Author's response to reviews

Title: The Epidemiology of Varicella Zoster Virus Infection in Italy

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Author's response to reviews: see over
Sir,

please find enclosed the answers to each further comment on our manuscript.

Regarding ethics approval, we can answer as follows:

(1) Clarify, within your manuscript, whether the data in the National Hospital Discharge Database is openly available to the public; if not, please confirm whether you obtained permission to access this and give the name of the body which granted this.

The Hospital discharge forms database (SDO) was officially established in 1991 (MoH Decree dated December 28th, 1991). The clinical information is coded by the international ICD9-CM system (International Classification of Diseases, 9th revision, Clinical Modification), currently used in Italy, and transmitted to the Regions and to the National Ministry of Health to be included in the regional and national SDO database.

Please note that the Italian SDO database is freely available from the website of the national Ministry of Health.

We have added the following sentence in the Materials section:

We also examined the National Hospital Discharge Database, created in 1994, which collects information on all hospitalizations recorded in Italy [9]. For the analysis of the data from this latter database, which is [freely available from the web site of the national Ministry of Health], we considered the main reason for hospitalization, which is codified using ICD9-CM (code 052 for varicella and code 053 for zoster).

(2) The UK would require ethical approval for your seroprevalence study - please inform us of the procedure followed for these types of studies in Italy and provide us with documentary evidence that you adhered to this procedure.

Regarding the ethical approval for our seroprevalence study, we followed the procedure already adopted for all studies performed during the European Seroepidemiology Network (ESEN) project. In detail, specimens were collected anonymously and only age, sex and date of sampling were recorded. Sera from
individuals known to be affected by an immunodepressive condition or by an acute infection or to have recently undergone a blood transfusion were excluded. No other information about health status or symptoms was recorded at the time of blood sampling. All individuals who provided serum samples gave verbal informed consent; consent for minors was provided by parents. These explanations are already described in the Methods section, and for this reason we would prefer not to add any sentence on this specific point.

Please note that this procedure has also been explained and accepted in the following publications:


Regarding Reviewer’s report:
The multivariable analysis would seem to provide no evidence that antibody prevalence to VZV varies by region in Italy. This is strongly suggestive that the epidemiology of VZV does not vary geographically in Italy. The authors may therefore want to review the discussion (page 11, final paragraph). Some comment on the convenience sample of sera used might also be useful (e.g. how representative might it be of the general population, could any bias in this sampling frame be contributing to some of the findings?)
Regarding the first point, we have added this sentence in the Discussion section:

**Multivariate analysis showed that the only variable associated with antibody titre is age group.** This is strongly suggestive that the epidemiology of VZV does not vary geographically in Italy. As a matter of fact, regional differences……..

Regarding the convenience sample, we added the following sentence in the Discussion section:

**In designing the sero-prevalence study, the representativeness of the sample was pursued following indications provided by the European Project for the Sero-epidemiological Surveillance of Vaccine-preventable diseases.** Although the samples from very young subjects could have been collected from children affected by health problems, the inclusion and exclusion criteria adopted in this study should have allowed to exclude these children, thus avoiding an overestimation of seroprevalence. **This study shows that** the sero-epidemiological profile in Italy is different……..

Please note that the new changes included in the text have been highlighted in green, while the changes included in the previous revision of the manuscript have been highlighted in yellow.

I hope that the comments and the changes included in the text will make the new revision of our paper suitable for publication in BMC Public Health.

Please do not hesitate to contact me if you need further explanation.

Yours sincerely,

Giovanni Gabutti