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Sputum colour and bacteria in chronic bronchitis exacerbations: a pooled analysis

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Running title: Sputum colour and bacteria in exacerbations

ABSTRACT

We examined the correlation between sputum colour and the presence of potentially pathogenic bacteria in acute exacerbations of chronic bronchitis (AECB).

Data were pooled from six multicentre studies comparing moxifloxacin with other antimicrobials in patients with an AECB. Sputum was collected before antimicrobial therapy, and bacteria were identified by culture and Gram staining. Association between sputum colour and bacteria was determined using logistic regression.

Of 4089 sputum samples, a colour was reported in 4003; 1898 (46.4%) were culture-positive. Green or yellow sputum samples were most likely to yield bacteria (58.9% and 45.5% of samples, respectively), compared with 18% of clear and 39% of rust samples positive for potentially pathogenic microorganisms. Factors predicting a positive culture were sputum colour (the strongest predictor), sputum purulence, increased dyspnoea, male sex and absence of fever. Green or yellow versus white sputum colour was associated with a sensitivity of 94.7% and a specificity of 15% for the presence of bacteria.

Sputum colour, particularly green and yellow, was a stronger predictor of potentially pathogenic bacteria than sputum purulence and increased dyspnoea in AECB patients. However, it does not necessarily predict the need for antibiotic treatment in all patients with AECB.

Keywords: acute exacerbations of chronic bronchitis, bacteria, chronic obstructive pulmonary disease, sputum colour

INTRODUCTION

One of the most difficult decisions faced daily in primary care clinical practice is whether or not to prescribe an antimicrobial in patients with an exacerbation of chronic bronchial disease (i.e. chronic bronchitis, bronchiectasis or chronic obstructive pulmonary disease [COPD]). Such decisions are made empirically, based on clinical evidence. Overuse of antimicrobials in the community is clearly associated with an increased risk of the development of bacterial resistance [1]. A diagnostic tool that can be implemented at the point of care to identify patients who may be safely managed without an antimicrobial may reduce the occurrence of inappropriate prescribing.

Anthonisen *et al*. [2] reported that patients presenting with at least two of increased dyspnoea, sputum production and sputum purulence were more likely to recover if prescribed an antimicrobial vs those with only one of the symptoms. However, their study included individuals with severe and very severe COPD, and these criteria have never been validated in patients with non-obstructive chronic bronchitis. More recently, Stockley *et al*. [3] observed that purulent sputum alone, compared with mucoid sputum, was significantly associated with the presence of bacteria during an exacerbation. The change to a darker colour of sputum during an exacerbation is clinically detectable and would be consistent with increased neutrophil recruitment, indicative of a new or significant bacterial stimulus. This darkening of sputum colour represents the presence of myeloperoxidase, which is the green-coloured enzyme from neutrophil azurophil granules [3].

To provide further evidence that darker sputum colour is indicative of the presence of bacteria during acute exacerbations of chronic bronchitis (AECB), data were collected from randomised clinical trial results of moxifloxacin for the treatment of this condition. They were used in a pooled analysis to determine the correlation between sputum colour and the presence of a potentially pathogenic microorganism (PPM) in the sputum of patients with an AECB. All the studies had similar inclusion and exclusion criteria, and used the same questionnaire to record sputum colour and aspect. As previous investigations of sputum colour as a diagnostic marker were single-centre studies [3–5], these data from many different centres in Europe and North America may provide new insights into the usefulness of sputum colour as an aid to treatment decisions in clinical practice in patients with an AECB of varying severity.

METHODS

Study design

Baseline data were pooled from six clinical trials with similar methodologies comparing moxifloxacin with other antimicrobials in patients with an AECB (table 1) to determine the relationship between infection and sputum colour [6–11]. All clinical trials were prospective, randomised, controlled, multicentre studies conducted in Europe and North America.

