

**Short-term change in self-reported COPD symptoms
after smoking cessation in an Internet sample**

Running title Smoking and COPD symptoms

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ABSTRACT

Background. Smoking is the first risk factor for COPD. Some recent reports suggest that, unexpectedly, some respiratory symptoms may increase transiently after smoking cessation, but there is a dearth of short-term data to test this hypothesis.

Aim. To assess the validity of an online screening tool and to describe short-term associations between smoking behaviour and self-reported respiratory symptoms, in cross-sectional and longitudinal data.

Methods. Internet survey in 2003-2009, on a smoking cessation website, with a follow-up survey after 30 days.

Findings. There were 15,916 participants at baseline and 1,831 at follow-up. In the 252 baseline smokers who had quit smoking at 30-day follow up, there was a substantial decrease in the proportion of participants who declared that they often coughed even without a cold (from 51.6% at baseline to 15.5% at follow-up), expectorated when they coughed in the morning (from 47.6% to 19.4%), were out of breath after climbing stairs or after a quick walk (from 75.0% to 48.4%), and who had a wheezing respiration (from 33.7% to 10.3%, $p<0.001$ for all before-after comparisons). In participants who did not change their smoking behaviour between assessments, the test-retest reliability was $r=0.87$ for a score summing these 4 symptoms.

Interpretation. Smoking cessation was followed by a rapid and substantial improvement in self-reported respiratory symptoms. COPD is largely underdiagnosed and undertreated. Internet screening is reliable and may allow for the early detection of COPD symptoms at a large scale, in patients who may otherwise have no access to COPD case-finding efforts.

MeSH Key Words. Tobacco Use Disorder; Smoking; Internet.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major public health problem, and the number of COPD patients is increasing worldwide. In the U.K., 13% of the population over the age of 35 have spirometry-defined COPD,(1) most (73%) COPD deaths are attributable to smoking and COPD mortality accounts for 4.8% of the total mortality.(2)

Effect of quitting smoking on respiratory symptoms

Smoking cessation is the most effective way to prevent COPD and to alter its progression, at any stage of the disease.(3) The long-term benefits of smoking cessation on COPD are well documented,(4-6) but recent literature reviews found surprisingly few studies on the short-term (i.e. after a few days or weeks) effects of smoking cessation on respiratory symptoms.(7, 8) Furthermore, the few available short-term studies were often conducted in small samples and some of them are decades old.(8) Older studies may not reflect the current situation, as cigarette consumption among smokers and the composition of cigarettes changed substantially in the past decades.(9, 10) The few available short-term studies show that respiratory symptoms (cough, expectoration, breathlessness, wheezing) improve since the first days and weeks after smoking cessation.(8, 11, 12) However, increased coughing has been described anecdotally as a cigarette withdrawal symptom,(7) and a recent study also suggests that cough and common cold symptoms may increase transiently after smoking cessation,(13) an effect that could be explained by a reduction in secretory immunoglobulin A.(14) In spite of the dearth of short-term data, both the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) list increased cough among tobacco or nicotine withdrawal symptoms. There is a need for more short-term data to resolve this apparent contradiction. Also, as the DSM-V and ICD-11 are under development, it is important to document whether or not increased cough is a tobacco or nicotine withdrawal symptoms.

Screening for COPD

Spirometry is essential to the diagnosis of COPD, but it is not always available in primary care settings, and even when it is available, spirometry is often underused.⁽¹⁵⁾ As a result, COPD is largely underdiagnosed, and only 47% of people with severe COPD report any diagnosed respiratory disease.⁽¹⁾ COPD symptoms may remain unnoticed and considered normal by patients (e.g. smoker's cough), who may not present to their doctor until they have severe, irreversible symptoms.⁽¹⁵⁾ Wider case-finding efforts are necessary, but screening the general population with spirometry, although it has been done,⁽¹⁶⁾ is costly and is unlikely to be widely adopted. Questionnaire screening may be a cost-effective way to select patients eligible for spirometry, but a 2005 review found surprisingly few validated COPD questionnaires,⁽¹⁵⁾ and few other questionnaires were published since this review.⁽¹⁷⁻¹⁹⁾ These studies show that questionnaire screening is useful and feasible in clinical practice, but COPD screening questionnaires have not been tested on the Internet. However, COPD screening over the Internet may reach large numbers of patients and may allow for the early detection and referral for clinical assessment and spirometry, thereby improving patients' prognosis. Online screening tools are available 24/7/365, at no charge to participants, even in rural or deprived areas where patients may otherwise have no access to COPD screening. Online screening may be particularly useful and cost-effective in low- or middle income countries, e.g. China, which is the country with the largest number of Internet users, and where smoking prevalence is very high among men.^(20, 21) Online COPD screening questionnaires need to be brief and written in simple language, criteria that some of the available COPD questionnaires may not fulfil. However, before Internet screening can be recommended, there is a need to test the validity of this approach.

