Format for ANSWERING REVIEWERS

December 25, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5529-Review.docx).

Title: Colorectal carcinoma in a southern Mediterranean country: the Libyan scenario.

Author: Zuhir Bodalal, Riyad Bendardaf

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 5529

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 00505544:

Abstract section:

Q1: "What authors want to mention by "determined using the direct method and the standard population"."

A1: The direct method and the standard population are techniques that are well known in the Cancer Epidemiology field. Every registry in the world uses this technique and it was established by the IARC – Lyon, who publish "Cancer in Five Continents". This is considered to be the most basic form of calculation of cancer incidence. Involves the normal calculation of incidence however taking into consideration a standardized equation (used worldwide) and a standardized age distribution.

Q2: "Conclusion section should be started with their actual results. How they have just concluded about the screening programms?"

A2: The conclusions are based on the results mostly, however the point regarding the screening programs was mentioned in the discussions and it is based on our observation from the daily activities in the Oncology department. Screening programs, in our belief, would greatly help in catching these patients early on when the treatment options are significantly better. In other words, it is based on the discussions and can also be considered a recommendation.

In the text:

Q1: "The whole manuscript should be edited for grammer and language seriously. There are so many language mistakes."

A1: This comment actually surprised us, considering that both authors are fluent English speakers. Furthermore, the main/corresponding (the one who wrote the manuscript) is a native English speaker and has earned 670 in TOEFL (a full mark, *which is very rare in the world*) as well as a 6.0/6.0 in the TWE (Test of Written English). The authors have revised the manuscript and would be really interested to see where these spelling and grammar mistakes are. Perhaps, the reviewer has confused this manuscript with another? Interestingly, we counted 16

grammar and spelling mistakes in the reviewer's comments which is much more than anything that could possibly exist in the manuscript.

Q2: "There is no requirement for abbrevations for :microscopic verification (MV), Benghazi Medical Center (BMC), Eastern Mediterranean Regional Office (EMRO)."
A2: These abbreviations have been removed at the request of the reviewer.

Q3: "Instead of 5 year analysis, it would be better to use decades to analyse the incidences among patients."
A3: The age distribution table has been modified to function on a 10-year basis. We appreciate the comment and we believe that it looks better now. Thank you.

Q4: "This study does not reflect the whole Libya, therefore heading of the manuscript should be corrected."
A4: The running title of the manuscript is "Colorectal Carcinoma in **Eastern** Libya", and the heading of the manuscript mentions that it represents the Libyan scenario (not necessarily all of Libya). Cancer epidemiology research rarely covers an entire country, usually it takes a representative sample and generalizes it. The title clearly indicates that we are speaking about Libya and the running title which will be seen on every page by the readers will specify that our data is from Eastern Libya (which is actually a very large geographical area). However, your point is valid and we appreciate your addition. Your concern has been addressed in the limitations portion of the discussion.

Q5: "Missing patients should be omitted from the tables. The whole manuscript should be based on the patients with available finding and results."
A5: The missing patients were removed from the tables. In the parameters for which there was missing data, these cases were not included in the calculations. When the results were available for another parameter, these cases were re-included. In Libya, documentation is poor and data gathering is extremely difficult (especially in a post-war situation). These cases are only missing a single parameter and they were excluded for the missing parameter.

Q6: "Therefore whole tables should be revised. The manuscrit mentions that the age of incidence decreases. They have to discuss this point in discussion section with other studies."
A6: We looked at the results, we never mentioned that the age is decreasing. This is impossible for us to say since this study does not speak about age trends (or any other trends, for that matter). Additionally, this is the first study ever done about colorectal cancer in Libya. The manuscript says that "younger ages are being affected with colon cancer" and we are of course referring to the <40, <50 and <55 year old age groups. We have compared our figures with a number of studies. (please see references 24, 25 and 26).

Q7: "It would be better to give most metastatic sites at presentation. "
A7: We agree that it would be an interesting parameter however, as we mentioned above, documentation is poor and this information was not available for enough cases. Hence, it was not included in the studies. This point has been included in the limitations.

Q8: "There is no knowledge about the survival of these patients. If available the authors should give the survival rates of the study group."

A8: We agree that it would be an interesting parameter however, as we mentioned above, documentation is poor and this information was not available for enough cases. Hence, it was not included in the study**.** This point has been included in the limitations.

Q9: "The authors should give more information about the changes in food habbits of Libyan patients."
A9: These additions have been made to the journal and can be found in the discussions section.

