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### ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>EPIDEMIOLOGY OF SYPHILIS-RELATED HOSPITALISATIONS IN SPAIN BETWEEN 1997 AND 2006: A RETROSPECTIVE STUDY.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Laura García García*, M Carmen Ariza Megía, Alba González-Escalada, Alejandro Álvaro, Ángel Gil de Miguel, Ruth Gil Prieto.</td>
</tr>
</tbody>
</table>

### VERSION 1 - REVIEW

| REVIEWER          | Dr Ian Simms  
| Description       | Epidemiologist  
| Health Protection Agency | London, United Kingdom |
| REVIEW RETURNED   | 18/08/2011 |

| THE STUDY         | None |
| RESULTS & CONCLUSIONS | None |
| REPORTING & ETHICS | None |

| GENERAL COMMENTS | I have a few suggestions which the authors should take into consideration when revising the manuscript.  
1 The paper would be improved if the standard of written English was improved, but this could be done at the editorial stage. Eg. there is a spelling mistake in the title to figure 2.  
2 For the international audience it would be helpful if the authors included a brief explanation of which clinical settings manage STDs in Spain. Are all the cases likely to be seen as hospital inpatients? If this isn't the case then the authors should account for the missing cases and explain the omission of these cases on their study.  
3 The number of cases looks high compared to other European countries - this could also be discussed.  
4 The authors should show the antenatal screening data together with the relevant discussions around policy. It would also be good to have the congenital cases (with the appropriate international case definition) shown in the paper.  
5 Under Article Focus, the authors should omit the second two bullet points as these aren't addressed effectively in the paper.  
6 Determinants of incidence should be discussed in more detail, if the data are available.  
7 Discussion (para 3) The comment around antenatal screening is too simplistic. The authors need to discuss the impact of antental screening in Spain within the context of the international literature and WHO guidelines on antenal screening and the prevention of congenital syphilis. |

| REVIEWER | Kevin A. Fenton, M.D., Ph.D., F.F.P.H | Director | National Center |
Reviewer completed checklist only, no further comments.

**VERSION 1 – AUTHOR RESPONSE**

I have a few suggestions which the authors should take into consideration when revising the manuscript.

1 The paper would be improved if the standard of written English was improved, but this could be done at the editorial stage. Eg. there is a spelling mistake in the title to figure 2.

Title to figure 2 has been modified. Thank you
Paper has been reviewed by a native speaker.

2 For the international audience it would be helpful if the authors included a brief explanation of which clinical settings manage STDs in Spain. Are all the cases likely to be seen as hospital inpatients? If this isn't the case then the authors should account for the missing cases and explain the omission of these cases on their study.

Syphilis infections are of mandatory notification in Spain through the notifiable disease system (EDO). New cases are recorded in a weekly basis at both the Primary Care and Hospital level, where patients with ITS are treated and followed. There are also ITS regional centers. Hospitalisations occur in the most severe cases, latent and terciary syphilis or comorbidities. Our results do not show the real incidence of syphilis infection. Primary and secondary infections are mainly treated in Primary Care centers.
That is the reason why we don't talk about incidence, but about hospitalisation rates.
Paper has been substantially modified in order to address this limitation.

3 The number of cases looks high compared to other European countries - this could also be discussed.

By comparing the figures obtained in the present study with the total of cases reported to the EDO (1), we can estimate a 42% of the syphilis infections needing hospitalisation. Both hospitalisation rates and incident estimates obtained in this study are higher than those published for other European countries (18). Possible explanations for these figures could be different sexual behaviours and the increasing immigrant population since 2000 coming from different regions with higher syphilis incidences.

4 The authors should show the antenatal screening data together with the relevant discussions around policy. It would also be good to have the congenital cases (with the appropriate international case definition) shown in the paper.

Congenital syphilis case definition has been included in the text: “Syphilis in the newborn due to maternal-fetal transmission in utero” (Global burden of Sexually Transmitted Diseases (excluding HIV)

The following paragraph has been included taking into account reviewers comment:

Pregnant women are tested twice for syphilis infection during the routine pregnancy controls in the National Health System in Spain, a first serology in the first antenatal consultation and a second one in the third trimester. Treatment is given both to the woman or her couple when needed. If the woman tests positive for the infection, a second serology will be done during delivery, both to the mother and the newborn to check its serological status (3, 4). The increase of congenital syphilis during the study period reflects an increase in the primary and secondary syphilis cases among women in Spain. It could be due to the increasing immigrant population from countries where syphilis incidence is higher. These women can have a lower adherence to the health system and less access to prenatal consultation and can be at a higher risk of syphilis and HIV transmission.

5 Under Article Focus, the authors should omit the second two bullet points as these aren't addressed effectively in the paper. The Key Messages also need to be revised and amended.

• They have been modified taking into account reviewers comments.

6 Determinants of incidence should be discussed in more detail, if the data are available.

Different determinants have been discussed throughout the discussion section following reviewer´s comments.

7 Discussion (para 3) The comment around antenatal screening is too simplistic. The authors need to discuss the impact of antenatal screening in Spain within the context of the international literature and WHO guidelines on antenatal screening and the prevention of congenital syphilis.

A new paragraph has been introduced taking into account this comment

Reviewer: Kevin A. Fenton, M.D., Ph.D., F.F.P.H | Director | National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention | Centers for Disease Control and Prevention |

No competing interests.

A few grammatical errors noted in the paper.

Final version has been reviewed by a native speaker.
Epidemiology of syphilis-related hospitalisations in Spain between 1997 and 2006: a retrospective study

Laura García-García, M Carmen Ariza-Megía, Alba González-Escalada, Alejandro Álvaro-Meca, Ángel Gil-deMiguel and Ruth Gil-Prieto

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