# Predictors of mortality in chronic pulmonary aspergillosis (CPA)

## Supplementary materials

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## Methods:

**Further details on inclusion and exclusion criteria:**

Concurrent infection with non-tuberculous mycobacteria (NTM) and pyogenic bacteria were allowable as co-infections; tuberculosis, histoplasmosis and coccidioidomycosis were not. In those with negative serology, biopsy showing characteristic histological features of *Aspergillus* spp. or a positive culture from a percutaneous aspiration/biopsy were required. The presence of *Aspergillus* spp. by culture and PCR in respiratory secretions was recorded, but not required for diagnosis. Patients with a simple aspergilloma with a view to complete resection or subacute invasive (chronic necrotizing) pulmonary aspergillosis at referral were excluded from this analysis. Underlying disease diagnoses were accepted if the data supporting them was provided in the referral documentation and the radiological characteristics were consistent, although a prior history of pulmonary tuberculosis was only accepted if the patient had received treatment.

**Consent and audit**

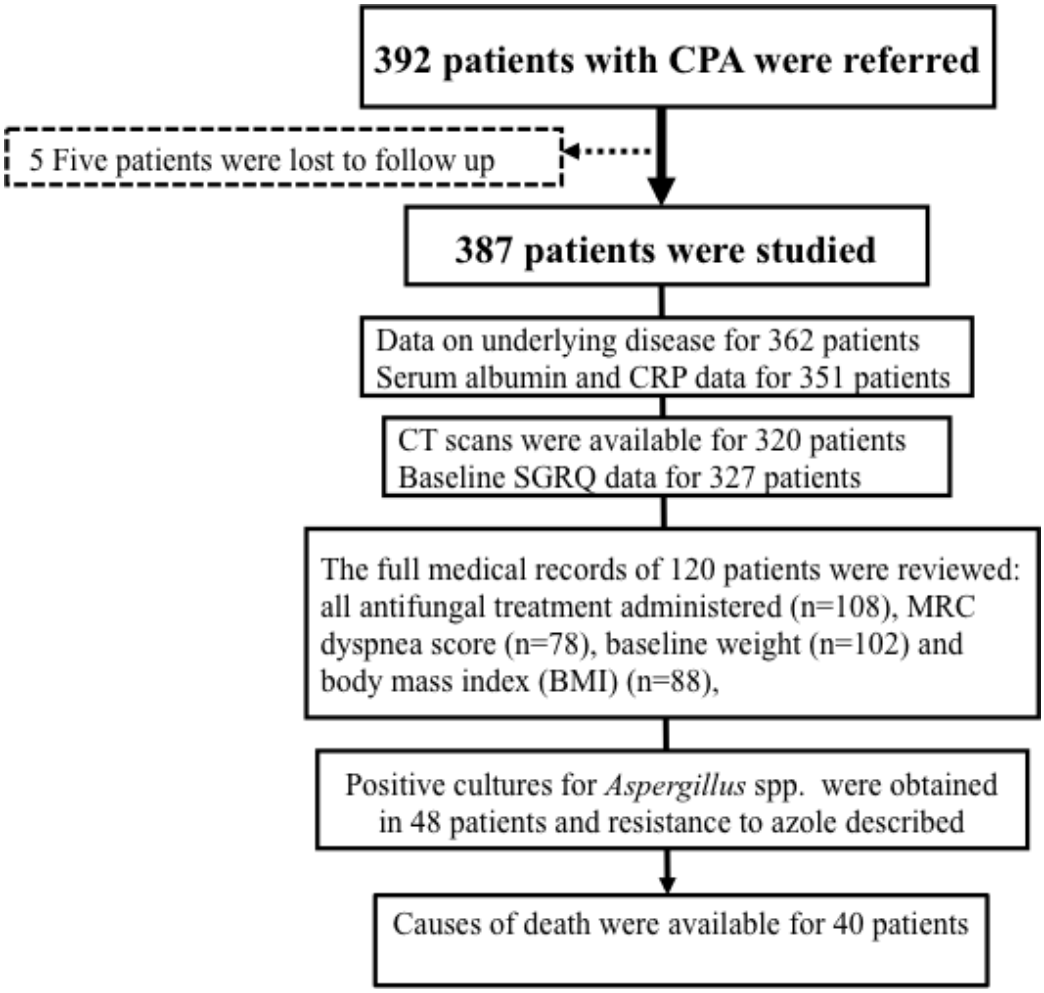
Patients gave informed consent for several ongoing diagnostic and genetic research studies, approved by the local Ethical Research Committee. This project was approved by the University Hospital of South Manchester (UHSM) Audit department in January 2013.

