Author's response to reviews

Title: Construction of a Traditional Chinese Medicine syndrome-specific outcome measure: The Kidney Deficiency Syndrome questionnaire (KDSQ)

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Construction of a Traditional Chinese Medicine syndrome-specific outcome measure: The Kidney Deficiency Syndrome questionnaire (KDSQ)

Run Qiu Chen \(^1\), Chit Ming Wong \(^2\), Tai Hing Lam \(^2\)

Dear Editors of BMC Complementary and Alternative Medicine,

We thank you and the reviewers for reviewing our manuscript and providing review comments. We have addressed each of the comments in our document “Responses to Reviewers’ Comments” as follows.

The revised manuscript text, tables and figures are re-submitted for your consideration of publication in BMC Complementary and Alternative Medicine. In addition, we have attached the revised version of our manuscript with tracked changes (file name: “ChenRQ-KDSQtext_revised.pdf”) with this document for your references to know how we have responded to the reviewers comments and what we have revised.

Best regards

Dr Chen, Run Qiu
School of Chinese Medicine
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Responses to Reviewers’ Comments
Reviewer1: Ali Montazeri

COMMENT: This manuscript reports on psychometric properties of the Traditional Chinese Medicine Kidney Deficiency Syndrome questionnaire. Overall the paper reads well and merits publication.
RESPONSE: We sincerely thank the reviewer for reviewing our manuscript and providing the comment.
Reviewer 2: darong wu

Major compulsory revisions:

COMMENT (point1): Background: For the background section, I believe that the Kidney Deficiency Syndrome Questionnaire (KDSQ) is useful in describing individual’s health status, i.e. similar as a diagnostic instrument. However, I’m not quite sure whether it could be used, as the author stated, to evaluate the efficacy of TCM therapies. Effect size of KDS-Yin, KDS-Yang and their domains listed in table 3 may partly explain my concerns. For deficiency heat domain of KDS-Yin and deficiency cold domain of KDS-Yang the effect size is close to or even less than 0.2 (which means that the ES is small).

RESPONSE: We sincerely thank the reviewer for reviewing our manuscript and providing the comments. We understand the reviewer’s concern on the small effect size of deficiency heat domain of KDS-Yin and deficiency cold domain of KDS-Yang. The deficiency heat domain symptoms and deficiency cold domain symptoms are mainly those of menopausal vasomotor symptoms. As what Lam and colleagues (Ref. 18) have reported from their community survey that intensity of menopausal vasomotor symptoms is lower than that of menopausal psychological and somatic symptoms in Hong Kong Chinese women aged 40-60 years, and that of the vasomotor symptoms is significantly lower in Hong Kong middle-aged women than in Dutch middle-aged women, as shown in the figure on the right. Consistently, our participants were found to have relatively mild deficiency heat symptoms or deficiency cold symptoms at baseline test and the magnitudes of change over the period of 66-74 days were relatively small. Thus, these might have contributed to the small effect sizes of deficiency heat domain and the deficiency cold domain. On the other hand, the rest of the KDSQ domains were found to have about medium to large effect sizes, suggesting that those KDSQ domains could detect changes. We have added this point to the discussion section of the revised manuscript (The last paragraph, page 15).

This figure is copied from ref.18. AN: anxiety domain; DE: depression domain; SO: somatic domain; VA: vasomotor domain; SE: sexual domain; UR: urogenital domain of menopausal symptoms.
COMMENT (point 2): Moreover, the author shall explain clearly that KDSQ belongs to which type of instrument. Is it a diagnostic one or an evaluative one? For if it is a diagnostic instrument, accepted levels of sensitivity and specificity to avoid as much as possible the rates of false negative or false positive are important. But if it is an evaluative instrument, it shall be good at detecting changes.

