

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH: A multi-region and cross-section study in China
AUTHORS	Chen, Yuke; Yu, Wei; Zhou, Liqun; Wu, Shiliang; Yang, Yang; Wang, Jianye; Tian, Ye; He, Dalin; Xu, Yong; Huang, Jian; Huang, Xiaobo; Gao, Xin; Li, Hanzhong; Ma, Lulin; Zhang, Ning; Zhao, Shengtian; Wang, Muwen

VERSION 1 - REVIEW

REVIEWER	Jian Guo Wen Urodynamic Center, The First Affiliated Hospital of Zhengzhou University, China
REVIEW RETURNED	21-Jan-2016

GENERAL COMMENTS	It is well known that multiple factors contribute LUTS and sexual function in LUTS/BPH adults. Therefore, the discussion should be included as much as possible to discuss or exclude these factors.
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REVIEWER	Limin Liao Department of Urology, China Rehabilitation Research Centre, Beijing, China ; Department of Urology of Capital Medical University, Beijing, China
REVIEW RETURNED	25-Jan-2016

GENERAL COMMENTS	<p>This article reported that the relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH, and it concluded some very interesting statements.</p> <ol style="list-style-type: none"> 1. I would like suggest the authors change the title of article as "Relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH: A multi-region and cross-section study in China". The structure of article would be revised according to this title. 2. There are some contradictions for the results, sentence and conclusions: e.g. "The PV was largest amongst men residing in southern China and smallest amongst men residing in northwestern China." and "The IPSS was highest in northwestern China and lowest in southern China." are contradictory for "A larger PV and a higher IPSS increased the IIEF-5 score, while a larger PV resulted in a higher IPSS." 3. The readers could not believe that "Subjects in southern China consumed the highest amounts of meat, fish, and eggs, while subjects in northern China and northwestern China consumed the
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	<p>highest amounts of vegetables, and milk and dairy products”, because southern China produces more vegetables than northern and northwestern China during all year, could you please provide the references to support your statement.</p> <p>4. You said that “The PV was largest amongst men residing in southern China and smallest amongst men residing in northwestern China”. Could please compare this statement with the previous data from China published in 1990’s, and discuss it.</p> <p>5. “The IPSS was highest in northwestern China and lowest in southern China”; it means that the larger PV has the lower IPSS, the smaller PV has the higher IPSS. It would be difficult to believe this. Even if it is true, please explain why.</p> <p>6. “More frequent meat, fish, and egg intake decreased the IPSS”, this statement needs to be supported by the references.</p> <p>7. “A larger PV and a higher IPSS increased the IIEF-5 score, while a larger PV resulted in a higher IPSS.” A larger PV resulted in a higher IPSS; here you said a different statement. Please explain it.</p> <p>8. There are many ambiguous data and statements, so you should draw conclusions carefully. Maybe have some possible speculations at first; then have an investigation based on community population to confirm them.</p> <p>9. Please add some published references related to China in this field, and discuss.</p>
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REVIEWER	Andrew Vincent The University of Adelaide Australia
REVIEW RETURNED	16-Mar-2016

