Research article

Telephone Follow-Up to Identify Incident Lung Cancer Symptoms in COPD Patients

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Abstract

Background: COPD patients are at very high risk of lung cancer, yet new respiratory symptoms of lung cancer may be particularly hard to identify. Aim: We sought to assess the feasibility of actively seeking lung cancer symptoms to improve the timeliness of diagnosis in this group. Design and setting: Observational study to evaluate the feasibility and practicability of the intervention. Patients were recruited from a primary care COPD register and were contacted by telephone 4-monthly over 12 months. Chest X-ray rates were assessed over the 20 months before, during the intervention and for 20 months following it, in both the study group and in patients on the register who did not volunteer for the intervention. Results: Most symptoms were identified at the first call, with 13 (17%) subjects admitting to a new persistent cough and 7 (9%) to a change in their cough. As a result of symptoms identified on the first call, 21 (27%) of the participating patients were referred for a chest X-ray and 4 (5%) were referred urgently to secondary care. Incident symptoms continued frequently to be identified at all subsequent calls, with an overall total of 49% of patients qualifying for and receiving a chest X-ray. Interestingly, the chest X-ray rate remained significantly elevated for the 20 months following the intervention, whilst there appeared to be little change in the non-study COPD patients. Conclusion: The intervention was readily practicable and lung cancer symptoms were frequently identified. The intervention may have resulted in a behavior change leading to a persistently higher chest X-ray rate, although the comparator group was not a formal control group and further assessment in a randomized control trial appears justified.

Keywords: lung neoplasms, pulmonary disease, chronic obstructive, early diagnosis; primary health care, signs and symptoms, respiratory

Introduction

Lung cancer is a common and frequently lethal complication of COPD. Cross-sectional studies show that in subjects diagnosed with lung cancer, 40–70% have COPD [1-3]. Papi et al. [4] found that the presence of COPD increased the risk of squamous cell cancer more than four fold. In a large US study, Mannino et al. [5] reported that moderate to severe obstructive lung disease was associated with a hazard ratio of 2.8 (95% confidence interval, 1.8-4.4) for incident lung cancer. In a large cohort of male Swedish construction workers, the rates of squamous and small cell lung cancer were increased, with relative risks of 1.5 and 2.2 for those with mild and moderate-to-severe COPD, respectively, indicating a "dose-response" [6]. The Inhaled Steroids in Obstructive Lung Disease (ISOLDE) investigators [7] reported that 14% of deaths in patients with moderate to severe COPD were due to lung cancer. In a large cohort of 1,927 patients with a first record-

ed diagnosis of COPD included in the General Practice Research Database, the relative risk of lung cancer was 3.33 (95% confidence interval, 2.33-4.75) [8]. Interestingly, this excess risk persisted after adjustment for age, sex and smoking status suggesting that COPD is itself an important risk factor, rather than merely being a surrogate marker of smoking [9].

Resection rate and survival of British lung cancer patients remain poor by international comparison [10]. Whilst the cause of this is uncertain, the reform of lung cancer management after primary care referral has had limited impact. British lung cancer patients are identified at a later stage [11] likely to reflect late presentation of symptomatic disease and/or late recognition of symptoms in primary care. Furthermore, the outcome of British lung cancer patients with COPD has been found to be substantially worse than for those without COPD, but whether

this is due to delayed presentation, to comorbidity or other factors is uncertain [12]. Identifying early lung cancer in COPD poses a particular challenge, because of the background noise of chronic respiratory symptoms. Even when new respiratory symptoms are identified, they are prone to being attributed to an exacerbation of COPD, rather than a second pathology.

Early diagnosis remains as important in patients with COPD as those without. Many patients with COPD may still be suitable for radical therapy, including surgical resection and radiotherapy. Even when not, earlier diagnosis has numerous potential benefits, including increasing eligibility for palliative treatments and addressing psychosocial issues.

We previously reported a social marketing study that showed that chest X-ray rates were significantly increased, with a trend to more lung cancer diagnoses, by increasing awareness of cough in particular as a lung cancer symptom in the general public and in primary care [13]. In the present study, we have sought to extend the reach of symptom identification by actively enquiring about lung cancer symptoms. COPD registers are now well established in primary care, supported by the Quality Outcomes Framework. We hypothesized that a pro-active review of respiratory symptoms in patients with COPD may facilitate earlier identification and diagnosis of lung cancer in this patient group. Key questions to assess feasibility were willingness of participants to be recruited, follow-up rates, duration of call times and nurse time required.

