PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	EPI-ASTHMA study protocol - a population-based multicentre stepwise study on the prevalence and characterisation of patients with asthma according to disease severity in Portugal
AUTHORS	Jácome, Cristina; Brito, Dinis; João, Catarina; Lopes, Filipa; Santos, Janete; Amorim, Liliana; Barbosa, Maria João; Pardal, Marisa; Teixeira, Pedro; Bernardo, Filipa; Fonseca, Joao A.; Correia-de-Sousa, Jaime

VERSION 1 – REVIEW

REVIEWER	Hassan, Maged Alexandria University Faculty of Medicine, Chest Diseases Department
REVIEW RETURNED	22-Jun-2022

GENERAL COMMENTS	The authors have formulated a protocol for a study to measure the prevalence of asthma and in particular difficult to treat and severe subtypes in Portugal. The protocol is very well written and the planned study addresses an important subject which evolves over time; that is the prevalence of a chronic respiratory disease. In my opinion the methods are sound and are well described. I have only minor comments/suggestions to the authors as follows: - The study ID and registration date on Clinitrials.gov are incorrect. Please amend. - The authors refer to the GINA guidelines for the definition of 'severe' and 'difficult to treat' asthma. I suggest the authors briefly describe the diagnostic criteria for each entity. - The study dates are mentioned as 2021-2022. This means the study has already started. If so, I suggest the authors mention the actual start date and at what stage the study is at the moment. - The authors mention that an 'interim analysis' by region will be conducted after all stages have been completed. Do they mean to say a subgroup analysis? - In table 2 the abbreviation ETS is not expanded in the table footnotes. Please expand. - I think it is important to mention whether the funding body has had any role in the design of the study and whether they will be involved in the conduct or reporting of the study.

REVIEWER	Soyiri, Ireneous University of Hull, Hull York Medical School
REVIEW RETURNED	05-Jul-2022

GENERAL COMMENTS	The protocol paper is well designed and the anticipated analysis also well described. I believe this population-based study, when

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	completely implemented would contribute new knowledge to help characterise asthma.

VERSION 1 – AUTHOR RESPONSE

	Reviewer 1	
The authors have formulated a protocol for a study to measure the prevalence of asthma and in particular difficult to treat and severe subtypes in Portugal. The protocol is very well written and the planned study addresses an important subject which evolves over time; that is the prevalence of a chronic respiratory disease. In my opinion the methods are sound and are well described. I have only minor comments/suggestions to the authors as follows:	Thank you for your kind words and for your comments/suggestions.	-
The study ID and registration date on Clinitrials.gov are incorrect. Please amend.	Thank you for pointing this error out for us. The study ID and registration date have now been amended.	Please see: Abstract>Trial registration (page 3, lines 55).
The authors refer to the GINA guidelines for the definition of 'severe' and 'difficult to treat' asthma. I suggest the authors briefly describe the diagnostic criteria for each entity.	We followed the reviewer's suggestion and described in more detail the criteria used for classifying patients with severe and difficult to treat asthma. We have now added GINA definitions of uncontrolled, difficult to treat and severe asthma and also the	Please see: Methods and analysis > Diagnosis criteria and definitions (page 11, lines 225-237).

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	way we plan to operationalise these definitions. A subheading “ Diagnosis criteria and definitions ” has been added to the “ methods and analysis” section.	
The study dates are mentioned as 2021-2022. This means the study has already started. If so, I suggest the authors mention the actual start date and at what stage the study is at the moment.	Thank you for your suggestion. Indeed, the data collection of the study has already started. The study will be conducted in a total of 38 primary care centres and data collection was concluded in 4 of them. We have now added the study´s starting date as well as its current status.	Please see: Methods and analysis> Study Design (page 5, 1st paragraph).
The authors mention that an 'interim analysis' by region will be conducted after all stages have been completed. Do they mean to say a subgroup analysis?	Interim analysis will be conducted to monitor the safety of study procedures and completeness of data collection . However, we agree that this needs to be clarified. We added a more detailed clarification to the text.	Please see: Methods and analysis > Data storage, blinding and statistical analysis plan (page 12, line 264).
In table 2 the abbreviation ETS is not expanded in the table footnotes. Please expand.	Indeed, only the acronym was mentioned. We added the corresponding words - ETS=Environmental tobacco smoke.	Please see: Table 2. > Footnotes (page 11)
I think it is important to mention whether the funding body has had	We have now specified the role of the funding body. This study was designed	Please see: Statements > Funding (page 16, line 362-

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any role in the design of the study and whether they will be involved in the conduct or reporting of the study.	by two academic institutions (University of Minho and University of Porto) together with AstraZeneca Portugal - Evidence Generation team. Nevertheless, the funding body will have no influence on the conducting and reporting of the study. Moreover, the funding body did not influence the writing of the paper. This has now been clarified.	363)
Reviewer 2		
The protocol paper is well designed and the anticipated analysis also well described. I believe this population-based study, when completely implemented, would contribute new knowledge to help characterise asthma.	Thank you for your kind words and appreciation of our work.	-

VERSION 2 – REVIEW

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GENERAL COMMENTS	

REVIEWER	
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GENERAL COMMENTS	

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GENERAL COMMENTS	

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VERSION 2 – AUTHOR RESPONSE

VERSION 3 – REVIEW

REVIEWER	
REVIEW RETURNED	

GENERAL COMMENTS	

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GENERAL COMMENTS	

VERSION 3 – AUTHOR RESPONSE

VERSION 4 – REVIEW

REVIEWER	
REVIEW RETURNED	

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GENERAL COMMENTS	

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VERSION 4 – AUTHOR RESPONSE

VERSION 5 – REVIEW

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GENERAL COMMENTS	

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GENERAL COMMENTS	

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VERSION 5 – AUTHOR RESPONSE

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