## Statistical analysis

SPSS statistics package version 20 was used for statistical analysis. Normally distributed data is presented as mean ± standard deviation (range), and non-normally distributed as median, interquartile range (range). Kaplan-Meier analysis was used to assess survival, and results are presented as two year survival ± standard error. Survival curves were produced for chosen variables. Log-Rank tests were used to compare survival between groups. The Cox proportional hazards model with the forward Wald method was used to calculate the hazard ratio of chosen variables, and presented as hazard ratio (HR) (95% CI). A $p$ value of $<0.05$ was considered significant for all statistical tests.

The study conforms to the STROBE criteria (http://strobe-statement.org/index.php?id=strobe-home ) and a checklist of key points is provided ans well as flow diagram to show the disposition of patients.

Figure S1. STROBE flow diagram showing disposition of patients.




## Results:

In a sub-sample of 120 patients, we assessed the interval between the likely onset of CPA and referral. Of these, 30 patients were excluded due to significant missing data. Of the remaining 90 patients, the median time from probable onset of disease to referral to the NAC was 7 months (range 0-256 months).

Figure S1. Change in albumin over time in surviving and non-surviving patients. Loess curve fit to 75% of data points.

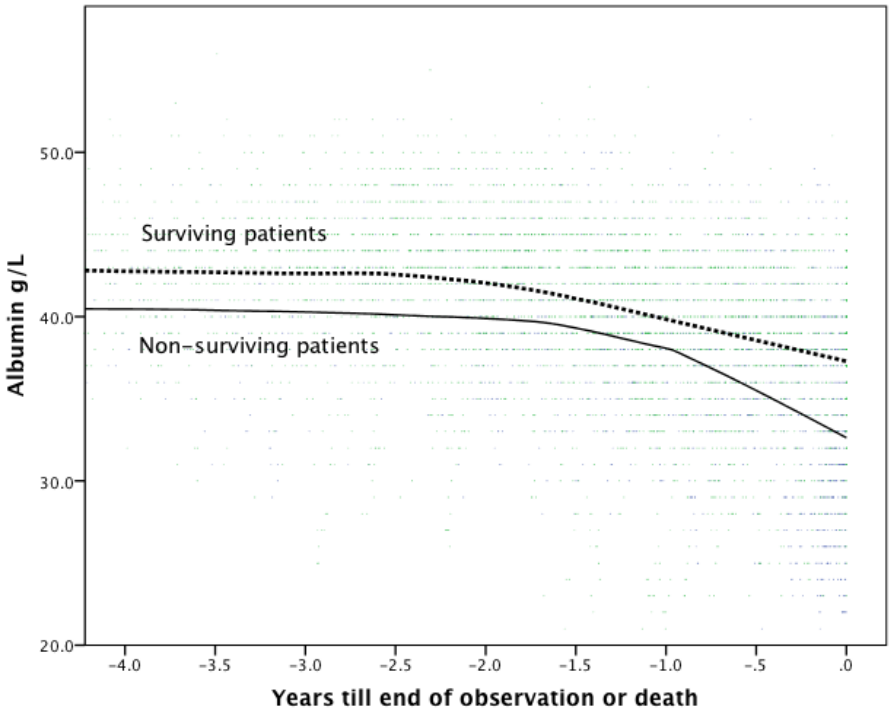



**Table S1.** Causes of death in a random subset of patients with CPA (n = 40 (31.5% of 127 deaths)

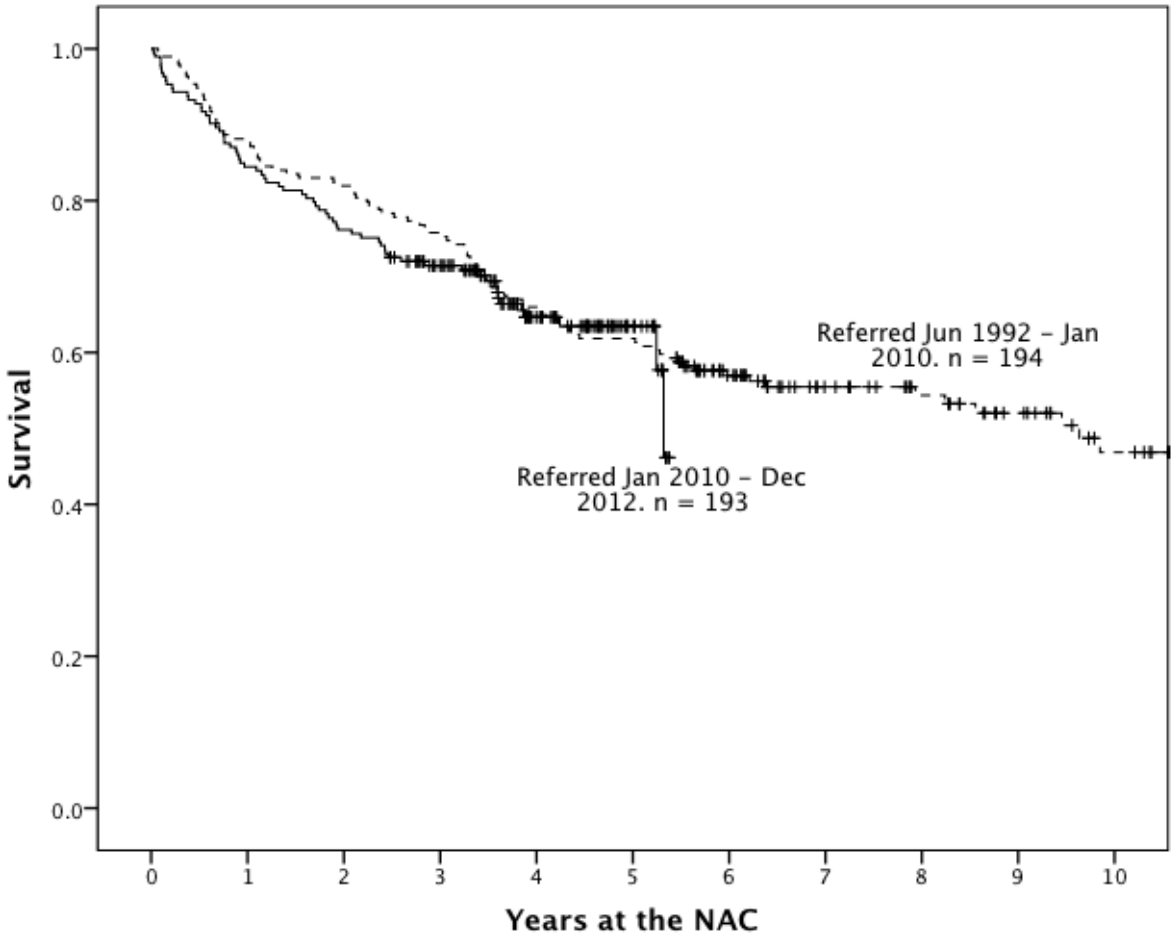
