Author's response to reviews

Title: Utilization Pattern of Traditional Chinese Medicine for Liver Cancer Patients in Taiwan

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Author's response to reviews: see over
Dear Editor:

Thank you very much for giving us the chance to reply the reviewers’ comments for our paper "Annual fasting plasma glucose variation increases risk of cancer incidence and mortality in patients with type 2 diabetes: The Taichung Diabetes Study ". We have made revision according to your comments point-by-point.

Your sincerely
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Reviewer: Laura Weeks
Reviewer's report:
1. I have reviewed the resubmission by Liao and colleagues. Comments to my prior report have been well addressed, in addition to those of the other reviewer. The manuscript is now stronger. I have a few suggestions and comments for the authors to consider, as outlined below. Further, there are several grammatical errors throughout that likely result from English being a second language for this team. The manuscript would benefit from a careful read from and editor.

Reply: Thank you for your suggestion. To improve the quality of written, we have sent our manuscript for English-editing by a professional expert.

Minor Essential Revisions
1. Introduction, 2nd paragraph: The sentence should be changed to "The motives for the use of CAM include A PERCEIVED failure" (i.e. not "the failure")

Reply: Thank you for your suggestion. We have followed your suggestion to make change. In addition, we separate the statements regarding CAM and TCM into two paragraphs according to the other reviewer’s comments. The revised sentence is as follows:

*The motives for the use of CAM include a perceived failure of standard health care, the patients’ need for autonomy, and a preference for holistic or natural therapy in Western populations [4-5,6].*

2. Results, Expenditures, 1st paragraph - in the last sentence, an error seems to have
been made when calculate US$ from NT$.

**Reply:** Thank you for pointing out our mistake. We have made correction. The last calculation is “NT$754.38 = US$23.28.”

3. Results, 2nd paragraph, last sentence - no need to repeat exchange rate between US$ and NT$ from paragraph above.

**Reply:** Thank you for your suggestion. We have deleted the repeat description in the results of the second paragraph, last sentence for Expenditure.

4. Abbreviation: CAM should be "Complementary and Alternative Medicine"

**Reply:** Thank you. We have followed your suggestion to make correction.

Discretionary Revisions

1. It seems to be a very important result that TCM costs are consistently lower than WM costs. This point should be highlighted more clearly in the discussion as it has the potential to inform policy decisions. The point could be made stronger in the first paragraph of the discussion, and in the conclusion for example by editing the corresponding sentence to read..."The costs of insurance covered TCM were CONSISTENTLY lower than those of WM."

**Reply:** The authors would like to thank you for judicious reading of the manuscript and valuable comments which greatly improved this manuscript. We have followed your suggestion to make correction in the conclusion of the Abstract, the first paragraph of the discussion, and in the conclusion. The revised paragraphs are as follows:

**Conclusion of the Abstract**

**Conclusion:** TCM was widely used by the patients with liver cancer and the prevalence of TCM use remained stably high during the study period. This study found the costs of insurance covered TCM were consistently lower than those of WM in patients with liver cancer. The findings of this study should be useful for health policy makers and those considering the integration of TCM and WM.

The first paragraph of the discussion

**This study is the first large-scale survey in the literature focusing on TCM use among liver cancer patients. In the present study, the overall prevalence of insurance-covered TCM use in outpatient services among liver cancer patients was 19.50% and remained stably high during the study period. TCM outpatient services accounted for 27.28% of the visits and 22.39% of the outpatient service expenditures of patients with**
liver cancer. And the costs of insurance covered TCM were consistently lower than those of WM.

Conclusion
In Taiwan, the NHI program is a comprehensive and universal health insurance program. This program covers both conventional WM services and TCM services. The prevalence of TCM use among liver cancer patients remained stably high. The costs of insurance-covered TCM were consistently lower than those of WM. This study provides information about TCM use frequency and existing diseases treated by WM and TCM in liver cancer patients, which should be useful to health policy makers and those who consider the integration of TCM and WM.

2. Conclusion - I agree with the change to report "no trend" for the rate of TCM use, but it seems worthwhile here to state that it is still a consistent and stable (and substantial?) proportion of LC patients who use TCM.

