

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Validating malignant melanoma ICD-9-CM codes in Umbria, ASL Napoli 3 Sud, and Friuli Venezia Giulia administrative healthcare databases: a diagnostic accuracy study
AUTHORS	Orso, Massimiliano; Serraino, Diego; Abraha, Iosief; Fusco, Mario; Giovannini, Gianni; Casucci, Paola; Cozzolino, Francesco; Granata, Annalisa; Gobbato, Michele; Stracci, Fabrizio; Ciullo, Valerio; Vitale, Maria Francesca; Eusebi, Paolo; Orlandi, Walter; Montedori, Alessandro; Bidoli, Ettore

VERSION 1 – REVIEW

REVIEWER	Ivan Marquez-Rodas Servicio de Oncología Medica, Hospital General Universitario Gregorio Marañón, Madrid, Spain
REVIEW RETURNED	17-Nov-2017

GENERAL COMMENTS	I have nothing to add to this work. It address a difficult topic, that is monitoring incidence of a tumor, melanoma, that in many countries has no clear registries in order to have a proper information about incidence and prevalence. Since the international coding matches almost perfectly with the data present in theses regional databases, it could help to pothers to implement similar databases registries.
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REVIEWER	Dr Veronique Bataille Kings College, London
REVIEW RETURNED	22-Jan-2018

GENERAL COMMENTS	This is an interesting paper checking the accuracy of ICD-9-CM codes for melanoma in several regions in Italy. The data is sound and the conclusions appropriate. The only confusing aspect is the data extracted from clinical notes when it is not clear how many patients had diagnostic biopsies and how many had full excision biopsies. For melanoma, the standard of care is the latter. The mean age is also older than most other melanoma cohorts where the mean age would be 51 to 55 years of age. The fact that most melanomas were diagnosed in surgical units does suggests that those were more advanced melanomas as thin melanomas are diagnosed by dermatologists usually. The low number of females in the Napoli Sud needs to be explained as well. The other curious data is the fact that only a small percentage of the patients had a skin lesion as the primary clinical issue and it is unclear why not all of them were not a skin lesion at the onset for the diagnosis of cutaneous melanoma. It would have been nice to add the thickness
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	of the tumours as this was accessible if the authors looked at the clinical notes and histology reports. The same for the justification of CT scan/US/PET scans which are often not performed for early melanoma and therefore the high percentage of these investigations in some centres needs to be justified.
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REVIEWER	Stacey DaCosta Byfield Optum, USA
REVIEW RETURNED	31-Jan-2018

GENERAL COMMENTS	<p>This paper was clear, succinct and well-written. Overall, investigation/assessment of claims-based algorithms to identify study populations of interest for analysis using claims data is important and warranted.</p> <p>Though I understand that there may timing considerations that influence when this study was initiated and the data available, the relevance of this article would be greatly improved if ICD-10-CM codes were also investigated, or at least some discussion of why ICD-9-CM code investigation is still relevant and how results with ICD-10-CM codes may be similar or different to the results using the ICD-9-CM .</p> <p>A few minor edits to be considered are: Page 3, line 25: Should 'STAR' be 'STARD'? Page 5, line 11: The 's' should not be superscript, instead, consider 'From the early 90s' Tables and Figures: Consider uniformly referring to Friuli Venezia Giulia as Unit 3. It is Unit 2 or Unit 3 in the current Tables and Figures.</p>
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VERSION 1 – AUTHOR RESPONSE

Editorial Requirements:

- Our in-house editors would like some further clarification about the data used in your study.

-Was the data used fully anonymised?

** Despite each resident has a unique anonymous identification code at a national level, within each administrative database there is a second process of anonymization to fully secure the id of the patients.

-Please can you confirm how you gained access to the data?

**We first obtained approval from the ethics committee of Umbria (CEAS), subsequently, to gain access to the medical chart consultation, each Operative Unit obtained permission from the Head Offices of the Local Health Units and Hospital Trusts to consult a list of medical charts.

-Is it publicly available and is it possible for someone else access it?