Patients

Male and female patients aged over 18 years with chronic bronchitis presenting with clinical symptoms of an exacerbation were eligible to join the studies. Inclusion criteria included type I Anthonisen exacerbations (all studies) or type II Anthonisen

exacerbations (one study). A type I exacerbation was defined as the presence of increased dyspnoea, sputum production and sputum purulence [2]. Diagnosis of a type II Anthonisen exacerbation required two of these symptoms to be present. Chronic bronchitis was defined as daily production of sputum on most days for at least 3 consecutive months for more than 2 consecutive years [12]. Fever was assessed at inclusion in all studies. Exclusion criteria were: significant renal or hepatic impairment; severe respiratory tract infection requiring parenteral antimicrobial therapy or mechanical ventilatory support; a diagnosis of pneumonia; unresolved chest malignancy; tuberculosis; cystic fibrosis; bronchiectasis; history of severe cardiac failure; pregnancy or lactation; radiological evidence of bronchopulmonary infiltrates or the requirement for concomitant systemic antimicrobial therapy with agents not specified in the study protocols; allergy to fluoroquinolones, carboxyquinolone derivatives or comparator antimicrobials; a prolonged QTc interval or receipt of medication to increase the QTc interval; tendinopathy related to fluoroquinolones; any illness likely to lead to death within 6 months; receipt of systemic antimicrobial therapy for more than 24 hours within 7 days of enrolment; or the receipt of any investigational drug within 30 days of enrolment.

All studies were conducted in accordance with the Declaration of Helsinki, and received appropriate approval from local ethical committees and regulatory authorities. Each patient provided written, informed consent before the start of the study. Individual patient data were obtained in all studies.

Microbiological assessment

In each study, sputum was collected before initiation of antimicrobial therapy (baseline). All sites and investigators used the same questionnaire to record sputum aspect, including sputum colour. All samples of sufficient quality were analysed by culture and Gram stain at each investigator's local laboratory. Only samples with less than 10 squamous cells/low-powered field and more than 25 polymorphonuclear leukocytes/ low-powered field identified by Gram stain were included. The presence of PPMs (*Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Moraxella catarrhalis* and other *Haemophilus* spp.) was determined by culture.

Statistical analysis

All parameters related to the impact and treatment of an AECB were analysed using descriptive statistics. To define the utility of using green or yellow sputum colour as a diagnostic test for the presence of a PPM, the following diagnostic test statistics including 95% confidence intervals (CIs) were calculated for each of the six clinical trials: sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio. Pooled estimates were calculated for sensitivity and specificity using the bivariate method [13]. As recommended by the Cochrane Collaboration [14], pooled estimates were not calculated for positive and negative predictive values because these depend on the underlying prevalence which varied somewhat across the six trials. Additionally, no pooled estimates for positive and negative likelihood ratios were calculated as recommended by Zwinderman and Bossuyt [15].

A logistic regression model was used to examine whether or not sputum colour was a statistically significant predictor of the presence of a microorganism. First, a stepwise logistic regression was performed using the following potential explanatory variables: sex, age group (<65 years vs ≥65 years), long-term use of inhaled bronchodilators and/or corticosteroids, geographical region, study, sputum aspect (purulent/mucopurulent/mucoid), number of previous exacerbations, increase in dyspnoea, pre-treatment C-reactive protein (CRP) level and white blood cell count, presence of fever and duration of exacerbation before the study. In this stepwise procedure each variable was added to the existing model, one at a time. If the p-value for the new variable was <0.05 (meaning that it was probably a significant predictor of microorganism presence even accounting for the other variables already in the model), it was added to the model. If a new variable was added, the overall model was run again; if any variable in the new model had a p-value >0.05, it was then dropped from the model. This step was followed for each of the potential variables. Once the stepwise procedure was complete a final model was run with just the variables identified by the stepwise procedure. P-values, point estimates and 95% CIs for the odds ratios were provided for each variable in the final model. The main purpose of the logistic regression model was to show that sputum colour is a significant predictor of PPM presence, even when adjusting for other important predictor variables in the model. A model with random study effects was fitted as a sensitivity analysis to confirm the findings from the model with fixed study effects.