The motivational impact of testing for respiratory symptoms

In addition to allowing for early detection of COPD and referral for spirometry, COPD screening questionnaires are also useful as motivational tools. Smokers are more motivated to stop smoking if they realize that their respiratory problems are caused by smoking rather than by other causes,(22) and if they believe that health gains will result from quitting smoking.(23)

Aim

Thus, the aims of this study were to assess the feasibility and validity of Internet-based COPD screening, and to describe short-term associations between self-reported respiratory symptoms and smoking status.

METHODS

Participants

Participants were visitors of the smoking cessation website Stop-tabac.ch, aged 18 or more.(24) We posted the questionnaire, in French, between September 2003 and March 2009, on Stop-tabac.ch. A link to the questionnaire was posted on several pages of this website, which was visited by over 80 000 people per month.(24) During much of the data collection period, the survey was listed 3rd in Google.ch when typing “BPCO” (French for COPD). From August 2005 onwards, participants who agreed and who indicated an e-mail address were invited by e-mail to answer the same survey again, after 30 days.

Questionnaire content

The questionnaire covered age and sex, whether participants smoked tobacco or cannabis daily or occasionally (not daily), or whether they were former smokers or never smokers. Current smokers indicated the number of cigarettes they smoked per day and the time (minutes) to their first cigarette of the day, both indicators of addiction.(25) Former smokers indicated the date when they had quit smoking. We used a brief questionnaire recommended by the Swiss

Pulmonary League to assess COPD symptoms (http://www.lung.ch/fr/test-bpco.html?no_cache=1). Participants answered (yes/no) the following questions: “Do you often cough even without a cold?”, “Do you expectorate when you cough in the morning?”, “Are you out of breath after an effort like climbing stairs or a quick walk?”, “Do you have a wheezing respiration?” and: “Did you ever have asthma diagnosed?”. We computed a 0-4 sum score, counting 1 point for each symptom (cough, expectoration, breathlessness, wheezing). These 4 symptoms, in particular expectorating without a cold, are good indicators of COPD.⁽¹⁷⁾ We used a yes/no response format because previous research showed that for respiratory symptoms, multiple response options add only marginal discriminatory power over a yes/no response format.⁽¹⁹⁾ In clinical and Internet settings, the simplicity of the yes/no response format outweighs any minor advantage of multiple response formats. We also recorded participants’ computer numbers and Internet protocol (IP) addresses, to identify duplicate records. Participants were informed that their answers were stored on a computer file and given the option of declining to have their answers retained on file.

Validity of the data

Three criteria of data validity were considered: the percentage of missing answers, test-retest reliability and construct validity, reflected by the ability of the questionnaire to detect expected effects (e.g., change over time). We used intraclass correlation coefficients to assess test-retest reliability of individual symptoms and of the 0-4 sum score. We assessed whether reliability coefficients were above the recommended threshold of 0.7.⁽²⁶⁾ The test-retest analysis was performed only in the 428 participants in whom we hypothesized that symptoms levels would be stable over time: the 266 daily smokers who did not change their cigarette consumption by more than 10% between baseline and follow-up, and the 162 former smokers who had quit smoking >365 days before baseline and were still ex-smokers at follow-up.

Associations between smoking status and respiratory symptoms

In cross-sectional data, we tested whether respiratory symptoms differed between current-, former- and never-smokers. In daily smokers, we tested whether respiratory symptoms were associated with cig./day and with time to the first cigarette of the day. In former smokers, we tested whether respiratory symptoms were associated with duration of abstinence.

