PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Optimal body fat percentage cut-off values for identifying cardiovascular risk factors in Mongolian and Han adults: A Population-based Cross-Sectional Study in Inner Mongolia, China
AUTHORS	Li, Yanlong; Wang, Hailing; Wang, Ke; Wang, Wenrui; Dong, Fen; Qian, Yonggang; Gong, Haiying; Xu, Guodong; Li, Guoju; Pan, Li; Zhu, Guangjin; Shan, Guangliang

VERSION 1 - REVIEW

REVIEWER	Bing Zhang National Institute for Nutrition and Health, China CDC. P. R. of China
REVIEW RETURNED	21-Oct-2016

GENERAL COMMENTS	It is valuable study to identify cut off point for BF% of Chinese Han and Mongolian. However, there is some questions: 1. for general understanding, BF% will change according to aging. but this study, age groups was do not considered sufficiently, foe examples, 20-39, 40-59, 60-80.. 2. In page 3, methods part. some subjects who suffered on cancer, diabetes, have to exclude. 3. Description in method was not clearly, for exampled, BF% examination did not be explained which was done in the morning or afternoon. 4. we want to see samples distribution by age and race. 5. limitation, it did not state any limitation in the paper. In reality, limitation was exactly. especially, for Han, there is lot han living in different area, north and south, maybe quite different. Therefore, Only Han living in one area could not represent real Han.

REVIEWER	Takahisa Kondo Nagoya University Graduate School of Medicine, Japan.
REVIEW RETURNED	02-Nov-2016

GENERAL COMMENTS	In the present study, the authors examined 3221 Chinese adults (2308 Han and 913 Mongolian) aged 20-80 years to clarify the optimal cut-off values of body fat percentage (BF%) for cardiovascular risk. They concluded that the optimal BF% cut-offs to detect cardiovascular disease (CVD) risk factors in Chinese men and women were 24% and 34% for Han adults, and 25% and 35% for Mongolian adults. The present study is of clinically importance in that the authors estimated BF% by bioelectrical impedance analysis (BIA), a simple

	method to estimate body In the present study, the authors examined 3221 Chinese adults (2308 Han and 913 Mongolian) aged 20-80 years to clarify the optimal cut-off values of body fat percentage (BF%) for cardiovascular risk. They concluded that the optimal BF% cut-offs to detect cardiovascular disease (CVD) risk factors in Chinese men and women were 24% and 34% for Han adults, and 25% and 35% for Mongolian adults. The present study is of clinically importance in that the authors estimated BF% by bioelectrical impedance analysis (BIA), a simple method to estimate body adiposity. However, there are some concerns that should be discussed in the present paper. Major 1. The authors adopted the optimal cut-off values of BF% to detect subjects with two or more CVD risk factors. The reviewer agree that BF% is useful in detecting subjects with hypertension and/or dyslipidemia. However, BF% may not be useful in detecting subjects with diabetes, especially among men in a Han population, judged by Figure1. low AUC of ROC. Low AUC of ROC in detecting diabetes may be related with heterogeneous population of diabetes subjects (ex. diabetes with or without insulin resistance, diabetes who developed at a young age or who developed with age). Moreover, smoking status could affect the development of diabetes. Analysis stratified by age, insulin resistance (or BMI), and smoking status should also be shown. 2. In connection to the comment above, the reason why optimal cut-off values of BF% was low in a Han population should be mentioned in Discussion. 3. It is more desirable that the way to use BF% as a public health tool in dealing with the obesity is mentioned. Minor 1. In abstract, abbreviation should be spelled out. 2. Page 3, line 11: underweight >>> overweight 3. Throughout paper: bioelectrical imendence analysis >>> bioelectrical impedance analysis

REVIEWER	Yonghong Zhang Soochow University, China
REVIEW RETURNED	03-Nov-2016

GENERAL COMMENTS	The article " Optimal body fat percentage cut-off values for identifying cardiovascular risk factors in Mongolian and Han adults: A Population-based Cross-Sectional Study in Inner Mongolia, China" by Yanlong Li, and colleagues showed that optimal BF% cut-off points for men and women were around 24.0% and 34.0% in Han adults, and 25.0% and 35.0% in Mongolian population, respectively. This manuscript is of interest but there are several issues that need to be addressed by the authors: Major issues: 1. Introduction: I think it's hard to get the point that "Therefore, the appropriate BF% cut-off points for Chinese remains inconclusive and needs to be further studied" based on references #8 and #9. Reference #8 showed that the optimal BF% cut-offs for obesity for the prediction of MetS and T2DM in Chinese men and women were around 25% and 35%, respectively. Reference#9 showed that BMI had its limitations in the interpretation of subjects with BMI between 24 and 27.9 kg/m2.