RESPONSE: We agree with the reviewer’s comment. The objective of the present study was “to test content validity, internal consistency, construct validity, test-retest reliability and responsiveness of the KDSQ for the assessment of KDS-Yin and KDS-Yang in Hong Kong middle-aged women menopausal symptoms”. We have revised the word “assessment” to “evaluation” in the objective of study in the introduction section (The last paragraph, page 4). We have already discussed the use of the KDSQ in the discussion section: “Also, the KDSQ is designed to be an outcome measurement tool, but for use as a diagnostic devise more rigorous tests are warranted.” (The second paragraph, page 15).

Minor essential revisions:
COMMENT (point 3): Method: In page 7, 3rd paragraph, the “…IFI were equal to or greater than 0.09”, here it shall be “0.90”.

RESPONSE: Thank the reviewer for pointing out the mistake. We have revised the figure to “.90” (page 7).

COMMENT (point 4): Result: The author shall show the detailed results from EFA and from SEM using figures or tables.

RESPONSE: Initially, we had considered using more tables and figures to report the results of EFA and SEM. But we thought it would occupy less space to summarize and interpret the EFA results that were more relevant to the present study (The second paragraph, page 10). Also, more details on the EFA including a table of the EFA factor loadings together with the results of a discriminant analysis study showing the symptom characteristics of KDS-Yin and KDS-Yang have already been reported elsewhere (Ref. 28, this table is copied below for your reference). We have added a sentence telling audiences who may want to know more details about the EFA in the last paragraph, page 10.

For the same reason, we prefer to summarize the SEM results on the measurement models of KDS-Yin (Figure 1) and KS-Yang (Figure 2) that were more relevant to the present study in four lines (The third paragraph, page 11). Also, more details about SEM on the multi-collinear models showing multiple measurement relationships in figures and tables have already been reported elsewhere (ref.
As indicated in the second paragraph, page 11.

This table is copied from ref.28 for your reference.

COMMENT (point 5): Discussion: In the discussion section, the sentence “construction of the KDSQ was evidence-based…” might not be proper. If the author wants to make this conclusion, he/she shall prove that the results either from exploratory factor analysis (EFA) or from structural equation modeling (SEM) are robust. Only women and those who were middle-aged with menopausal
symptoms were included, external validity of the results is limited. The author shall state this point in the limitation part.

RESPONSE: We understand the reviewer’s concern. The KDSQ was constructed on middle-aged women with menopausal symptoms. The use of the KDSQ is limited to this population of women. We have already stated this limitation in the discussion section with the last sentence: “Cautiousness should be taken in generalizing the validity and reliability of the KDSQ to middle-aged women of other ethnic backgrounds without prior testing.” (The end of page 13 and the top of page 14)

The background of discussing “Construction of the KDSQ was evidence-based…” is that validation of traditional Chinese medicine (TCM) syndromes and development of TCM instruments are the evolving fields of study; however, in published literature, validation has been based on expert opinions, and content validity of the instruments has been established by expert opinions (ref. 11). Different from previous studies, in contrast, the present study tested expert opinions in the construction of the KDSQ. We have now rephrased the paragraph for a more concise discussion as follow. “Scientific evidence is recognised to be a higher form of knowledge than expert opinion. We tested expert opinions in our construction of the KDSQ for expert opinion is subjective in nature. TCM syndromes are defined by expert opinion in plain language with domain changes and symptoms. Similar to what is reported by Birch et al., we found that the description of KDS-Yin and KDS-Yang was vague and varied in the literature despite experts had attempted to standardize TCM syndromes for decades. Content validity of the KDSQ could not be established by expert opinion. Therefore, after excluding those KDS items which were not related to KDS in middle-aged women (e.g., retarded growth and development, impotence), we tested the KDSQ for content validity by the pilot-test, the EFA exploratory test, and the SEM confirmatory and model-strengthening tests on different samples of participants.” (Discussion section, the second paragraph, page 13)

Nevertheless we did try to make our EFA and SEM studies more robust by careful planning and implementation, i.e., estimation and justification of sample sizes.

