Direct costs were not discounted, but this was appropriate as the time frame of the cost analysis was less than 12 months. No statements of potential conflicts of interest were presented.

The effect of financial coverage on abstinence from smoking

The effects of financial interventions were separately analysed for the comparisons: full versus no coverage, full versus partial coverage and partial versus no coverage. Two studies presented the self-reported continuous abstinence rate at 12 months for full versus no coverage,^{15,38} and two studies presented the self-reported point prevalence abstinence rate at six months.^{24,32} In all four studies, the abstinence rate in the treatment group was higher than in the control group. Pooling the data of the four studies resulted in an OR of 1.48 (95% CI 1.17-1.88) and a RD of 0.02 (95% CI 0.00-0.05). (Figure 5.1)

Two studies compared full coverage with partial coverage.^{17,24} In both studies, more participants quit smoking at six months in the full coverage group. The pooled OR for the self-reported point prevalence abstinence was significantly higher for the full coverage group compared with the partial coverage group

(OR=2.49; 95% CI 1.59-3.90). The pooled RD did not show a significant effect (RD=0.05; 95% CI -0.07-0.16).

No statistically significant difference was found in the one study²⁴ that compared partial coverage with no coverage for self-reported abstinence at six months (OR=0.69; 95% CI 0.11-4.37; RD=-0.02; 95% CI -0.14-0.09).

Figure 5.1 Effect of full versus no coverage on abstinence from smoking.

The effect of financial coverage on the number of participants making a quit attempt

Four studies assessed the effects of full coverage compared with no coverage on the number of participants who tried to quit.^{15,24,32,38} In all four studies more smokers in the intervention group tried to quit smoking compared with the control group. The pooled OR was 1.32 (95% CI 1.18-1.49) and the pooled RD was 0.05 (95% CI 0.03-0.08). Only Hughes et al.²⁴ collected data on the number of participants with quit attempt and partial coverage. No significant differences were observed in number of participants attempting to quit between full coverage and partial coverage (OR=1.54; 95% CI 0.45-5.31; RD=0.07; 95% CI -0.12-0.25). There were also no significant differences between partial coverage and no coverage (OR=1.82; 95% CI 0.65-5.11; RD=0.12; 95% CI -0.08-0.32).

The effect of financial coverage on the use of smoking cessation treatment

Four studies^{15,24,32,38} assessed the effects of full coverage versus no coverage for NRT and all showed an increased use of NRT. The pooled OR was 1.99 (95% CI 1.17-3.40) and the pooled RD was 0.05 (95% CI 0.01-0.09). The effect of full coverage compared with no coverage on the use of bupropion was extracted from two studies.^{15,38} The pooled OR for the use of bupropion was not statistically significant (OR=2.47; 95% CI 0.86-7.13). The pooled RD was significantly higher for full coverage when compared with no coverage (RD=0.04; 95% CI 0.02-0.06). The number of smokers who participated in a behavioural programme were registered in Kaper et al.³⁸ and Schauffler et al.³² The pooled OR and RD were not significantly higher (OR=2.56; 95% CI 0.66-9.94; RD=0.02; 95% CI -0.02-0.06).

When the effect on the use of NRT with full coverage was compared with partial coverage, all three studies^{17,20,24} showed an increased use in favour of full coverage. The pooled OR was statistically significant (OR=5.03; 95% CI 1.52-16.62), while the pooled RD was not significant (RD=0.23; 95% CI -0.09-0.55). Only Curry et al.¹⁷ assessed the effect of full coverage compared with partial coverage for behavioural interventions. Full coverage increased the number of participants in a behavioural intervention by 8% (OR=3.67; 95% CI 3.06-4.39; RD=0.08; 95% CI 0.07-0.09).

Only one study²⁴ assessed the effects of partial coverage compared with no coverage on the use of NRT. There was no significant difference between the partial coverage and no coverage group (OR=1.56; 95% CI 0.62-3.90; RD=0.11, 95% CI -0.12-0.34).

Cost effectiveness of financial coverage

Three studies presented data on the costs of the intervention.^{17,24,32} As pooling of the different economic evaluations is only allowed when there is no interaction between the setting and the effect of the intervention,¹³ we have not pooled the results of the individual studies. None of the studies calculated the costs per quality-adjusted life year saved.

Curry et al.¹⁷ presented the direct costs of NRT and a behavioural intervention programme for the different coverage groups. With full coverage, the average costs per benefit user who quit were US\$21 for users and US\$1171 for the health plan. With partial coverage, the costs per benefit user who quit were respectively US\$326 and US\$801. We also calculated the incremental cost effectiveness ratio: when full coverage is introduced instead of partial coverage, the financial gain for users would be US\$5316 for each benefit user who quit. For the health plan, the costs would be US\$7646 per benefit user who quit.

Hughes et al.²⁴ included the following direct costs: nicotine gum, a smoking cessation booklet and healthcare provider's time. Participant's time was regarded as an indirect cost. The calculated financial gain per participant enrolled was US\$1120 for the full coverage group, US\$280 for the partial coverage group and US\$413 for the no coverage group. For the incremental analyses, we calculated the costs per additional quitter per comparison. If full coverage was compared with partial coverage, the costs per additional quitter were US\$260. When comparing full coverage with no coverage, the costs were US\$716. Partial coverage was not cost effective compared to no coverage.

Schauffler et al.³² reported the total costs of NRT, the behavioural programme and the self-help kit for the treatment group, but no control group costs. The authors have subsequently advised us that the control group costs amounted to US\$29 per participant, for the self-help kit. The average costs per quitter were US\$1495. The costs per additional quitter of our own incremental analysis for full compared with no coverage were US\$1247.

Discussion

The objectives of this review were to assess the effect of healthcare financing interventions on the abstinence rate, on the number of participants that attempted to quit and on the use of smoking cessation treatments, and where possible to assess cost effectiveness.

Our extensive literature search resulted in the inclusion of four randomised trials and two controlled trials. All the included studies assessed the effects of financial interventions directed at participant smokers rather than at healthcare providers. Four studies compared full coverage with no coverage, and showed that the smokers in the full coverage group had a 1.5 times higher chance of achieving abstinence. The chance of making a quit attempt was 1.3 times higher in the full coverage group than in the no coverage group. The use of NRT was 2.0 times higher and use of bupropion was 4% higher for full coverage smokers than for no coverage smokers. The number of smokers who participated in a behavioural programme was not significantly higher for full coverage compared with no coverage. Three studies compared full coverage with partial coverage. The chance of being abstinent was 2.5 times higher with full coverage than with partial coverage. The chance of using smoking cessation treatments was 5.0 times higher for NRT and 3.7 times higher for behavioural interventions compared with partial coverage. No significant difference was found for the number of participants making a quit attempt. Only one study compared partial coverage with no coverage. There was no increase in abstinence rate, no significant increase in number of participants making a quit attempt and no significant increase in the use of NRT.

Three studies presented data on the costs of the financial benefit. When full coverage was compared with partial coverage or no coverage, the costs per quitter varied between US\$260 and US\$2330. Financial coverage was not cost effective in the one study that compared partial coverage with no coverage.

This is the only review to assess the effects of financial interventions aimed at encouraging the prescription and use of smoking cessation treatments. We found two reviews^{39,40} examining the effects of financial interventions, but they included studies which offered a financial benefit for abstinence rather than the utilization of smoking cessation treatment. Bains et al.³⁹ discussed the use and impact of incentives in population-based smoking cessation programmes. Smokers participated in contests and lotteries or received financial incentives. Moher et al.⁴⁰ addressed the effectiveness of workplace interventions for smoking cessation. The results of this review should be interpreted in the light of the issues discussed below, i.e. the comparability and the methodological quality of the included studies.

Comparability

This review shows that the included studies were heterogeneous with respect to the study setting, motivation to participate in the study, motivation to quit smoking and the intervention. Because of this heterogeneity, the results have to be interpreted with care.

The setting of the included studies ranged from family practices in the UK and USA to health insurance organizations in the USA and the Netherlands. As each country has a different healthcare system, comparisons between studies in various settings should be made in the knowledge of these differences.

The included studies also differed with respect to the motivation of smokers to participate or to quit smoking. In Dey et al.,²⁰ for example, participants had to be motivated to quit in order to participate. On entry in the study, motivated participants received free prescriptions for nicotine patches, and as a result, 97% of the participants in the full coverage group used at least one prescription. Omitting the Dey study²⁰ reduced the statistical heterogeneity of the NRT meta-analysis, and changed the pooled OR from 5.03 (95% CI 1.52-16.62) to 2.96 (95% CI 2.15-4.09), and the pooled risk difference (RD) from 0.23 (95% CI -0.09-0.55) to 0.06 (95% CI -0.01-0.13).

On the other hand, Kaper et al.³⁸ and Schauffler et al.³² offered coverage in a general population. As participants were not obliged to quit smoking, the use of NRT was 21% in the study of Schauffler et al.³² and 4% in Kaper et al.³⁸.

