

Peer Review File

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Comment 1: Considering the broad scope of LCM's audience (younger clinicians and experienced ones), we suggest authors

- Add a paragraph at the very beginning to briefly introduce the background of the BC (e.g., the role, importance, classification);
- Explain the relationship between Blood-Stasis and cardiovascular disease, simply stating "previous studies (3,6) have linked Blood-Stasis to cardiovascular disease and coronary heart disease" (lines 32-33) is not sufficient.

This would effectively avoid younger peers from getting lost.

Response: We added a brief introduction of background for BC and the relationship between Blood-Stasis and cardiovascular disease (see Page 2, lines 18-25, 39-42).

Changes in the text:

Traditional Chinese Medicine (TCM) has guided health maintenance and surveillance for thousands of years in the East. The theory of body constitutions (BC) originated from the Yellow Emperor's Canon of Medicine and played an important role in the evolution of TCM. BC theory summarizes balanced and imbalanced health states according to individual's innate and acquired body features and classifies individuals into nine categories of BC: Gentleness type, Qi-deficiency type, Yang-deficiency type, Yin-deficiency type, Phlegm-dampness type, Dampness-heat type, Blood-stasis type, Qi-depression type, and Special diathesis type (1). Although TCM BC types have been standardized and extensively studied in recent years, studies conducted among populations other than Chinese are sparse except one study of White students living in China (2).

Finally, previous evidence showed that from 23.0% to 45.6% of coronary atherosclerotic heart disease (CAHD) cases, the leading cause of mortality globally, were linked to the Blood-Stasis constitution type (7).

Comment 2: Lines 27-32: "Zhu et al. reported ... in sex and age (4)". Not entirely clear why you mention these three articles here; did the authors intend to show that there are many influencing factors that cause international differences in BC? And why did the authors choose to discuss mainly cardiovascular disease? Please explain clearly.

Response: These three articles published together in this special issue provide additional evidence indicating that the TCM BC types differ in US population from that in Chinese populations which is the basis for the current study.

The reason we chose cardiovascular disease because 1) it is the leading cause of death worldwide; 2) previous studies showed that a large proportion of cardiovascular disease cases were linked to BC types, i.e. the Blood-Stasis constitution type. See our response to comment #1; 3) the incidence is higher in the US and other Western countries and lower in Chinese populations; 4) the first BC study conducted in the US population found Blood-Stasis type constitutes the largest proportion (17.3%) among white individuals in the US which is higher than that in the Chinese population; and 5) We used cardiovascular disease as an example. Future studies from other groups can address other diseases.

Through the review of immigration studies, the current study generated a hypothesis that different environmental factors across populations and countries lead to the different BC types and different incidence rates of cardiovascular diseases.

Changes in the text: [None](#)

Comment 3: Line 34: This article focuses on "immigration studies" (as the title shows), so does the "US populations" mean "Chinese immigrants" in the sentence "We examined whether US populations had...Blood-Stasis BC type"? Please specify it.

Response: [To clarify, we have modified the description of study populations \(See Page 2-3, lines 42-44\).](#)

Changes in the text:

[We examined whether white Americans had higher risk of cardiovascular disease and/or coronary heart disease compared to Chinese immigrants in western countries and Chinese population in China.](#)

Comment 4: Line 27, line 30: Please explain "in this issue" ("Zhu X" is not the author of this article) otherwise it will confuse the readers.

Response: [In the current issue in Longhua Chinese Medicine, there are three reports, including the current report together with two other reports by Tao M and Zhu X, respectively \(see the following citations\), supporting the findings from the first BC study conducted in an US population \(Shu L\). To make it clear, we have modified the text on page 2, lines 32-34.](#)

[See two citations below.](#)

Tao M, Zhu X, Yin X. Different Traditional Chinese Medicine Body Constitution in White and Chinese Patients with Colorectal Polyp. Longhua Chinese Medicine 2023, in press.

Zhu X, Yin X, Deng X, et al. Associations between Traditional Chinese Medicine Body Constitution and Obesity Risk among US adults. Longhua Chinese Medicine 2023, in press.

Changes in the text:

[This finding has been supported by other two reports by Tao et al \(5\) and Zhu et al \(6\) in this special issue that...](#)

Comment 5: Lines 67-69: According to table 1 in reference 3, the proportion of Blood-Stasis in Chinese in China seems to range from 1.5% to 3.83%, while that in caucasian in China was ranging from 2.5% to 8.1%. Please kindly confirm the accuracy of the data and the statement about the "Chinese immigrants" and "Chinese in China" in the text.

Response: [We apologize for the confusion of the numbers. We have confirmed that in the Personalized Prevention of Colorectal Cancer Trial \(PPCCT\), the first study of TCM BC types conducted in the US population, proportions of Blood-Stasis were much higher in white Americans \(17.3%\)\(3\) than those from the studies conducted in Chinese population in China ranging from 1.5% to 8.1% \(9-11\). Young Caucasian college students in China were young college students, but not immigrants. Thus, they are not included in the current study. We have corrected this number on Page 4, lines 77-81. To avoid confusion, we have further specified "Chinese immigrants in Western countries" in comparison to "Chinese in China" throughout the manuscript.](#)

Changes in the text: [In the Personalized Prevention of Colorectal Cancer Trial \(PPCCT\), the first study of TCM BC types conducted in the US population, proportions of Blood-Stasis were much higher in white Americans \(17.3%\)\(3\) than those from the studies conducted in Chinese population in China ranging from 1.5% to 8.1% \(9-11\).](#)

Comment 6: The conclusion is not drawn reasonably enough. From two articles studying the prevalence of CHD in Chinese immigrants and two articles studying the BC of white Americans alone, the authors conclude that blood stasis may be associated with cardiovascular disease, which we do not

think is feasible. We suggest the authors add specific data related to blood stasis and cardiovascular disease. For example, in the study by Shu et al., it is recommended to report the number and percentage of the 191 participants with cardiovascular disease and those with blood stasis.

Response: In the study conducted by Shu et al., there was no incident cardiovascular disease outcome. We have clarified that the current study leads to a new hypothesis which should be tested in future studies. We have substantially revised the conclusion section on Page 5, lines 93-98.

Changes in the text: In conclusion, we hypothesize that higher proportions of Blood-Stasis in white Americans compared to Chinese immigrants in Western countries and Chinese in China may provide a possible explanation for the higher risk of CHD in white Americans compared to both Chinese immigrants in Western countries and Chinese population in China. If this hypothesis is confirmed in future studies, one promising strategy for the prevention of CHD is to modify the environmental factors associated with both Blood-Stasis and CHD.

Comment 7: Similar to the point in comment 3, the purpose mentions "immigration studies of cardiovascular disease", but the conclusion does not mention any information about the Chinese immigrants. The conclusion should include answers to the priority questions posed by the research.

Response: Please see our detailed response under the response to the comment #3. In brief, we have specified the comparisons among three populations including White Americans, Chinese immigrants in Western countries and Chinese in China in the conclusion section on Page 5, lines 93-98.

Changes in the text: In conclusion, we hypothesize that higher proportions of Blood-Stasis in white Americans compared to Chinese immigrants in Western countries and Chinese in China may provide a possible explanation for the higher risk of CHD in white Americans compared to both Chinese immigrants in Western countries and Chinese population in China. If this hypothesis is confirmed in future studies, one promising strategy for the prevention of CHD is to modify the environmental factors associated with both Blood-Stasis and CHD.

Comment 8: Lines 83-84: "If confirmed in future studies, assessment of Blood-Stasis will be used to identify individuals at high-risk of CHD for the prevention and treatment of CHD". If it is motivated by this hypothesis, the authors need to clarify: What are the advantages of BC assessment over traditional cardiovascular disease screening methods? What is the accuracy of the BC assessment? How to address extrapolation?

Response: Based on the current literature and the reviewer's comment, we have changed the last sentence of the conclusion to "If this hypothesis is confirmed in future studies, one promising strategy for the prevention of CHD is to modify the environmental factors associated with both Blood-Stasis and CHD."

Changes in the text: In conclusion, we hypothesize that higher proportions of Blood-Stasis in white Americans compared to Chinese immigrants in Western countries and Chinese in China may provide a possible explanation for the higher risk of CHD in white Americans compared to both Chinese immigrants in Western countries and Chinese population in China. If this hypothesis is confirmed in future studies, one promising strategy for the prevention of CHD is to modify the environmental factors associated with both Blood-Stasis and CHD.

Comment 9: Please kindly confirm the accuracy of the references cited and revise accordingly. For example,

- In the reference list, list all authors, but if the number exceeds three, give three followed by "et al."

- Also, please add the URL if the preprinted article is available online, e.g., Reference 3: "3. Shu L, Yin X, Zhu X, et al. Associations between Traditional Chinese Medicine Body Constitution and Cardiovascular Disease Risk in a White population. medRxiv 2022;2022.12.13.22283433. Available at: <https://www.medrxiv.org/content/medrxiv/early/2022/12/20/2022.12.13.22283433.full.pdf>).

- Lines 24-26: "whereas in a previous large study with 8,448 participants ... and Yang-deficient (9.0%) (3)". Please cite the original reference (Zhu YB, Wang Q, Chen KF, et al. Stratified analysis of the relationship between traditional Chinese medicine constitutional types and health status in the general population based on data of 8,448 cases. Zhong Xi Yi Jie He Xue Bao. 2011 Apr;9(4):382-9. Chinese.).

Please check the entire manuscript to address similar concerns.

Response: [We have corrected the format of references.](#)

Changes in the text: [See references.](#)

Comment 10: Please paraphrase the sentences marked in the attached Similarity Report, mainly source 1.

Response: [We have modified the sentences marked in Similarity Report.](#)

Changes in the text: [Although TCM BC types have been standardized and extensively studied in recent years, studies conducted among populations other than Chinese are sparse except one study of White students living in China \(2\).](#)

[Specifically, the study revealed that a large proportion of white individuals in the US exhibited Blood-Stasis type \(17.3%\) whereas in a previous large study conducted among 8,448 Chinese participants in China, the most common pathologic BC subtypes are Qi-deficient \(13.4%\), Dampness-Heat \(9.1%\) and Yang-deficient \(9.0%\), respectively \(4\).](#)