

Dear Editor of *World Journal of Gastroenterology*,

Our sincere thanks for your consideration of the manuscript, “Areas of research and clinical approaches to the study of liver abscess” (ESPS Manuscript NO: 28993) and for the peer reviewers’ comments, which we believe have helped to deepen the discussion of the interest in case reports. Please find attached our revised manuscript, in which we have incorporated all the suggested changes, as well as our detailed response to the peer reviewers.

We remain at your disposal for any additional clarifications.

Sincerely,

Gregorio González Alcaide, on behalf of all coauthors

## RESPONSE TO REVIEWER 1

Following the reviewer's recommendation, we expanded the discussion regarding the implications and application of clinical case studies from two perspectives: considering the interest of this document type, and providing different bibliographic examples that report and describe the creation and use of information sources based on case studies.

Specifically, we have included the following text and bibliographic references in the manuscript:

Although individually, clinical case studies may be insufficient grounds on which to base treatment decisions, when they are considered together and adequately codified and integrated into structured information systems, they can provide early insight toward characterizing rare diseases, as they allow physicians to compare cases and check diagnoses. They may also be useful in identifying emerging trends or studying the geographical distribution of diseases. Case studies could even be apt for integration into simulators for use in an educational context, as shown through different initiatives (Kansagra et al., 2004; Selmi et al., 2013).

**Kansagra S**, Chang C, Hussain S, Hulka G, Leithe LG. Online medical teaching case database. In: Proceedings 17th IEEE Symposium on Computer-Based Medical Systems, CBMS 2004; Bethesda, MD; United States; 24-25 June 2004. Piscataway, NJ: Institute of Electrical and Electronics Engineers,; 420-422.

**Selmi SY**, Fiard G, Promayon E, Vadcard L, Troccaz J. A virtual reality simulator combining a learning environment and clinical case database for image-guided prostate biopsy. In: Rodrigues PP, Pechenizkiy M, Gama J, Cruz-Correia R, Liu J, Traina A, et al., editors. Proceedings of CBMS 2013. 26<sup>th</sup> IEEE International Symposium on Computer-Based Medical Systems. Piscataway, NJ: Institute of Electrical and Electronics Engineers, 2013: 179-184.

Different projects have highlighted the utility of international case report registers describing unusual clinical cases in different medical specialties or in relation with rare diseases whose low prevalence makes them very difficult to investigate in studies with a more traditional design. By drawing from a wide body of case reports, investigators can develop an ad hoc cohort for analysis (Cervera, 2012; Ohmann et al., 1999; Sancho et al., 1996).

**Cervera R**, CAPS Registry. *Lupus* 2012;**21**: 755-757 [PMID: 22635223 DOI: 10.1177/0961203312436866].

**Ohmann C**, Eich HP, Sancho JJ, Diaz C, Faba G, Oliveri N, Clamp S, Cavanillas JM, Coello E.. European and latin-american countries associated in a networked database of outstanding guidelines in unusual clinical cases (ELCANO). *Stud Health Technol Inform* 1999; **68**: 59-63. [PMID: 10724957]

**Sancho JJ, Oliveri NC, Faba G, Campos M, Sanz F, de Dombal FT**. ELCANO: European and Latin-American countries associated for a networked database of outstanding guidelines in unusual clinical cases. In: Brender J, Christensen HL, McNair P, editors. Medical Informatics Europe. Amsterdam: IOS Press, 1996.

Different initiatives have been proposed to promote the use of clinical case reports for rare diseases and to lay the groundwork for the generation of higher level evidence. Although the BioMed Central project “Cases Database” has unfortunately not been maintained (Kettermann, 2014), other international registers could base their case report databases on the models described in the literature (LaPook, 2000). The dissemination of this document type could also be expanded through specialized journals dedicated to case studies or clinical case reports, and specific identifiers could be used to locate these types of studies in bibliographic databases, particularly the main multidisciplinary databases.

**Kettermann E.** Cases Database. *J Med Lib Assoc* 2014; **102**: 137-138. [doi: 10.3163/1536-5050.102.2.023]

**LaPook JD.** Proposal of an international case-report database. *Lancet* 2000; **356**: 169-170 [PMID: 10963280 DOI: 10.1016/S0140-6736(05)73188-3]

## RESPONSE TO REVIEWER 2

We analyzed the presence of the study topic in the Scopus database because this is the international multidisciplinary database with the largest coverage of journals, and in Copernicus, incorporating brief comments related to the results obtained in these sources of bibliographic information and to the interest in specifically identifying case studies (or clinical case reports) as a document type in the main bibliographic databases, particularly the large multidisciplinary ones.

We have incorporated the following paragraphs and bibliographic references into the manuscript:

Performing this same search in the Scopus database yields similar results (1303 articles, reviews and letters in the 2001–2014 period, compared to 1226 records of the same document types in MEDLINE). More specialized databases such as Copernicus present a lower number of documents, so we consider that the source used (MEDLINE) provides a complete and comprehensive picture of the existing research on the topic.

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dissemination of this document type could also be expanded through specialized journals dedicated to case studies or clinical case reports, and specific identifiers could be used to locate these types of studies in bibliographic databases, particularly the main multidisciplinary databases.

**Ketterman E**, Cases Database. *J Med Lib Assoc* 2014; **102**: 137-138. [doi: 10.3163/1536-5050.102.2.023]

**LaPook JD**, Proposal of an international case-report database. *Lancet* 2000; 356: 169-170 [PMID: 10963280 DOI: 10.1016/S0140-6736(05)73188-3]