Furthermore, the interventions varied in the extent of financial coverage, the methods of smoking cessation treatment for which the coverage was available, the conditions for receiving the coverage and the information concerning the new benefit. In four of the six studies, coverage was available for different types of smoking cessation treatment. As the effect of the financial intervention can be spread out over the different types of products, studies with coverage for more than one type cannot formally be compared with studies that offered coverage for only one product. Similarly, studies which offered coverage for two different types of smoking cessation treatment can not be compared with the study that offered coverage for three different types. Since participants in four studies could use more than one type of product, summing the use of the different products could overestimate the number of smokers who used smoking cessation treatments. For clarity, we have therefore summarized the effects by type of smoking cessation treatment. However, one should keep the limitations of this summary in mind.

Methodological quality

Only two of the six studies scored positively on more than half of the quality checklist items. An important limitation was that not all of the studies used random or concealed allocation. Only four of the six studies randomly

allocated the participants to the treatment or control groups, and only two of those concealed the allocation. In the remaining studies, the possibility exists that the effect is biased.

Furthermore, not all the studies blinded the participants, healthcare providers and outcome assessors. Only two of the six studies blinded the participants. In studies which assess the effect of a financial intervention, blinding the control group may be important, since control participants who knew that they would not receive financial coverage for treatment might feel disadvantaged and change their behaviour. Such a change would be a threat to the internal validity of the study. Only one study explicitly blinded the healthcare provider and three studies blinded the outcome assessors. We therefore cannot rule out the possibility of biased results in the unblinded studies.

Another methodological problem is the low follow-up rate, which was below 80% in all the included studies, and may be related to the intervention. If participants are less interested in the financial intervention, for example, when they do not want to use smoking cessation treatments or are not motivated to quit, then the number of dropouts can increase. In an intention-to-treat analysis, drop-outs would be considered to be continuing smokers. However, intention to treat analyses were not performed by three of the included studies. For this review, we have recalculated the results of those studies on an intention-to-treat basis.

We have preferred to present the most conservative measure of abstinence at the longest follow up. Only two studies biochemically validated participants' smoking status.^{20,38} In Dey et al.,²⁰ however, abstinence was assessed at 14 weeks rather than six months from the start of the intervention, and in Kaper et al.³⁸ the smoking status of only 57% of the self-reported quitters was biochemically validated. Those outcomes were therefore not reported in this review. Reported outcomes are restricted to self-reported abstinence rates for all the included studies apart from Dey et al.,²⁰ for which no abstinence rate is presented. This could have introduced bias, as participants with a financial incentive might be more likely to give socially desirable answers than participants in the control group.

We used a separate methodological quality assessment for the economic evaluation; the Consensus Health Economic Criteria (CHEC) list.¹² We preferred to use two separate lists to be able to cover all items, which we considered important. From the methodological quality assessment of the economic evaluations, it became clear that none of the three studies reporting on cost effectiveness had performed a full economic evaluation. Only costs of the intervention were calculated. Other important data like duration and number of contacts with healthcare providers and sources of cost valuation were not presented. No study examined cost effectiveness in terms of quality-

adjusted life years saved. Results were presented in terms of costs per additional quitter or costs per subject enrolled. Furthermore, no assessment was made for uncertainty in the estimation of costs and consequences, and no incremental analyses were performed. As a result, a precise estimate of the costs cannot be presented and no comparisons can be made with economic evaluations of other preventive healthcare treatments.

Conclusions

Full financial coverage for smoking cessation treatment increases the number of successful quitters, the number of participants making a quit attempt and the use of smoking cessation treatment at low cost when compared with partial or no coverage. As the difference in abstinence rate, number of participants making a quit attempt and use of smoking cessation treatments is only small, coverage for smoking cessation treatment is not the one intervention that can turn all smokers into permanent non-smokers. However, with one third of the world population being a smoker, a small difference in abstinence rates can have a huge societal impact.

Because of heterogeneity between the settings, interventions and participants of the included studies, the conclusions from this review have to be interpreted cautiously. More randomised controlled trials should be performed that are comparable with the studies that are included in this review, so that future analyses can be stratified on setting, intervention and participants. No randomised trials examining the effects of financing systems directed at healthcare providers have yet been reported. Future randomised trials should assess whether financial interventions aimed at healthcare providers can affect the prescribing pattern and uptake for smoking cessation treatments, or the smoking behaviour of their patients.

Furthermore, no full economic evaluations have been performed. To assess the financial impact of healthcare financing interventions for smoking cessation, it is important to determine more precisely the cost effectiveness of these interventions. A full economic evaluation is needed to be able to compare the cost effectiveness with other preventive healthcare treatments.

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Chapter 6

Encouraging smokers to quit:
The cost-effectiveness of reimbursing the costs of
smoking cessation treatment

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Abstract

Introduction

Smoking cessation should be encouraged in order to increase life expectancy and reduce smoking related health care cost. Results of a randomised trial suggested that reimbursing the costs of smoking cessation treatment (SCT) may lead to an increased use of SCT and an increased number of quitters versus no reimbursement.

To assess whether reimbursement for SCT is a cost-effective intervention (from the Dutch societal perspective), we calculated the incremental costs per quitter and extrapolated this outcome to costs per quality adjusted life year (QALY) saved versus no reimbursement.

Methods

In the reimbursement trial, 1266 Dutch smokers were randomly assigned to the intervention or control group using a randomised double consent design. Reimbursement for SCT was offered to the intervention group for a period of six months. No reimbursement was offered to the control group.

Prolonged abstinence from smoking was determined six months after the end of the reimbursement period. The QALYs gained from quitting were calculated until 80 years of age using data from the US. Costs (year 2002 values) were determined from the societal perspective during the reimbursement period (May 2002–November 2002). The uncertainty of the incremental cost-effectiveness ratios was estimated using non-parametric bootstrapping.

Results

Eighteen participants in the control group (2.8%) and 35 participants in the intervention group (5.5%) successfully quit smoking. The costs per participant were €291 and €322, respectively. If society is willing to pay €1000 or €10000 for an additional 12-month quitter, the probability that reimbursement for SCT would be cost-effective was 50% or 95%, respectively. If society is willing to pay €18000 for a QALY, the probability that reimbursement for SCT would be cost-effective was 95%. However, the external validity of the extrapolation from quitters to QALYs is uncertain and several assumptions had to be made.

Conclusion

Reimbursement for SCT may be cost-effective if Dutch society is willing to pay €10000 for an additional quitter or €18000 for a QALY.

Introduction

Smoking is one of the most avoidable causes of death and disability in developed countries¹ and accounts for up to 15% of the total annual health care costs.² To increase life expectancy and to reduce smoking related health care cost, smoking cessation needs to be encouraged.^{1,2} Many studies have demonstrated that smokers are more successful in their attempt to stop smoking when they use some form of smoking cessation treatment (SCT), like nicotine replacement therapy (NRT), bupropion or behavioural interventions.³⁻⁶ Despite this evidence, few smokers use SCT. It is expected that smokers do not use these interventions because of the costs.⁷

We previously conducted a randomised trial to evaluate whether reimbursing the costs of SCT would lead to an increased use of SCT and an increased number of quitters, we previously conducted a randomised trial.⁸ Results showed that during the reimbursement period, 132 participants (20.8%) in the control group and 148 participants (23.4%) in the intervention group tried to quit smoking at least once and that the use of SCT by these participants increased from 20% in the control group to 45% in the group with reimbursement.⁸ Moreover, reimbursement for SCT not only increased its use, but also increased the number of prolonged abstinent quitters.⁸ The results of this trial are supported by a Cochrane review examining the effects of health care financing systems on the utilisation of SCT.⁹ This review was based on five other studies that assessed the effects of reimbursement.¹⁰⁻¹⁴ However, even though three of these studies collected data on the costs, no study performed incremental cost-effectiveness analyses.¹⁰⁻¹²

As monetary resources are limited, establishing the cost-effectiveness of an intervention can assist policymakers in their decisions on the reimbursement of various treatments. In general, the cost-effectiveness ratios of smoking cessation interventions seem similar to those of other public health interventions, such as treating mild-to-moderate hypertension and lowering cholesterol levels,^{2,15,16} but the cost-effectiveness of reimbursement for SCT remains unknown. The present study primarily aimed to assess the short-term cost-effectiveness of reimbursement for SCT in terms of costs per quitter. We also assessed the cost per additional quality adjusted life year (QALY) for reimbursed SCT and compared this with that of other public health interventions.