Reviewer 3: LIU Fengbin
COMMENT 1: Title of paper should be “the Kidney Deficiency Syndrome questionnaire (KDSQ) of middle-aged women with menopausal symptoms”
RESPONSE: We sincerely thank the reviewer for reviewing our manuscript and providing the comments. We understand this change of manuscript title is to show the limitation of the KDSQ. TCM syndromes have age, gender and cultural differences. We recognized these differences in the construction of the KDSQ, as described in the results section, “From all the symptoms and signs described in the literature, we included 39 symptoms to the KDS item reduction list by excluding the items appear only in children (retarded growth and development), men (impotence, nocturnal emission, premature ejaculation, infertility) and women of reproductive stage (infertility, oligomenorrhea)…”. (The last paragraph, page 9). In the discussion section, we pointed out “Cautiousness should be taken in generalizing the validity and reliability of the KDSQ to middle-aged women of other ethnic backgrounds without prior testing.” (The end of page 14 and the top of page 15). Thus, the title of manuscript could be “Construction of a Kidney deficiency syndrome questionnaire (KDSQ) in Hong Kong Chinese middle-aged women with menopausal symptoms”.

We used the title “Construction of a Traditional Chinese Medicine syndrome-specific outcome measure: The Kidney Deficiency Syndrome questionnaire (KDSQ)” because we wanted to emphasize the methods we developed for the construction of a TCM syndrome-specific outcome measure. We did not include “in Hong Kong Chinese middle-aged women with menopausal symptoms” in the title as this limitation statement would make a lengthy title, but the limitation is clearly presented in the paper. Also, we wondered if audiences who are not TCM professionals know that “Kidney deficiency syndrome” is a TCM syndrome. Thus, we prefer to keep the title as it is; however, if editors of BMC Complementary and Alternative Medicine believe the other title is better for the journal audiences, we are happy to change the title of the manuscript.

COMMENT2: I don’t know if the symptom list for a Kidney Deficiency Syndrome Questionnaire (KDSQ) has the representativeness.

RESPONSE: One of the issues in planning the construction of the KDSQ was to ensure representativeness of the KDSQ items. We took the following measures to ensure representativeness (appropriateness and completeness) of the KDSQ symptoms in Hong Kong Chinese women aged 40-60 years with menopausal symptoms.

1) We included ALL 39 symptoms and signs of KDS-Yin and KDS-Yang from “a TCM diagnosis textbook for Chinese national tertiary education,” a commonly cited clinical research guideline for diagnosis and assessment of TCM syndromes, the World Health Organization (WHO) international standard terminologies on TCM, the Chinese national standard on the diagnosis of TCM syndromes for clinical practice, and TCM classic literature. (Methods section, second paragraph, page 5). We discussed the rationale and limitation of using the references. “The classic literature was recognized to have built the foundation of TCM theory” and the contemporary
literature had been most frequently cited in TCM education, research and practice.\textsuperscript{2,7,8,15} We considered these references were representative of the TCM theory for the study of KDS-Yin and KDS-Yang. In future studies, guidelines are needed for the selection of references from TCM literature contributed by scholars of the last two thousand years and the present time.” (Discussion section, the last paragraph, page 14)

2) “For content validity, we set inclusion and exclusion criteria for the selection of symptoms for the KDSQ. The items included were those directly related to KDS-Yin and KDS-Yang in middle-aged women. The items excluded were those directly related to syndromes other than KDS-Yin and KDS-Yang; those have weak consensus in the literature (i.e., listed in only one or two of the references); and the signs appeared only in the contemporary literature but not in the classic literature.” (Methods section, the second paragraph, page 5).