Methods

The study was designed to assess the feasibility of using regular, telephone-based review of respiratory symptoms experienced by patients registered in a primary care COPD database, to identify the emergence of NICE-recommended lung cancer symptoms. The outcomes of main interest were: a) recruitment rate b) staff-time required to undertake the telephone interviews, to facilitate the resourcing of a definitive study and to inform the health economic evaluation c) yields of the outcome measures. The ideal outcome measures would be the number of cancers identified as a result of the intervention, radical treatment rates and, ultimately, mortality. Given the small scale of this pilot study, no case of cancer was expected to be identified, but the rates of chest X-rays requiring further evaluation to exclude lung cancer was expected to be evaluable and was chosen as the primary outcome measure.

Inclusion criteria

Inclusion on a primary care COPD register; provision of informed consent; ability regularly to be contacted by telephone; age 40 years or above.

Exclusion criteria

Current or previous (within 5 years) lung cancer diagnosis; presence of any other condition likely to cause death within the next 3 years, including active malignancy (excluding skin cancer, superficial bladder cancer and stable CLL); severe cardiac failure (NYHA IV); dementia or active psychosis; unwillingness to give informed consent; inability to communicate in English. Conducting telephone interviews with non-English speaking participants was regarded as being impractical,

at least without the use of expensive and cumbersome interpreting resources.

The study was undertaken in a single, large, primary health care practice in Conisbrough, a socially deprived town within the metropolitan borough of Doncaster, UK, from August 2013 to December 2014. The exploratory nature of the study and the resources available determined that only one practice was used and this determined the number of participants. A staged consent process was employed. Potentially eligible patients were sent an invitation letter and information sheet regarding participation in the study, along with a consent form, in which consent or otherwise could be indicated, for return in a stamped addressed envelope. The invitation letter was sent from and returned to the practice. Patients returning the form with provisional consent were then telephoned to confirm the consent by the practice nurse (DB).

At the first telephone contact, baseline data were collected, including smoking history, the type and frequency of usual respiratory symptoms (specifically cough, sputum production, haemoptysis, wheeze and breathlessness). Thereafter, the nurse contacted the patient 4-monthly for 12 months to identify the emergence of the features recommended by NICE as requiring a chest X-ray. It was asked specifically whether:
- a new cough or a change in the character of a longstanding cough had developed;
- there had been haemoptysis;
- there had been an increase in breathlessness;
- there had been a new chest pain;
- there had been unintentional loss of 2 kg or more in weight.

If the symptom had persisted for less than 3 weeks, a repeat call was scheduled to check whether it had resolved. If any of the NICE criteria were met, subjects were asked to attend for a chest X-ray, unless they had had a normal chest X-ray in the previous 2 months. If the chest X-ray was normal, subjects were asked to make an appointment with the general practitioner for evaluation including the need for a secondary care referral. The questions to be asked in the interviews were provided in a Microsoft Access © database.

Chest X-ray reports were returned in the normal way to the practice. If a report raised the possibility of lung cancer it was copied to the local lung cancer multi-disciplinary team and an urgent outpatient appointment arranged, in line with our usual practice.

Statistical analyses

The proportion of patients referred for a chest X-ray for each month in the study was calculated. Descriptive statistics were calculated for the pre-, during, and post-intervention period for the intervention and non-intervention cohorts.

Linear regressions were carried out to establish whether rates of referrals varied systematically over time or seasons in the pre- or post- intervention intervals, and to establish the base referral rate (intercept) for each of these intervals. These were performed separately for pre- and post- intervention intervals, for both intervention and non-intervention cohorts.

Results
Recruitment

281 patients identified on the COPD register meeting the inclusion/ exclusion criteria were approached. Only 77 (27%) consented and were contactable for the first call. The characteristics of the study participants are shown in Table 1.