RESULTS

Patient characteristics

A total of 4089 patients provided a sputum sample. Patients were mainly male (55.0%), white (78.6%) and over 45 years old (74.8%) (table 2). Overall, 44.5% of patients had experienced three or more exacerbations in the previous year. While the characteristics of the overall population and patients with positive or negative cultures were generally similar, one notable difference was that patients with positive cultures were more likely to be past or current smokers than those with negative cultures (85.8% vs 75.4%, respectively; $p<0.001$).

Sputum characteristics and microbiology

Of the 4089 sputum samples, a colour was reported in 4003 (97.9%) and 1898 (46.4%) were culture-positive at baseline. Most patients had yellow (56.7%) or green (29.8%) sputum; a further 466 patients had white (8.6%) or rust-coloured (2.8%) sputum (table 3). Following culture, 2331 PPMs were found from the 1898 samples.

Infecting organisms were most likely to be isolated from green or yellow sputum, with 58.9% and 45.5% of these samples, respectively, being bacteriologically positive (figure 1). Patients with clear or white sputum were least likely to have a PPM (18.4%).

H. influenzae was the most frequently isolated organism in sputum of all colours (table 3). Green or yellow was the most commonly seen sputum colour where PPMs were present, followed by rust or white. The patterns of colours were similar for all species of PPMs isolated; therefore no specific colour can be associated with a given microorganism (figure 2).

Having green or yellow sputum versus white sputum had a sensitivity for the presence of a PPM between 91.1% and 96.8% across trials with a pooled estimate of 94.7%, and a specificity of between 4.7% and 24.4% with a pooled estimate of 15.0%. The positive predictive value varied between 41.6% and 56.6% and the negative predictive value between 65.2% and 87.9% across trials. All positive likelihood ratios across trials were above 1 and the negative were below 1 (table 4).

Regression analysis: predicting bacterial infection from patient and sputum characteristics

In the logistic regression analysis, factors that predicted the presence of an infecting organism were sputum colour, sputum purulence, increased dyspnoea, male sex and absence of fever (table 5). Sputum colour was found to be a stronger predictor for the presence of a PPM than other factors (table 5), although all factors were significant. Chi-square analysis of the null hypothesis ('no association between sputum colour and the presence of a PPM') gave a p-value of <0.001 (Chi-square = 108, 3 degrees of freedom [d.f.]) indicating a strong association between sputum colour and bacterial presence. The presence of bacteria was also strongly predicted by sputum purulence ($p<0.001$, Chi-square = 27, 4 d.f.). The model with random study effects confirms that sputum colour remains the strongest predictor for the presence of a PPM.

DISCUSSION

The present study has shown sputum colour to be the best marker for the presence of a PPM in sputum during an AECB compared with sputum aspect, dyspnoea or presence of fever. A PPM was isolated in 46.4% of samples from patients with a type I or II exacerbation, with almost 60% of culture-positive samples being from green sputum

and only 18.4% from white sputum. Consistent with other studies [16], *H. influenzae* was the PPM most often isolated in our large series and we found no specific colour pattern for the different PPMs present in sputum samples.

The Anthonisen criteria (i.e. increased dyspnoea, sputum production and sputum purulence) have been considered the most reliable predictors of bacterial infection as a cause of an exacerbation, requiring antimicrobial treatment, for more than 20 years [2]. However, these criteria were described for COPD, with all patients having a forced expiratory volume in the first second (FEV_1) below 80% of predicted; in fact, the mean FEV_1 was only 33% in Anthonisen's study, which represents a population with severe to very severe COPD. These criteria have never been validated in simple, non-obstructive chronic bronchitis. Moreover, the most relevant advance in our ability to predict bacterial involvement in exacerbations of chronic bronchial disease was the observation that not all three criteria had the same predictive value. Stockley *et al*. [3], with the aid of a colour chart, demonstrated that a change in sputum colour in the course of an exacerbation was a sensitive and specific marker for bacterial presence and was also predictive of a high bacterial load in bronchial secretions. These findings have been repeated by other groups [4,5] and have been validated using more specific and sensitive sampling methods, such as the protected specimen brush technique in hospitalised patients. This method has demonstrated that a change in sputum purulence described by the patient had a sensitivity of 89.5% and a specificity of 76.2% for the presence of a PPM during the episode of exacerbation [17].

