

## **The SMOKE study**

### *Background*

Chronic Obstructive Pulmonary Disease (COPD) is a widespread and growing health problem merely due to the smoking trends of the last decades, smoking is the only avoidable cause of the disease. Approximately 15% of the cases develop COPD and only 5% of the COPD patients never smoked. Smoking cessation is the only evidence based intervention that reduces the accelerated decline of pulmonary function and improves the prognosis of COPD. The urgency of developing an effective smoking cessation programme is therefore high. Previous research also indicates that the quality of life will increase if a smoker becomes an ex-smoker.

COPD patients generally have a long smoking history and are heavily addicted to smoking. COPD patients have a strong nicotine dependency which is illustrated by the fact that they maintain their smoking behaviour despite the fact that they experience smoking related complaints. In addition, most COPD patients have undertaken several quit attempts. The LMIS is currently recommended in the Netherlands as the preferred smoking cessation programme in COPD patients. Unfortunately, this intervention seemed to be unsatisfying for this specific target group. A more intensive smoking cessation programme might be more effective for these outpatients.

The SMOKE study is a randomised controlled multi-centre trial. This trial compares the effectiveness of a new developed high-intensity smoking cessation programme targeted at COPD outpatients, the SmokeStopTherapy (SST), with the Minimal Intervention Strategy for Lung patients (LMIS). Both interventions are based on theories of behavioural change: the Attitude-Social influence-Efficacy-model (ASE-model), the Transtheoretical Model (TTM), and Marlatt's Relapse Prevention model. Motivational Interviewing (MI) was used as a counselling tool throughout the whole intervention.

*Effectiveness of the new developed intervention*

Outpatients with moderate to severe COPD, willing to quit smoking, were randomly assigned to the SST or LMIS. 234 patients were randomised but due to 9 drop outs before the baseline measurements, 225 patients were eventually followed up. The SST consists of both individual and group counselling, telephone contacts and bupropion free of charge. Additionally, patients can re-enter the individual sessions after they experienced a lapse within three months after the start of the intervention ('recycling') to prevent a total relapse. The LMIS consists of individual counselling and telephone contacts which could be combined with pharmacological support at the patients' own expenses.

The primary outcome measures are continuous and point prevalent abstinence from smoking after one year, validated by salivary cotinine. Analysis was by intention-to-treat. The cotinine validated continuous abstinence rates after 12 months are 19% for SST and 9% for the LMIS (RR= 2.22; 95% CI: 1.06-4.65;  $p=0.03$ ). The 12-month point prevalent abstinence rates are 22% for patients receiving SST versus 12% for patients receiving LMIS (RR= 1.80; 95% CI: 0.97-3.37;  $p=0.06$ ). Discrepancy between the self-reported and validated smoking status was found in 12% in the SST group and in 20% in the LMIS group. The SST is therefore concluded to be more effective than the LMIS after one year follow-up based on validated continuous abstinence rates.

*Baseline characteristics predicting continuous abstinence*

Another aim of this study was to identify characteristics of smoking COPD patients participating in a smoking cessation programme that predict successful quitting.

A wide range of social-cognitive, demographic, smoking related and medical characteristics were measured at baseline. Only variables that showed a (marginally) significant ( $p < .20$ ) univariate relationship with cotinine-validated continuous abstinence at 12 months were included in a full logistic regression model. Subsequently, variables that did not remain independent predictors of continuous abstinence were removed, one by one.

A positive attitude with regard to smoking cessation (OR 11.8; 95% CI: 1.7-81.5) and the cotinine level at baseline (OR 2.1; 95% CI: 1.08-3.93) were independent predictors of continuous abstinence for the LMIS. For the SST subjects no independent significant

predictor for continuous abstinence remained. It can be concluded that the LMIS is only suitable for COPD patients with a strong positive attitude regarding smoking cessation at baseline. The SST can be seen as an alternative for patients not possessing such baseline characteristic. This stepwise approach may be useful in clinical practice and will lead to increased efficiency by matching the interventions to the patients' needs.

### **CAMOXI study**

Biochemically validated smoking status should be the primary outcome measure when investigating the effectiveness of smoking cessation programmes because of the high 'deceiving-rate' in such circumstances. Because Carbon Monoxide (CO) measurements have several advantages over the measurement of cotinine (e.g. non-invasive, direct feedback, less costly) the use of CO measurements might be very useful. CO monitors are also widely used in research concerning the effectiveness of smoking cessation interventions. These factors contribute to the relevance of validating CO monitors for their use in smoking cessation research.

The CAMOXI study validates three carbon monoxide (CO) monitors regarding their ability to distinguish smokers from non-smokers, in participants with and without COPD. Salivary cotinine measures were also validated. 26 'healthy' smokers, 25 healthy non-smokers, 25 smoking and 24 former smoking stable COPD patients (age 40-72 years) were included (N=100). Smokers were determined by self-report and non-smokers by a combination of self-report and cotinine measurements (< 20ng/ml) and COHb in blood. The exhaled CO level of the 51 smokers was measured before, and 1 through 6 hours after smoking one cigarette. Because the 49 non-smokers naturally did not smoke a cigarette after one hour, they solely served as control group for the measurements beyond one hour. All smoking participants were measured following a 12-hour abstinence period. Sensitivity, specificity, positive predictive values and negative predictive values were calculated for range of cut-off points for both CO and cotinine measurements.

The Breath CO<sup>®</sup> generates a sensitivity of 68% for COPD patients and 42% for the healthy participants, using the factory-prescribed cut-off point of 9 ppm. The 10 ppm factory-prescribed cut-off point of the Smokerlyzer<sup>®</sup> generates 56% sensitivity for COPD

patients and 23% for healthy participants. Both monitors generate 100% specificity in both groups. The factory-prescribed cut-off point for the Micro CO meter<sup>®</sup> (5 ppm) generates 88% sensitivity and 92% specificity for COPD patients, and for healthy people 92% sensitivity and 88% specificity. Salivary cotinine has a 100% sensitivity, specificity, positive predictive value, and negative predictive value over the range of 15 ng/ml through 40 ng/ml for healthy participants and at 10 ng/ml for COPD patients. For this specific analysis, self-reported smoking status was used as the ‘gold standard’.

The validation of the CO monitors over time was also investigated. Six hours after smoking one cigarette, Breath CO<sup>®</sup> detects 48% of the COPD patients and 15% of the ‘healthy’ smokers at the prescribed 9 ppm cut-off point. The Smokerlyzer<sup>®</sup> (10 ppm factory-prescribed cut-off point) detects 36% and 12% respectively. The Micro CO meter<sup>®</sup> (5 ppm factory-prescribed cut-off point) detects 92% and 85%. Remarkably, the CO-values, as measured with the three monitors, are actually quite similar with minor deviations of 1 or 2 ppm. This contradiction is caused by the different factory-prescribed cut-off points.

The prescribed cut-off points for all three CO monitors generate misleading results concerning the determination of the smoking status in both populations after a 12-hour period of abstinence. For the measurement of CO over time, it can be concluded that smokers are able to deceive CO monitors by short-time abstinence, unless the cut-off points are being adjusted properly. The optimal cut-off points depend upon the goal of the study but salivary cotinine measurements outperforms the CO measurements and can therefore be considered the ‘gold standard’. Cotinine measurements are relatively costly; a cost-effective validation procedure combining both tools is therefore recommended.