

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 and 3	A retrospective analysis of a data from cohort of 387 chronic Pulmonary Aspergillosis (CPA) patients over > 10-year period to identify predictors of mortality in CPA.
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3	Fully addressed in abstract.
<b>Introduction</b>				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4	Fully covered in page 4 eg., Chronic pulmonary aspergillosis (CPA) is an infectious disease that often progressively destroys lung tissue. It occurs principally in immunocompetent individuals ... we found only seven studies with sample sizes of 11–194 subjects reporting divergent data on the survival of CPA patients.... Using data from a cohort of 392 CPA patients, we...
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4	Addressed eg., we present data on long-term survival from a well-experienced single center

				with a consistent approach to antifungal therapy. Using a wide range of objective and subjective measures, we also examine factors associated with mortality risk in CPA.
<b>Methods</b>				
Study design	4	Present key elements of study design early in the paper	Page 4	Described, eg., this retrospective study reviewed patients referred to...
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4	Mentioned, eg., patients referred to UK's National Aspergillosis Centre for medical management of CPA from June 1 <sup>st</sup> 1992 until June 1 <sup>st</sup> 2012... The clinical records of all patients were examined and the diagnosis of CPA confirmed using criteria modified...
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Page 4 and page 1 in the e-supplement.	Information on inclusion and exclusion criteria were provided in the e-supplement. Moreover, survival data was collected in June 2015, resulting in a minimum follow up of three years for surviving patients. The clinical records of all patients were examined and the diagnosis of CPA confirmed using criteria modified from Denning <i>et al</i> 2003 (3), and

[illegible]

measurement		(measurement). Describe comparability of assessment methods if there is more than one group		
Bias	9	Describe any efforts to address potential sources of bias	Page 4 and 5	<p>- Major effort for data accuracy was made eg., for diagnosis accuracy: all patients were examined and the diagnosis of CPA confirmed using criteria modified from Denning <i>et al</i> 2003 (3), and described in detail recently by Farid <i>et al</i> (5) and consistent with the recently published European guideline on CPA (Denning, et al 2016) (19)...</p> <p>-The diagnosis was made by trained physicians.</p>
Study size	10	Explain how the study size was arrived at	Page 4 and 5	<p>We demonstrate our experience over more than a decade, and we present the largest -so far- cohort on this uncommon disease.</p>

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Several qualitative and quantitative variables were collected. Data analysis was performed by a trained doctor with considerable help of experienced medical statistician and clinical scientist.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 5-7. Page 2 in the e-supplement	Different types of statistical tests were performed including multiple regression analysis to examine the possible effect of confounding factors.
		(b) Describe any methods used to examine subgroups and interactions	Page 2 in the e-supplement	Categorical data such as MRC dyspnoea grades, gender were examined considerably using number of types of statistical tests. Other tests were performed including eg., Kaplan-Meier analysis.
		(c) Explain how missing data were addressed	Page 4 and 5	We were keen to collect accurate data and we presented the number of patients in each variable involved in this analysis..
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	Page 4	Only 5 patients were lost to follow up.
		(e) Describe any sensitivity analyses		N/A
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 5	Fully described eg., overall, the one, five and ten survival rates in our 387 patients were 86%, 62% and 47% (Table 1)...

		(b) Give reasons for non-participation at each stage		N/A
		(c) Consider use of a flow diagram		Please see a new flow diagram.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 5	Please see results (page 5) and table 1
		(b) Indicate number of participants with missing data for each variable of interest		Please see a new flow diagram with data on number of patients available for different variables.
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Pages 6 and 7	Please see detailed results
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Pages 6 and 7	Several outcomes were reported using univariate and multivariate analyses eg., survival was 86%, 62% and 47% at one, five and 10 years from first visit. Increased mortality was associated with non-tuberculous mycobacterial infection and COPD as well as higher age, lower albumin, lower activity in St. George's Respiratory Questionnaire Activity Domain and having one and especially bilateral aspergillomas.
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure		
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Pages 5, 6, 7 and 8	We paid considerable attention for this key point using particularly multivariate analysis to correct the effect of confounding factors eg., the median number of underlying pulmonary conditions was 2 (IQR 1-3, range 0-6). As shown in table 2, COPD was the most common underlying disease (n=145 patients, followed by pneumonia and TB (n=79 and 76 patients,

respectively). Several co-existing pulmonary illnesses were associated with increased mortality risk in CPA; however, multivariable Cox regression analysis (including all underlying conditions and age) showed that NTM infection (HR 2.212,  $p<0.001$ ) and COPD (HR 1.580,  $p=0.006$ ) were associated with worse survival (Table 2). Furthermore, multivariate analysis including age, gender, underlying pulmonary conditions, location and presence of aspergillomas, serum albumin and CRP, and SGRQ activity found that previous NTM (HR 2.07,  $p = 0.007$ ), previous COPD (HR 1.57  $p = 0.029$ ), age (HR 1.053  $p<0.001$ ), SGRQ activity score (HR 1.021 per unit increase,  $p<0.001$ ), and albumin (HR 0.917 per g/L,  $p<0.001$ ), were independent predictors of mortality.

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(b) Report category boundaries when continuous variables were categorized

N/A

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(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

N/A

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 7	Precisely reported eg., A sub-sample of 120 patients was reviewed in further detail to collect baseline MRC dyspnea score (n=78), baseline BMI (n= 88) and baseline weight (n=102). Those more breathless with a higher baseline MRC score have shorter survival ( $p<0.001$ ) as demonstrated in figure 4. MRC scores 3 and 4 have been grouped for analysis due to ambiguity in the questions used. A unit increase....
<b>Discussion</b>				
Key results	18	Summarise key results with reference to study objectives	Page 8	Addressed, eg., We present a large retrospective cohort analysis of 387 CPA patients whose care was delivered at our specialist center. We found that poor outcomes in CPA were associated with several objective and subjective variables. NTM infections, prior COPD, pleural involvement
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11	Carefully mentioned eg., although we presented key prognostic factors that would assist in identifying patients at risk of poor prognosis, our study has limitations. We could not achieve a full dataset for all our patients, a common limitation in retrospective analysis. Substantial



				effort was made to collect reliable data, and develop the largest dataset so
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9	Reported eg., BMI is a functional marker of poor prognosis in CPA, and our finding confirms results of previous smaller studies (15, 18). We observed that a unit increase in baseline BMI was associated with an 11% decrease in mortality risk. Moreover, we found low weight to be a useful indicator of poor prognosis as in other chronic progressive respiratory illnesses e.g. COPD (33, 34), possibly....
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 10	Discussed with consideration of results of other studies eg., This finding is not surprising since the SGRQ is a respiratory-specific and sensitive tool in identifying patients at risk of mortality (11) and detects response to anti-fungal treatment (9). ...
<b>Other information</b>				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 16	We acknowledged funding from National Aspergillosis Centre.

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).