3) “Then, we pilot-tested the KDSQ on participants who fulfilled the participant inclusion and exclusion criteria for the present study”. (Methods section, second paragraph, page 5). Together with the pilot test of the KDSQ, we pilot tested a translated Chinese version of the Greene Climacteric Scale (GCS) as one of the steps in testing validity and cultural equivalence of the GCS in Hong Kong Chinese middle aged women (ref. 17). The KDSQ, the GCS and a urogenital symptom domain (ref. 18) in Chinese language were stabled together with an open-ended space for participants to fill in any additional symptoms they experienced which they thought were related to either their menopause transition or Kidney deficiency syndrome. The pilot test results showed that the participants did not provide additional symptoms in the open-ended space. This pilot test result suggested the KDSQ items were representative in the participants; however, the limitation of the pilot test was “(the) sample size of the pilot-test was small (n=10) and that could be increased to reduce bias.” (Discussion section, the last paragraph, page 14)

4) After the pilot test, in order to ensure representativeness of the KDSQ items, “and finally three senior TCM experts who had over forty years of experience in TCM teaching, research and practice reviewed the items for appropriateness and completeness.” (Methods section, the second paragraph, page 5).

5) The items generated from the measures above were based on expert opinions. Since expert opinion is subjective in nature, we further tested content validity of the KDSQ items on two samples of Hong Kong Chinese women aged 40-60 years with menopausal symptoms as described in the statistical analysis sub-section: “We tested content validity of the KDSQ in four steps…..” (Methods section, page 6-7). In the exploratory factor analysis (EFA), importantly, we included a control item to the test. “The item ‘loose stools’ listed only in the textbook\textsuperscript{2} for the diagnosis of KDS-Yang was added as a control to the KDSQ, but was not found to be grouped to the domains of KDS-Yang by the EFA indicating this control item was independent from the domains of KDS-Yang.” (Results section, the last paragraph, page 10). We then performed a confirmatory test (Structural Equation Modelling, SEM) on the symptoms of KDSQ. Evidence from the EFA and SEM supports content validity of the KDSQ symptoms.
In summary, the KDSQ symptoms were reviewed from representative TCM theory, which were then evaluated by TCM experts, and finally were tested on samples of Hong Kong Chinese women aged 40-60 years with menopausal symptoms. The results suggested that the KDSQ items were appropriate and complete for the evaluation of KDS-Yin and KDS-Yang in the population of women.

Reviewer 4: Einar Kristian Borud
COMMENT (general): Interesting concept. The objective of the present paper is first stated as an attempt "to find out whether TCM syndrome-specific PRO instruments can be constructed for use in
TCM clinical studies”, and then as a test of the psychometric properties of a newly developed "Kidney Deficiency Syndrome Questionnaire” or KDSQ.

RESPONSE: We sincerely thank the reviewer for reviewing our manuscript and providing the comments. We have re-edited the whole manuscript in this revised version for a more concise presentation. We have attached this revised version with tracked changes at the end of this responses to reviewers’ comments.

We have revised the introduction section to avoid confusing audiences as if there were two objectives. We have deleted “In the present study, we attempted…” in the second last paragraph of the introduction section (page 4) and re-edited the sentence to as follow: “Next, it is interesting to find out whether TCM syndrome-specific PRO instruments can be constructed for evaluative use in TCM clinical studies.” The objective of the present paper is rephrased in the last paragraph in the introduction section: “The present study attempted to construct a Kidney Deficiency Syndrome Questionnaire (KDSQ) and test content validity, internal consistency, construct validity, test-retest reliability and responsiveness of the KDSQ for the evaluation of KDS-Yin and KDS-Yang in Hong Kong middle-aged women menopausal symptoms.” (page 4)

Major Compulsory Revisions

COMMENT1: When a new questionnaire is presented, I would like to see the questionnaire, how the items are formulated, a description of the scoring of the questionnaire and an interpretation of the score. How will the questionnaire be used in research and clinical practice? None of these are present in this paper.

RESPONSE: We have reviewed the manuscript to make sure these comment points are clearly presented for the audiences. In the methods section, under the sub-heading of “The KDSQ” (page 5), we have already presented how the items are formulated as follows.