Reply: Thank you. We have followed your suggestion to delete the description of “no trend” for the rate of TCM use. It has changed as “The prevalence of TCM use among liver cancer patients remained stably high.”
Reviewer's report

Title: Utilization Pattern of Traditional Chinese Medicine for Liver Cancer Patients in Taiwan

Version: 2 Date: 6 February 2012

Reviewer: Vincent Chung

Reviewer's report:

Reviewer’s report

Major compulsory revisions:

1. Introduction:

   Overall comments:

   The content of the introduction part has greatly improved by the authors’ professional input. However, it could be better organized by (1) giving sub-title each paragraph;

   Reply: Thank you. We have followed your suggestion by adding sub-title for each paragraph. The sub-titles we add are as followed:

   Incidence and mortality of liver cancer

   Use of Complementary and Alternative Medicine worldwide

   Use of traditional Chinese medicine in Asian countries

   Therapeutic effect of TCM against hepatocellular carcinoma in previous studies

   How the current study helps resolve the uncertainties regarding TCM use

   (2) clarifying issues as listed in the following:

   Second paragraph:

   A. The authors discussed TCM together in CAM usage which I believe to be inappropriate from both cultural and policy perspectives. CAM is a term that denotes a wide range of non-allopathic therapies while TCM is a very specific type of CAM with its own theories and systems. The context of how CAM gained popularity in the West, and how it mainstreamed within health systems outside the Chinese speaking world is complete different from how TCM has evolved within Chinese health system in the past few thousand years. For instance, TCM is well covered in the Taiwanese social insurance system but in the West funding of CAM service via private or social insurance is not widespread. I believe that the second paragraph can be improved by separating discussion on CAM and TCM, and possibly highlight how Chinese and western populations differ in their choice of TCM as well CAM. This will help the readers to interpret findings better under a culturally specific lens.

   Reply: Thank you for your valued comments. We have followed your suggestion by
separating the second paragraph into two parts: one is use of complementary and alternative medicine worldwide and the other is use of traditional Chinese medicine in Asian countries. In addition, we add several statements regarding how TCM use in Taiwan population is different from CAM use by Western population. These two paragraphs are as follows:

**Use of Complementary and Alternative Medicine worldwide**

The use of Complementary and Alternative Medicine (CAM) has gained worldwide popularity. The motives for the use of CAM include perceived failure of standard health care, the need of a patient for autonomy, and preference for holistic or natural therapy in Western populations [4-6]. CAM is commonly used together with conventional medicine and has entered mainstream society and culture [7-9]. According to the 2007 National Health Interview Survey, the prevalence of CAM use is about 38% in American adults [9]. In a survey across a number of European countries, the percentages of CAM use range from 22.7% for head and neck cancer patients to 56.3% for pancreatic cancer patients [10].

**Use of traditional Chinese medicine (TCM) in Asian countries**

TCM is one of the most popular CAM forms worldwide. The motives for TCM use include cultural belief about TCM in managing illness symptoms, maximizing conventional treatment effect, and preventing recurrence in Chinese populations [11-13]. TCM is commonly used together with conventional medicine and has entered mainstream society and culture. In Chinese and East Asian societies, TCM plays an active role in the modern health care system. Unlike CAM that is not funded by either private or social insurance companies in most Western societies, TCM is covered by the National Health Insurance (NHI) Program of Taiwan. Thus, one important feature of the NHI Program is the coverage of both biomedicine (Western) and TCM. By 2003, after implementing the NHI Program, more than 99% of the 23 million persons residing in Taiwan had been covered by this universal health insurance plan.

Compared with CAM use by Western populations, TCM has a higher level of accessibility due to lesser financial barrier. A study on the determinants of TCM and acupuncture utilization of cancer patients in Taiwan has shown that the prevalence of TCM ranges from 14.81% for cervical cancer to 30.13% for breast cancer [8].

B. Third paragraph: The use of the term “western medicine” is not specific enough as it also includes non-conventional western medicine like homeopathy. I recommend the use of the term “biomedicine” is a more specific term that denotes only allopathic medicine.

**Reply:** We have followed your suggestion by changing “western medicine” into
“biomedicine” through the entire manuscript.