GENERAL COMMENTS	<p>Statistical review of: “Effect of diet habit on lower urinary tract symptoms and sexual function in LUTS/BPH adults: A multi-region and cross section study in China”.</p> <p>Overall this is a clearly written paper presenting a well-measured reasonably sized cohort. The analyses are for the most part straight forward, allowing for the data to speak for themselves. However there a couple of areas that need tightening.</p> <p>1: The main conclusion of the paper is that there are distinct differences in PV, IPSS and ED across the three regions of China, and that these differences may be explained by the distinct diets observed in these regions. To test this hypothesis the authors examine associations between the severity of the clinical outcomes and both region and diets. One notes that with the inclusion of the 1624 of non LUTS/BPH men, it would be possible to assess the association between BPH/LUTS prevalence and diet. Given that such an analysis would greatly strengthened their thesis, is there any reason why this analysis has not been performed?</p> <p>2: On page 10 a sample size calculation is presented. However it appears to be a post-hoc power calculation testing a prevalence of 38% against a non-specified null hypothesis (0%?). Being an association study this power calculation is not appropriate. Please delete and/or replace with a power calculation for an association study. On a related note, the first sentence of the discussion thereby questionable.</p> <p>3: At present there is no presentation of the cohort demographics</p>
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	<p>(eg differences by region in age, BMI, education etc.). Please include as the first table of the manuscript.</p> <p>4: There is excessive use of pairwise comparisons in Table 1. Please only reporting the ANOVA comparisons. If there is reason to highlight a specific pairwise comparison please do so in the text only. Furthermore please include:</p> <ul style="list-style-type: none"> - A sentence in the description detailing that the comparisons for the three clinical outcomes are within age subgroups. - The sample sizes in Table 1 for each of the regions, and also for age subgroups. - The thresholds for dietary tertiles. <p>5: Table 2 – One-way ANOVAs are not appropriate when the 3 groups are ordered predictor variables, eg diets. Please use linear regressions with continuous predictor variables (instead of tertiles). For example Table 2 reports a very significant difference in IPSS dependant on meat fish and eggs consumption. However IPSS is maximal for moderate consumption. The significance of this test is very likely due to the inappropriate comparison of 3 discrete groups (in combination with the large sample size and lack covariate adjustment).</p> <p>6: The multivariable analyses (Table 3) are the most important analyses of the manuscript. These will indicate which diets and regions are associated with the clinical outcomes, after adjusting for known confounders. However one would expect two models for each clinical outcome, one with the regions, and one with diets. Given the very strong differences in diet across regions, it is not clear what conclusions can be drawn by inclusion of both factors simultaneously. Furthermore only some diets were included for some outcomes, please include all diets for each outcome.</p> <p>Minor comments</p> <ul style="list-style-type: none"> - The title subclause should read: ‘A multi-region cross-sectional study in China’. - On page 10 please replace “sampling size” with “sample size”. - Please include confidence intervals or SEs in Table 3.
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VERSION 1 – AUTHOR RESPONSE

#Reviewer: 1

Jian Guo Wen

Institution and Country

Urodynamic Center,

The First Affiliated Hospital of Zhengzhou University,

China

It is well known that multiple factors contribute LUTS and sexual function in LUTS/BPH adults.

Therefore, the discussion should be included as much as possible to discuss or exclude these factors.

Thank you for the advice. The factors involved in the current study concluded age, BMI, education level, history of smoking or drinking, diet habit and geographic factors. Generally, prostate

enlargement was greatest in south China. LUTS and MSD were most severe in northwest China. Age

and BMI were risk factors for all the three clinical outcomes (PV, IPSS and IIEF-5 score). Population

with high education level tended to have less severe symptoms in terms of the three clinical

outcomes. However, the influence of smoking, alcohol consumption and diet habit were inconsistent

according to different clinical outcomes. Except for citing more references related to China in this field,

we also add some extra analysis and comparison for the three clinical outcomes, which would be

presented in the revised manuscript as follows.

“Regional difference in demographic characteristics like diet habit, education level, economic development, natural environment and etc. might contribute to the geographic variation of PV and LUTS to some extents.”

“Morphologic differences of prostate due to genetics and races might also act on the geographic distribution of PV and LUTS.”

“Regional variation of diet structure might attribute to the different dwellers' taste, cuisine areas and economy level in China”

#Reviewer: 2

Limin Liao

Institution and Country

Department of Urology, China Rehabilitation Research Centre, Beijing, China ; Department of Urology of Capital Medical University, Beijing, China

This article reported that the relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH, and it concluded some very interesting statements.

1. I would like suggest the authors change the title of article as “Relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH: A multi-region and cross-section study in China”. The structure of article would be revised according to this title.

Thank you for the advice. First, leaflets, printed with health education concerning prostate disease and information about a clinical check-up on prostate, were handed out in the communities in the above three regions. Then, our sample consisted of 5484 native males who attended the clinic for a prostate check-up at medical centers. We would add the detailed description of sampling process and change the title to “Relationship among diet habit and lower urinary tract symptoms and sexual function in outpatient-based males with LUTS/BPH: A multi-region and cross-section study in China” in our revised manuscript.

2. There are some contradictions for the results, sentence and conclusions: e.g. “The PV was largest amongst men residing in southern China and smallest amongst men residing in northwestern China.” and “The IPSS was highest in northwestern China and lowest in southern China.” are contradictory for “A larger PV and a higher IPSS increased the IIEF-5 score, while a larger PV resulted in a higher IPSS.”