Table 1. Baseline characteristics of the study participants

Characteristic	Number (percent)
Number of patients	77 (100)
Age at enrolment	
<55 yr	3 (4)
55–59 yr	9 (12)
60–64 yr	14 (18)
65–69 yr	17 (22)
70–74 yr	10 (13)
75–79 yr	13 (17)
80–84 yr	8 (10)
≥85 yr	3 (4)
Sex	
Male	43 (56)
Female	34 (44)
Smoking status	
Never	5 (6)
Current	17 (22)
Former	55 (71)
Pack-year smoking history	
< 10	16 (20)
10-20	10 (13)
20-29	12 (16)
30-39	13 (17)
40-49	9 (12)
50-59	8 (10)
≥60	9 (12)

Delivery of the intervention

Call durations are shown in Table 2. The first call took less than 5 minutes in 13 (18%), 5-10 minutes in 54 (74%) and 10-15 minutes in 6 (8%) cases. The subsequent calls were quicker due to the fewer questions being asked, with only 1-3% taking longer than 10 minutes and none more than 15 minutes.

Some difficulty was found contacting patients for follow up calls: 8 patients were unable to be contacted for call 2 and of these 4 patients were not contactable at the third call either, although 2 of these were contacted for the final call. Of the 69 patients contacted at both first and second calls, 33 were not contactable for the fourth call, one having died and another withdrawing. Of the remaining 31, 14 were contactable for the final call.

Table 2. Call durations. The number of calls falling within the time ranges specified are shown, with the percentage of calls of that series in parenthesis

Call Duration: number (percent)			
Call number	<5 min	5 - 9 min	10 - 15 min
1	13(18)	54 (74)	6 (8)
2	8 (12)	58 (86)	1 (1)
3	3 (8)	35 (88)	1 (3)
4	3 (6)	48 (92)	1 (2)

Symptoms and referrals

The symptoms identified are reported in Table 3. Most symptoms were found at the first call, with 13 (17%) subjects admitting to a new persistent cough and 7 (9%) to a change in their cough that had been present for 3 weeks or longer. 4 (5%) had had haemoptysis, 6 (8%) chest pains, and 8 (10%) had lost more than 2 kg in weight. As a result of symptoms identified on the first call, 21 (27%) patients were referred for a chest X-ray and 4 (5%) were referred urgently to secondary care as a possible case of lung cancer.

18 patients required additional calls to check whether a new cough identified at a previous call had persisted for 3 weeks. In 7 (39%) of these the symptom had fully resolved, 7 (39%) patients were reviewed by the GP. Six (33%) patients received a chest X-ray, 2 after the GP's review. Incident symptoms continued frequently to be identified at all subsequent calls, with an overall total of 38 patients having a CXR requested (49% of the whole cohort) over the 12-month intervention period. No further target wait appointments were made after the first call.

Chest X-ray referral rates

A sensitivity analysis was undertaken showing that using season as a covariate did not affect the interpretation of the results (see appendix). Figures 1 and 2, respectively, show the chest X-ray referral rates, taking account of seasonality, for the intervention and non-intervention cohorts. For the intervention cohort, linear regressions showed there was no effect of time on the proportion of patients referred during the pre-intervention interval (β=0.0001, 95% CI -0.0005, 0.0008), suggesting a steady rate of referral during this interval that was not significantly different from zero (intercept = 0.002, 95% CI = -0.008, 0.013). However, the post-intervention interval saw higher rates of referral (intercept = 0.033, 95% CI = 0.012, 0.053). There was no significant change in the rate of referral during the post-intervention period (β=-0.0003, 95% CI= -0.0008, 0.0003), although figure 1 suggests the possibility of a slowly decreasing trend in the rate of referral after the intervention, as may be expected. For the non-intervention cohort, there was a similar lack of effect of time on referral rates, for both the pre- (β = 0.0002, 95% CI = -0.0005, 0.0008) and post (β = -0.0001, 95% CI = -0.0005, 0.0002) intervention intervals. For this cohort, the baseline referral rate during the pre-intervention period was higher than for the intervention cohort (intercept = 0.014, 95% CI = 0.003, 0.024), but for the post-intervention period, the baseline referral rate was slightly lower than for the

Table 3. Numbers of patients contacted, symptoms identified and actions taken after each call. Values are absolute numbers (percentage of total numbers of calls)