	2. Results: Could the authors provide comparisons of baseline characteristics by ethnic? 3. Results: Why chose 24% and 34% for the male and female Han adults, and 25% and 35% for the male and female Mongolians, respectively, considering the fact that optimal cutoff values of BF% were different for young and old groups (20-49 years and 50-80 years old). 4. Discussion (page 12 lines 5-6): consider rewriting the sentence “BF% has been found to have a stronger association with multiple CVD risk factors in several studies conducted in China [8], Korea[14], and other ethnic groups[15-17]”. Although BF% provided more information than BMI to predict diabetes, metabolic abnormalities, and dyslipidemia et al., I could not find any evidence for stronger associations as stated by the authors between BF% and CVD risk factors compared to BMI in these references. 5. Discussion (page 12 line 31): consider adding an appropriate reference to the sentence “Zhang, et al reported the prevalence of overweight or obesity was higher in Mongolian people than Han people using WHO criteria (26.1% vs 21.3%, respectively)”. 6. Discussion (page 12 line 37): “The current definitions of obesity using BF% are based on Western populations and probably need to be modified for Chinese population. The present study showed the optimal BF% cut-off points for men and women were around 24.0% and 34.0% in Han adults, and 25.0% and 35.0% in Mongolian population, respectively.” What is the widely used definition in China? Why did the definition of obesity need to be modified for Chinese population based on results from a cross-sectional study conducted in Inner Mongolia, China? Moreover, the author also mentioned that “Li and colleagues [8] showed that the BF% cut-off values for Chinese adults were similar to those proposed by the WHO” in the introduction. 7. Conclusion: “The optimal BF% cut-offs for obesity for the prediction of CVD risk factors in Chinese men and women were approximately 24% and 34% for Han adults, and 25% and 35% for Mongolian population, respectively.” The study population was selected using a multistage cluster sampling method from Inner Mongolia (an autonomous region in northern China) in 2014. Since the dietary patterns and lifestyles are very different between southern and northern China, I am afraid that the results cannot be applied to all Han population across China. 8. Language needs editing. Please carefully check for grammatical errors. Minor issues: 1. Discussion (page 11 lines 34-36): I think the optimal BF% cut-offs of 24% and 34% for male and female Han adults in this study were only a little lower than those in the WHO criteria (25% and 35%), instead of “relatively lower” as the authors stated in the manuscript. 2. Discussion (page 12 line 35): I think the author might want to say “Because of different genetic backgrounds, lifestyles and dietary patterns, the optimal BF% cut-offs of Han adults may not be the same as Mongolian” instead of “Because of different ethnicities, the optimal BF% cut-offs of Han adults may be not the same as Mongolian”.

REVIEWER	Amado D. Quezada Instituto Nacional de Salud Publica Mexico

REVIEW RETURNED	05-Nov-2016

GENERAL COMMENTS	I found the topic interesting in an area that requires more research. The paper addressess whether BF% cutoffs are useful for the detection of cardiovascular desease risk factors in Han and Mongolian adult populations. I suggest a deeper consideration of the issues on the development of population specific BF% cutoffs and to provide an assessment of the benefits in comparison to using BMI. Major modifications suggested: 1. On optimality of cutoffs. The youden index is used to find the optimised cutoffs but given that the sample comes from a well defined population I would suggest taking into consideration missclasification costs as well as the population prevalence of the CVD risk factors (hypertension, diabetes and dyslipidemia) if available or if the sample is representative of the population of interest. The provided cutoffs based on the Youden Index give the same importance to sensitivity as to specificity, when missclassifications costs differ (e.g. higher cost of a false negative vs a false positive) or when the prevalence of a condition is different than 50% then sensitivity and specificity should not have the same weight if classification costs are to be minimised. I suggest the authors to at least mention these issues and how the cutoff may change. One reference to consult: jstatsoft.org/article/view/v061i08/v61i08.pdf 2. It is mentioned that there are WHO recomendations for BF% cutoffs in caucasian populations (25% for men and 35% for women). Please provide the corresponding pages of the WHO document (reference #6) where this is found. I'm not totally sure but it seems that these values are not to be understood as oficial WHO BF% cutoffs. If there are no clear recommendations yet in regard to BF% cutoffs it should be mentioned along with the variation on BF% cutoffs provided by different studies. 3. In the discussion it is said that it is preferable to measure BF% directly since BMI accuracy is limited for detecting excess body adiposity (page 11, lines 38-40). The accuracy of the type of BF% measurements employed in the analysis should be discussed more thoroughly, that is, what we know about the accuracy of BF% measures obtained with bioelectrical impedance and how it compares with other methods? I would suggest to compare the performance of BMI to that of BF% for classification purposes, that is, a comparison of the AUC between classifiers. BMI is available in the data and this also would give perspective to the actual benefits of using BF% measured with bioimpedance vs using BMI. Another altertative would be to use both classifiers as predictors in a probit or logit regression, and then using the linear predictor from this regression as the classifier. BF% measured by bioimpedance and BMI are both indirect measures of the true adipositiy. Is the performance improved when both are used or not so much? It would be interesting to perform this excercise but more importantly to compare the BF% performance with BMI using the appropiate statistical methods to compare the AUC between these two classifiers. Please clarify the sentence in line 5-6 in page3 where it is mention that BF% measured with bioimpedance "...tends to underestimate body fat in all subjects and in men and women separately".

