Format for ANSWERING REVIEWERS

May 27th, 2015

Dear Editor,

Enclosed please find the edited manuscript in Word format (file name: 17291-review.doc).

Title: Signs and genetics of rare cancer syndromes with gastroenterological features

Author: William Bruno, Giuseppe Fornarini, Paola Ghiorzo

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 17291-review

1 I wish to thank the reviewers for their suggestions. The manuscript has been revised according to the reviewers' and editor's suggestions and I believe the manuscript is now greatly improved. Major changes have been highlighted in *Italics* throughout the text.
The manuscript has been reviewed for grammar and spelling mistakes by an English proofreader who is a native speaker and has been editing scientific papers for international journals in the fields of medicine and computer science for the last 20 years. A CV is available upon request.

2.
(1) Reviewer **02536288**:
"1. In introduction part: The knowledge of these findings and the ability to recognize thm (misprint) can help clinicians 2. In Beckwith-Wiedemann Syndrome: newborns. (misprint)".
Misprints have been corrected.
"3. In The Bloom's Syndrome: "Associated neoplasias" and "Genetics" are in differ places than in other parts".
The position of the paragraphs has been corrected.
"4. In Hereditary hemorrhagic telangiectasia Associated neoplasias is missing".
A paragraph entitled "Associated neoplasias" has been added to the Hereditary Hemorrhagic Telangiectasia section.
"5. Please include a part "Methodology" with information about your scientific search for information - web systems, prefers journals ect."
A description of how the scientific search was carried out is now provided in a new "Methodology" section.

(2) Reviewer **02445450**:
"1. Please make the definition of rare cancer syndromes."
A/ ***The - choose*** *definition of rare cancer syndromes has been added to the "Introduction".*
"2. In the introduction, please let the readers know how BWS, Bloom's Syndrome, etc are selected more precisely. It is odd that HNPCC, FAP, Peutz-Jegher's syndrome, etc are not included".
The aim of the review was to focus greater attention on syndromes that are often neglected, little recognized, or even unknown among clinicians. Colon cancer prone syndromes, such as HNPCC or FAP, are well known since a great deal of reviews and studies are available, and the diagnosis and management of these patients is currently part of standardized, routine protocols. We felt that it was of no particular interest to provide further information

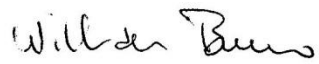
on any of the syndromes already described in several papers, some of which have even been published in the WJG and are cited among the references. Furthermore, our aim was to describe cancer prone syndromes that show gastroenterological signs, thus not necessarily those that include colon cancer.
As a team involved in the management of rare tumors we know the difficulties that need to be faced by patients affected by rare syndromes and how these difficulties are often related to a late or missing diagnosis. We are aware that our proposal is about very rare and misdiagnosed syndromes, but this is exactly why our approach to writing about them does not start from oncological gastrointestinal signs.
Therefore, in the Introduction section we strengthened the rationale of the study.

"3.What is the order of the described syndromes? Is it frequency? It is better to add information of incidence and prevalence."
Information about incidence and prevalence has been checked and implemented when available (this kind of data is still approximate or unknown for these syndromes). With regard to order, see below.
"4.Please try categorization depending upon the manifestations, such as cystic lesions, vascular lesions, and intestinal polyps."
There is an overlapping of clinical signs among the syndromes we illustrated, so strict categorization is not possible or is still inaccurate. Nonetheless, we created four subsets (Syndromes with vascular or cystic lesions, Syndromes with GEP endocrine tumors, Syndromes with colon polyps/cancer, Syndromes with childhood onset tumors and gastrointestinal anatomical defects). These subsets are described at the end of the Methodology section which states the possible inaccuracy due to clinical overlapping, as illustrated in a new Table (Table 2).

3 References and typesetting were corrected.

I hope the reviewers will find this version satisfactory, and am grateful for this opportunity to publish in the *World Journal of Gastroenterology*.

Sincerely yours,



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