We conclude that for the same degree of lung function impairment females tend to report more (severe) dyspnoea and cough, but less phlegm. Knowledge of this difference in reporting symptoms is important as symptoms often are the first step to a diagnosis of underlying airway disease.

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For the same degree of lung function impairment females tend to report more (severe) dyspnoea and cough, but less phlegm http://ow.ly/mp2CF

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Do we need bacteriological confirmation of cure in uncomplicated tuberculosis?

To the Editor:

Using data from English tuberculosis (TB) services, we investigate whether European guidelines recommending high levels of culture confirmation of pulmonary tuberculosis (PTB) cases and proof of bacteriological cure are achievable or needed.

The European Centre for Disease Prevention and Control (ECDC) recommends that 80% of pulmonary cases should be culture-confirmed [1]. In England, the Chief Medical Officer's action plan for TB [2], aims

for 65% of PTB cases to be confirmed by laboratory culture. Currently, although the UK target has been met, the ECDC goal has yet to be achieved in the UK [3]. In 2011 70% of notified cases in the UK were culture-confirmed. As part of treatment outcome monitoring the international guidelines in Europe, including the Wolfheze and International Standards for TB Care documents [4, 5], recommend that clinicians report evidence of bacteriological cure, defined as documented conversion (to culture-negative) during the continuation phase [6], but monthly sputum smear and culture samples are recommended when treating multidrug resistant (MDR)-TB [7]. In the UK, despite the existence of national treatment outcome monitoring programme for 9 years, data on bacteriological cure are frequently not reported. We investigated: 1) why not all cases of notified PTB have microbiological confirmation, and from this suggest methods to improve rates of microbiological confirmation; and 2) the feasibility of obtaining objective evidence for bacteriological cure among culture-confirmed cases. Three respiratory centres in the UK were chosen from metropolitan areas (two in London and one in Bristol). These have large TB case loads and generate adequate sample sizes for analysis. Furthermore, the London TB register and records in Bristol made the data particularly suitable and accurate for retrospective analysis.

A retrospective case note and pathology dataset review was performed, and a bespoke data collection tool completed. This tool collected information about: demographic data (table 1); the site of TB disease; sputum smear and culture status at the start and end of treatment; whether the sample obtained at the start and end of treatment was from spontaneously expectorated sputum, induced sputum or *via* bronchoscopy; if sputum smear status and/or mycobacterial cultures were not done, not known, or if data were missing whether reasons for this were documented in the case notes; drug sensitivity patterns; and relapse rates 2 years after the study.

TABLE 1 Demographics, acid-fast bacilli smear and mycobacterial culture results at diagnosis of incident pulmonary tuberculosis cases, 2009

Sex	
Female	52
Male	71
Age years	40±16
Ethnic group	
Black	43 (35)
ISC	34 (28)
White	28 (23)
Other	18 (14)
Previous TB diagnosis	
Yes	8 (6)
No	103 (84)
Missing data	12 (10)
HIV status	
Positive	10 (8)
Negative	97 (79)
Missing data	16 (13)
UK born	
Yes	24 (20)
No	95 (77)
Missing data	4 (3)
Years in UK if non-UK born	11±15
Smear positive	69 (56)
Smear negative	49 (40)
Smear not performed[#]	3 (2)
Smear data missing[¶]	2 (2)
Culture positive	98 (80)
Culture negative	19 (15)
Culture not performed[#]	4 (3)
Culture data missing[¶]	2 (2)

Data are presented as n, n (%) or mean±SD. n=123. Black: Black African, Black Caribbean, Black Other; ISC: Indian Subcontinent (Indian, Pakistani, Bangladeshi). [#]: Not performed = test not requested; [¶]: Data missing = test requested elsewhere, but unavailable at time of case note review.

All new notified cases of pulmonary *Mycobacterium tuberculosis* in 2009 who were ⩾18 years at the time of diagnosis at three hospitals in England (Imperial College Healthcare NHS Trust London; Royal Free London NHS Foundation Trust; and University Hospitals Bristol NHS Foundation Trust) were included.

Across the three hospitals, there were 123 newly notified PTB cases in 2009 (table 1). Of these, 8% were known to be HIV positive. 112 (91%) PTB cases had sputum or lung fluid samples sent for acid-fast bacilli (AFB) smear and mycobacterial culture at diagnosis. 5% had lung biopsy or lymph node samples similarly examined.