Our results agree with previous observations, demonstrating a relationship between darker sputum colour and higher frequency of isolation of a PPM. We have extended the total number of observations by including a very large sample of patients from many centres in Europe and North America, including not only individuals with COPD but also those with non-obstructive chronic bronchitis. The results suggest that the yellow, and particularly green, sputum colour is a good marker for the presence of a PPM across the spectrum of chronic bronchial disease, including acute cough [18], stable COPD [19], and bronchiectasis [20].

One limitation of the present study is that, unlike in previous investigations [3–5], a standardised colour chart was not used. However, the consistency of the results in this large multinational sample suggests that sputum colour is easily recognised by physicians, and even by patients. In the study by Soler *et al*. [17], the sputum samples were not seen by the investigators; their colour was described exclusively by the patients themselves and provided good diagnostic accuracy for the presence of PPMs.

Information about sputum purulence was also collected. Purulence is strongly related to colour, but is even more subjective. In prospective studies mucoid sputum is usually described as colourless to white and purulent sputum as ranging from pale yellow to dark green [21]. We found a significant and consistent relationship between purulence and the presence of a PPM in sputum, although it had less predictive value than the colour of the sample.

The second limitation of the present study is that only patients with type I and II exacerbations were included because the population comprised candidates in an antimicrobial trial in AECBs. We were able to demonstrate the relationship between sputum colour and the presence of a PPM studying only patients with a high probability of bacterial exacerbation. It is likely that extending the study to include patients with type III exacerbations, even with the same severity of the underlying disease [22], would show an even stronger relationship between sputum colour and bacterial infection. This is reflected in the low specificity observed in our study (15%). This is probably due to the very low number of patients with white sputum in our sample, because only one of the trials enrolled patients with a type II exacerbation (i.e. patients who could potentially have white sputum). Our results show greater similarity to those observed by Daniels *et al*. (23), who reported a sensitivity and specificity of 70% and 39% respectively for reported sputum colour, but contrary to our study, up to one-third of their patients had mucoid sputum. An important implication of our results is that white sputum is a good predictor of a negative sputum culture, and it may help prevent the use of antibiotics in those patients unlikely to benefit.

The results obtained in our selected population of patients fulfilling the inclusion criteria of clinical trials may not be extrapolated to a more heterogeneous population of patients with chronic bronchitis in primary care. However, our results are consistent with those of other studies performed in patients in usual clinical practice, with different degrees of severity [3–5,17,19].

No information was collected about viral infection. Viruses may be isolated in up to 45% of exacerbations of severe COPD, either alone or together with bacteria [24]. Viral exacerbations in COPD are likely to present with fever [25]. The presence of fever was consistently significantly associated with a lower probability of bacterial isolation in our patients, suggesting again that febrile exacerbations are more likely related to viruses. In another study, febrile exacerbations of COPD were not significantly associated with purulent sputum compared with exacerbations without fever [26].

Plasma CRP level did not predict the presence of a PPM in sputum. A previous study indicated that point-of-care testing for CRP in lower respiratory tract infections in primary care significantly reduced antimicrobial prescribing without compromising patient recovery [27]. However, the patients had mild disease and a mean age of 50 years, and only 7% had a diagnosis of COPD. In individuals with more severe disease, Gompertz *et al*. [21] and Stockley *et al*. [3] reported significantly higher concentrations of CRP in patients with purulent compared with mucoid exacerbations; the patients with positive sputum cultures in the present study also had higher (although not significantly higher) concentrations of CRP. Perhaps the inclusion of patients with type III exacerbations would have made this difference more evident. In multivariate analysis, CRP was not predictive of the presence of a PPM in sputum; in a systematic review, testing for CRP was consistently neither sufficiently sensitive to rule out nor sufficiently specific to rule in an infiltrate on chest radiography and a bacterial aetiology of lower respiratory tract infection [28]. In the field of biomarkers, measurement of procalcitonin level shows promise as a means of identifying patients with exacerbations of COPD who require antimicrobial treatment [29].