Methods

The reimbursement study

The incremental cost-effectiveness of reimbursement for smoking cessation treatment was assessed by means of data obtained from a reimbursement study described in Kaper et al.⁸ This study included a general population of smokers aged at least 18 years who did not have to be motivated to quit smoking. From random samples of inhabitants of Friesland, a province in the north of the Netherlands, 1266 smokers were found to be eligible and randomly assigned to the control group (n=634) or the intervention group (n=632). Only smokers assigned to the intervention group had the opportunity to apply for reimbursement for NRT, bupropion, and behavioural counselling during a period of six months. The intervention group also received a description of the SCT for which reimbursement was available and the way they could apply for reimbursement. To receive reimbursement, participants had to send the receipt of the smoking cessation treatment they bought and a proof of two contacts with a health care professional to the health insurance company. To avoid selective dropout or changes in behaviour due to disappointment, we used a double randomised consent design in which the control group was blinded for the existence of the intervention group and the reimbursement they were offered. Control group participants were told that the study objective was to collect data on the use of SCT and smoking behaviour. They were not offered reimbursement. Assessments were performed at the start of the reimbursement period, after five weeks, at the end of the reimbursement period (i.e. after six months) and six months after the end of the reimbursement period (i.e. after 12 months). The study was approved by the Medical Ethics Committee of the Trimbos Institute in Utrecht, The Netherlands.

Short-term cost-effectiveness

The time horizon, that is the duration of the short-term economic evaluation, was equal to the 6-month reimbursement period. The outcome of the short-term economic analyses was the cost per quitter. A participant was considered to have prolonged abstinence if they reported no smoking for seven days preceding the 6- and 12-month follow-up assessment and no smoking between the two assessments.¹⁷ Self-reported abstinence was biochemically confirmed by an expired air carbon monoxide level of <7 parts per million (ppm). The direct and indirect smoking-related healthcare and productivity costs during the 6-month reimbursement period were calculated according to the societal perspective. All costs relating to smoking cessation and health were calculated including reimbursed costs. Smoking-related disease was identified as a

disease or health complaint in which smoking was judged to be one of the main causes. Productivity costs were included because we expected that, during the first months of smoking cessation, quitters might be more absent from work as was demonstrated by Sindelar et al.¹⁸; recent quitters could have quit because of poor health, but the mental and physical stress of quitting could also increase absences. It was assumed that no appreciable decrement in life expectancy or quality of life was introduced by using SCT. However, adverse events could have led to sick leave or healthcare consumption, which were included in the cost calculation. Table 6.1 describes all costs included.¹⁹⁻²¹

Table 6.1 Costs included in the control and intervention groups based on the societal perspective (€, 2002 values).

Overhead cost consisted of sending a letter and leaflet about their new benefits and the process of applying for reimbursement to participants of the intervention group.

Using SCT was recorded via the 6-month questionnaire. We did not use receipts to estimate costs, as the intervention group did not always apply for reimbursement and as participants used treatment methods for which no reimbursement was available. Information about the price of SCT was provided by the companies concerned or requested from the users.

Consultations for SCT and smoking-related diseases were calculated using standard rates. The consultations were offered by general practitioners, general practice nurses, community health workers, and physicians and recorded via the 6-month questionnaire.

Travel cost were calculated for consultations with general practitioners (€3.07), hospitals (€4.74) and community health services (€4.74).

Cost of lost productivity resulted from sickness, absenteeism, inability to work and/or death of persons with paid jobs, excluding retirement.¹⁹ These costs were calculated using the friction cost method, which assumes that organisations need a certain time (the friction period) to restore the initial production level when an employee is absent from work.

The length of the friction period may depend on the availability of labour and hence, of unemployment. In the Netherlands, the maximum period of adaptation was set at 154 days in 2002. If the period of absence was <154 days, then only the actual days of absence were calculated.

Participants were asked how many days they had been sick. To convert the days of sickness into days of absenteeism from work, we divided the total number of contract based working hours in the Netherlands per year by the total number of working people and divided by 365,25 days. This resulted in 3.7 working hours per day for employed men and 2.6 working hours per day for employed women. (Statistics Netherlands: www.cbs.nl)

The productivity costs per hour varied between €20 and €47 depending on age and gender. As numerous studies have demonstrated that a reduction of annual labour time causes a less than proportional decrease in labour productivity, a correction factor of 0.8 was used for the estimated elasticity regarding lost work time and productivity.^{20 21}

Long-term cost-effectiveness

We extrapolated the short-term cost-effectiveness to the lifetime cost-effectiveness. When extrapolating the short-term costs to future medical costs, contradicting literature was found.²² For example, MacKenzie et al.²³ reported that the lifetime medical costs for smokers exceeded those for non-smokers. In contrast, Barendregt et al.²⁴ found that if all smokers quit, health care costs would be lower at first, but after 15 years they would become higher as quitters live longer and incur more healthcare costs at older ages. Eventually, smoking cessation would lead to a reduction of smoking related health care costs, but a net increase in total health care costs. Taking the conflicting findings and uncertainty together, the net impact of smoking and cessation on health care costs is likely to be modest.²² The effect of quitting on total health care costs is likely to be modest. Therefore, we assumed that the future medical costs were equal for both quitters and smokers and as a result, the difference in long-term costs in the control group and intervention group was the same as the short-term costs.

The effect of quitting on QALYs was estimated in two steps. We first calculated the long-term effects of smoking and smoking cessation on life expectancy. Because proper information concerning differences in life expectancy and utilities were not available for people >80 years of age, we assumed equal mortality rates and quality of life for smokers and quitters after age 80. Second, the remaining life years of both smokers and quitters were corrected for quality-of-life weights (utilities). The difference in quality-adjusted life expectancy between quitters and smokers at age 80 years is presented as the number of QALYs gained by quitting.

To calculate the benefits of smoking cessation in terms of life expectancy, we derived mortality rates from data on never-smokers, light and heavy smokers. The mortality rates of smokers were obtained from the National Mortality Followback Survey (NMFS), conducted in the United States in 1986. Rogers and Powell-Griner²⁵ presented these mortality rates for both light (<25 cigarettes/day) and heavy smokers (≥ 25 cigarettes/day). In the current study, there were 9-fold more light than heavy smokers at baseline, so we used a 9:1 ratio to calculate weighted mortality rates. Next, the mortality rates of quitters were estimated by extrapolating mortality rates from smokers to never-smokers. As the long-term health effects of smoking cessation mainly result from the prevention of smoking-related diseases,²⁶⁻²⁸ these health benefits only become fully visible after about 20 years.²⁷ Therefore, we used a 20-year phase-in period corresponding to this delay.²⁷ During this phase-in period, the mortality rates of smokers were linearly extrapolated to never-smokers over four 5-year categories. After 20 years of abstinence, quitters were assumed to have the same chances of dying as never-smokers (Table 6.2).

The life expectancy of quitters was corrected for relapse. We assumed that the lifetime relapse rate after one year of abstinence was 35%.²⁷ For the percentage of quitters who relapsed, we used the mortality rate of smokers. As we only incorporated the effects originating from the reimbursement period, the control group represented the natural quit rate. As no mortality rates were available for smokers and quitters in the 18-19 years and 20-24 years age groups, mortality rates of the Centers for Disease Control and Prevention were used instead.²⁹ However, no distinction in mortality rate could be made between smokers and quitters in these age groups.

To calculate the quality-adjusted life expectancy, the remaining life years were multiplied by the utility score per 5-year age category that corresponded with the gender and smoking status of the participant. The utility scores of smokers and never-smokers were presented by Fiscella and Franks³⁰ who derived the scores from Healthy People 2000.³¹ The utility scores of quitters were estimated by linearly extrapolating the utilities from smokers to never-smokers using a 15-year phase-in period including three 5-year age categories. After 15 years of abstinence, the utilities of quitters approximated those of never-smokers.³⁰ No utility scores were available for smokers and quitters aged 18 to 25 years and 70 to 80 years. We assumed that the utility scores of smokers and quitters aged 18 to 25 years were equal to those of the 25-29 years age group. The utilities of quitters aged 70 to 80 years were derived from data on a general population presented by Burström et al.³² The utility scores of smokers in this age group were calculated as the utility scores for quitters minus the difference in scores between smokers and quitters at the age of 65 to 70, which was 0.05 for females and 0.09 for males (Table 6.2).

Table 6.2 Mortality rates and quality of life scores for smokers and quitters per 5-year age group.