C. The authors mentioned that “fee for consultation and diagnosis” for WM and TCM were US 9.88 and US 8.95 respectively. Is that what the patients have to pay at the point of care then get reimbursed later? Same confusion exists for herbal fee. Please clarify as this will aid interpretation of table 4.

Reply: The expenditure we considered in our study is the fee that was covered by NHIP. In Taiwan, patients only pay copayment and expenditure that was not covered by NHIP at the time point of outpatient visit. They don’t need to pay any expense that was covered by NHIP and reimburse later. We have added some sentences, which are underlined, to describe this in the second paragraph of method section. These sentences are as follows:
The LHID2005 database contains comprehensive information, such as demographic data, dates of clinical visits, diagnostic codes, expenditure amounts, and others. The amount of expenditure in the dataset was that covered by NHIP, which represent the consumption of medical resources. NHIP has a committee to review new treatments, drugs or procedures. Those treatments, drugs or procedures proved to have evidence-based effectiveness are covered by NHIP. The expenditure can be classified into 3 categories: fees for consultation, treatment, and medical supply, diagnosis fee, and drug fee.

D. Fourth paragraph: Commonly used Chinese herbal medicine should be named using proper Latin names in italics.

Reply: Thank you for pointing out our errors. We have had these Chinese herbal medicine names in italics.

E. Method: In the eighth paragraph, the authors mentioned that clinicians are required to input three ICD-9 items into the electronic database. What if the patients have more than 3 co-existing condition like liver cancer, diabetes, hypertension and acute upper respiratory infection? Will the last one be omitted? If so, this will under – count coexisting disease listed in table 3. I strongly suggest the authors to use only 95% CI instead of using different statistical indicators liberally. From the result section and the tables I can see SD, p values etc. They may not be the most informative indicators.

Reply: Yes, the least important existing condition for a specific visit will be omitted if the patients have more than 3 existing conditions. Usually only the main diseases or conditions for each outpatient visit are recorded into the electronic database. To enhance the validity of claimed data, expert reviews on a random sample for every
50-100 ambulatory and inpatient claims in each hospital and clinic were conducted quarterly. A severe penalty would be placed on every false report of diagnosis by the NHI Bureau. We have added these two sentences for enhancing the validity of claim data in the method section. Yes, our data will under-count coexisting disease listed in table 3. We have followed your suggestion by adding 95% CI for mean and proportions in Tables 2 and 3.

F. Results: The tenth paragraph is too long and I suggest the authors to split it into two. Currently, the text only focus on univariate findings and none of the multivariate findings is being reported. Emphasis should be given to the reporting of logistic regression findings as they illustrate differences between users and non-users without influences of confounding factors. For example, after controlling for various confounding factors, compared to liver cancer patients in northern Taiwan, residence of the central parts are more likely to use TCM but the contrary was observed in Taipei. Is this a cultural variation? Similarly, farmers and fishermen are less likely to use TCM compared to government and school employee. Does this represent a type of comparative inequality within the TCM coverage system? Discussion on these interesting findings will make this paper a very valuable contribution to the literature. In table 1, full name of the statistic “odd ratios” should be given, not just “adjusted”.

Reply: We have followed your suggestion by splitting the tenth paragraph into two paragraphs. We deleted the description regarding univariate findings and added the description of multivariate findings. We have also added one paragraph to discussion why patients residing in the central Taiwan and farmers and fishermen are more likely to use TCM compared with their counterparts. In table 1, the full name of the statistic “odds ratios” has been added to the heading.

Our results suggested that TCM services were utilized more often by females and residents of central Taiwan, but less often by patients >70 years old, residents of Taipei, as well as farmers and fishermen. The higher TCM use of central Taiwan residents may probably be due to the higher availability of TCM providers in this area. Before 1998, the only medical university that provided formal TCM education was located in central Taiwan; thus, the ratio of TCM physicians to 10 000 residents was 1090 for Taichung city in central Taiwan compared with 771 for the second highest area in 2010. There are two possible reasons that can explain the low TCM use of farmers and fishermen. One is that farmers and fishermen live in areas with less access to TCM providers. Another is that their economic status is usually lower and the extra expenditure for TCM use may be a financial burden. Further research on the barriers for TCM use is warranted.
G. In the twelfth paragraph, why would “malignant neoplasm of the liver and hepatic bile ducts” a coexisting condition with liver cancer??