“In the validation of KDS-Yin and KDS-Yang,11 we developed a KDS item reduction list with the symptoms of KDS-Yin and KDS-Yang listed in a TCM diagnosis textbook for Chinese national tertiary education,2 a commonly cited clinical research guideline for diagnosis and assessment of TCM syndromes,7 the World Health Organization (WHO) international standard terminologies on TCM (including TCM syndromes),8 the Chinese national standard on the diagnosis of TCM syndromes for clinical practice,15 and TCM classic literature.16 The contemporary textbook and references are written by groups of national or international renowned experts in TCM.2,7,8,15 The classic literature16 is recognized to have established the foundation of TCM theory and generally, contemporary TCM literature is written with authors’ interpretation to the classic literature.1

For content validity, we set inclusion and exclusion criteria to select items into the KDSQ.11 The items
included were those directly related to KDS-Yin and KDS-Yang in middle-aged women. The items excluded were those directly related to syndromes other than KDS-Yin and KDS-Yang; those have weak consensus in the literature (i.e., listed in only one or two of the references); and the signs appeared only in the contemporary literature but not in the classic literature. The items included were given indicative guidelines for severity scores ranging from 0 (absent) to 1 (mild), 2 (moderate) and 3 (severe). Then, we pilot-tested the KDSQ on participants who fulfilled the participant inclusion and exclusion criteria for the present study, and finally three senior TCM experts who had over forty years of experience in TCM teaching, research and practice reviewed the items for appropriateness and completeness.” Then, under the sub-heading “statistical analysis” in the methods section (page 6-7), we describe how we used exploratory factor analysis (EFA) and structural equation modeling (SEM) to test whether the KDSQ items could measure what it supposed to measure. We included a ‘control item’ in the EFA and the results showed this control item should not be a KDSQ item. We consider that the EFA and SEM tests were important in the construction of the KDSQ.

We have already given descriptions on the scoring of the questionnaire and an interpretation of the score as follow: “The items included were given indicative guidelines for severity scores ranging from 0 (absent) to 1 (mild), 2 (moderate) and 3 (severe).” (page 5) We used the EFA and SEM tests to determine the domains of KDS-Yin and KDS-Yang and their measurement models (page 6-7). “The scaling structure of KDS-Yin and KDS-Yang was defined based on these measurement models, and the scoring method for the domains of KDS-Yin and KDS-Yang was the sum of scores reported by women to the symptoms within the domains.” (page 7-8).

How will the questionnaire be used in research and clinical practice? As described in our response to the general comment above, we describe the use of the KDSQ in the objective of study. The results showed that “the KDSQ is a valid and reliable tool for the measurement of KDS-Yin and KDS-Yang in Hong Kong Chinese middle-aged women with menopausal symptoms.” (Discussion section, first paragraph, page 13) We concluded that “The KDSQ is a valid and reliable measure for KDS-Yin and KDS-Yang in Hong Kong Chinese middle-aged women with menopausal symptoms. TCM syndrome-specific measurement tools may be developed for outcome measurement in TCM clinical research.”(page 16)

We agree that the points raised by this reviewer are important for the presentation of a new questionnaire. We hope that these points we have addressed in the present paper are clear for the audiences to read.

COMMENT2: One of my main concerns is that the development of the KDSQ is based on textbook descriptions and expert opinions of the symptoms and signs of Kidney Deficiency Syndrome (KDS) as the "true source of knowledge", and the "fact" that the symptoms and signs of KDS per definition
is found among menopausal women. These assumptions are however under dispute, see for instance Scheidet al. (ref. 36, as attached below). In a sample of postmenopausal London women they found that “a majority of the factors can be matched with patterns... that do not reflect the treatment of any significant Kidney deficiency. In my opinion it is important to discuss these considerations and their importance regarding the construction of the KDSQ.