Q10: "The figure 1 should be omitted."
A10: We believe that Figure 1 is important since it provides the reader with an idea of the location of the different cities/town/villages that were studied and the eastern part of Libya where data was collected. Apart from Benghazi and Tripoli, no other cities here in Libya are known to the outside world. This map will at least be helpful in appreciating the distances and geography of the locations.

Reviewer <u>00506105</u>:

Q1: "This is a simple age-standardized reporting of colorectal cancer – based on a retrospective chart analysis of ONE year data. This is the major weakness of the study. It has to be trend of minimum five years to a decade to pronounce that CRC is on the rise."
A1: The authors agree with this statement, however determining any form of trend (i.e. whether it is on the rise or not) was not listed as an objective of this study. We only discussed the features of colorectal carcinoma patients. In the long term, we plan to prospectively collect data regarding colorectal carcinoma for the purpose that you mentioned. Any attempt at forming a trend, either by ourselves or any future generation of authors needs to have a benchmark placed in the past and that is what we are hoping to do.

Q2: "The study should have more information regarding dietary habits, clinical symptomatology, how many of them were incidentally diagnosed, what was the management strategies – how many of then underwent surgery / radiotherapy / palliation etc."
A2: We agree that this would have been interesting additions to the study however, as we mentioned in the methodology, our data was obtained from patient records. Data is very difficult to obtain in Libya and in the current climate, potentially life-threatening. In developing countries, the quality of patient files is notoriously poor (this is especially true for Libya and is evident from the low medical research output). Most of our cases present at such a stage that only palliation is given and hence only scanty information is present in the patient's file. The parameters that we presented in this study were the only reliable data available.

Q3: "The authors have listed their own article (submitted and under review) as a reference (ref 10) – this will give the reviewer an impression that the current paper may be salami publication of the same information."
A3: The paper that was submitted and under review is only concerned with the results of our efforts at reactivating the Benghazi Cancer Registry, which has been dormant for around 10 years now. A year's worth of data was gathered and due to the wide variety of cancers covered, only superficial information was provided on each one. This study is devoted whole-heartedly to CRC patients and hence includes parameters like histopathological grade and detailed clinical staging.

Q4: "Part of Table 1 and Figure 2 have the same information – Figure 2 should be enough to show the age-group differences."

A4: Figure 2 is a graphical representation of the patient distribution of age *when split for gender*. Statistically speaking, this is different and also data labels are not present and hence the readers would not determine the percentages. This will only give them a broad visual feel of the numbers but not the analytical aspect present in the table. We had hoped to keep the "best of both worlds" and provide both of them for our valued readers.

Reviewer 00068546:

Q1: "The introduction for the CRC mortality rate (ie, 60%) is not right."

A1: The authors agree with this comment and it appears to have been a typographical error. It has been removed.

Q2: "Please clarify and cite a paper that reflect data from either worldwide or Libya. In addition, it is unclear why the authors cited the incidence rate from Finland. Please use data that are more representative to the country. Please also make sure the citations are up to date."

A2: The authors agree with this comment and the Finnish reference has been removed. Most of studies cited in this study are from similar countries (i.e. Egypt, Iran etc…). Our citations are up to date and have been changed to meet the requirements.

Q3: "How representative are the patients in the study? The data were from only one clinic and thus the data can't be generalized to the general Lybians. Please mention this as a limitation in the discussion section."

A3: As mentioned in the methodology, the oncology clinic at the Benghazi Medical Center (BMC) is the sole oncological center in all of eastern Libya (which is a large geographical area). Virtually all patients have to register with our center, however your point is valid and we have added it to our limitations.

Q4: "Please comment on the health care system in Lybia. How accessible are most Lybians to the clinical care? What are the plausible factors that the patients were not diagnosed earlier? Is socioeconomic playing a role? Please also comment on the lifestyle factors of most Libyans. Which potential risk factors might have affected the present findings? There are many well-known risk factors (eg, fat meat intakes, physical activity, obesity, insulin resistance, screening) for CRC."

A4: These additions have been made to the journal and can be found in the discussions section.

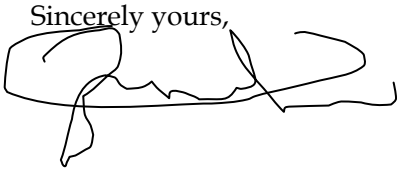
Q5: "Please offer distribution (N, %) on tumor location (ie, colon, rectum)."

A5: This parameter has been added as Table 3 and was referred to in the results section (i.e. rectal carcinoma was the most common form).

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Oncology*.

Sincerely yours,



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