The fourth limitation of our study was the use of sputum culture as the marker for bacterial involvement in the aetiology of the exacerbation. It is well known that a negative sputum culture does not rule out bacterial infection [30]. In fact, studies using invasive techniques in more severe, hospitalised patients, such as the protected specimen brush method, have demonstrated the high prevalence of bacteria in patients with coloured sputum [17], which is more reliable than the percentage of positive cultures. More importantly, these studies have demonstrated the high accuracy of using mucoid sputum to rule out bacterial infection [3,17]. Clearly, it is not feasible to use invasive diagnostic techniques in routine clinical practice, and sputum sampling is yet irreplaceable in the diagnostic approach to lower respiratory tract infections in the community. However, it should be noted that the presence of a PPM in the sputum does not confirm its role as a cause of an exacerbation and does not necessarily imply that antibiotic therapy will be beneficial in aiding resolution of the exacerbation.

Conclusion

This pooled analysis of clinical trial results in AECB showed sputum colour to be a stronger predictor of the presence of a PPM than other factors, including sputum purulence and increased dyspnoea. The greatest association between sputum colour and bacterial presence was found with darker (green and yellow) sputum. The change in colour of sputum in the course of an exacerbation can be used in self-management plans [31,32], leading to early antimicrobial therapy that may reduce the duration of the exacerbation and improve outcomes [33,34]. In addition, avoiding the use of antimicrobials to treat exacerbations when sputum is white will reduce inappropriate

antibiotic prescribing in the community and help slow the development of bacterial resistance [1].

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TABLE 1. Designs of the six studies included in the sputum analysis

Study reference (trial no.)	**Design**	**Treatment (moxifloxacin and comparator)[#]**	**No. of patients**	**No. of patients with a causative organism**
Schaberg *et al.*, 2001 (84) [6]	Prospective, multicentre, multinational, non-blind, randomised study in Europe	Moxifloxacin, 400 mg q.d. for 5 days; amoxicillin/clavulanate, 625 mg t.i.d. for 7 days	575	251
Chodosh *et al.*, 2000 (100033) [7]	Prospective, randomised, double-blind, multicentre study in the USA	Moxifloxacin, 400 mg q.d. for 5 days; moxifloxacin, 400 mg q.d. for 10 days; clarithromycin, 500 mg b.i.d. for 10 days	926	491
Bayer Schering Pharma, data on file (100034 [previously D96-022]) [8]	Prospective, randomised, double-blind, multicentre study in the USA and Canada	Moxifloxacin, 400 mg q.d. for 10 days; moxifloxacin, 200 mg q.d. for 10 days; cefuroxime axetil, 500 mg b.i.d. for 10 days	682	274
DeAbate *et al.*, 2000 (100160) [9]	Prospective, randomised, double-blind, multicentre study in the USA and Canada	Moxifloxacin, 400 mg q.d. for 5 days; azithromycin, 250 mg q.d. (500 mg on day 1) for 5 days	567	280

Hautamaki *et al.*, 2002 (100243) [10]	Prospective, randomised, double-blind, multicentre study in the USA	Moxifloxacin, 400 mg q.d for 5 days; levofloxacin, 500 mg q.d. for 7 days	594	315
Wilson *et al.*, 1999 (240017) [11]	Prospective, randomised, double-blind, multicentre study in Europe	Moxifloxacin, 400 mg q.d. for 5 days; clarithromycin, 500 mg b.i.d. for 7 days	745	287

[#]All treatments were administered orally.
q.d.: once daily; t.i.d.: three times daily; b.i.d.: twice daily.