| CPA listed in causal sequence (Part la, b or c)* | | CPA listed as contributing towards death (Part 2) | | CPA not listed | |
|---|---|---|---|---|---|
| Cause 1a | Frequency (%) | Cause 1a | Frequency (%) | Cause 1a | Frequency (%) |
| CPA | 3 (7.5%) | Aspiration pneumonia | 1 (2.5%) | Pneumonia | 3 (7.5%) |
| Hemoptysis | 1 (2.5%) | Multi-organ failure | 2 (5%) | Lung Carcinoma | 2 (5%) |
| Pneumonia | 12 (30%) | Pneumonia | 1 (2.5%) | Small bowel | 1 (2.5%) |

| | | | | | |
|---|---|---|---|---|---|
| | | | | infarction | |
| Respiratory failure (type 2) | 4 (10%) | | | COPD exacerbation | 1 (2.5%) |
| Septicemia | 2 (5%) | | | Invasive aspergillosis | 1 (2.5%) |
| | | | | Multi-organ failure | 1 (2.5%) |
| | | | | Ovarian Ca | 1 (2.5%) |
| | | | | Pulmonary sarcoid | 1 (2.5%) |
| | | | | Septicaemia | 1 (2.5%) |
| | | | | Respiratory failure | 1 (2.5%) |
| | | | | Respiratory failure (type 2) | 1 (2.5%) |
| Total | 22 (55%) | | 4 (10%) | | 14 (35%) |

* Causes of death in the UK are recorded as 1 (a, b or c) if they are considered to have directly contributed to death. Part 2 refers to significant underlying disorders, not directly responsible for death.

CPA = chronic pulmonary aspergillosis, COPD = chronic obstructive pulmonary disease.

**Figure S4**. Comparison of survival stratified by date of referral. (p = 0.722). 1 and 5 year survival for patients referred before January 10th 2010 was 88 and 62% respectively. 1 and 5 year survival for patients referred after January 10th 2010 was 84 and 63% respectively.


Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6
7
8
9
10
Years at the NAC
Referred Jun 1992 – Jan 2010. n = 194
Referred Jan 2010 – Dec 2012. n = 193