RESPONSE: As one of the limitations we have discussed in the discussion section that “Cultural variation of menopausal symptoms is well reported; but there is little literature on that of KDS symptoms. Cautiousness should be taken in generalizing the validity and reliability of the KDSQ to middle-aged women of other ethnic backgrounds without prior testing.” (the last paragraph, page 14). The menopausal symptoms in Hong Kong Chinese women have been found to be different from those in some European women (ref. 18). Thus, one must perform prior tests to find out whether one can generalize study results from European women to Hong Kong Chinese women.

We would want to discuss the differences between our study and the study conducted by Scheid et al (ref.36). Firstly, the present study was part of a project studying TCM syndromes and menopause in Hong Kong Chinese middle-aged women. We studied the symptoms of menopause in Hong Kong Chinese middle-aged women (refs. 17,18). On the other hand, Scheid et al used a general symptom checklist, with symptoms considered to be related to menopause embedded within it; however, there about one third of the symptoms studied are not considered to be related to menopause (ref.36). Secondly, we had studied the symptom characteristics of KDS-Yin and KDS-Yang using exploratory factor analysis (EFA) and discriminant analysis on a sample of Hong Kong Chinese women aged 40-60 years (ref.28), and then validated KDS-Yin and KDS-Yang in Hong Kong Chinese women aged 40-60 years with menopausal symptoms using EFA and structural equation modeling (SEM) on two different samples of Hong Kong Chinese women aged 40-60 years (ref. 11). We identified the pathogenic domains and the domain symptoms of KDS-Yin and KDS-Yang (ref. 11). The symptoms we studied are the symptoms of Kidney deficiency in Hong Kong Chinese middle-aged women (ref.11,28). On the other hand, Scheid et al used the general symptom checklist to survey on a sample of London menopausal women; rather, they did not identify the symptoms of Kidney deficiency in their study (ref. 36). With reference to the 33 symptoms surveyed and included to their EFA (ref. 36), the 10 symptoms listed below were not considered to be related to menopause or Kidney deficiency: diarrhoea or constipation, upset stomach, nausea, persistent cough, pain/discomfort in chest, pain or discomfort in stomach, pain or discomfort low abdomen, sore throat, increased libido, puffiness anywhere on body. In TCM, these symptoms listed here are rather the symptoms of disorders of the spleen, stomach, lung, heart and heat (sore throat, increased libido). Importantly, Scheid et al conducted a postal survey (with a low response rate of 58%) on London middle-aged women but did not report whether their participants were suffering from concurrent medical conditions or discomforts during the survey reporting period. Critically, the symptoms of the general symptom check list in their
study participants might be caused by concurrent illnesses and different causes might have
confounded EFA factor grouping and interpretation; and also, Scheid et al interpreted their EFA
results based on their expert opinion (ref. 36). With a study designed by Scheid et al as above, it could
be expected that “a majority of the factors can be matched with patterns (due to the subjective nature
of expert opinions in interpretation of the EFA results)... that do not reflect the treatment of any
significant Kidney deficiency (the symptoms may be caused by concurrent illnesses).” However,
these results (ref. 36) may not dispute “the fact that the symptoms and signs of KDS per definition is
found among menopausal women”.

The problem of interpretation EFA results based on expert opinion in TCM studies has been pointed
out in our previous paper and we have reported an evidence-based validation of TCM syndromes as a
better approach (ref. 11). Since expert opinion is subjective in nature, one can almost freely interpret
some EFA results based on his opinion because of the philosophical nature of TCM theory. For
instance, Scheid et al interpreted the factor (sore throat, sweating from the head only, dislike to
draughts, tendency to cold feet) as “This COULD be yang deficiency with upward floating of empty
fire OR yang deficiency with heat excess”. However, in practice, I as a TCM practitioner do not find
empty fire floating from yang deficiency in patients who can participate in a postal survey but only in
patients with critical illnesses when Yin and Yang are separating from each other; and there is no such
a TCM syndrome of “yang deficiency with excess heat” from TCM literature; Yang deficiency
produces COLD but not HEAT. If Scheid et al wants to argue that there is such a TCM syndrome, then
they must point out where does the excess heat come from: the menopause transitional changes or
from an exogenous pathogenic heat attack?