Thank you for the comments. First, we make the comparison on PV and IPSS among the three different regions, and draw the conclusion that “The PV was largest amongst men residing in south China, who had the lowest IPSS.” Second, we analyzed the relationship among PV and IPSS of the whole 2584 subjects, and made the conclusion that “A larger PV resulted in a higher IPSS.”

Therefore, we concluded that “the dissociative trend of PV and LUTS in terms of geographic variation was detected.” We would further clarify it in our revised manuscript.

3. The readers could not believe that “Subjects in southern China consumed the highest amounts of meat, fish, and eggs, while subjects in northern China and northwestern China consumed the highest amounts of vegetables, and milk and dairy products”, because southern China produces more vegetables than northern and northwestern China during all year, could you please provide the references to support your statement.

Thank you for the comments. It is widely accepted that regions located in south China might harvest more green vegetables for warmer climate. However, in Zhao et al. [1] research about food consumption in China, elderly men in south China (Guangzhou) consumed more meat food and less green vegetables than correspondence in north China (Shandong). Further, Zhao et al. [1] attributed the dietary variation to the different dwellers' taste, cuisine areas and economy level. And more large-scale studies on different dietary habit distribution in China are needed. We would add Zhao et al. [1] study and clarify it in our revised manuscript.

4. You said that “The PV was largest amongst men residing in southern China and smallest amongst men residing in northwestern China”. Could please compare this statement with the previous data

from China published in 1990's, and discuss it.

In 1997, Yu et al. [2] conducted the survey on prevalence of prostatic hyperplasia and its relative factors in six cities of China. And diagnosis of prostatic hyperplasia mainly depended on prostate volume from digital rectal examination. According to results of Yu et al. [2] study, population in Guangzhou had more severe prostate enlargement than Xi'an, which is consistent with the current study. We would add Yu et al. [2] study and make a further comparison in our revised manuscript. 5. "The IPSS was highest in northwestern China and lowest in southern China"; it means that the larger PV has the lower IPSS, the smaller PV has the higher IPSS. It would be difficult to believe this. Even if it is true, please explain why.

Thank you for the comments. Although the PV was positively associated with LUTS for in the 2584 LUTS/BPH subjects (Table 1 in supplementary materials), the PV was largest amongst men residing in South China, who had the lowest IPSS. First, regional difference in demographic characteristics like diet habit, education level, economic development, natural environment and etc. might contribute to the geographic variation of PV and LUTS to some extents. Second, morphologic differences of prostate due to genetics and races might also act on the geographic distribution of PV and LUTS [3]. For instance, compared with Caucasian population, Korean men have an incidence of LUTS similar to that in men in the Western hemisphere, despite having smaller average prostate volume [4, 5]. Third, BPH, especially in the early stage, might be more relative to voiding symptoms of LUTS [5]. We would clarify the point in our revised manuscript.

6. "More frequent meat, fish, and egg intake decreased the IPSS", this statement needs to be supported by the references.

Thank you for the comments. According to the results of our multivariate analysis, we claimed that "The frequency of meat, fish, and egg consumption was inversely correlated to the IPSS ($\beta=-0.11$, $P=0.031$)". Meanwhile, Maserejian et al. [6] also reported that men who consumed more protein were less likely to report LUTS, which might be supported by the evidence that high-protein diets suppress sympathetic nervous system (SNS) activity. We would add Maserejian et al. [6] study in our revised manuscript.

7. "A larger PV and a higher IPSS increased the IIEF-5 score, while a larger PV resulted in a higher IPSS." A larger PV resulted in a higher IPSS; here you said a different statement. Please explain it.

Thank you for the comments. First, we must make the correction. According to univariable and multivariable linear analyses performed for the PV, IPSS, and IIEF-5 scores of the whole 2584 subjects (Table 1 in supplementary materials). A larger PV ($B=-0.02$, $P<0.001$) and a higher IPSS ($B=-0.17$, $P<0.001$) decreased (but not increased) the IIEF-5 score, and a larger PV resulted in a higher IPSS ($B=0.14$, $P<0.001$). We would clarify it in the revised manuscript.

8. There are many ambiguous data and statements, so you should draw conclusions carefully. Maybe have some possible speculations at first; then have an investigation based on community population to confirm them.

Thank you for the advice. We would make the improvement in the current and following studies.

9. Please add some published references related to China in this field, and discuss.

Thank you for the comments. Xu et al. study concerning prevalence of BPH in Tianjin, Zhao et al. study exploring diet structure in China, Yu et al. survey on geographic difference of prostate enlargement in six cities in China, and etc. would be compared with the current study and further discussed in the revised manuscript.