	Minor modifications and suggestions: 1. It is mentioned that the data support the good discrimitation of BF% for each CVD risk factor (page 12). It seems that this statement comes from the area under the ROC Curves (AUC) obtained in the results. I suggest to provide a better assessment of the AROC values. E.g. AUC ranged from 0.589 to 0.699 for Han men, is this a fair performance, a good performance? Hosmer and Lemeshow (2000) in chapter 5 of Applied Logistic Regression provided a classification of AUC values that may be helpful as a rough guideline. 2. In the objective I'm not sure whether it is appropiate to say that the cutoff values of BF% are for obesity given the approach used, I would suggest to say "cut-off values for the detection of CVD risk factors" or "..for the purposes of classification of CVD risk conditions" 3. I would suggest to mention something about the AUC in the abstract. In general, did the classifiers perform well? A general description of AUC values observed, and specificity/sensitivity achieved at the optimised cutoffs. 4. In the introduction it is mentioned that the global prevalence of underweight has risen dramatically but in the reference cited it seems that underweight has decreased. 5. Please add the prevalence for BMI categories (overweight, obesity) in table 1. I would suggest to refer overweight as 25<=BMI<30 instead of BMI>=25. Please clarify definitions in line 17 of page 3. 6. In tables 4 and 5, and in the paper in general, a certain cut-off is highlighted across the table but the optimal cut-off as indicated by the Youden Index varies between CVD risk factors, especially for Han men (21 for diabetes, 26 for dyslipidemia). It is not clear why the highlited cutoffs are the optimal given this variation (lines 38-40 of page 8) 7. There are no standard errors or some measure that indicates precision of estimates for sensitivity, specifitivy and the cutoffs. If you can generate those, it would allow to determine whether there are significant differences between Han and Mongolian populations (line 35, page 12). Not all statistical packages provide confidence intervals or standard errors for these. Please explore whether in the statistical package used confidence intervals or standard errors are implemented for sensitivity, specificity and the cutoffs. 8. Provide more details on the sampling desing. Is this a probabilistic representative sample? Was stratification used in the sampling design? Is a multistage sample? 9. On question. The attributable fractions are calculated using ORs. Is the original formula in terms of relative risks (RRs)? In case ORs were used to approximate RRs how well does this work given that prevalence of CVDs are far from zero? Is the approximation

	appropriate?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
1. For general understanding, BF% will change according to aging. but this study, age groups were do not considered sufficiently, for examples, 20-39, 40-59, 60-80.
Reply: In our study, the prevalence of obesity(BMI≥28kg/m2), hypertension, diabetes, dyslipidemia were markedly higher in subjects≥50 years of age than in those <50 years of age (obesity 23.94%vs.15.29%, p<0.0001; hypertension 48.98vs.16.85, p<0.0001; diabetes 13.46vs.2.88, p<0.0001; dyslipidemia 46.42vs.30.29, p<0.0001). We also calculated those by age groups (according to your advice: 20-39, 40-59, 60-80), however, the prevalence of some important outcomes in different age groups was similar, such as dyslipidemia (40-59, 41.00%; 60-80, 44.74%). Therefore, subjects in our study were divided into two age groups: (1) those 20–49 years of age; and (2) those 50–80 years of age.
We also calculated
2. In page 3, methods part. some subjects who suffered on cancer, diabetes, have to exclude.
Reply: Thanks for your comments. The present study was based on data from the China National Health Survey (CNHS) in Inner Mongolia Autonomous region in 2014, which was conducted by the Chinese Academy of Medical Sciences for evaluating the Physiological Constant and Health Condition in Chinese. Subjects without severe diseases such as disability or psychiatric disturbances and those who were not pregnant were eligible to participate in this study. We also investigated "whether subjects had cancer or not" and "what kind of cancer subjects had". Subjects with cancer in this study were only 14 (0.43% in all subjects), which was too small to affect the results. Therefore, subjects with cancer were not excluded from this subjects. The present study was cross-sectional design and diabetes was one of primary endpoints in this study, so subjects with diabetes cannot be excluded. Some studies exploring the relationship between anthropometric indices of obesity and diabetes, such as Bhowmik B, et al. (Obes Res Clin Pract 2014;8:e201-298) and Jayawardana R, et al. (Diabetes Res Clin Pract 2013;99:292-299) also included subjects with diabetes.
3. Description in method was not clearly, for example, BF% examination did not be explained which was done in the morning or afternoon.
Reply: Anthropometric measurements in method section has been detailly rewritten.
4. we want to see samples distribution by age and race.
Reply: Samples distribution by age and race were added into Table 1.
5. limitation, it did not state any limitation in the paper. In reality, limitation was exactly. especially, for Han, there is lot Han living in different area, north and south, maybe quite different. Therefore, Only Han living in one area could not represent real Han.
Reply: The limitations of this study have been added into the discussion section on Page 7. Indeed, Han adults in this study conducted in Inner Mongolia could not represent whole Han in China. We have seriously considered our conclusions and rewritten them to limit them to Han living in Inner Mongolia, China. But we still want to provide evidences for making criterion of the optimal BF% cut-off points for Chinese population, especially considering ethical and regional differences in China.