**The data from the healthcare databases are not available to the public. Access to the medical charts for consultation is possible to the personnel of the National Health System only for specific administrative issues. Researchers can obtain access only after approval from the ethics committee.

-We note that you have not obtained ethical approval for the study - can you provide details of the ethical oversight and methods used to compile and protect the data?

**A copy of the approval by the Regional Ethics Committee of Umbria (CEAS), authorization number: 2656/15 (04/11/2015) was sent to the BMJ Open during the first submission of the protocol (doi: 10.1136/bmjopen-2015-010547).

We are attaching again copy of the ethical approval.

The following sentence was added in the methods section: "Patients were not directly involved. This was a retrospective study based on the consultation of medical charts. Ethical approval for the present study including the access to medical charts was obtained from the Ethics Committee of the Umbria Region Health Authority (CEAS)."

- Please revise your title to state the research question, study design, and location. This is the preferred format for the journal.

**We have revised the title as follows: "Validating malignant melanoma ICD-9-CM codes in Umbria, ASL Napoli 3 Sud, and Friuli Venezia Giulia administrative healthcare databases: a diagnostic accuracy study"

Reviewer(s) Reports:

Reviewer: 1

Reviewer Name: Ivan Marquez-Rodas

Institution and Country: Servicio de Oncologia Medica, Hospital General Universitario Gregorio Marañon, Madrid, Spain

Please state any competing interests: None declared for the present work.

Please leave your comments for the authors below

I have nothing to add to this work. It address a difficult topic, that is monitoring incidence of a tumor, melanoma, that in many countries has no clear registries in order to have a proper information about incidence and prevalence. Since the international coding matches almost perfectly with the data present in these regional databases, it could help to others to implement similar databases registries.

**We really thank the reviewer for his positive comment about our work.

Reviewer: 2

Reviewer Name: Dr Veronique Bataille

Institution and Country: Kings College, London

Please state any competing interests: None

Please leave your comments for the authors below

-This is an interesting paper checking the accuracy of ICD-9-CM codes for melanoma in several regions in Italy. The data is sound and the conclusions appropriate.

**We thank very much Dr. Bataille for her positive comment.

-The only confusing aspect is the data extracted from clinical notes when it is not clear how many patients had diagnostic biopsies and how many had full excision biopsies. For melanoma, the standard of care is the latter.

**We thank Dr. Bataille for this question. We have collected all the available info regarding the biopsies performed. Actually, some patients may have performed a diagnostic biopsy before the complete removal of the lesion by excision. We modified the variables in Table 1 as (a) Diagnostic

biopsy and (b) Excision biopsy with a new row (c) where the number of subjects that received both approaches was displayed. We would like to underline that these information were collected from the first medical chart of each patient. Further info might be present in the subsequent charts.

-The mean age is also older than most other melanoma cohorts where the mean age would be 51 to 55 years of age.

** We thank Dr. Bataille for raising this question. We included this sentence in the discussion: "The mean age of our sample population ranged between 60 to 61 years that is higher than the mean age (55 years) reported in the medical literature²⁸. Age variability can be due to thickness and histological subtype of the melanoma but we were able to plan the acquirement of these data."

-The fact that most melanomas were diagnosed in surgical units does suggests that those were more advanced melanomas as thin melanomas are diagnosed by dermatologists usually.

**Yes, this is a possible explanation. However, we have to state that in some settings (e.g., FVG) several surgical departments have a dermatological sub-unit where melanomas are diagnosed by dermatologists. In a few other circumstances it is possible that departments of dermatology have a restricted number of beds and patients are subsequently referred to week-surgery.

-The low number of females in the Napoli Sud needs to be explained as well.

**In the ASL Napoli 3 Sud there was 45% of males comparing to 57% in Umbria and 53% in FVG. Each Unit randomly selected its own population. The difference in proportions of males/females might be due to chance. Applying the Pearson chi² test the differences in proportion across the three Operative Units resulted not statistically significant (p-value = 0.16) with 95% CI of prevalence rates largely overlapping between the three Units.

-The other curious data is the fact that only a small percentage of the patients had a skin lesion as the primary clinical issue and it is unclear why not all of them were not a skin lesion at the onset for the diagnosis of cutaneous melanoma.