TABLE 2. Demographics of patients included in the sputum analysis

Characteristic	**All patients** N = 4089	**PPM+** N = 1898	**PPM–** N = 2191	**P-value**[¶] PPM+ vs PPM–
Male sex (%)	55.0	61.0	49.8	<0.001
Mean ± SD age (years)	56 ± 15.3	55.3 ± 15.5	57.2 ± 15.0	<0.001
Mean ± SD number of exacerbations in previous year[#]	2.5 ± 1.9	2.4 ± 1.6	2.5 ± 2.1	0.614
Median (IQR) duration of exacerbation before study entry (days)	2 (5)	2 (5)	2 (6)	0.130
Past or present smoker, n (%)[#]	3280 (80.2)	1629 (85.8)	1651 (75.4)	<0.001
Use of long-term bronchodilators or steroids, n (%)	261 (6.4)	116 (6.1)	147 (6.7)	0.135
Median (IQR) CRP level (mg/L)[#]	0.70 (1.79)	0.69 (2.17)	0.71 (1.56)	0.551
Fever present, n (%)	74 (18.2)	294 (15.5)	389 (20.5)	0.005

IQR = interquartile range; PPM = potentially pathogenic microorganism; SD = standard deviation; CRP = C-reactive protein.

[#]Data were not collected for all patients in the study for these characteristics.

[¶]Cochran–Mantel–Haenszel test, adjusting for study, categorical variables, and using an analysis of variance, also adjusting for study, for the continuous variables.

TABLE 3. Commonly isolated potentially pathogenic microorganisms: number overall and proportion by sputum colour

Microorganism	Total no. of isolates (n)	Samples (%) containing specific pathogen[#]			
		Yellow sputum (N = 2319)	Green sputum (N = 1218)	White sputum (N = 353)	Rust sputum (N = 113)
Haemophilus influenzae	605	14.1	20.0	10.6	5.9
Streptococcus pneumoniae	313	7.4	9.5	12.4	2.5
Moraxella catarrhalis	319	7.3	11.2	2.3	4.4
Haemophilus parainfluenzae	262	5.8	9.2	2.5	5.3
Staphylococcus aureus	158	3.4	5.4	1.7	5.3
Klebsiella pneumoniae	133	3.9	3.1	0.8	1.8
Pseudomonas aeruginosa	105	2.4	3.1	2.5	1.8
Haemophilus spp.[¶]	64	1.4	2.4	0.3	0.0
Negative culture[+]	2191	54.5	41.1	81.6	61.1

[#]Percentage of isolates of each species based on the total number of culture samples.

[¶]*Haemophilus* spp. other than *H. influenzae* and *H. parainfluenzae*.

[+]Total number of negative cultures.

N = number of samples of each colour; one sample obtained per patient.

TABLE 4. Performance parameters of the colour of sputum in the diagnosis of the presence of a potential pathogen microorganism by study

Study reference	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR
84 [6]	96.8 (93.8, 98.6)	4.6 (2.6, 7.6)	44.1 (39.3, 48.4)	65.2 (42.7, 83.6)	1.02 (0.98, 1.05)	0.68 (0.30, 1.59)
100033 [7]	91.8 (88.9, 94.0)	19.2 (15.6, 23.3)	56.6 (53.1, 60.1)	66.9 (57.8, 75.2)	1.14 (1.08, 1.20)	0.43 (0.30, 0.61)
100034 [8]	95.3 (92.0, 97.5)	24.4 (20.2, 29.0)	47.0 (42.8, 51.3)	88.0 (80.3, 93.4)	1.26 (1.18, 1.34)	0.19, (0.11, 0.34)
100160 [9]	96.8 (93.9, 98.5)	16.5 (12.3, 21.5)	54.1 (49.6, 58.6)	83.3 (97.7, 92.10	1.16 (1.09, 1.23)	0.20 (0.10, 0.39)
100243 [10]	95.6 (92.7, 97.6)	13.6 (9.7, 18.2)	56.1 (*51.7, 60.3)	72.6 (58.3, 84.1)	1.11 (1.05, 1.17)	0.33 (0.18, 0.59)
240017 [11]	91.1 (87.2, 94.2)	18.9 (15.4, 22.9)	41.6 (37.6, 45.6)	77.1 (68.0, 84.6)	1.12 (1.06, 1.19)	0.47 (0.31, 0.72)
Pooled	94.8 (92.1, 97.4)	15.0 (6.7, 23.3)	n/c	n/c	n/c	n/c

n/c = not calculated; NLR = negative likelihood ratio; NPV = negative predictive value; PLR = positive likelihood ratio; PPV = positive predictive value.