Reviewer: 2
Major comments:
1. The authors adopted the optimal cut-off values of BF% to detect subjects with two or more CVD risk factors. The reviewer agrees that BF% is useful in detecting subjects with hypertension and/or dyslipidemia. However, BF% may not be useful in detecting subjects with diabetes, especially among men in a Han population, judged by Figure1. low AUC of ROC.
Low AUC of ROC in detecting diabetes may be related with heterogeneous population of diabetes subjects (ex. diabetes with or without insulin resistance, diabetes who developed at a young age or who developed with age). Moreover, smoking status could affect the development of diabetes.

Analysis stratified by age, insulin resistance (or BMI), and smoking status should also be shown.
Reply: Analysis stratified by age groups (20-49 and 50-80 years old) had been shown in Table 2-3 and the effects of age had been taken into account. Actually, compared to hypertension or dyslipidemia, BF% is similarly useful in detecting subjects with diabetes (shown Table 2-3), of course, except among men in Han population. We are also interested why men in Han population were excluded and exploring relationship between body fat and diabetes in men adults in another study. We sincerely thanks for your suggestions about this part, but BF% is still useful anthropometric parameter for detecting cardiovascular risk factors.
2. In connection to the comment above, the reason why optimal cut-off values of BF% was low in a Han population should be mentioned in Discussion.
Reply: Overall, the optimal BF% cut-offs of Han adults may be not the same as Mongolian because of different genetic backgrounds, lifestyles and dietary patterns. Detail discussion has been shown on Page 7.
3. It is more desirable that the way to use BF% as a public health tool in dealing with the obesity is mentioned.
Reply: As this paper mentioned "It is now identified that obesity essentially increases the risk of hypertension, diabetes and dyslipidemia, which has a great influence on the morbidity and mortality of Cardiovascular disease (CVD)", "BMI is the most widely used measure to diagnose obesity. However, the accuracy of BMI in detecting excess body adiposity in the general adult population is limited, because BMI cannot measure BF% directly and poorly distinguishes among total body fat, total body lean, and bone mass. To overcome misclassifications, direct measurements of BF% would be a better tool for diagnosing obesity". The aim of this study was to determine the optimal BF% cut-off values for the detection of cardiovascular risk factors in Mongolian and Han adults, which was helpful to deal with the obesity.
Minor comments:
1. In abstract, abbreviation should be spelled out.
Reply: Abbreviation in abstract on Page 2 has been spelled out.
2. Page 3, line 11: underweight >>> overweight
Reply: The spelling errors have been corrected.
3. Throughout paper: bioelectrical impendence analysis >>> bioelectrical impedance analysis
Reply: The spelling errors have been corrected.

Reviewer: 3
Major comments:
1. Introduction: I think it's hard to get the point that "Therefore, the appropriate BF% cut-off points for Chinese remains inconclusive and needs to be further studied" based on references #8 and #9. Reference #8 showed that the optimal BF% cut-offs for obesity for the prediction of MetS and T2DM in Chinese men and women were around 25% and 35%, respectively. Reference#9 showed that BMI had its limitations in the interpretation of subjects with BMI between 24 and 27.9 kg/m2.
Reply: On the one hand, Reference#9 showed the best cutoff point of BMI for BF% obesity (according to WHO BF% criteria) was 23.7kg/m2, however, the BF% cut-off points for obesity proposed by the WHO are 25% for men and 35% for women, corresponding a BMI of 30 kg/m2 in young Caucasians. On the other hand, Reference#8 showed that the BF% cut-off values for the prediction of MetS and T2DM in Chinese adults were similar to those proposed by the WHO, but Reference#9 showed the risks of subjects with intermediate BF% (>20/30[male/female]-25/35[male/female]) and high BF% (>25/35[male/female]) for future diabetes were significantly higher with RRs (95% CI) of 2.35 (1.23-4.48) and 2.89 (1.43-5.81), respectively, compared to those of subjects with low BF% (≤20/30[male/female]), which can be deduced that intermediate BF% and high BF% two groups were not different in predicting diabetes--- 25% for men and 35% for women are not optimal cutoff points for BF% to detect diabetes. Therefore, the appropriate BF% cut-off points for Chinese remains inconclusive and needs to be further studied
2. Results: Could the authors provide comparisons of baseline characteristics by ethnic?

Reply: The comparisons of baseline characteristics by ethnic have been added to the results on Page 5 and Table 1.

3. Results: Why chose 24% and 34% for the male and female Han adults, and 25% and 35% for the male and female Mongolians, respectively, considering the fact that optimal cutoff values of BF% were different for young and old groups (20-49 years and 50-80 years old).