#Reviewer: 3

Andrew Vincent

Institution and Country

The University of Adelaide

Australia

Statistical review of: "Effect of diet habit on lower urinary tract symptoms and sexual function in LUTS/BPH adults: A multi-region and cross section study in China".

Overall this is a clearly written paper presenting a well-measured reasonably sized cohort. The analyses are for the most part straight forward, allowing for the data to speak for themselves.

However there are a couple of areas that need tightening.

1: The main conclusion of the paper is that there are distinct differences in PV, IPSS and ED across the three regions of China, and that these differences may be explained by the distinct diets observed in these regions. To test this hypothesis the authors examine associations between the severity of the clinical outcomes and both region and diets. One notes that with the inclusion of the 1624 of non LUTS/BPH men, it would be possible to assess the association between BPH/LUTS prevalence and diet. Given that such an analysis would greatly strengthen their thesis, is there any reason why this analysis has not been performed?

Thank you for the comments. 1624 subjects were excluded for their IPSS <8. And the main aim of the study was to explore the association between diet habit and prostate volume, IPSS and IIEF-5 score, especially in LUTS/BPH adults. If the 1624 subjects were added to the analysis, it would be possible to compare the diet habit between subjects with IPSS ≥8 and IPSS <8 or perform the correlation analysis between food intake amount and IPSS. But when we analyze the relationship between diet habit and prostate volume and IIEF-5 score, the subject of our study as well as the sample size would change. In other words, we aim to detect the association between diet habit and PV, IPSS and IIEF-5 score without the influence from non-BPH/LUTS subjects.

2: On page 10 a sample size calculation is presented. However it appears to be a post-hoc power calculation testing a prevalence of 38% against a non-specified null hypothesis (0%?). Being an association study this power calculation is not appropriate. Please delete and/or replace with a power calculation for an association study. On a related note, the first sentence of the discussion thereby questionable.

We aimed to study the association between demographic factors (eg diet habit, education, etc.) and prostate volume, IPSS and IIEF-5 score in LUTS/BPH adults. And the main clinical parameters of our study were prostate volume, IPSS and IIEF-5 score, which should have been referred to calculate the sample size. As there were no consistent cutoff value relating to the three clinical parameters, we choose to delete the sentence about power calculation and correct the first sentence of the discussion.

3: At present there is no presentation of the cohort demographics (eg differences by region in age, BMI, education etc.). Please include as the first table of the manuscript.

Thank you for the comments. We would add cohort demographics in our revised manuscript.

4: There is excessive use of pairwise comparisons in Table 1. Please only reporting the ANOVA comparisons. If there is reason to highlight a specific pairwise comparison please do so in the text only. Furthermore please include: A sentence in the description detailing that the comparisons for the three clinical outcomes are within age subgroups; The sample sizes in Table 1 for each of the regions, and also for age subgroups; The thresholds for dietary tertiles.

Thank you for the advice. We would make the correction.

5: Table 2—One-way ANOVAs are not appropriate when the 3 groups are ordered predictor variables, eg diets. Please use linear regressions with continuous predictor variables (instead of tertiles). For example Table 2 reports a very significant difference in IPSS dependant on meat fish and eggs consumption. However IPSS is maximal for moderate consumption. The significance of this test is very likely due to the inappropriate comparison of 3 discrete groups (in combination with the large sample size and lack covariate adjustment).

Thank you for the comments. We would make the correction in the revised manuscript.

6: The multivariable analyses (Table 3) are the most important analyses of the manuscript. These will indicate which diets and regions are associated with the clinical outcomes, after adjusting for known confounders. However one would expect two models for each clinical outcome, one with the regions, and one with diets. Given the very strong differences in diet across regions, it is not clear what conclusions can be drawn by inclusion of both factors simultaneously. Furthermore only some diets were included for some outcomes, please include all diets for each outcome.

Thank you for the advice. We would separate diet factors (all diets for each outcome) and region factors into two model in the multivariable analysis. Meanwhile, factors of age, BMI and diet were used in the form of continuous variable, being consistent with the univariate analysis.

Minor comments

- The title subclause should read: 'A multi-region cross-sectional study in China'.
- On page 10 please replace "sampling size" with "sample size".
- Please include confidence intervals or SEs in Table 3.