In longitudinal data, we hypothesized that after 30 days, respiratory symptoms would:

- improve in the 252 baseline daily smokers who had quit smoking at the time of the 30-day survey, compared with the 266 daily smokers who did not change their cigarette consumption by more than 10% between baseline and follow-up, in whom we hypothesised that symptoms would remain stable.
- improve in the 34 baseline smokers who had ever had asthma diagnosed and who had quit smoking at follow-up.(27)
- improve in the 220 baseline recent quitters who quit smoking <31 days before baseline and were still ex-smokers at follow-up, compared with the 162 people who quit smoking >365 days before baseline and were still ex-smokers and follow-up, in whom we hypothesised that symptoms would remain stable.

Statistical analyses

We used χ^2 tests to compare proportions, ANOVA F tests to compare means, and Mann-Whitney U tests to compare medians. We used McNemar tests to assess change over time in respiratory symptoms, within groups.(26) To assess between-group differences in change over time, we computed a follow-up minus baseline score for each symptom and used χ^2 tests to compare groups on these difference scores. We used linear regression models to assess associations between continuous variables, with and without adjustment for age, sex and asthma diagnosis (since these variables were associated with respiratory symptoms).

RESULTS

Participation

After deletion of 1,437 duplicate records (8.3% of the 17,353 records in the raw database), there remained 15,916 participants at baseline, of whom 4,668 (47.0% of the 9,927 who answered after August 2005, that is, after we started to collect e-mail addresses) agreed to take part in the follow-up survey and indicated an e-mail address (Figure 1). Of these, 1,831 (39.2% of 4,665) answered the 30-day survey. Baseline participants were on median 35 years old, 47% were men, 69% were daily smokers, 4% occasional (non-daily) smokers, 24% former smokers and 4% had never been smokers. An asthma diagnosis was reported by 14.2% of participants. Daily smokers smoked 18 cigarettes per day and they smoked their first cigarette within 23 minutes of waking up (medians). Former smokers had quit smoking 65 days (median) before the baseline survey (25th and 75th percentiles: 13 and 386 days). The follow-up survey was answered 31 days (median) after baseline (25th and 75th percentiles: 30 and 34 days). Compared to those who did not take part in the 30-day follow-up survey, those who answered this survey were older and more likely to be women and former smokers, and they were slightly less likely to report respiratory symptoms (Table 1).

Validity

For the 4 questions on respiratory symptoms, there were 0.4 to 1.3% of missing answers. There were 1.5% of missing answers to the question on asthma. The test-retest intraclass correlation coefficients were $r=0.87$ (95% CI: 0.85-0.90) for the 0-4 sum score, $r=0.80$ (0.75-0.83) for cough without a cold, $r=0.76$ (0.71-0.80) for expectorating in the morning, $r=0.78$ (0.73-0.82) for breathlessness, and $r=0.76$ for wheezing (0.71-0.80).

Cross sectional analysis

Respiratory symptoms were higher in daily smokers than in occasional-, former- and never-smokers, but the prevalence of respiratory symptoms was high in all groups (Table 2). In daily smokers, there was a linear, dose-response association between cig./day and the presence of respiratory symptoms (+0.32 symptoms for each additional 10 cig./day, 95% confidence interval (CI): 0.30-0.34, $p<.001$). This association was only slightly modified after adjustment for age, sex and asthma (+0.31 symptoms per 10 cig./day, 95% CI: 0.29-0.34, $p<.001$). Compared with smokers of 1-9 cig./day, about twice as many smokers of 25+ cig./day reported each symptom (Table 3). Most smokers of 25+ cig./day reported cough without a cold (62.0%), expectorating in the morning (57.9%) and breathlessness (82.6%). In daily smokers, there was an inverse, linear association between minutes to the first cigarette of the day and the number of respiratory symptoms (0-5 minutes: 2.5 symptoms; 6-30 minutes: 2.0 symptoms, 31-60 minutes: 1.8 symptoms; 61+ minutes: 1.5 symptoms, $F=149.7$, $p<.001$).

In former smokers, the duration of abstinence was strongly, negatively associated with the presence of all 4 symptoms. For instance, twice as many recent quitters who had quit 0-7 days before baseline reported cough and expectoration, compared to former smokers who had quit 92-365 days ago (Table 4). Respiratory symptoms were less frequent in recent quitters who had quit 0-7 smoking days before baseline than in daily smokers ($\chi^2=7.6$ and $p\leq 0.006$ for between-group differences in all 4 symptoms).