Reply: It has been surely found that the optimal BF% cut-off points varied greatly by age and CVD risk factors in our study, so we further confirm the range of optimal BF% cut-off points in Table 4 and Table 5. BF% cut-off points of preferable sensitivity and specificity to detect each CVD risk factor and clustering of ≥2 risk factors were selected as optimal values.

4. Discussion (page 12 lines 5-6): consider rewriting the sentence “BF% has been found to have a stronger association with multiple CVD risk factors in several studies conducted in China [8], Korea [14], and other ethnic groups [15-17]”. Although BF% provided more information than BMI to predict diabetes, metabolic abnormalities, and dyslipidemia et al., I could not find any evidence for stronger associations as stated by the authors between BF% and CVD risk factors compared to BMI in these references.

Reply: The sentence has been rewritten into “BF% has been found to have a strong association with multiple CVD risk factors in several studies conducted in China [8], Korea [14], and other ethnic groups [15-17]”.

5. Discussion (page 12 line 31): consider adding an appropriate reference to the sentence “Zhang, et al reported the prevalence of overweight or obesity was higher in Mongolian people than Han people using WHO criteria (26.1% vs 21.3%, respectively)”.

Reply: The missing reference has been added into the revised manuscript.

6. Discussion (page 12 line 37): “The current definitions of obesity using BF% are based on Western populations and probably need to be modified for Chinese population. The present study showed the optimal BF% cut-off points for men and women were around 24.0% and 34.0% in Han adults, and 25.0% and 35.0% in Mongolian population, respectively.”

What is the widely-used definition in China?

Reply: In the present, there is few research studying the appropriate BF% cut-off points for Chinese, so the criterion is not clearly. WHO proposes criterion that the BF% cut-off points are 25% for men and 35% for women.

Why did the definition of obesity need to be modified for Chinese population based on results from a cross-sectional study conducted in Inner Mongolia, China? Moreover, the author also mentioned that “Li and colleagues [8] showed that the BF% cut-off values for Chinese adults were similar to those proposed by the WHO” in the introduction.

Reply: Although Li and colleagues [8] showed that the BF% cut-off values for Chinese adults were similar to those proposed by the WHO, attention should be paid to the different methods they used. The definition proposed by WHO corresponded a BMI of 30 kg/m2 in young Caucasians, however, Li determined the optimal BF% cut-off points according to predicting MetS and T2DM and the study included Chinese adults at 30-70 years of age. We agree with the method Li has used, but younger and older adults should be considered, more importantly, substantial CVD risk factors such as hypertension should not be ignored. Therefore, our study aimed to get the optimal body fat percentage cut-off values for identifying cardiovascular risk factors (diabetes, hypertension, dyslipidemia) and clustering of risk factors in Mongolian and Han adults aged 20-80 years, which will provide a comprehensive frame of reference of the optimal cut-off values of body fat percentage. Of course, it's hard to deny the study’s cross-sectional design, but we still want to provide evidences for making criterion of the optimal BF% cut-off points for Chinese population.

7. Conclusion: “The optimal BF% cut-offs for obesity for the prediction of CVD risk factors in Chinese men and women were approximately 24% and 34% for Han adults, and 25% and 35% for Mongolian population, respectively.”

The study population was selected using a multistage cluster sampling method from Inner Mongolia (an autonomous region in northern China) in 2014. Since the dietary patterns and lifestyles are very different between southern and northern China, I am afraid that the results cannot be applied to all

Han population across China.
Reply: Indeed, Han adults in this study conducted in Inner Mongolia could not represent whole Han in China. We have seriously considered our conclusions and rewritten them to limit them to Han living in Inner Mongolia, China. But we still want to provide evidences for making criterion of the optimal BF% cut-off points for Chinese population, especially considering ethical and regional differences in China.
8. Language needs editing. Please carefully check for grammatical errors.
Reply: The spelling and syntax errors have been checked and corrected.
Minor comments:
1. Discussion (page 11 lines 34-36): I think the optimal BF% cut-offs of 24% and 34% for male and female Han adults in this study were only a little lower than those in the WHO criteria (25% and 35%), instead of "relatively lower" as the authors stated in the manuscript.
Reply: The corresponding sentence has been rewritten "Compared with WHO criteria, the optimal BF% cut-offs in this study were a little lower in Han adults, but similar in Mongolian".
2. Discussion (page 12 line 35): I think the author might want to say "Because of different genetic backgrounds, lifestyles and dietary patterns, the optimal BF% cut-offs of Han adults may not be the same as Mongolian" instead of "Because of different ethnicities, the optimal BF% cut-offs of Han adults may be not the same as Mongolian".
Reply: The corresponding sentence has been rewritten "Because of different genetic backgrounds, lifestyles and dietary patterns, the optimal BF% cut-offs of Han adults may not be the same as Mongolian".