Thank you for the comments. We would make the correction in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Limin Liao China Rehabilitation Research Center, China
REVIEW RETURNED	29-Apr-2016

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.
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REVIEWER	Andrew Vincent University of Adelaide Australia
REVIEW RETURNED	27-Apr-2016

GENERAL COMMENTS	<p>In the discussion the second clause of the sentence: "we found that LUTS/BPH subjects who consumed meat, fish, and eggs more frequently tended to have larger PVs (B=0.05, P=0.711)" (page 19 line 7) is not appropriate given the confidence interval. Please remove or reword.</p> <p>The acronym MSD undefined.</p> <p>Please include SE or 95%CIs in Supplementary Table 1.</p> <p>Missing sign in the confidence interval of Table 4 Meat, fish & eggs (line 30) for IIEF-5.</p> <p>There are sporadic spelling and grammar issues that require correcting, eg page 6 line 32 and page 18 line 25.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 3

Reviewer Name

Andrew Vincent

Institution and Country, University of Adelaide, Australia

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below.

(1) In the discussion the second clause of the sentence: "we found that LUTS/BPH subjects who consumed meat, fish, and eggs more frequently tended to have larger PVs (B=0.05, P=0.711)" (page 19 line 7) is not appropriate given the confidence interval. Please remove or reword.

Thank you for the comment. We choose to remove the sentence in the revised manuscript.

(2) The acronym MSD undefined.

Thank you for the advice. We would add the definition of MSD as "male sexual dysfunction" in our revised manuscript.

(3) Please include SE or 95%CIs in Supplementary Table 1.

Thank you for the comment. We would revise the point in the manuscript. Meanwhile, factors of age,

BMI and weekly diet were used in the form of continuous variable.

(4) Missing sign in the confidence interval of Table 4 Meat, fish & eggs (line 30) for IIEF-5.

Thank you for the advice. We would re-upload the revised manuscript.

(5) There are sporadic spelling and grammar issues that require correcting, eg page 6 line 32 and page 18 line 25.

Thank you for the comment. We would enhance the quality of language expression.

VERSION 3 – REVIEW

REVIEWER	Andrew Vincent University of Adelaide Australia
REVIEW RETURNED	20-Jun-2016

GENERAL COMMENTS	<p>Issues</p> <p>1: Given some surprising associations between diet and outcome (eg vegetable intake associated with worse PV and ED) it would be informative to present the correlation matrix of factors included in the multivariable analyses (eg Model 1) to ensure that, for example, vegetable intake is not simply a surrogate for another highly correlated factor.</p> <p>2: Last sentence page 14 is incorrect. There was no increasing trend between PV and meat intake. Although the point estimate is positive, the analysis does not preclude negative trends or non-association.</p> <p>3: Are the coefficients (Betas) reported in tables 3 and 4 standardized? If not please include units, eg Age (yrs), in the tables.</p> <p>4: The choice of English phraseology is non-standard, to the extent that the intended meaning is sometimes unclear. For example - “be more relative to voiding symptoms of LUTS” - “future research ... should be preformed targetedly.” - “the scale gap of medical centers” And in some cases incorrect: “lack of association between PV and LUTS”, and contradicted by the subsequent subclause, with the following discussion relating meat intake to IPSS and PV being difficult to follow.</p> <p>Minor changes:</p> <p>5: Pg 13 – line 10 “in the whole subject” replace with “in the entire cohort”.</p> <p>6: Pg 6 line 30 and pg 15 line 7 – “vegetables intake” with “vegetable intake”</p> <p>7: pg 8 line 31 – erectile should be lower case.</p> <p>8: Page 13 line 17 – please replace ‘subjects’ with ‘subject’.</p> <p>9: Page 21 line 15. – please replace ‘extents’ with ‘extent’</p> <p>10: Table 2 – please replace “70-8” with “70-80”.</p> <p>11: Table 2 – PV/IPSS/IIEF – please include “yrs” with each age category, eg 50-60yrs.</p> <p>12: Table 2 – PV/IPSS/IIEF – please replace ‘Total’ with ‘All’.</p> <p>13: Table 4 - Model 1 – The confidence intervals for the IIEF-5 Beta for meat does not matching the reported p-value, possible missing minus sign.</p> <p>14: Supplementary Table 1 – please replace ‘variables’ with</p>
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'variables' (twice).