	Call number			
	Call 1	Call 2	Call 3	Call 4
Patients contacted	77 (100)	69(100)	40 (100)	52 (100)
New persistent cough	13 (17)	5 (7)	1 (3)	4 (8)
Changed cough	7 (9)	2 (3)	2 (5)	1 (2)
Changed cough for >3 weeks	7 (9)	2 (3)	1 (3)	1 (2)
Haemoptysis	4 (5)	1 (1)	2 (5)	2 (4)
Chest pain	6 (8)	3 (4)	1 (3)	1 (2)
>2 kg weight loss	8 (10)	6 (9)	3 (8)	1 (2)
Chest X-ray ordered	21 (27)	6 (9)	1 (3)	4 (8)
Medical review	1 (1)	7 (10)	4(10)	6 (12)
Lung cancer referral	4 (5)	0 (0)	0 (0)	0 (0)
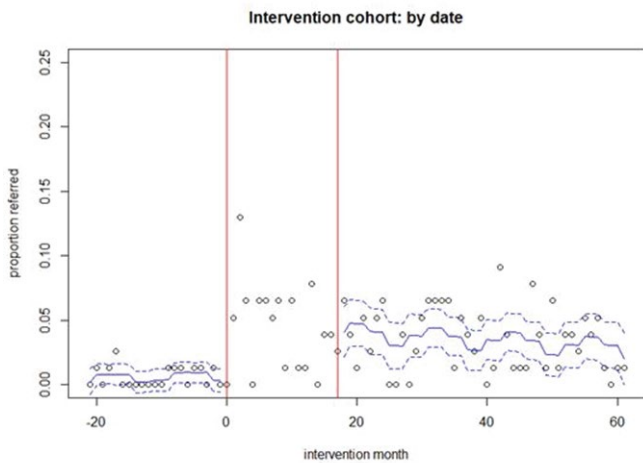
Figure 1. The proportion of patients referred for a chest X-ray in the intervention cohort in the 20 months prior to the intervention, the intervention (between the red bars) and post intervention periods, taking account of seasonality
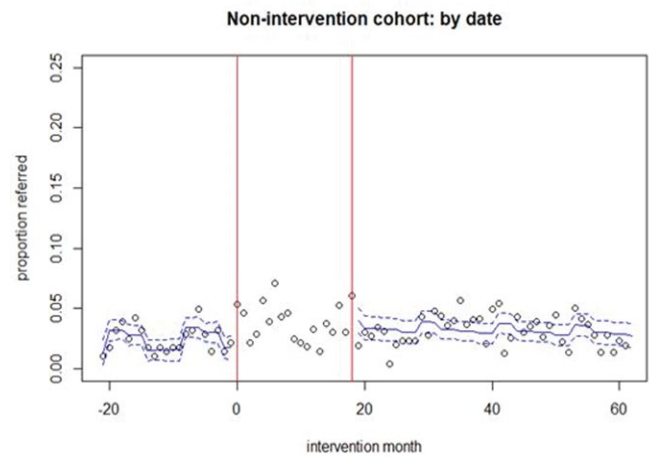
Figure 2. The proportion of patients referred for a chest X-ray in the non-intervention cohort in the 20 months prior to the intervention in the other cohort, the intervention period in the other cohort (between the red bars) and the post intervention periods, taking account of seasonality
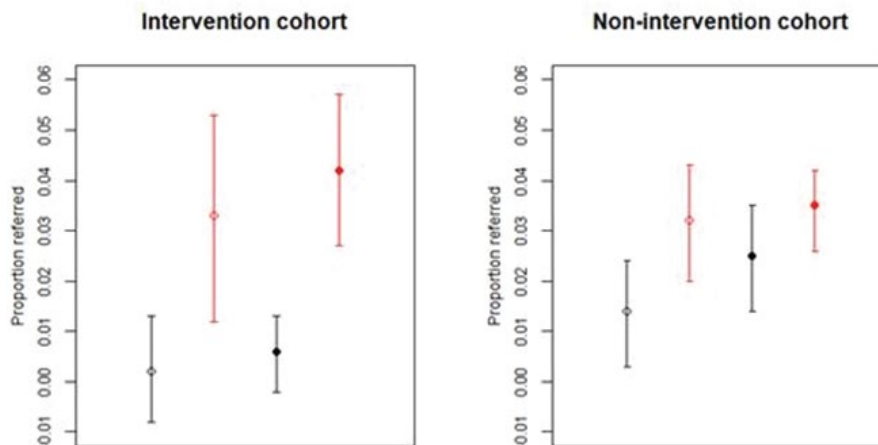
Figure 3. Regression co-efficients and CIs for intercepts (baseline referral rates) for intervention and non-intervention cohorts. Black points show pre-intervention baseline, red points show post intervention baseline. Empty circles show results accounting for season, filled circles show results without effects of season

intervention cohort (intercept = 0.031, 95% CI = 0.020, 0.043). It is possible that the higher rates of referral in the non-intervention cohort during the pre-intervention period may indicate some self-selection for the intervention by those patients who had had fewer referrals in the months prior to the study. There appeared to be an increase in the referral rate for the non-intervention cohort for the post-intervention period, compared with the pre-intervention period, but this rise was not nearly as marked as that seen in the intervention cohort (Figure 3). It is possible that this reflected an increased awareness of lung cancer as a concern in COPD patients amongst the primary care team.