Reviewer: 4
Major comments:
1. On optimality of cutoffs. The Youden index is used to find the optimized cutoffs but given that the sample comes from a well-defined population I would suggest taking into consideration misclassification costs as well as the population prevalence of the CVD risk factors (hypertension, diabetes and dyslipidemia) if available or if the sample is representative of the population of interest. The provided cutoffs based on the Youden Index give the same importance to sensitivity as to specificity, when misclassifications costs differ (e.g. higher cost of a false negative vs a false positive) or when the prevalence of a condition is different than 50% then sensitivity and specificity should not have the same weight if classification costs are to be minimized. I suggest the authors to at least mention these issues and how the cutoff may change. One reference to consult: jstatsoft.org/article/view/v061i08/v61i08.pdf
Reply: Sensitivity measures the proportion of positives that are correctly identified and Specificity measures the proportion of negatives that are correctly identified. Therefore, sensitivity quantifies the avoiding of false negatives, and specificity does the same for false positives ("Detector Performance Analysis Using ROC Curves - MATLAB & Simulink Example". www.mathworks.com). Youden's index (sensitivity+specificity-1) summarizes the performance of a diagnostic test (Cancer 1950; 3:32-35). For getting optimal BF% cut-off points, sensitivity and specificity for identifying each CVD risk factor at different cut-off points of BF% were analyzed (shown in Table 4-5). As paper wrote, "Clearly, specificity gradually increased but sensitivity conversely decreased with the increase cut-off values of BF% in men and women. BF% cut-off points of preferable sensitivity and specificity to detect each CVD risk factor and clustering of ≥2 risk factors were selected as optimal values.", which avoided relative high false positive rate. Meantime, population-attributable risks percent at BF% cut-off points were estimated and showed that if intervention started at these points, it would be possible to prevent the percentage of risk factors in the population (shown in Table 6). Based on the above results, the study determined the optimal cut-off points for BF% for Han and Mongolian adults and kept relatively low level of misclassifications costs.
2. It is mentioned that there are WHO recommendations for BF% cutoffs in Caucasian populations (25% for men and 35% for women). Please provide the corresponding pages of the WHO document (reference #6) where this is found. I'm not totally sure but it seems that these values are not to be understood as official WHO BF% cutoffs. If there are no clear recommendations yet in regard to BF%

cutoffs it should be mentioned along with the variation on BF% cutoffs provided by different studies.
Reply: It has also been mentioned below references [1-4] that there are WHO recommendations for BF% cutoffs in Caucasian populations (25% for men and 35% for women)

[1]. Deurenberg P, Yap M, van Staveren W A. Body mass index and percent body fat: a meta analysis among different ethnic groups.[J]. International Journal of Obesity & Related Metabolic Disorders Journal of the International Association for the Study of Obesity, 1998, 22(12):1164-71.
[2]. De L A, Deurenberg P, Pietrantuono M, et al. How fat is obese?[J]. Acta Diabetologica, 2003, 40 suppl 1(1 Supplement):s254-s257.
[3]. Arroyo M, Rocandio A M, Ansotegui L, et al. Comparison of predicted body fat percentage from anthropometric methods and from impedance in university students.[J]. British Journal of Nutrition, 2004, 92(5):827-32.
[4]. Deurenberg P, Weststrate J A, Seidell J C. Body mass index as a measure of body fatness: age- and sex-specific prediction formulas.[J]. British Journal of Nutrition, 1991, 65(2):105-14.

3. In the discussion it is said that it is preferable to measure BF% directly since BMI accuracy is limited for detecting excess body adiposity (page 11, lines 38-40). The accuracy of the type of BF% measurements employed in the analysis should be discussed more thoroughly, that is, what we know about the accuracy of BF% measures obtained with bioelectrical impedance and how it compares with other methods? I would suggest to compare the performance of BMI to that of BF% for classification purposes, that is, a comparison of the AUC between classifiers. BMI is available in the data and this also would give perspective to the actual benefits of using BF% measured with bioimpedance vs using BMI. Another alternative would be to use both classifiers as predictors in a probit or logit regression, and then using the linear predictor from this regression as the classifier. BF% measured by bioimpedance and BMI are both indirect measures of the true adiposity. Is the performance improved when both are used or not so much? It would be interesting to perform this exercise but more importantly to compare the BF% performance with BMI using the appropriate statistical methods to compare the AUC between these two classifiers. Please clarify the sentence in line 5-6 in page3 where it is mention that BF% measured with bioimpedance "...tends to underestimate body fat in all subjects and in men and women separately".

Reply:

Discussion about the accuracy of BF% measures obtained with bioelectrical impedance has been added into the limitations on Page 7.

Several studies have discussed comparison of BMI with BF% in the evaluation of obesity in Chinese (Biomed Environ Sci 2010;23:173-179) and in saudi adults (Biomed Environ Sci 2013;26:94-99), but the results were inconsistent. Therefore, it’s helpful suggestion to compare the performance of BMI to that of BF% for classification purposes, we are now conducting another study about this part and considering the combined usage of BMI and BF% to better define obesity.