VERSION 3 – AUTHOR RESPONSE

Reviewer: 3

1: Given some surprising associations between diet and outcome (eg vegetable intake associated with worse PV and ED) it would be informative to present the correlation matrix of factors included in the multivariable analyses (eg Model 1) to ensure that, for example, vegetable intake is not simply a surrogate for another highly correlated factor.

Thank you for the comment. Here we would present the Variance Inflation Factor (VIF) and the correlation matrix of variables in multiple linear regression (model 1) to further explain the probability of multicollinearity.

Table. VIF and correlation matrix of variables in multiple linear regression (model 1).

variables X1 X2 X3 X4 X5 X6 X7 X8

VIF(a) 1.052 1.015 1.126 1.188 1.195 1.095 1.045 1.103

X1(b) - -0.07** -0.09** -0.08** -0.10** 0.01 0.02 0.12

X2(b) -0.07** - -0.01 0.06* 0.06* 0.01 0.07** 0.02

X3(b) -0.09** -0.01 - -0.04* -0.02 0.20** 0.06** 0.18**

X4(b) -0.08** 0.06* -0.04* - 0.30** -0.03* -0.03 -0.01

X5(b) -0.10** 0.06* -0.02 0.30** - 0.03 -0.02 0.03

X6(b) 0.01 0.01 0.20** -0.03* 0.03 - 0.08** 0.14**

X7(b) 0.02 0.07** 0.06** -0.03 -0.02 0.08** - 0.18**

X8(b) 0.12 0.02 0.18** -0.01 0.03 0.14** 0.18** -

x1=age (yrs); x2=BMI (kg/m²); x3=education (≤9yrs/>9yrs); x4=smoking (No/Yes); x5=alcohol consumption (No/Yes); x6=Meat, fish and eggs (times/week); x7=vegetables(times/week); x8=Milk and dairy products (times/week); VIF=variance inflation factor.

(a): VIF of variables in multiple linear regression (model 1) were listed.

(b): correlation matrix of the variables included in model 1- the correlation coefficients were listed.

* indicates that the correlation of the two variabls was significant for P<0.05.

** indicates that the correlation of the two variabls was significant for P<0.01.

2: Last sentence page 14 is incorrect. There was no increasing trend between PV and meat intake. Although the point estimate is positive, the analysis does not preclude negative trends or non-association.

Thank you for the comment. We would replace the sentence with “the association between PV and meat, fish, and egg intake failed to reach a statistical significance (B=0.05, P=0.711)”

3: Are the coefficients (Betas) reported in tables 3 and 4 standardized? If not please include units, eg Age (yrs), in the tables.

Thank you the advice. The unstandardized coefficients (Beta) had be reported in the manuscript. And the main purpose of the present study was to explore the influence factors of PV, IPSS and IIEF-5 but not to make comparisons of the effect of these factors on PV, IPSS and IIEF-5. The units of influence factors would be included in tables 3 and 4.

4: The choice of English phraseology is non-standard, to the extent that the intended meaning is sometimes unclear. For example

- “be more relative to voiding symptoms of LUTS”

- “future research ... should be preformed targetedly.”

- “the scale gap of medical centers”

And in some cases incorrect: “lack of association between PV and LUTS”, and contradicted by the subsequent subclause, with the following discussion relating meat intake to IPSS and PV being difficult to follow.

Thank you for the advise. We would make the language expression more clear and authentic in the revised manuscript .

Minor changes:

5: Pg 13 – line 10 “in the whole subject” replace with “in the entire cohort”.

6: Pg 6 line 30 and pg 15 line 7 – “vegetables intake” with “vegetable intake”

7: pg 8 line 31 – erectile should be lower case.

8: Page 13 line 17 – please replace ‘subjects’ with ‘subject’.

9: Page 21 line 15. – please replace ‘extents’ with ‘extent’

10: Table 2 – please replace “70-8” with “70-80”.

11: Table 2 – PV/IPSS/IIEF – please include “yrs” with each age category, eg 50-60yrs.

12: Table 2 – PV/IPSS/IIEF – please replace ‘Total’ with ‘All’.

13: Table 4 - Model 1 – The confidence intervals for the IIEF-5 Beta for meat does not matching the reported p-value, possible missing minus sign.

14: Supplementary Table 1 – please replace ‘variabiles’ with ‘variables’ (twice).

Thank you for the comment. We would make the above minor changes point to point.