Discussion

The primary aim of confirming the feasibility of a telephone-based programme of actively seeking potential lung cancer symptoms amongst patients included on a primary care COPD register was achieved. Minimal additional resource was required –mostly the time taken to make the calls by the practice nurse and extra reviews required by the practice doctors. Our study has shown a very high prevalence of symptoms for which NICE lung cancer guidelines recommend a chest X-ray or urgent secondary care referral, both at the initial call and subsequent ones. No increase in the chest X-ray rate was seen in COPD patients on the register who had not volunteered for the study. The increase in chest X-ray rate in the intervention group persisted over the 20 months after the intervention had finished, suggesting that participation in the study had led to a behavior change, presumably by breaking down barriers to disclosure of symptoms and an understanding of the appropriateness of attending for this investigation.

New symptoms continued frequently to be identified at the follow up calls and beyond. As "background symptoms" should have been accounted for, these new symptoms may potentially be more specific for new pathology. This would include lung cancer, but also, inevitably, exacerbations of COPD.

The main methodological finding was the low proportion of patients who consented to participate (27%), using the 2-stage consent process employed. In contrast, the practice manages to see about 80 % of these patients for their annual "QOF" checks through the use of up to 3 invitation letters as well as calls from administrative staff for non-attenders. The recruitment process will need to be modified for the next phase of the investigation. When calling patients there was always the difficulty of catching them in. Over the last 2 years the practice concerned, probably reflecting a more general trend, has dramatically increased their database of mobile phone numbers, reflecting the increase in use of triage calls prior to making appointments. Additionally, text reminders are now employed and this method may well increase recruitment for the planned, definitive, clinical trial possibly augmented by the use of "cold calling" invited subjects by telephone.

It seems likely that the uptake of the intervention would be improved if it could be "piggy-backed" onto the annual QOF review, thereby obviating much of the extra effort in reaching patients for the interviews. If the intervention were incorporated into standard clinical care in this way, the main additional resource required would be 2 additional calls per year, beyond the current annual review, requiring about 10 additional minutes of nurse time per COPD patient.

As expected from the small size of the study and its limited power, the differences seen, whilst promising, just fell short of statistical significance. Similarly, no new lung cancer cases were found. We believe this justifies a larger, fully randomised study.

If this approach were confirmed to be effective in improving lung cancer diagnosis, it could potentially be funded through locally enhanced services or an extension of the QOF process. The time for the review of X-ray reports was minimal. We believe that the additional GP reviews of symptomatic patients may be particularly cost-effective, as many of these patients would eventually need review anyway and would merely be seen earlier. The annual COPD review is often carried out using a computerized template. Incorporating the additional questions, either as free text or a READ code question within a COPD template, would be a straightforward process and could be linked with a protocol to aide a decision to generate an X-ray request.

Conclusion

The intervention was readily practicable and lung cancer symptoms were frequently identified. The intervention may have resulted in a behavior change leading to a persistently higher chest X-ray rate even after the intervention, although the comparator group was not a formal control group and further assessment in a randomized control trial appears justified.

Abbreviations: COPD: chronic obstructive pulmonary disease, NICE: National Institute for Health and Care Excellence, Chronic lymphatic leukaemia, NYHA: New York Health Association, CI: confidence interval, QOF: Quality Outcomes Framework

Ethical Approval

Research ethics approval was obtained from the Sheffield LREC.

Contributorship

TKR conceived and designed the study, and wrote the first draft. AMT and SPB were primarily involved in a qualitative study to explore acceptability of the intervention to patients, to be reported separately, but actively contributed to the planning of the study. JL performed the statistical analyses. MB was responsible for the practicalities of integrating the study into the primary care practice. DB undertook the regular telephone enquiries. All authors reviewed and contributed to the final manuscript.

Conflicts of Interest

None declared.

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compared to men around the time of diagnosis of primary lung cancer. Chest. 2006;129(5):1305-12.

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