Longitudinal analysis

Quitters - At 30-day follow-up, 27.0% (252/935) of baseline smokers had quit smoking. In these 252 quitters, the median duration of abstinence at follow-up was 31 days (25th and 75th percentiles: 20 and 35 days). In quitters, all respiratory symptoms improved substantially between baseline and follow-up, as hypothesized (Table 5). The between-group difference in change over time in respiratory symptoms between recent quitters and continuing smokers was

statistically significant ($p \leq .003$) for all symptoms (Table 5). The total number of symptoms (0-4 sum score) decreased in 61.5% of recent quitters, remained stable in 31.7% and increased in 6.8% of them. Of the 252 quitters, 34 had ever had asthma. In this subgroup too, all respiratory symptoms improved after smoking cessation (cough: from 67.6% at baseline to 35.3% at follow-up, $p=0.01$; expectoration: from 70.6% to 38.3%, $p=0.007$; out of breath: from 91.2% to 58.8%, $p=0.001$; wheezing: from 76.5% to 32.4%, $p<.001$).

Recent quitters vs. long-term former smokers - In the 220 recent quitters who had quit <31 days before baseline and who remained ex-smokers at 30-day follow-up, all respiratory symptoms improved over time, as hypothesized, whereas in the 162 long-term ex-smokers (who had quit >365 days before baseline), respiratory symptoms remained stable. The differences in change over time between these 2 groups were statistically significant for all symptoms (Table 6).

DISCUSSION

Our results have two broad types of implications. First, they document that online screening for COPD symptoms is feasible at a low cost in very large samples and can produce data of good quality. We assessed three criteria of validity. First, we showed that these items produced very few missing data. Second, we showed that test-retest reliability was high for the 0-4 sum score and adequate for the 4 individual items. Third, by showing that brief, simple questions on respiratory symptoms are sensitive to change over time in smoking behaviour, our data provide a test of construct validity for this questionnaire.(26) These results suggest that this questionnaire can be a valid and reliable COPD screening tool, used either online, to detect at-risk patients and refer them for clinical assessment, or in clinical practice, to select patients eligible for spirometry. A brief COPD questionnaire can also be used to teach smokers and make them aware that their symptoms are not normal, that they can be a sign of COPD and are probably due to smoking. This information can motivate smokers to quit.(16, 22, 23)

Second, this is one of relatively few studies documenting the short-term effects of smoking cessation on respiratory symptoms.(7, 8) In cross-sectional data, in former smokers, respiratory symptoms were strongly, inversely associated with the duration of abstinence, but this association may not be necessarily causal, because usually, only the less addicted smokers (those who may also, on average, have less severe respiratory symptoms) reach long-term abstinence. However, in longitudinal data, quitting smoking was rapidly followed by a substantial improvement in cough, expectoration, breathlessness and wheezing. Thus, our results disagree with the ICD-10 and DSM-IV definition of nicotine/tobacco withdrawal. They also disagree with recent data showing that there is a short-term deterioration in cough and cold symptoms after smoking cessation,(13, 14) and with the common but anecdotal belief that cough increases after smoking cessation.(7) In contrast, our results are in agreement with the few previous short-term studies reporting an improvement in cough and other respiratory symptoms in the first days or weeks after smoking cessation,(8, 11, 12) including in patients with asthma.(27) Even though on average, respiratory symptoms improved substantially after smoking cessation, the number of symptoms increased in a minority (6.8%) of quitters, which may explain the occasional observation that these symptoms increase after smoking cessation.(7, 13)

Study strengths and limitations

Our data collection procedure, based on the self-selection of visitors of a smoking cessation website and on a Google link, probably selected people concerned about COPD and resulted in a sample with a high prevalence of smoking and of respiratory symptoms. The prevalence of cough and expectoration was higher in our sample (>45% in smokers) than in the general population of smokers (10-40%),(8) and the prevalence of asthma was also higher in our sample (14%) than in the general population (~10% in Europe).(28) Furthermore, participants were

somewhat young (median=35 years) for an assessment of COPD. Thus, our results may not be generalizable to other populations, and this study should not be interpreted as a prevalence study. However, our aim was not to produce prevalence estimates, but to assess the validity of online COPD screening and to test associations between smoking and respiratory symptoms in the short term. Studies in representative samples are still necessary because of the paucity of short-term longitudinal data on this topic, and because of the small size of many previous samples.(7, 8) Even though it resulted in a selected sample, the Internet-based data collection was a very effective (and cost-effective) way to enrol one of the largest longitudinal samples described to date in a study of smoking and respiratory symptoms.