Guang Sun, et al. (reference #29) showed that bioelectrical impedance analysis tends to underestimate body fat in all subjects and in men and women separately, meanwhile this bias depends on the degree of adiposity. However, reference methods such as dual-energy X-ray absorptiometry (DXA), air-displacement plethysmography, and underwater weighing can provide accurate adiposity; however, these methods are costly and often inaccessible to the public. In most situations, Bioelectrical impedance analysis (BIA) and other field methods are the only techniques available for body-composition measurements, especially in large-scale epidemiological investigations.

Minor comments:

1. It is mentioned that the data support the good discrimination of BF% for each CVD risk factor (page 12). It seems that this statement comes from the area under the ROC Curves (AUC) obtained in the results. I suggest to provide a better assessment of the AROC values. E.g. AUC ranged from 0.589 to 0.699 for Han men, is this a fair performance, a good performance? Hosmer and Lemeshow (2000) in chapter 5 of Applied Logistic Regression provided a classification of AUC values that may be helpful as a rough guideline.

Reply: In present study, confidence intervals of AUC values had been calculated (shown in Table 2), which allowed to determine that almost AUC values were significant (compared with 0.5). We have carefully read the chapter 5 of Applied Logistic Regression mention, which provided a general rule about the classification of AUC values. However, as this book wrote, “In practice it is extremely unusual to observe areas under the ROC curve greater than 0.9”, actually, the AUC values for anthropometric parameters such as BMI and WC to detect CVD risk factors were not very high, which mostly were round 0.6-0.8 (Postgrad Med J 2011;87:251-256/J Diabetes 2015;7:386-392/Br J Nutr 2014;112:1735-1744), Our study found that in Han population, the AUCs for BF% ranged from 0.589 to 0.699 for men and from 0.711 to 0.763 for women, and the AUCs for BF% in women (0.685-0.783) were similar with those in men (0.686-0.736) for CVD risk factors in Mongolian. We thought the data supported the “good” discrimination of BF% as an anthropometric parameter for each CVD risk factor. The “good” is not at all excellent in statistics, but, more importantly, means a good performance as a public health tool to deal with CVD risk factors.

2. In the objective I'm not sure whether it is appropriate to say that the cutoff values of BF% are for obesity given the approach used, I would suggest to say "cut-off values for the detection of CVD risk factors" or “...for the purposes of classification of CVD risk conditions"

Reply: The corresponding sentence has been rewritten “The present study was designed to determine the optimal cut-off values of body fat percentage (BF%) for the detection of cardiovascular disease (CVD) risk factors risk factors in Mongolian and Han adults”

3. I would suggest to mention something about the AUC in the abstract. In general, did the classifiers perform well? A general description of AUC values observed, and specificity/sensitivity achieved at the optimized cutoffs.

Reply: AUCs of BF% for CVD risk factors among Han and Mongolian adults have been added into abstract.

4. In the introduction it is mentioned that the global prevalence of underweight has risen dramatically but in the reference cited it seems that underweight has decreased.

Reply: It’s a spelling error and “underweight” has been corrected into “overweight”.

5. Please add the prevalence for BMI categories (overweight, obesity) in table 1. I would suggest to refer overweight as 25<=BMI<30 instead of BMI>=25. Please clarify definitions in line 17 of page 3.

Reply: The prevalence for BMI categories (overweight, obesity) were added in table 1 and corresponding definitions “Overweight and obesity were defined as a subject with BMI≥25 and <30 kg/m2, and BMI≥30kg/m2, respectively” have been added into the revised manuscript.

6. In tables 4 and 5, and in the paper in general, a certain cut-off is highlighted across the table but the optimal cut-off as indicated by the Youden Index varies between CVD risk factors, especially for Han men (21 for diabetes, 26 for dyslipidemia). It is not clear why the highlighted cutoffs are the optimal given this variation (lines 38-40 of page 8)

Reply: It has been found that the optimal BF% cut-off points varied greatly by age and CVD risk factors in our study (Table 3), so we further confirm the range of optimal BF% cut-off points in Table 4 and Table 5. BF% cut-off points of preferable sensitivity and specificity to detect each CVD risk factor and clustering of ≥2 risk factors were selected as optimal values.

7. There are no standard errors or some measure that indicates precision of estimates for sensitivity, specificity and the cutoffs. If you can generate those, it would allow to determine whether there are significant differences between Han and Mongolian populations (line 35, page 12). Not all statistical packages provide confidence intervals or standard errors for these. Please explore whether in the statistical package used confidence intervals or standard errors are implemented for sensitivity, specificity and the cutoffs.

Reply: Unfortunately, we haven’t found appropriate statistical packages to calculate the confidence intervals or standard errors sensitivity, specificity and the cutoffs yet. We will continue to seek related statistical method.

8. Provide more details on the sampling design. Is this a probabilistic representative sample? Was stratification used in the sampling design? Is a multistage sample?