Age group	Mortality rate				Quality of life			
	Male		Female		Male		Female	
	smoker	quit ≥20 years	smoker	quit ≥20 years	smoker	quit ≥15 years	smoker	quit ≥15 years
18 - 19	0.0010	0.0010	0.0004	0.0004	0.91	0.93	0.89	0.92
20 - 24	0.0015	0.0015	0.0005	0.0005	0.91	0.93	0.89	0.92
25 - 29	0.0026	0.0012	0.0007	0.0005	0.91	0.93	0.89	0.92
30 - 34	0.0023	0.0012	0.0007	0.0006	0.88	0.93	0.87	0.90
35 - 39	0.0031	0.0018	0.0009	0.0009	0.86	0.92	0.84	0.89
40 - 44	0.0038	0.0020	0.0014	0.0012	0.83	0.90	0.82	0.87
45 - 49	0.0047	0.0023	0.0021	0.0015	0.81	0.89	0.80	0.86
50 - 54	0.0115	0.0044	0.0050	0.0022	0.78	0.87	0.78	0.84
55 - 59	0.0126	0.0083	0.0082	0.0035	0.76	0.85	0.76	0.82
60 - 64	0.0212	0.0136	0.0102	0.0065	0.74	0.83	0.74	0.79
65 - 69	0.0335	0.0182	0.0199	0.0107	0.71	0.80	0.72	0.77
70 - 74	0.0526	0.0386	0.0377	0.0177	0.67	0.76	0.61	0.66
75 - 79	0.1076	0.0902	0.0750	0.0622	0.67	0.76	0.61	0.66

Analyses

Intention-to-treat analyses were performed in which all withdrawals were considered to be smokers. The costs of the withdrawals were imputed by the mean costs of smokers in both the control and treatment group. In the intervention group, we added the costs of sending information. For the long-term cost effectiveness, the effects in terms of life years gained or QALYs gained were corrected for the difference in timing between costs and benefits by discounting the benefits by 4%.¹⁹ All costs included were incurred in one year, so the costs were not discounted.³³ To assess the robustness of the incremental cost-effectiveness ratio (ICER) to changes in effectiveness, we varied the relapse rate of quitting between 20% and 50% in a one-way sensitivity analysis. In addition, the uncertainty of both short-term and long-term ICERs was estimated using non-parametric bootstrapping, a method based on random sampling with replacement of a number of the participants in the trial.³⁴ The 1000 bootstrap replicates were used to generate acceptability curves, representing the probability that reimbursement for smoking cessation treatment is cost-effective in terms of quitters and QALYs over a range of cost-effectiveness thresholds.

Results

Participants

The baseline characteristics of the participants in the intervention group and control group are presented in Table 6.3. For the economic evaluation, we used data of 517 participants in the control group (81.5%) and 462 participants in the intervention group (73.1%) for whom outcome and cost data were available. Insufficient information was available for the other participants and they were regarded as withdrawals. There were no differences between the participants and withdrawals in terms of age ($t=1.8$, $df=12.1$, $p=0.07$), gender ($X^2=0.01$, $df=1$, $p=0.93$), educational level ($X^2=3.44$, $df=2$, $p=0.18$) or type of health insurance ($X^2=0.04$, $df=1$, $p=0.84$).

Table 6.3 Baseline characteristics.

	Control group (n=634)	Intervention group (n=632)
Age in years, mean (sd)	39.9 (12.8)	39.5 (12.9)
Males, n (%)	338 (53.3)	362 (57.3)
Educational level, n (%)*		
low	169 (26.7)	180 (28.5)
intermediate	299 (47.2)	268 (42.4)
high	125 (19.7)	115 (18.2)
missing	41 (6.5)	69 (10.9)
Health care insurance, n (%)		
private insurance	125 (19.7)	102 (16.1)
national health insurance	496 (78.2)	517 (81.8)
missing	13 (2.1)	13 (2.1)

Educational level: low = primary and lower-level vocational school; intermediate = lower-level secondary and intermediate-level vocational school; high = higher-level secondary and higher-level vocational school and university.

Short-term cost-effectiveness

After the reimbursement period had ended (after six months), 35 participants in the control group (5.5%) and 49 participants in the intervention group (7.8%) reported to have quit smoking. Six months later, at the 12-month assessment, 18 participants in the control group (2.8%) and 35 participants in the intervention group (5.5%) were still abstinent ($RD=2.7$; 95% CI 0.5-4.9). Table 6.4 shows the volumes and costs incurred during the reimbursement period per category for the intervention and control group. Costs per participant were €291 in the control group and €322 in the intervention group. The difference between the intervention and control group was about €30 and ranged from -€161 (2.5th percentile) to €217 (97.5th percentile).

Table 6.4 Costs (€, year 2002 values) included in the control and intervention group based on the societal perspective.

	Cost per unit	Control group		Intervention group	
		Volume	Cost (€)	Volume	Cost (€)
Overhead costs	Only intervention group, €6.96 per participant (pp) + €4,65 pp who applied for reimbursement	-	-	632 pp +38 pp	4575
Costs of SCT	€7.71 (nicotine gum) - €167.26 (bupropion)	26 pp	1281	68 pp	6081
Costs of consults	€18.40 (GP) - €45.28 (specialist)	97 visits	4014	193 visits	7007
Travel costs	€3.07 (GP) or €4.74 per visit (hospital/comm. health services)	97 visits	477	193 visits	856
Costs due to lost productivity	Mean days of sickness/7 x working hours per day (=2.6 female or 3.7 male) x productivity cost per hour (=€20 - €47 depending on age and gender) x 0.8.	3.2 days of sick- ness pp	179003	3.3 days of sick- ness pp	184746
Total costs			184777		203265

Figure 6.1 shows the 1000 bootstrap replicates indicating the uncertainty around the mean cost-effectiveness ratio of €1118 per quitter. Of the bootstrap replicates, 63% are in the northeast quadrant, indicating that reimbursement is more effective and more costly. Thirty-six percent of the replicates are in the dominant southeast quadrant indicating greater effects at lower costs. One percent of the replicates are in the northwest or southwest quadrant indicating less effect.

Figure 6.2 presents the acceptability curves deduced from these bootstrap results, representing the probability that reimbursement for smoking cessation treatment is cost-effective over a range of cost-effectiveness thresholds (λ -value). Figure 6.2 shows that if society is willing to pay €1000 for an additional quitter, there is a 50% chance that the intervention will be cost-effective. If society is willing to pay €10000, this chance rises to 95%.

Figure 6.1 Bootstrap replications indicating the incremental costs (€, year 2002 values) per quitter for reimbursement for SCT versus no active intervention.

Figure 6.2 Acceptability curve showing the probability that reimbursement for SCT (in terms of cost per quitter, €, year 2002 values) is cost effective versus no active intervention for varying values of willingness to pay (λ).

Long-term cost-effectiveness

To calculate the number of QALYs gained by reimbursing SCT, we first calculated the number of life years that could be gained by quitters assuming a relapse rate of 35%. Figure 6.3 shows that, as expected, smokers who quit at a young age could gain more life years than smokers who quit when they are older. However, in the incremental cost-effectiveness analyses we had to account for time preference by discounting the benefits. In addition, Figure 6.3 shows that, when discounting was applied, the greatest number of life years could be gained by quitting between the age of 35 and 45. We then corrected the number of life years gained for quality of life. The general effects of quitting on the number of QALYs gained are presented in figure 6.4. When discounting was applied, the greatest number of QALYs could be gained by quitting between the age of 30 and 40.

Figure 6.3 Discounted and undiscounted life-years that could be gained by quitting smoking in general (i.e. not related to this study) for men and women, different ages and a relapse rate of 35%.

Figure 6.4 Discounted and undiscounted QALYs that could be gained by quitting smoking in general for (i.e. not related to this study) for men and women, different ages and a relapse rate of 35%.

The discounted numbers of QALYs gained from quitting were integrated with the effect of reimbursement on quitting. The total number of QALYs gained was 11.8 in the control group and 22.4 in the intervention group. Taking the costs of the short-term analyses into account, the mean costs were €1802 per QALY. Undiscounted, the mean costs were €900 per QALY. Figure 6.5 shows the 1000 bootstrap replicates of the incremental costs per QALY for a relapse rate of 35%. In 2% of the replicates, reimbursement yielded less effect. Figure 6.6 presents the acceptability curves indicating the probability that reimbursement for SCT is cost-effective in terms of QALYs.

Sensitivity analyses were performed by varying the relapse rates between 20% and 50%. The maximal difference in the probability of cost-effectiveness was 6% between the various relapse rates over the full range of cost-effectiveness thresholds. Figure 6.6 indicates that if society is willing to pay €1000 for a QALY there is a 43% to 46% probability that the intervention will be cost-effective for relapse rates between 20% and 50%. If society is willing to spend €10000, this probability rises to 86% for a relapse rate of 50% and to 91% for a relapse rate of 20%.

Figure 6.5 Bootstrap replications indicating the incremental costs (€, year 2002 values) per QALY gained for reimbursement for SCT versus no active intervention.

Using an accepted Dutch cut-off point of €18000,³⁵ the probability that reimbursement for SCT will be cost-effective at a relapse rate of 35% is 95%.

Figure 6.6 Acceptability curve showing the probability that reimbursement for SCT (in terms of costs per QALY, €, year 2002 values) is cost effective versus no active intervention for varying values of willingness to pay (λ) and relapse rates.