The response rate at follow-up (39.2%) was relatively low, but close to the average response rate of 39.6% observed in a meta-analysis of Internet surveys.(29) Participants in the follow-up survey differed from non-participants. This may limit the generalizability of the longitudinal analysis, but it does not affect the validity of this analysis. Collecting follow-up data after 30 days ensured that we captured the short-term effects of smoking cessation, but all the benefits of smoking cessation on respiratory symptoms do not materialize after such a short interval, and these effects can only be documented in long-term data. At follow-up, the average duration of abstinence in recent quitters was 31 days, which may have been too long to detect very short-term effects (e.g. a peak in cough 2-3 days after quitting). Studies with very short follow-ups would be necessary to detect these effects.

Another limitation of this study is that we conducted a limited set of validity tests only. Further tests of construct validity would be useful. Ideally, tests of sensitivity and specificity should also be conducted, with a clinical diagnosis of COPD as the reference, and results should be compared with the performance of other COPD screening questionnaires.(15, 17-19, 30)

Conclusion

Respiratory symptoms improved substantially and rapidly after smoking cessation. This information can be used to motivate smokers to quit. The currently published data are probably not sufficient to justify the inclusion of increased cough as an ICD-10 and DSM-IV criterion of tobacco or nicotine withdrawal. Our data also suggest that, based on a very brief and simple questionnaire, screening for COPD on the Internet is feasible and can detect, at a low cost, very large numbers of COPD patients who may otherwise not have access to COPD screening.

COPD is largely underdiagnosed and undertreated,(1) and Internet screening may contribute to the early detection of COPD at a large scale, and to the subsequent improvement of prognosis in many patients. This could represent a significant public health advance.

Authors and Contributors

JF Etter is the sole author of this paper, he designed the study, collected and analyzed the data and wrote the manuscript.

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Conflict of interest statement

No conflict of interest.

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Figure 1. Flow chart of study participants

17,353 records		
1,437 duplicate (deleted)		
15,916 valid records		
9,927 after August 2005 (start of follow-up)		
1,831 answer the 30-day survey		
935 baseline daily smokers ↓	48 occasional smokers, 14 never smokers, 7 missing	827 baseline former smokers ↓
252 quit smoking at follow-up, 683 still smoking, of whom 266 did not change cig./day >10%		713 still ex-smokers at follow-up, of whom 220 had quit smoking <31 days before baseline, 162 quit >365 days before baseline

Table 1. Comparison of participants and non-participants in the 30-day follow-up survey

	No e-mail address	E-mail address, but no answer to 30-day survey	Answer 30-day survey	Chi ²	P
N	5259	2837	1831		
Age (years, median)	36.0	33.0	39.0	192	<.001
Men (%)	48.8	47.9	40.9	34.8	<.001
Daily smokers (%)	68.2	75.2	51.3	715	<.001
Former smokers (%)	20.0	20.5	45.3	715	<.001
In daily smokers, cig./day	17.0	15.0	17.0	17.8	<.001
In former smokers, days of abstinence	93.0	37.5	49.0	38.6	<.001
Do you often cough even without a cold? (%)	41.3	37.8	34.5	29.0	<.001
Do you expectorate when you cough in the morning? (%)	41.7	40.1	38.0	8.0	0.02
Are you out of breath after an effort like climbing stairs or a quick walk? (%)	67.2	72.7	69.6	26.2	<.001
Do you have a wheezing respiration? (%)	30.8	33.0	28.7	9.8	0.007
None of the above 4 symptoms (%)	16.6	14.1	18.1	21.3	0.006
Ever diagnosed with asthma (%)	14.9	15.6	14.8	0.8	0.66

Table 2. Respiratory symptoms at baseline in daily, occasional, former and never smokers

	Daily smokers	Occas. smokers	Former smokers	Never smokers	Chi ²	P
N	10853	565	3837	578		
Age (years, median)	34.0	32.0	38.0	30.0	356.7	<.001
Men (%)	46.6	48.0	48.0	35.8	30.1	<.001
Do you often cough even without a cold? (%)	45.8	23.2	22.8	29.1	716.8	<.001
Do you expectorate when you cough in the morning?	45.6	26.0	28.3	24.4	468.7	<.001
Are you out of breath after an effort like climbing stairs or a quick walk?	73.8	56.8	59.3	57.1	360.1	<.001
Do you have a wheezing respiration? (%)	34.3	18.8	19.2	17.8	389.3	<.001
None of the above 4 symptoms (%)	10.3	27.4	27.4	30.3	1250.0	<.001