**Our intention was to report as much rigorously as possible the description of the lesions that were present in the medical chart. In several occasions there was not a detailed clinical description of the lesion. This might give a different impression but we would like to confirm that almost all the lesions were skin lesions as confirmed in the subgroup of ICD-9 codes.

In the Table 1, we modified the related variable as "Detailed clinical description of the skin lesion".

-It would have been nice to add the thickness of the tumours as this was accessible if the authors looked at the clinical notes and histology reports.

**For the present study, the thickness of the tumours was not our primary aim. However, we noticed that part of the medical chart evaluators reported the data at their discretion. Hence, the data regarding tumour thickness is incomplete as reported here:

a) In Umbria, the thickness of the tumours was available for 34/112 (30%) and it ranged from 0.28 to 7.75 mm.

b) In ASL Napoli 3 Sud, the thickness of the tumours was available for 27/116 (23%) and it ranged from 0.80 to 7.10 mm.

c) In FVG, the thickness of the tumours was available for 22/130 (17%) and it ranged from 0.38 to 11.0 mm.

-The same for the justification of CT scan/US/PET scans which are often not performed for early melanoma and therefore the high percentage of these investigations in some centres needs to be justified.

**Yes. For the same issues raised above (age, surgical departments,...), the diagnostic examinations usually used for disease staging might explain that part of the cases were of advanced disease. The percentages of diagnostic instrumental examinations were variable between the three Units as follows: CT scans 11%-51%, Ultrasound 13%-26%, PET/CT 2%-3%, CT or MRI of the brain 0%-4%, lymphoscintigraphy 28%-55% (percentages are now added in Table 1). Since we have not recorded the stage of the disease we cannot conclude whether the underwent examinations were appropriate or not. However, in order to show the number of patients that did not undergo any instrumental examination, we have also added in the Table 1 a row with the variable "None instrumental examinations"

Reviewer: 3

Reviewer Name: Stacey DaCosta Byfield

Institution and Country: Optum, USA

Please state any competing interests: None

Please leave your comments for the authors below

This paper was clear, succinct and well-written. Overall, investigation/assessment of claims-based algorithms to identify study populations of interest for analysis using claims data is important and warranted.

**We thank the reviewer for his positive comment.

-Though I understand that there may timing considerations that influence when this study was initiated and the data available, the relevance of this article would be greatly improved if ICD-10-CM codes were also investigated, or at least some discussion of why ICD-9-CM code investigation is still relevant and how results with ICD-10-CM codes may be similar or different to the results using the ICD-9-CM.

**In our study we considered ICD-9-CM codes because in Italy they are still used in the hospital discharge databases. We added this sentence in the Limitation paragraph:

"A possible limitation of our results for future research is that validation studies of administrative databases are related to the context where they are generated, and may not be generalizable to other settings. Another limitation is that we are unsure whether the results presented for the ICD-9 code 172.x related to malignant melanoma of the skin could be also valid for the corresponding ICD-10 code C43.x."

A few minor edits to be considered are:

Page 3, line 25: Should 'STAR' be 'STARD'?

**We amended the text accordingly.

Page 5, line 11: The 's' should not be superscript, instead, consider 'From the early 90s'

**We amended the text accordingly.

Tables and Figures: Consider uniformly referring to Friuli Venezia Giulia as Unit 3. It is Unit 2 or Unit 3 in the current Tables and Figures.

**Thank you for highlighting the mistake. We amended the order of Unit 2 and Unit 3.

VERSION 2 – REVIEW

REVIEWER	IVAN MARQUEZ RODAS
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	HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑON
REVIEW RETURNED	03-Mar-2018
GENERAL COMMENTS	Accept, since the questions from other reviewers have been appropriately answered
REVIEWER	Dr Veronique Bataille Kings College London
REVIEW RETURNED	06-Mar-2018
GENERAL COMMENTS	The reviewers' comments have been addressed
REVIEWER	Stacey DaCosta Byfield Optum, USA
REVIEW RETURNED	06-Mar-2018
GENERAL COMMENTS	The updates are acceptable and I recommend acceptance for publication.