At diagnosis, the total proportion of sputum smear-positive cases was 56% across all three hospitals and 40% were smear-negative (table 1). From all 123 TB cases, the majority were confirmed with sputum culture. When sputum culture was negative, bronchoscopy contributed to the detection of another 15 (12%) of the cases. In total, 80% were culture positive at diagnosis. Culture data were unavailable in six cases (5%). The reasons identified for no culture data being available were: two samples were obtained by surgical teams who did not send them to microbiology; one had absence of respiratory symptoms; one had an initial diagnosis made external to the site of treatment; and in two cases no cause was found.

At treatment completion, the majority did not undergo a repeat culture for *M. tuberculosis* (82%), 15% had a negative culture result and 2% had unavailable data. The main reasons for no culture sample being sent at the end of treatment were the individual: 1) was clinically asymptomatic (28%); 2) had documented radiological resolution (20%); 3) defaulted from care (9%), or 4) transferred out from the local TB service (6%). Ten (8%) of the 123 cases were on an extended treatment period, due to either drug resistance or treatment interruption. They did not have further culture results available at the time of the initial audit. 2 years after treatment completion for those treated in 2009, we found that only one case had relapsed, who was known to have been non-adherent with initial treatment and to have pulmonary and pleural disease.

This study sought to evaluate why not all notified cases of pulmonary tuberculosis have diagnostic microbiological confirmation. We found that the great majority (96%) had documented evidence of sputum, lung fluid or tissue samples being sent for smear and culture during diagnostic evaluation. This meets ECDC recommendations and is above the current UK threshold. Therefore, we recommend that the UK Chief Medical Officer should review and revise the UK guidelines upwards to conform with the European recommendations. In the few cases that did not have samples sent at diagnosis, this was mainly because clinicians without specialist experience in TB were involved in the diagnostic procedure and appeared less likely to consider mycobacterial disease, and hence send relevant material.

It is of interest that, despite cases where our *post hoc* analysis suggested a high pretest likelihood of TB, surgically-obtained samples were not always sent for mycobacterial culture. Surgical pathology checklists, that have been used successfully elsewhere [8], may help here by acting as a prompt for clinicians to consider infections such as TB in certain populations who would be regarded as being at ''at risk'' of TB, such as Asians presenting with lymph node masses.

At diagnosis, 56% of subjects had AFB smear-positive disease and 80% had culture-positive results. This exceeds the national target for the latter (of 65%), and meets that recommended by the ECDC. We reviewed information from three large English metropolitan TB services (two in London and one in Bristol). We cannot, therefore, extrapolate our findings to all national TB care providers. However, the results suggest that in most cases samples for mycobacterial diagnosis can be obtained, and that achieving improved culture confirmation actually requires better microbiological techniques, in addition to sending surgical specimens for culture.

We also investigated the practicality of obtaining bacteriological confirmation of cure among treated pulmonary culture-positive cases. At treatment completion, four-fifths were not tested for cure. This was because they were in good health and invasive tests were felt to be inappropriate by their managing clinicians. Both national and local data indicate low rates of relapse post anti-TB treatment [9], suggesting that the majority of subjects are cured with therapy. We believe it is not indicated, in the UK, to pursue end of therapy samples for mycobacterial culture when a patient has successfully completed treatment and is well. In light of this, we recommend that each European country, based on their treatment completion and disease relapse rates plus local drug resistance prevalence, should review their policy and decide whether a final sputum culture is likely to be of value and cost-effective.

We conclude that microbiological diagnosis of PTB is performed appropriately. However, obtaining evidence of cure is impractical and unnecessary in the majority of treated individuals in our UK hospital settings. We recommend that the European guidelines are revised. The World Health Organization allows for the reporting of treatment completion (*i.e.* those who complete a treatment regimen and do not have a

negative smear or culture sample sent in the last month of treatment) as a successful outcome. This could be emphasised in future guidelines, with the proviso that if there is no proof of bacteriological cure, greater efforts should be made to improve initial microbiological TB diagnosis. This would enable individualised patient-specific drug susceptibility results to inform regimen choice and ensure that treatment completion is a robust indicator of success. In light of the new information from this study, we would suggest similar studies are performed in different settings both in the UK and elsewhere. The information obtained may allow for better selection of patients to be tested at treatment completion.

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In UK hospitals obtaining evidence of TB cure is impractical and unnecessary in the majority of treated individuals http://ow.ly/mxhQM

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Adherence to positive airway pressure in non-sleepy patients with obstructive sleep apnoea

To the Editor:

Complaints of excessive daytime sleepiness (EDS) are absent in many individuals with obstructive sleep apnoea (OSA). The influence of EDS prior to treatment on continuous positive airway pressure (CPAP) adherence has not been clearly determined [1, 2]. The aim of this prospective cohort study was to evaluate the adherence and perceived benefit during long-term CPAP therapy in a "real life" population of non-sleepy OSA patients.