Discussion

This study showed that since the societal cost for offering reimbursement is about €30 per participant, and the quit rate increases by 2.7%, compared with no reimbursement, the point estimate of the cost per additional quitter is €1148. Furthermore, taking into account the uncertainty of the outcome, reimbursement for SCT seems a cost-effective intervention if society is willing to pay €10000 for an additional quitter. In addition, we extrapolated the effects in terms of quitters to QALYs. Results showed that the intervention seems cost-effective at a cut-off point of €18000 per QALY. As we do not know what the lifetime relapse curve looks like, we assessed the robustness of this outcome by varying the relapse rates between 20% and 50%. As the maximum difference in probability of cost-effectiveness was 6%, we consider the outcome of the economic analyses robust for changes in relapse.

From additional analyses, it appeared that the health care costs and the costs for sick leave from work were higher for quitters than for continuing smokers. At baseline, quitters had a lower health score than continuing smokers. This was to be expected because smokers who quit recently, could have quit because of poor health or could have been newly diagnosed with smoking related health problems. However, the mental and physical hardships of quitting could also have increased absences and health care consumption as the quitting process is arduous and withdrawal can be difficult to manage.¹⁸

Some important study limitations have to be discussed. Firstly, not all self-reported quitters could be biochemically validated, as an appointment could not always be made. Therefore the analyses were generally performed with self-reported abstinence data.⁸ When performing the same analyses with the biochemical validated data, only small differences were observed. The mean cost effectiveness ratio was €1058 per biochemically validated quitter compared with €1118 per self-reported quitter.

Our extrapolation of the effect in terms of self-reported quitters to the effect in terms of QALYs was based on mortality rates and utility data from the United States, which was at least one decade old. Unfortunately, no recent European or Dutch data are available for male and female smokers, quitters or never-smokers of different ages in a general population. As a result, the generalisability of the results of the present study remain dependent on the generalisability of the original US data²⁵⁻²⁹ and as we also have no data ranges, we are not able to perform sensitivity analyses on the utility and mortality outcomes. Moreover, we were unable to find any data on how to extrapolate the mortality rates of smokers to quitters. We cannot be sure whether this

relation is linear over 20 years, as we assumed in the present study, or whether the reduction in mortality rate is greater in the first years after quitting. Having to make assumptions on these issues introduces uncertainty, which reduces the validity of the extrapolation. However, the assumptions made are partially supported by a number of studies. In the American Cancer Society Prevention Study II, it was found that the mortality rate for former smokers progressively approaches and finally rejoins the mortality rate for never-smokers approximately 20 years after quitting.²⁵ Based on the same study, Cornuz et al. assumed a conservative approach and applied a phase-in period to never-smokers mortality risk of 25 years after quitting.³⁶ Edwards reported that, within 15 years of smoking cessation, the absolute risk of heart disease is almost the same as in people who have never smoked, but that the risk for lung cancer remains raised even after 20 years of abstinence.¹

Another uncertainty is related to the costs. We only included direct and indirect health care costs and productivity costs incurred during the reimbursement period. The effect of reimbursement on the number of quitters in the first six months, however, was followed up for another six months and also extrapolated to 80 years of age. The costs from 6 to 12 months were not included, as no additional differences between the intervention and control group were expected after the reimbursement had ended. Furthermore, no life time costs of smoking were calculated as analyses of the medical costs have shown contradictory findings.^{23 24 37} That is, smoking cessation may decrease the costs of medical care for smoking-related diseases,²³ but it may increase the lifetime costs of healthcare as a result of life extension.^{24 37}

A Cochrane review into the effects of health care financing systems for increasing the utilization of SCT showed that the costs per benefit user who quit varied between \$260 and \$2330 when full coverage was compared with partial or no coverage.⁹⁻¹² In the present study, the mean costs per quitter were €1118, which seems consistent with findings of previous studies. However, in the current study we found considerable uncertainty in the cost-effectiveness estimates, as can be seen from the bootstrap simulations. Therefore, we presented the outcome as the probability that reimbursement for SCT is cost-effective over a range of cost-effectiveness thresholds. We found no other public health or smoking cessation study that used the same method to assess the statistical uncertainty of the ICER. It is therefore difficult to compare our results with those of other studies.

Moreover, this study did not assess the effectiveness of reimbursement alone, but included the effect of additional information about the reimbursed SCT for participants in the intervention group. As the main idea of the study was that reimbursement may lower the threshold to use SCT, an essential part of the

intervention was to make smokers aware of the reimbursement and for which means this was available. If smokers do not know about the offered reimbursement, then no effect of the intervention can be expected. Therefore, the information about reimbursement is an essential part of the intervention. A preventive intervention like reimbursement for SCT should always be accompanied by information concerning the reimbursed products to have an optimal effect.

Conclusion

Our results suggest that if society is willing to pay €10000 for an additional quitter, reimbursement for SCT seems to be a cost-effective intervention. More cautiously, we conclude that reimbursement for SCT may increase the quality adjusted life expectancy if society is willing to pay €18000 for a QALY. However, the external validity of this outcome can be reduced as several assumptions had to be made regarding the extrapolation of the effect in terms of quitters to QALYs. Future research should, therefore, focus on the existing gaps in our knowledge, like European mortality rates for smokers and never-smokers in the general population, the distribution of lifetime relapse rates over time, and the uncertainty of the cost-effectiveness ratios of public health and smoking cessation interventions.

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Chapter 7

General discussion

The previous chapters of this thesis considered the cost-effectiveness of SCT in patients with COPD and the effectiveness and cost-effectiveness of reimbursement for SCT in the Netherlands and in general. In this final chapter, first the main results of the different studies are summarized and their implications are discussed. Next, more detail is given on how the use of SCT and the number of successful quitters can further be increased. In the end, the future of reimbursement for SCT is discussed.

Main findings and considerations

To reduce the risk and costs of smoking related diseases and to increase life expectancy, smoking cessation needs to be encouraged strongly.^{1,2} Stopping smoking is however not easy, especially not for smokers with COPD, who are often more addictive and more susceptible to depression.³ In the study described in chapter 2, we assessed the cost-effectiveness of bupropion and nortriptyline compared to placebo in patients at risk for, or with existing COPD. In the nortriptyline group high costs were made for visits to health care professionals and sick leave from work. In patients with COPD, overall the costs were higher and the effects were lower than in patients at risk for COPD. Results showed that if willing to pay more than €2000 for a quitter or more than €4000 for a QALY, bupropion was the most cost-effective intervention according to both the societal and health care perspective.

Using SCT seems to be highly cost-effective even in smokers with COPD and the use of these treatment methods should be encouraged. In a randomised controlled trial described in chapter 3 and 4, we studied whether reimbursement for effective smoking cessation interventions would increase the use of SCT and would increase the number of successful quitters in the general population. As reimbursement is a popular intervention, smokers without reimbursement may be disappointed. To avoid this, we used a randomised consent design,⁴ in which the group without reimbursement was blinded with regard to the existence of the group with reimbursement. The use of this study design is considered a valid alternative for a traditional randomised design and the only possibility if the experimental condition is highly attractive for all participants and if the control group is at least offered standard treatment.⁵

In the study, no specific emphasize was put on smoking and smoking cessation, except in the questionnaires. Selective dropout due to unsuccessful quit attempts may as a result have been minimal. Filling in the questionnaires could however, due to the extra attention given to smoking cessation, have lead to additional quitters, but we do not expect that this Hawthorne effect has been different in the control or intervention group.⁶ Reimbursement for SCT

increased the use of SCT from 4.1% to 10.8%. The self-reported point prevalence abstinence rate was after six months 7.8% in the reimbursement group and 5.5% in the group of smokers who were not reimbursed.⁷ After 12 months, the self-reported point prevalence abstinence rates were 5.5% and 2.8%, respectively. Two years after the reimbursement period, still 4.3% in the reimbursement group and only 1.6% in the control group reported not having smoked. On the whole, the effectiveness of SCT after two years was 22% in the reimbursement group and 8% in the control group. In conclusion, reimbursing effective smoking cessation treatment may be an effective strategy to increase the prolonged abstinence rate, even after two years.

The findings of this Dutch study were supported by a Cochrane review presented in chapter 5, which described the general effect of reimbursement by comparing health care financing interventions for SCT in different countries.⁸⁻¹³ Healthcare financing systems, which offered full coverage, significantly increased the use of smoking cessation treatment, the number of participants who tried to quit smoking and prolonged/point prevalence abstinence rate(s). Although three of the six studies included the costs of the intervention, a full incremental cost effectiveness analysis was not performed yet.

Using the data from the Dutch reimbursement study, we carried out the first full economic evaluation on reimbursement for SCT. Results described in chapter 6 showed that reimbursement for SCT may not only be an effective intervention, but may also be cost-effective if society is willing to pay €10000 for an additional 12-month quitter or €18000 for an additional QALY.¹⁴ For the external validity of this last outcome, it is important to refer to the several assumptions that had to be made regarding the extrapolation of the effect in terms of quitters to the effect in terms of QALYs.