In addition, we would like to show some evidence on Kidney deficiency and the menopause. The
following paragraph is copied from the discussion section of our previous paper (ref.11)

“That Kidney deficiency causes permanent cessation of menstrual periods in middle-aged women is
documented in Huangdi’s Canon of Internal Medicine and in contemporary literature. This opinion is
challenged by another expert opinion that Kidney deficiency causing menopause is a product of
modernisation of TCM by copying oestrogen deficiency of menopause in biomedicine during the
China Cultural Revolution (ref.35). We compared KDS-Yin and KDS-Yang by menopausal status on
women pooled from the seminar sample and the survey sample because the difference of symptoms by
the GCS domains and the KDS domains were not found to be statistically significant between the
samples by menopausal status (p > 0.05). Our data show that the domains of KDS-Yin and the
domains of KDS-Yang were more severe in the post-menopausal women (n = 191) and the peri-
menopausal women (n = 145) than in the pre-menopausal women (n = 225) (p < 0.001), except
restlessness at night of KDS-Yin and deficiency cold of KDS-Yang (p > 0.05). Women, who had
hysterectomy (n=27), ovariectomy (n=23) and missing data on the GCS (n=2), were excluded from
this comparison. This finding supports Kidney deficiency and the menopause described in the TCM
“Kidney deficiency causes permanent cessation of menstrual periods in middle-aged women is documented in TCM classic and contemporary literature.\textsuperscript{14,16} We have shown evidence supporting the TCM theory on KDS and the menopause.\textsuperscript{11} In contrast, some authors have challenged that Kidney deficiency causes menopause is a product of modernization of TCM by copying estrogen deficiency of menopause in biomedicine during the China Cultural Revolution.\textsuperscript{35,36} The authors surveyed a sample of London middle-aged women using a general symptom check list consisting of menopausal symptoms and other symptoms (about one third of the total items) not related to menopause or Kidney deficiency in middle-aged women, and the survey did not exclude participants who might have concurrent medical conditions. The authors performed an EFA on the survey data and interpreted factors from the EFA into TCM patterns that could not reflect the treatments of Kidney deficiency.\textsuperscript{36} However, we do not find a subjective expert opinion-based interpretation of EFA on the symptoms that may have been confounded by concurrent illnesses can dispute the TCM theory on Kidney deficiency and the menopause.” (Discussion section, the second paragraph, page 16)

COMMENT3: To make it possible to follow the discussion of the psychometric properties of the KDSQ, I would also like table(s) with the results of the factor analyses, such as the factor loadings of each item.

RESPONSE: We agree that a table showing the factor loadings of the EFA may help audiences know how we tested content validity of the KDSQ. Initially, we did consider providing a table to report the EFA. We change the decision as a table listing the EFA factor loadings together with tables showing a discriminant analysis study on the symptom characteristics of KDS-Yin and KDS-Yang have been reported elsewhere (Ref. 28), and we thought it would occupy less space to summarize the EFA results as follow: “With reference to the theory,\textsuperscript{2,7,8,15,16} the four factors of KDS-Yin were found to correspond to Kidney-Essence deficiency, deficiency heat, impaired Kidney orifices and restlessness at night; whereas the five factors of KDS-Yang correspond to Kidney-Qi deficiency, deficiency cold, impaired Kidney orifices, abnormal water metabolism, and abnormal urine excretion. The item ‘loose stools’ listed only in the textbook\textsuperscript{2} for the diagnosis of KDS-Yang was added as a control to the KDSQ, but was not found to be grouped to the domains of KDS-Yang by the EFA indicating this control item was independent from the domains of KDS-Yang. More details on the EFA had been reported as part of a study on the symptom characteristics of KDS-Yin and KDS-Yang elsewhere.\textsuperscript{28}” (page 10). We have added the last sentence informing the audiences who may want to know more about the EFA (page 10). We also have copied the table on page 4 of this document for your reference.
References: