
Peer Review File

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Reviewer A

Comment 1: Could you better define TCIM. ? Integrative oncology allows patients, besides specific care, to access complementary therapies. In your paper, patients do not access to specific therapies so it is alternative medicine which is quite different from complementary or integrative medicine+++

Reply 1: Thank you very much for raising this point to our team. On reflection and reassessment of our piece, we do see that we mostly touched on traditional and alternative medicine rather than integrative oncology as a whole. We have thus revised the title and body of our piece by changing “integrative” (as TCIM) to “alternative” (as traditional, complementary, and alternative medicine [TCAM]), since this is more appropriate given our discussion.

Changes in the text: Changes are scattered throughout the title, abstract, and body of the piece. The word “alternative” has been highlighted in yellow to track the change from “integrative” to “alternative.”

Reviewer B

Comment 1: on the Abstract “*there exists a deep divide between TCIM and biomedicine.*” — where? In Philippines? Because it is not the case in all countries. you could say: in some countries more than others or “depending on the country”

Reply 1: Thank you for bringing this to our attention, and we agree that we have unintentionally generalized this statement inappropriately. We meant to refer to the Philippines, hence we have modified our text as follows (see page 3, line 46).

Changes in the text: “Despite the strong patronage for the paradigm, there exists a deep divide between TCAM and biomedicine in some countries like the Philippines.”

Comment 2: “*Prayers, vitamins, and herbal preparations are used to stabilize the present condition, boost the immune system, improve quality of life, and manage the side effects of conventional therapies.*” — replace with “are used for the purpose to stabilize”

Reply 2: We have modified the text as advised (see page 5, lines 101-103).

Changes in the text: Prayers, vitamins, and herbal preparations are used for the purposes of stabilizing the present condition, boosting the immune system, improving quality of life, and managing the side effects of conventional therapies.

Comment 3: “*Little interprofessional coordination and communication exists between conventional physicians and TCIM practitioners,*” — what about the other way? Is there communication between TCIM practitioner and conventional physicians?

Reply 3: Little is known about formal communication channels between TCAM practitioners

and conventional physicians since referral systems in the country are still underdeveloped. We have elaborated this in the text for better context (see page 5, lines 114-118).

Changes in the text: Little is known about formal communication channels between TCAM practitioners and conventional physicians, but referral systems in the country in general have yet to be developed. Without mechanisms in place, compounded by personal prejudices, it is less likely that patient management is coordinated and unified, especially with an existing distinct delineation between these two practices.

Comment 4: *“It is common for Filipino patients to opt for TCIM (12), deeming it safer, more accessible, and more affordable.”* — I think it is not the good reference. Would it be 11 ?

Reply 4: Thank you for bringing this to our attention. We have reviewed our text references and determined that the main reference for this line is reference 12, as originally cited. However, the study discusses patients in general and does not specify Filipinos. The inclusion of Filipino in this statement was an oversight on our part during our internal revisions. We have opted to remove the Filipino descriptor as follows (see lines 119-120).

Changes in the text: It is common for patients to opt for TCAM (12), deeming it safer, more accessible, and more affordable.

Comment 5: *“Though TCIM is meant to be utilized for supportive and palliative care, Filipino patients underserved by the healthcare system must rely on it as a primary form of treatment in the absence of accessible and affordable conventional cancer therapies, and this is regrettably linked to worse prognosis (12)”* — could you discuss if the results of this US study are applicable to Filipinos?

Reply 5: There is little published data on TCAM use in the Filipino setting and how it figures in the prognosis of patients who rely on it as primary treatment in the absence of conventional cancer therapies. To avoid misinterpretation, we have revised the statement to a more generalizable argument that does not discuss prognosis (see page 5-6, lines 122-125).

Changes in the text: “TCAM is meant to be utilized for supportive and palliative care. However, Filipinos underserved by the current healthcare system are left to rely on it as a primary form of treatment despite its limitations, in the absence of accessible and affordable conventional cancer therapies.”

Comment 6: *“patients who initially choose treatment with TCIM exclusively may delay or refuse conventional therapies altogether”* — do you have any exact figures on the percentage of patients who would refuse conventional cancer treatments due to taking TCIM, or is this an "impression" an "opinion". If you do not have a figure or an exact study on the subject, you should say: that this "could lead to"

Reply 6: This statement is an impression due to the lack of studies on TCAM in the Philippine setting. We have modified the text as advised. (see page 6, lines 124-127).

Changes in the text: It must also be acknowledged that choosing treatment with TCAM exclusively may lead to the delay or outright refusal of conventional therapies altogether, especially when discussions on TCAM use are not handled satisfactorily by their physicians.

Comment 7: *“With inadequate patient education and less stringent safety evaluations*

compared to conventional medicines, adverse side effects experienced by patients taking herbal preparations are often unrecognized or assumed to be part of the medicine's healing action, and remain unreported (16)." — you could indicate here the risk of induction or inhibition of cytochrome CYP 3A4 by certain plants and their consequences on certain targeted cancer therapies

Reply 7: Thank you for raising this important aspect of TCAM in relation to integrative oncology. We agree that this would be important to discuss as well, hence we have expounded with additional information in the text, as advised (see page 6, lines 140-143).

Changes in the text: Some plants commonly used in Traditional Chinese Medicine induce or inhibit the cytochrome P450 enzyme system, particularly CYP3A4, which may lead to either decreased effectiveness of some chemotherapeutic drugs or increase in their side effects and toxicity (17).

Comment 8: Reference 3 - Kong et al. — with or without DOI ?

Reply 8: We have modified the text without the DOI, in accordance with Vancouver citation guidelines.

Changes in the text:

3. Kong YC, Kimman M, Subramaniam S, et al. Out-of-pocket payments for complementary medicine following cancer and the effect on financial outcomes in middle-income countries in southeast Asia: a prospective cohort study. *The Lancet Global Health*. 2022;10(3):e416-e428.

Comment 9: Reference 6 - Tan ML. — Town?

Reply 9: We have modified the text as advised.

Changes in the text:

6. Tan ML. *Revisiting usog, pasma, kulam*. Student ed. Manila: University of the Philippines Press; 2008.

Comment 10: Reference 7 - Tan JZT — town

Reply 10: We have modified the text as advised.

Changes in the text:

7. Galvez Tan JZ. *Health in the hands of the people*. Manila: JZGalveztan Health Associates, Inc; 2013.

Additional edits from the authors:

We have removed the DOI's of references 5, 12, and 13, in accordance with the Vancouver citation guidelines.

Changes in the text:

5. Rondilla N, Rocha I, Roque S, et al. Folk medicine in the Philippines: A phenomenological study of health-seeking individuals. *International Journal of Medical Students*. 2020;9(1):25-32.

12. Johnson SB, Park HS, Gross CP, Yu JB. Complementary medicine, refusal of conventional cancer therapy, and survival among patients with curable cancers. *JAMA Oncol*.

2018;4(10):1375–1381.

13. Adams KE, Cohen MH, Eisenberg D, Jonsen AR. Ethical considerations of complementary and alternative medical therapies in conventional medical settings. *Annals of Internal Medicine*. 2002;137(8):660–664.