To be able to make a more accurate extrapolation from quitters to QALYs in the future, existing gaps in knowledge have to be filled like European mortality data for smokers and never-smokers in the general population, the distribution of lifetime relapse rates over time, and the uncertainty of the cost-effectiveness ratios of public health and smoking cessation interventions.

Implications of the findings

If one is willing to demonstrate that reimbursing smoking cessation treatment is a valuable tool to reduce the number of smokers and to increase life expectancy, then several steps need to be taken. These steps are described in the measurement iterative loop,¹⁵ and start and end with describing the burden of disease. The second and third step in the loop are to determine the causes of illness and to assess the effectiveness of potential interventions.

To reduce the burden of smoking related diseases, many studies have demonstrated that using SCT is both effective and cost-effective.^{2 16-20} In this thesis we also demonstrated that antidepressants for smoking cessation are cost-effective, if used by smokers at risk for or with COPD. Moreover, we evaluated the effectiveness of implementing a reimbursement system for SCT. From the findings presented in this thesis, it appeared that reimbursement can increase the number of quitters in the Netherlands and that these results can be extrapolated to other countries as well. As monetary resources are limited, determining the cost-effectiveness of reimbursement for SCT is an important next step in the measurement iterative loop. The reimbursement system used seems cost-effective if willing to pay €10000 for an additional quitter or €18000 for an additional QALY.

Taken all findings together, reimbursing SCT seems to be an effective and cost-effective intervention to reduce the costs of smoking related diseases and to increase life expectancy. Implementing reimbursement for SCT is consequently the only next step to make. To close the measurement iterative loop, an implemented reimbursement system for SCT has to be monitored and after some time the burden of smoking related diseases needs to reassessed.

In 2002, the Dutch House of Representatives already accepted a motion stating that smoking is an addictive disease.²¹ Like alcohol and drug addiction, nicotine addiction should be reimbursed on principal grounds. This thesis demonstrates that we now also have scientific evidence that reimbursement for SCT is both cost-effective and effective. Implementation of a reimbursement system in the Netherlands would not only lower the barrier for smokers to use SCT, but would also give health care providers more possibilities to set up or to expand their stop smoking activities.

At this moment, health care providers are not reimbursed for SCT they provide. Only if a patient consults the physician for smoking related health complaints, then SCT turns out to be an evident part of their work.²² As the position of prevention of smoking related diseases in primary care should be strengthened, reimbursement for the time and energy put into SCT by health care providers is important.⁶

Further increasing the use of SCT

Results presented in this thesis showed that reimbursement for SCT significantly increased its use to 10.8% and increased the one-year prolonged abstinence rate to 5.5%. This demonstrates that although reimbursement is an effective intervention, it cannot turn most smokers in to non-smokers. Qualitative data⁶ showed that a majority of the participants, 58% in the control

group and 65% in the intervention group, was in favour of reimbursement. However, for only 39% of the participants in the control group and 44% in the intervention group, reimbursement was an additional motivation to quit. Half of the participants in the intervention group, who did not apply for reimbursement, did not want to use smoking cessation treatment at all. This negative attitude towards SCT is a direct barrier for its use and needs to be opposed to further increase the effect of reimbursement. To overcome this barrier, more attention should be given to smoking as addictive disease. Information should be provided concerning the working mechanism of nicotine. Moreover, the different aids to quit smoking, their working mechanism and potential effects should be explained.

Further increasing the number of successful quitters

The most effective treatment currently available, pharmacotherapy combined with intensive behavioural counselling, has a success rate of maximal 24% after 12 months. Because there is still room for improvement, we should also look ahead for new pharmacological developments like nicotine vaccines, varenicline tartrate, and rimonabant,²³ but also the role of genetics, behavioural interventions and other restrictive and health promoting activities should not be underestimated;

- Nicotine vaccination causes the immune system to produce antibodies that bind nicotine and consequently prevents nicotine from entering the brain. As the positive stimulus by nicotine in the brain may no longer be present, this approach is expected to interrupt the vicious circle between smoking and nicotine-related gratification. Studies of three different vaccines have shown that multiple injections of a nicotine vaccine were safe and generated substantial amounts of nicotine-specific antibodies.^{24 25} The effect on smoking cessation needs however to be demonstrated.
- Varenicline tartrate is a selective nicotine receptor partial agonist for smoking cessation. It may relieve nicotine craving and withdrawal symptoms. In two parallel studies, 44% of varenicline-treated patients, 30% of the patients using bupropion and 18% in the placebo group quit smoking by the end of the 12-week treatment period.²⁶ These results are encouraging, however, since the intensity of smoking cessation interventions in clinical trials is much higher than in daily practice, the real effect may be overestimated.
- Rimonabant is a cannabinoid CB1 receptor antagonist. This drug reduces nicotine self-administration and is well tolerated, but its effects on smoking cessation are equivocal. It may have a valuable additional property of inhibiting post-cessation weight gain.

- Evidence has become available that nicotine addiction is related to genetic predisposition. For example, individuals with a genetic variant that decreases the function of the enzyme CYP2A6 may have greater resistance to nicotine addiction. The decrease in CYP2A6 slows the breakdown of nicotine and protects individuals against nicotine addiction. The DRD2 gene is more common in smokers who start smoking at an earlier age and who are less able to stop. Understanding the role of genetics in nicotine addiction may be a new target for developing more effective medications to help people stop smoking.
- Not only pharmacological treatment can increase the abstinence rate, but also behavioural interventions by health care providers can.²⁷ There is a positive dose-response relation between abstinence from smoking and the number of sessions with a health care provider, and between abstinence and the session duration.^{19,27} Yet, a single, short intervention can already significantly increase abstinence from smoking.^{19,28} Structural improvements within primary care could optimise the possibilities that health care providers have to assist smokers in their quit attempt.
- Other restrictive and health promoting activities, like increasing cigarette taxes, reducing cigarette sales to adolescents, smoke free work places and public areas can also have an important influence in the reduction of the number of smokers. The World Health Organisation even recently introduced a policy that bans the hiring of smokers in an effort to promote its public health campaign against tobacco use. This is in my opinion a step too far. One can promote healthy behaviour and make unhealthy behaviour less attractive, but people should in the end be free to live their own life. Since smoking has a strong addictive character, the choice to smoke may however often not be so voluntary as the smoker believes.

Reimbursement for SCT in the future?

Smoking is an addictive disease like alcohol and drug addiction.²¹ For these latter diseases reimbursement is available, but not for smoking since the Minister of Health in the Netherlands decided that smoking is a lifestyle and that smokers are consequently responsible for their own behaviour.

Using SCT is effective if willing to quit smoking and reimbursement can encourage its use. Reimbursement can encourage the use and assistance of health care providers, but the government and/or health insurance companies must be willing to invest. Although, reimbursement for SCT is a cost-effective intervention, one does have to be willing to pay €1000 for a quitter or €18000 for a QALY. In the battle of who needs to pay these costs, it is often heard that it is cheaper and consequently preferred, to continue smoking. This is in

contrast with MacKenzie et al.²⁹ who reported that the lifetime medical costs for smokers exceeded those for non-smokers. However, Barendregt et al.³⁰ found that if all smokers quit, health care costs would be lower at first, but after 15 years they would become higher and in the end, smoking cessation would lead to a net increase in health care costs. As long as there is no agreement whether smoking cessation increases or reduces lifetime medical costs, I suggest using a neutral budget like in the study concerning the cost-effectiveness of reimbursement.¹⁴ However, from a health care perspective increasing quality of life and life expectancy instead of making profit should be the priority of at least the Ministry of Health.

Results of a qualitative study showed that if reimbursement for SCT will be available after all, SCT has to be prescribed, since the contact with a health care provider is in that case guaranteed.⁶ However, it was also noticed that consequently the accessibility of the SCT is reduced, which is the opposite of what we want to achieve with reimbursement. A solution may be to reimburse the SCT on prescription, but to maintain the provision of SCT over the counter. Participants, health care providers and participating organizations preferred to only scientifically proven effective SCT that will be reimbursed. The opinions were mixed about providing full or partial reimbursement. The results of the Cochrane Review described in chapter 5, however showed that full reimbursement is more effective than partial reimbursement. There was no indication of providing reimbursement only for low-income groups.

Until now the debate of reimbursing SCT continues and maybe with the next shift of the government the focus goes from life style to addiction again. It is therefore necessary that reimbursement for SCT remains on the agenda and that its importance is being strengthened.