Table 3. Respiratory symptoms in daily smokers, by number of cigarettes per day

	Cigarettes per day				Chi ²	P
	1-9	10-19	20-24	25+		
N	1432	4056	2750	2236		
Age (years, median)	30.0	31.5	35.0	40.0	639.7	<.001
Men (%)	41.7	41.9	49.0	54.1	109.1	<.001
Do you often cough even without a cold? (%)	28.8	40.4	48.8	62.0	462.7	<.001
Do you expectorate when you cough in the morning?	30.3	41.1	50.2	57.9	329.4	<.001
Are you out of breath after an effort like climbing stairs or a quick walk?	57.8	72.1	77.9	82.6	311.0	<.001
Do you have a wheezing respiration? (%)	23.7	28.9	36.9	47.1	294.5	<.001
None of the above 4 symptoms (%)	22.8	11.3	7.6	4.2	921.1	<.001

Table 4. Respiratory symptoms in recent quitters at baseline, by interval since the quit date

	Has quit smoking for (days):				Chi ²	P
	0-7	8-31	32-91	92-365		
N	440	563	537	550		
Age (years, median)	32.0	35.0	38.0	39.0	123.8	<.001
Men (%)	35.0	41.4	47.5	49.5	25.8	<.001
Do you often cough even without a cold? (%)	34.1	24.0	13.8	14.9	78.1	<.001
Do you expectorate when you cough in the morning?	36.8	30.9	21.0	20.4	46.9	<.001
Are you out of breath after an effort like climbing stairs or a quick walk?	68.0	63.8	52.9	54.5	32.3	<.001
Do you have a wheezing respiration? (%)	25.2	16.3	14.9	14.9	23.3	<.001
None of the above 4 symptoms (%)	17.0	21.5	34.6	34.4	117.2	<.001

Table 5. Change in respiratory symptoms between baseline and 30-day follow-up in smokers who did not change their cigarette consumption at follow-up, and in baseline smokers who quit at follow-up

	Smokers who did not change cig./day at follow-up N=266		Recent quitters (smoked at baseline and quit at 30-day) N=252		Chi ²	p ^a
	Baseline %	30 days %	Baseline %	30 days %		
Do you often cough even without a cold?	46.6	49.2 ns	51.6	15.5**	70.5	<.001
Do you expectorate when you cough in the morning?	47.7	46.6 ns	47.6	19.4**	38.4	<.001
Are you out of breath after an effort like climbing stairs or a quick walk?	77.1	72.9 ns	75.0	48.4**	28.6	<.001
Do you have a wheezing respiration?	41.0	31.2 **	33.7	10.3**	11.9	0.003
None of the above 4 symptoms	9.4	10.9 *	9.1	40.1 **	89.7	<.001

* $p \leq 0.05$; ** $p < 0.001$; ns: not statistically significant, from McNemar tests, for change over time within groups.

a) p-value for difference between groups on change over time, from chi-square tests.

Table 6. Change in respiratory symptoms between baseline and 30-day follow-up in ex-smokers who had quit <31 days before baseline and ex-smokers who had quit >365 days before baseline

	Ex-smokers who had quit for <31 days at baseline N=220		Ex-smokers, who had quit for >365 days at baseline N=162		Chi ²	p ^a
	Baseline %	30 days %	Baseline %	30 days %		
Do you often cough even without a cold?	26.0	10.5 *	14.2	12.4 ns	17.0	<.001
Expectoration when you cough in the morning?	33.6	15.2 *	19.5	16.0 ns	12.9	0.002
Out of breath if effort (stairs, quick walk)?	67.5	48.0 *	56.2	58.0 ns	33.4	<.001
Do you have a wheezing respiration?	19.9	5.1 *	17.8	16.6 ns	15.9	<.001
None of the above 4 symptoms	19.5	42.3 *	38.5	34.9 ns	62.8	<.001

* p<0.001; ns: not statistically significant, from McNemar tests, for change over time within groups.

a) p-value for difference between groups on change over time, from chi-square tests.