TABLE 5. Regression analysis of significant factors predicting the presence of potentially pathogenic microorganisms in sputum

Variable	Wald Chi-square p-value	Odds ratio point estimate	95% confidence interval
Sputum colour	**108.4**		
	<0.001		
Yellow vs white		3.2	2.3, 4.2
Green vs white		4.9	3.6, 6.8
Rust vs white		2.3	1.4, 3.7
Study	**32.7**		
	<0.001		
84 vs 240017 [6,11]		1.0	0.8, 1.3
100033 vs 240017 [7,11]		1.6	1.3, 2.0
100034 vs 240017 [8,11]		1.1	0.8, 1.3
100160 vs 240017 [9,11]		1.3	1.0, 1.6
100243 vs 240017 [10,11]		1.4	1.1, 1.9
Sputum aspect	**27.0**		
	<0.001		
Purulent vs mucoid		2.0	1.6, 2.5
Purulent vs mucopurulent		1.1	1.0, 1.2
Dyspnoea	**6.6**		
	0.036		
Increased vs not increased		1.27	1.1, 1.5
Sex	**40.7**		
	<0.001		
Male vs female		1.5	1.3, 1.8
Fever	**14.8**		
	0.001		
Absent vs present		1.3	1.1, 1.6

FIGURE LEGENDS

FIGURE 1. Percentage of sputum samples with an identified pathogen according to sputum colour.

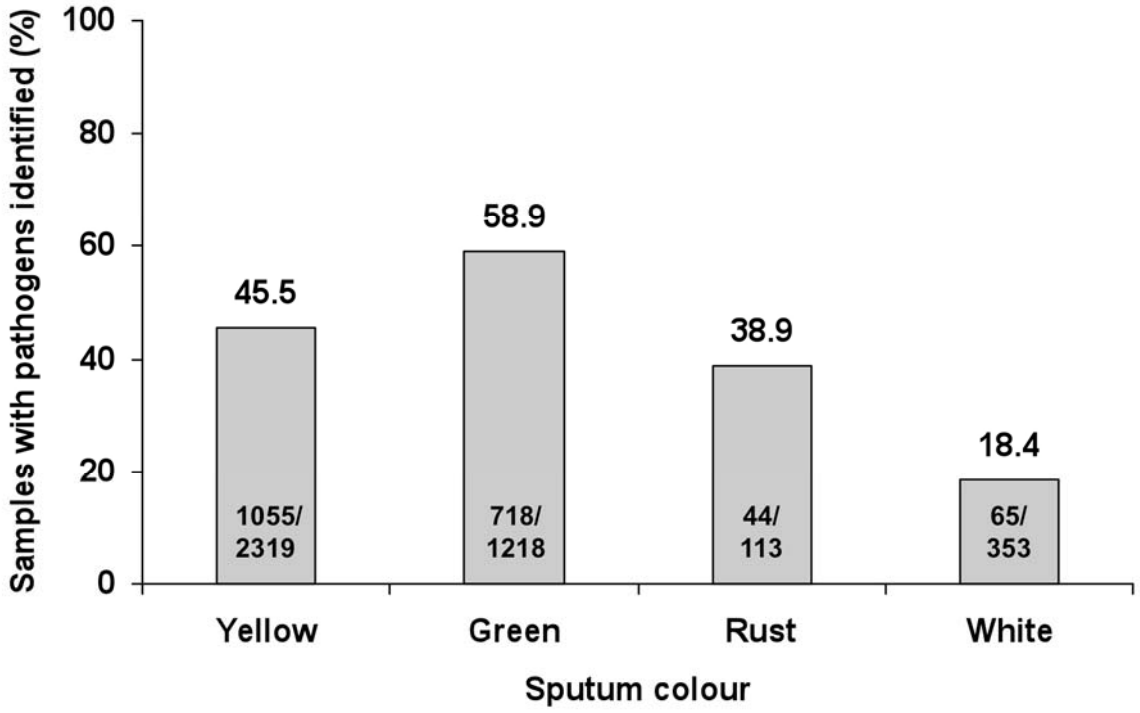

FIGURE 2. Distribution of sputum colour by infecting species.