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Summary

Summary

Smoking is one of the most avoidable causes of death and disability in developed countries. To reduce the costs of smoking related diseases and to increase life expectancy, smoking cessation strongly needs to be encouraged. However, stopping smoking is not easy. The addictive effects of nicotine and the psychosocial aspects of smoking make it difficult to quit. Many studies have demonstrated that smokers who stop smoking are more successful when using smoking cessation treatment (SCT) like nicotine replacement therapy (NRT), bupropion, nortriptyline and behavioural interventions. However, despite the knowledge that using SCT increases the abstinence rate, and is highly cost-effective, the use remains limited. One way to increase the use of SCT may be to offer reimbursement.

The research questions of the studies in this thesis are presented in **chapter 1** and concern the cost-effectiveness of SCT in patients with chronic obstructive pulmonary disease (COPD) and the effectiveness and cost-effectiveness of reimbursement for SCT in the Netherlands and in general.

In **chapter 2**, we described the cost-effectiveness of bupropion and nortriptyline versus placebo in patients at risk or with existing COPD. This study was performed using the data of a randomised controlled trial. We assessed which intervention was most cost-effective in stopping smoking and in increasing the number of quality-adjusted life years (QALYs) saved for a relatively short time horizon of one year.

Results showed that if willing to pay more than €2000 for a quitter or more than €4000 for a QALY, bupropion was most cost-effective according to both the societal and health care perspective. Nortriptyline was never the most optimal intervention due to high medical costs. These high costs may be related to poorer health at baseline or more frequent side effects. Future studies are needed to replicate these findings. In patients with COPD, overall, costs were higher and the effects were lower than in patients at risk for COPD.

Since using SCT seems to be highly cost-effective even in smokers with COPD, the use of these treatment methods should be encouraged. One way to increase the use of SCT may be to offer reimbursement. Commissioned by the Dutch Minister of Health, research institute CAPHRI and STIVORO, in collaboration with health insurance company De Friesland and community health centre Fryslân, a randomised controlled trial was set up to study the effects of reimbursement for all proven effective smoking cessation interventions in the Netherlands. In **chapter 3**, we assessed whether financial reimbursement for SCT would increase the use of SCT and would as a result increase the number of smokers who were abstinent six months after the start of the study.

For this study, we recruited 1266 smokers aged over 18 years insured by one health insurance company. Respondents in the intervention group received an offer of reimbursement for nicotine replacement therapy, bupropion, and behavioural counselling. No reimbursement was offered to the control group. To preclude a change of behaviour due to disappointment in the control group, we used a randomised consent design.

During the reimbursement period, 10.8% of the participants in the intervention group reported having used SCT compared with 4.1% in the control group. After six months, the self-reported point prevalence abstinence rate was 7.8% (n=49) in the intervention group and 5.5% (n=35) in the control group. Reimbursement for SCT seems efficacious in increasing the use of SCT and increasing the number of successful quitters after six months.

In **chapter 4**, we presented data concerning the effect of reimbursement on abstinence from smoking and on the effectiveness of SCT for up to two years. 35 participants (5.5%) in the intervention group and 18 participants in the control group (2.8%) reported to be prolonged abstinent for at least six months. Two years after the reimbursement period, still 4.3% in the intervention group and 1.6% in the control group had not smoked. The overall effectiveness of SCT with reimbursement was 25%, i.e. 17 participants of the 68 participants who had used SCT in the intervention group were prolonged abstinent for six months. Two years after the reimbursement period, the overall effectiveness was 22%. Without reimbursement, the overall effectiveness of SCT was 15% six months after the reimbursement period and 8% after two years.

At the end, we concluded that reimbursement may be an effective strategy to increase prolonged abstinence and can increase the effectiveness of SCT even after two years.

In a Cochrane Review presented in **chapter 5**, we described the general effect of reimbursement by comparing health care financing interventions for SCT of different countries. We performed a meta-analysis using a random effects model.

Six eligible studies were identified by a computer-aided search of several databases. Four studies compared full coverage with no coverage and all showed a significant increase in: abstinence rate, in number of participants with at least one quit attempt and in the use of SCT. When full coverage was compared with partial coverage, the abstinence rate, the number of participants making a quit attempt and the use of SCT were higher with full coverage in all three studies that examined this comparison, but the increase was not always significantly higher. One study compared partial coverage with no coverage and found no significant differences.

Three studies included the costs of the financial intervention, but no incremental cost analyses were performed. We calculated the incremental cost-effectiveness ourselves and showed that the costs per user who quit were relatively low and varied between \$260 and \$2330 when comparing full coverage with partial or no coverage.

Chapter 6 presents the first full economic evaluation on reimbursement for SCT. Based on data from the Dutch reimbursement study, we calculated the incremental costs per quitter and extrapolated this outcome to costs per quality adjusted life year (QALY) saved. However, assumptions had to be made to perform this extrapolation. We estimated the uncertainty of the incremental cost effectiveness ratios by using non-parametric bootstrapping.

The mean costs per participant were €322 in the intervention group and €291 in the control group. If society is willing to pay €1000 or €10 000 for an additional 12-month quitter, the probability that reimbursement for SCT would be cost-effective was 50% or 95%. If society is willing to pay €18 000 for a QALY, the probability that reimbursement for SCT would be cost-effective was 95%.

In **chapter 7**, the implications of this thesis and the future of reimbursement for SCT are subject of discussion. Taken all findings of the previous chapters together, reimbursing SCT would be an effective and cost-effective intervention to increase the use of SCT, the number of quitters and the quality adjusted life expectancy. Implementing reimbursement for SCT seems consequently the only thing that is left to do.

In 2002, the Dutch House of Representatives already accepted a motion stating that smoking is an addictive disease. Like alcohol and drug addiction, nicotine addiction should be reimbursed on principal grounds. We now also have scientific evidence that reimbursement for SCT is both cost-effective and effective. Implementation of a reimbursement system in the Netherlands would not only lower the barrier for smokers to use SCT, but would also give health care providers more possibilities to set up or to expand their stop smoking activities. Since reimbursement cannot turn all smokers in to non-smokers, we should also look ahead for new pharmacological developments, genetics, behavioural interventions and other restrictive and health promoting activities.

Currently no reimbursement is available for SCT since the Minister of health considers smoking a lifestyle and that smokers are consequently responsible for their own behaviour. Maybe with the next shift of the government the focus goes from life style to addiction again. It is therefore necessary that reimbursement for SCT remains on the agenda and that its importance is being strengthened.

Samenvatting

Samenvatting

Roken is één van de belangrijkste oorzaken van ziekte en voortijdige sterfte in de Westerse wereld. Stoppen met roken moet sterk worden aangemoedigd om de kosten van rookgerelateerde ziekten te verlagen en om de levensverwachting te verhogen. De verslavende effecten van nicotine en de psychosociale aspecten van roken maken stoppen met roken lastig. Veel studies hebben aangetoond dat stoppen met roken meer succesvol is wanneer men gebruik maakt van hulpmiddelen zoals nicotine vervangende middelen, bupropion, nortriptyline en gedragsmatige ondersteuning. Ondanks dat het gebruik van hulpmiddelen het abstinenteratio kan verhogen en dat de mate van kosteneffectiviteit hoog is, blijft het gebruik beperkt. Het vergoeden van deze hulpmiddelen zou een manier kunnen zijn om dit gebruik te verhogen.

De onderzoeksvragen van de studies in dit proefschrift staan beschreven in **hoofdstuk 1** en betreffen de kosteneffectiviteit van hulpmiddelen in patiënten met chronische obstructieve longziekten (COPD) en de (kosten)-effectiviteit van het vergoeden van hulpmiddelen voor stoppen met roken in Nederland en in het algemeen.

In **hoofdstuk 2** beschrijven we de kosteneffectiviteit van bupropion en nortriptyline ten opzichte van placebo bij patiënten “at risk” of met bestaande COPD. In een gerandomiseerde studie onderzochten we welke interventie het meest kosteneffectief was na 1 jaar in termen van stoppen met roken en het verhogen van het aantal voor kwaliteit gecorrigeerde levensjaren (QALYs).

Uit de resultaten bleek dat wanneer de maatschappij of de gezondheidszorg bereid is om meer dan €2000 te betalen voor een stopper of meer dan €4000 voor een QALY, dat dan bupropion de meest kosteneffectieve interventie was. Vanwege de hoge medische kosten was nortriptyline nooit de meest kosteneffectieve interventie. Deze hoge kosten zouden gerelateerd kunnen zijn aan een slechtere gezondheid op baseline of aan meer bijwerkingen bij het gebruik van nortriptyline. Meer studies zijn nodig om de bevindingen uit deze studie te repliceren. In het algemeen waren bij patiënten met COPD de kosten hoger en de effecten kleiner dan bij patiënten “at risk” voor COPD.

Aangezien het gebruik van hulpmiddelen voor stoppen met roken in hoge mate kosteneffectief is, zou het gebruik van deze methoden moeten worden gestimuleerd, bijvoorbeeld door het aanbieden van een vergoeding. In opdracht van de Minister van Volksgezondheid, Welzijn en Sport werd door onderzoeksinstituut CAPHRI en STIVORO, in samenwerking met De Friesland Zorgverzekeraar en GGD Fryslân, een gerandomiseerd onderzoek opgezet om het effect van het vergoeden voor alle bewezen effectieve middelen te bepalen in Nederland.