Reply: A sample of adult residents aged 20–80 years was selected using a multistage cluster sampling method. The sampling process was stratified according to degree of urbanization, and four

urban areas were selected from Inner Mongolia Autonomous Region including Bayan Nur, Xilingol League, Ulanqab and Hohhot. In each area, different districts were selected as sampling units, which has been described in Li, et al (Reference #11)
9. On question. The attributable fractions are calculated using ORs. Is the original formula in terms of relative risks (RRs)? In case ORs were used to approximate RRs how well does this work given that prevalence of CVDs are far from zero? Is the approximation appropriate?
Reply: Population-attributable risks percent at BF% cut-off points were estimated in present study, which showed that if intervention started at these points, it would be possible to prevent the percentage of risk factors in the population. Zhou BF, et al. (Asia Pacific Journal of Clinical Nutrition 2002;15: S685–S693) has calculated the population-attributable risks percent [PAR(%)] for different risk factors such as hypertension according to the following equation: PAR(%) = 100 * P (OR-1) / [P (OR-1)+1]%, which formula our study used too. Indeed, the PAR(%) may be overestimated by this method, but we cannot exactly calculate the extent of overestimation.

VERSION 2 – REVIEW

REVIEWER	Bing Zhang National Institute for Nutrition and Health, China CDC. P.R. China
REVIEW RETURNED	14-Dec-2016

GENERAL COMMENTS	The revised manuscript have answered my questions and suggestions. No other question.

REVIEWER	Takahisa Kondo Nagoya University Graudate School of Medicine, Japan
REVIEW RETURNED	20-Dec-2016

GENERAL COMMENTS	The authors responded well to the several Reviewer’s comments. However, the question “Analysis stratified by insulin resistance (or BMI), and smoking status was not shown in the Revised version. The authors should be answered to this question.

REVIEWER	Yonghong Zhang Soochow University, China
REVIEW RETURNED	09-Dec-2016

GENERAL COMMENTS	The authors have fulfilled the reviewer's indications.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 3
Reviewer Name: Yonghong Zhang
Institution and Country: Soochow University, China
Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below
The authors have fulfilled the reviewer's indications.
Reply: None.

Reviewer: 1

Reviewer Name: Bing Zhang
Institution and Country: National Institute for Nutrition and Health, China CDC. P.R. China
Please state any competing interests or state ‘None declared’: no

Please leave your comments for the authors below
The revised manuscript has answered my questions and suggestions. No other question.
Reply: None.

Reviewer: 2
Reviewer Name: Takahisa Kondo
Institution and Country: Nagoya University Graudate School of Medicine, Japan
Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below
The authors responded well to the several Reviewer’s comments. However, the question “Analysis stratified by insulin resistance (or BMI), and smoking status was not shown in the Revised version. The authors should be answered to this question.

Reply: Compared to hypertension or dyslipidemia, BF% is similarly useful in detecting subjects with diabetes (shown Table 2-3), however, except among men in Han population. The AUC of BF% for men in Han to identify diabetes was 0.589, but 0.686 for men in Mongolian. As your suggestion that this phenomenon may be related with heterogeneous population of diabetes subjects.

First, the prevalence of diabetes of men in Han and Mongolian was 9.58% and 9.86%, respectively (P=0.879) (shown Table1). Diabetes has 2 primary forms: type 1, previously called insulin-dependent or juvenile-onset diabetes, and type 2, previously called non–insulin-dependent or adult-onset diabetes; the latter accounts for about 90% to 95% of all diagnosed cases of diabetes (Am J Public Health. 2012;102(8):1482-97). Although we didn’t have the data of insulin resistance, the diabetes (especially type 2 diabetes) of men in Han we thought was like that of men in Mongolian.

Second, although smoking status was not analyzed in this paper, Li, et al has reported the status of cigarette smoking in Han was similar to that in Mongolian (BMC Public Health. 2016;16(1):1-10). Thus, smoking status was not likely a confounding factor.

In conclusion, low AUC of ROC in detecting diabetes of men in Han population may not be related with heterogeneous population of diabetes and the status of cigarette. Therefore, the analysis stratified by insulin resistance (or BMI), and smoking status is not necessary. However, why this happened? We thought that the BF% of men in Han and Mongolian was significantly different (22.54% vs 23.86%, respectively, P=0.0002), which was because of different genetic backgrounds, lifestyles and dietary patterns in Han and Mongolian (as this paper discussed). But some further studies about BF% and diabetes need to be conducted.

We sincerely thanks for your suggestions about this part, but overall BF% is still useful anthropometric parameter for detecting cardiovascular risk factors.

VERSION 3 – REVIEW

REVIEWER	Takahisa Kondo Nagoya University Graduate School of Medicine, Japan
REVIEW RETURNED	10-Mar-2017

GENERAL COMMENTS	The authors answered the questions raised by this reviewer sincerely. Now, reviewer expects the authors to pursue further studies about BF% and diabetes.