**Reply:** Thank you for pointing out our errors. We have changed “coexisting diseases” as “existing diseases”.

H. Is the prevalence of hypertension rather low amongst Taiwanese liver cancer patients? Or it is related to lack of comprehensive coding from clinicians? The use of hypertension code is only 4.47% for all outpatient visits amongst liver cancer patient. Also, the authors must address the related issue I raised on paragraph eight.

**Reply:** The figure of this proportion for hypertension does not reflect the prevalence of hypertension amongst Taiwanese liver cancer patients. For each outpatient visit, there are 3 disease codes. This proportion was calculated by using total number of disease code for all outpatient visits made by these liver cancer patients during study period as the denominator and number of hypertension disease code as numerator. Thus, this proportion was affected both by the hypertension prevalence amongst Taiwanese liver cancer patients and rate of outpatient utilization for hypertension by liver patients with hypertension. In addition, it is related to lack of comprehensive coding. For example, only 3 diseases will be coded if a patient seeks for outpatient care for more than 3 diseases. We have added several sentences to address this issue.

*Based on the ICD-9-CM codes, we found that chronic liver disease and cirrhosis, as well as general symptoms were the primary indications for TCM. In biomedicine, the top two primary indications, apart from malignant neoplasm of the liver and hepatic bile ducts, were chronic liver disease and cirrhosis, as well as diabetes. These findings on the disease pattern of health care use may be explained by the fact that patients seek TCM to relieve symptoms. We observed that the proportions of hypertension and diabetes only accounted for a small portion of all ICD-9 codes made by patients with LC. Caution should be taken when interpreting these proportions. This proportion was affected by both the disease prevalence among Taiwanese LC patients and the rate of outpatient utilization for each disease by LC patients with co-existing conditions. This proportion is also related to insufficient comprehensive coding. For example, only three diseases were coded if a patient sought outpatient care for more than three diseases. Our data underestimated the proportion of existing disease among all ICD-9 codes.*

I. In the thirteenth paragraph, authors must explain how these expenditure figures
represent financial barrier to access. Currently there is no text explaining how may we understand these expenditure figure as the reader would not know in what proportion of these expenditure would be covered by the national insurance system. Also, interpretation of the WM / TCM ratio in table 4 is not given on the related text.

Reply: The expenditure figures do not represent financial barrier to access. They represent the consumption of medical resources. All expenditure figures we present here were cover by NHI. There is no regulation for the number of outpatient visits. The only financial barrier to access is the amount of copayment. NHI Bureau once raised the upper limit of copayment to prevent patients from unnecessary outpatient visits. As we mentioned, some treatment or drug items were not covered by NHI because the effectiveness of the treatment or drug is controversial (please see C). We have added the interpretation of the WM/TCM ratio in the text.

J. Discussion: The current discussions merely repeat the papers’ finding and no interpretation of results is given. Also, no policy implications were discussed in this session. For example, the public sector constitute a very small proportion of TCM outpatient service supply – why is it so? Does it carry any implication on TCM access? A thorough rewrite after reorganization (as well as interpretation) of current results is warranted.

Reply: We have followed your suggestion by adding one paragraphs that discussed the important findings of the current study (please see reply for F). The public clinical institutes constitute a very small proportion of TCM outpatient service supply is because most public clinical institutes set up departments of TCM after 2000. Because these public clinical institutes constitute a very small proportion TCM care providers, it does not affect TCM outpatient service supply or access. Our study is mainly descriptive and the estimates from our study can provide information for health policy and allocation of health resources. We have followed the other reviewer’s comment by highlighting our study findings that has the potential to inform policy decisions. The revised paragraph of discussion (1st paragraph of discussion) is as follows:

This study is the first large-scale survey focusing on TCM use among LC patients in Taiwan. The overall prevalence of insurance-covered TCM use in outpatient services among LC patients was 19.50% and remained stably high during the study period. TCM outpatient services accounted for 27.28% of the visits and 22.39% of the outpatient service expenditures of patients with LC. The costs of insurance covering TCM were consistently lower than those covering biomedicine.