In **hoofdstuk 3** onderzochten we of een vergoeding het gebruik van hulpmiddelen zou verhogen en of het aantal mensen dat stopte met roken hoger was zes maanden na de start van de studie. 1266 rokers ouder dan 18 jaar en verzekerd bij één ziektekostenverzekering deden mee aan het onderzoek. Deelnemers in de interventiegroep kregen een aanbod om gedurende zes maanden een vergoeding te kunnen ontvangen voor nicotine vervangende middelen, bupropion, en gedragsmatige interventies. De controlegroep kon geen vergoeding ontvangen. Om verandering van gedrag door teleurstelling in de controlegroep te voorkomen gebruikten we een “randomised consent” design. Hierbij worden deelnemers alleen geïnformeerd over het specifieke doel van hun eigen onderzoeksgroep.

Tijdens de vergoedingsperiode werden door 10.8% van de deelnemers in de interventiegroep hulpmiddelen gebruikt. In de controlegroep was dit 4.1%. Na zes maanden was het percentage zelfgerapporteerde stoppers 7.8% (n=49) in de interventiegroep en 5.5% (n=35) in de controlegroep. Een vergoeding voor hulpmiddelen bij het stoppen met roken lijkt daarmee het gebruik van hulpmiddelen en het aantal stoppers na zes maanden te kunnen verhogen.

In **hoofdstuk 4** presenteerden we het effect van vergoeden op continue abstinentie voor een periode van zes maanden en een periode van twee jaar. Tevens keken we naar de effectiviteit van de gebruikte hulpmiddelen. Vijfendertig deelnemers (5.5%) in de interventiegroep en 18 deelnemers in de controlegroep (2.8%) waren tenminste zes maanden gestopt met roken. De algehele effectiviteit van de gebruikte stop-roken middelen was 25% in de vergoedingengroep; 17 van 68 deelnemers die ondersteuning hadden gebruikt waren nog gestopt met roken. In de controlegroep was dit 15%. Twee jaar na de vergoedingsperiode had 4.3% in de interventiegroep en 1.6% in de controlegroep nog niet gerookt. De algehele effectiviteit van de gebruikte middelen was nu nog 22% in de vergoedingengroep en 8% in de controlegroep. In dit hoofdstuk concludeerden we dat het vergoeden van hulpmiddelen bij het stoppen met roken een effectieve strategie kan zijn om het aantal stoppers te vergroten en de effectiviteit van de hulpmiddelen te verhogen, zelfs na twee jaar.

In een Cochrane Review gepresenteerd in **hoofdstuk 5** vergelijken we vergoedingssystemen voor hulpmiddelen bij het stoppen met roken van verschillende landen. We deden een meta-analyse en gebruikten een “random effects model”.

Zes studies werden geïdentificeerd met een computergestuurde zoekopdracht in verschillende databases. Vier studies vergeleken een volledige vergoeding met geen vergoeding en toonden een significante verhoging aan van het aantal stoppers, het aantal deelnemers met tenminste één stoppoging en het gebruik

van stop-rook middelen. Wanneer een volledige vergoeding werd vergeleken met een gedeeltelijke vergoeding stegen het aantal stoppers, het aantal deelnemers met tenminste één stoppoging en het gebruik van ondersteuning. Echter de stijging was niet altijd statistisch significant. Eén studie vergeleek gedeeltelijke vergoeding met geen vergoeding en vond geen significante verschillen.

Drie studies bepaalden tevens de kosten van de financiële interventie, maar presenteerden geen incrementele kosteneffectiviteitsratios. Wanneer we dit zelf berekenden dan waren met een volledige vergoeding de kosten per stopper relatief laag en varieerde tussen de \$260 en \$2330, indien vergeleken met een gedeeltelijke of geen vergoeding.

Hoofdstuk 6 beschrijft de eerste volledige economische evaluatie van het vergoeden van hulpmiddelen bij het stoppen met roken. Op basis van de gegevens uit de vergoedingenstudie beschreven in hoofdstuk 3 en 4, berekenden we de incrementele kosten per stopper en extrapoleerden deze uitkomst naar de kosten per QALY. Echter om deze extrapolatie te kunnen doen moesten verschillende aannames worden gemaakt. De onderzekerheid om de incrementele kosteneffectiviteitsratios werd geschat via non-parametrisch “bootstrapping”.

De gemiddelde kosten per deelnemer waren €322 in de interventiegroep en €291 in de controlegroep. Wanneer de maatschappij bereid is om €1000 of €10000 te betalen voor een extra stopper, dan is de waarschijnlijkheid dat het vergoeden kosteneffectief is respectievelijk 50% en 95%. Wanneer men bereid is om €18000 te betalen voor een QALY, dan is de waarschijnlijkheid dat het vergoeden een kosteneffectieve interventie is, 95%.

In **hoofdstuk 7** worden de implicaties van dit proefschrift en de toekomst van het vergoeden van hulpmiddelen voor stoppen met roken besproken. Wanneer alle bevindingen uit de vorige hoofdstukken worden samengevat, blijkt dat het vergoeden van hulpmiddelen voor stoppen met roken een effectieve en kosteneffectieve manier is om het gebruik van hulpmiddelen, het aantal stoppers en de voor kwaliteit gecorrigeerde levensverwachting te verhogen. Het implementeren van de vergoeding voor deze hulpmiddelen is eigenlijk het enige dat nog gedaan moet worden.

In 2002 werd in de Tweede Kamer een motie geaccepteerd waarin roken een verslavingsziekte werd genoemd. Net als alcohol- en drugsverslaving, zou nicotineverslaving op principiële gronden vergoed moeten worden. Uit dit proefschrift blijkt dat er nu ook wetenschappelijk bewijs is dat het vergoeden tevens een (kosten)-effectieve interventie is. Implementatie van een vergoedingensysteem zou in Nederland niet alleen de barrière verlagen voor rokers om ondersteuning te gebruiken, maar het zou daarbij zorgverleners

meer mogelijkheden geven om stop-roken activiteiten op te zetten of deze uit te breiden. Aangezien een vergoeding voor hulpmiddelen er niet voor zorgt dat alle rokers stoppen, moeten we ook verder kijken naar nieuwe farmacologische ontwikkelingen, genetica, gedragsmatige interventies en andere beperkende of gezondheidsstimulerende activiteiten.

Op dit moment is er geen vergoeding voor hulpmiddelen bij het stoppen met roken beschikbaar, omdat de huidige minister roken meer een leefstijl vindt en rokers vervolgens zelf verantwoordelijk zijn voor hun gedrag. Wanneer er een wisseling komt van regering wordt roken misschien weer benaderd als verslaving. Het is daarom belangrijk dat het vergoeden van hulpmiddelen voor stoppen met roken op de agenda blijft staan.

Dankwoord

Dankwoord

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“Where north meets south”

Het onderzoek naar het vergoeden van hulpmiddelen bij het stoppen met roken vond plaats in Friesland. Met de steun van de GGD Fryslân, De Friesland Zorgverzekeraar en STIVORO is dit een meer dan geslaagd project geworden. *Bert Soenveld*, *Siebre Wieling*, *Peter van Winsen*, *Mieke Riezebos*, *Grieto Zeeman* en *Marc Willemsen*, heel erg bedankt voor jullie inbreng en inzet!

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About the author

About the author

On October 13, 1978 Janneke Kaper was born in Goes, the Netherlands. Until the age of 7, she lived in the province of Zeeland, then moved to South Holland and 3 years later to Limburg.

After completing secondary school (VWO) in Geleen in 1997, she studied Movement Sciences at the Free University, Amsterdam, and took several courses on neuroscience, physiology, psychology, occupational health, rehabilitation and research skills. She graduated in November 2001 and in February 2002, she started working as a researcher at the Department of General Practice of Maastricht University on a project about reimbursement for smoking cessation treatment. Janneke performed qualitative and quantitative analyses and assessed the cost-effectiveness of reimbursement for smoking cessation in the general population and of antidepressants for smoking cessation in patients with COPD.

Besides the work for this thesis, she took courses on international comparison of health systems, medical technology assessment, statistics, fundraising and good clinical practice. Additionally, she coordinated a phase 3b trial of Varenicline tartrate and worked on the guideline "Treating tobacco dependence" of the Dutch Institute for Healthcare Improvement (CBO) and on the practice guideline "Smoking cessation" of the Dutch College of General Practitioners (NHG).

Since July 2006, she has been working as a senior researcher at the Department of General Practice and currently supervises a project on cardiometabolic risk reduction by rimonabant and lifestyle counselling.

Janneke lives in Guttecoven, a small village near Sittard, together with Dave Winkens.