PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Waist to height ratio as an indicator of 'early health risk': simpler and more predictive than using a 'matrix' based on BMI and waist circumference
AUTHORS	Ashwell, Margaret; Gibson, Sigrid

VERSION 1 - REVIEW

REVIEWER	David S Freedman Centers for Disease Control, USA
REVIEW RETURNED	16-Oct-2015

GENERAL COMMENTS	While it may be true that waist circumference (possibly divided by height) is a better indicator of health risk than is BMI, I feel the authors do not adequately address the difficulties in teasing out the relative importance of very highly correlated variables; I believe that the correlation between BMI and WHtR is ~0.80 to 0.95. Molarius and Seidell (Molarius & Seidell, 1998) emphasize the difficulties involved in attempting to determine the single best anthropometric indicator of disease risk It's troubling that the 1st cited article (Mokha et al., 2010) appears to completely ignore this strong correlation. The analysis largely consists of contrasting CVD risk factor levels between children who have a WHtR of ≥ 0.5 and those < 0.5 within very broad categories of BMI. The authors appear not to realize that 'normal-BMI' children with a high WHtR almost certainly have higher BMI levels than do normal-BMI children who have a low WHtR. Interestingly another paper published 3 years earlier (Freedman et al., 2007) using the same data, found that BMI-for-age and WHtR did not differ in their abilities to identify children with adverse risk factor levels. Other papers in the literature that purportedly support the superiority of WHtR also suffer from residual confounding by BMI (Khoury et al., 2012) It should also be realized that although WHtR may, in some studies, be found to be more accurate in the identification of adverse risk factor levels than is BMI, many of the observed differences have been very small (Bosy-Westphal et al., 2006). This can also be seen in the 3rd cited paper (Guasch-Ferré et al., 2012): for the most part, the C-statistics for BMI and WHtR were very similar, and BMI was actually a better predictor of hypertension than WHtR. The only outcome for which WHtR was appreciably better than BMI was for metabolic syndrome, but as one component of this syndrome is a high waist circumference, it is unsurprising that WHtR was a better predictor. In contrast to the many studies that the authors cite in support of

	WHtR, the authors fail to cite any studies that have found BMI and WHtR to be equivalent in the assessment of risk factor levels or in the assessment of disease risk (Stevens et al., 2001; Taylor et al., 2010; Tulloch-Reid, Williams, Looker, Hanson, & Knowler, 2003; Wannamethee, Shaper, Morris, & Whincup, 2005; Wormser et al., 2011). Some of these papers should be cited to provide a more balanced view of the literature, and the authors should consider replacing 'overwhelming' in the Abstract with some other description of the evidence. There are also some changes that should be made in the Results and Discussion sections of the paper. The table and Figure 2 present exactly the same information, and the figure should be deleted. Page 4 states that the authors have unpublished data showing that levels of TG and the HDL ratio are elevated in the group who are would be misclassified by the NICE matrix. I think the authors are referring to subjects who have a higher WHtR category than NICE category in the table, and these data should be shown in the article. It should be clarified if the reason for this finding is that these misclassified subjects have a higher BMI (or other covariate) than subjects who are classified identically by the 2 systems. Please check reference #20 as there is not enough information in the citation to obtain this article/working paper. Is the information available on a website? References Bosy-Westphal, A., Geisler, C., Onur, S., Korth, O., Selberg, O., Schrezenmeir, J., & Müller, M. J. (2006). Value of body fat mass vs anthropometric obesity indices in the assessment of metabolic risk factors. International Journal of Obesity (2005), 30(3), 475–83. doi:10.1038/sj.ijo.0803144 Freedman, D. S., Kahn, H. S., Mei, Z., Grummer-Strawn, L. M., Dietz, W. H., Srinivasan, S. R., & Berenson, G. S. (2007). Relation of body mass index and waist-to-height ratio to cardiovascular disease risk factors in children and adolescents: the Bogalusa Heart Study. American Journal of Clinical Nutrition, 86(1), 33–40. doi:86/1/33 [pii] Guasch-Ferré, M., Bulló, M., Martínez-González, M. Á., Corella, D., Estruch, R., Covas, M.-I., … Salas-Salvadó, J. (2012). Waist-to-Height Ratio and Cardiovascular Risk Factors in Elderly Individuals at High Cardiovascular Risk. PLoS ONE, 7(8), e43275. doi:10.1371/journal.pone.0043275 Khoury, M., Manlhiot, C., Dobbin, S., Gibson, D., Chahal, N., Wong, H., … McCrindle, B. W. (2012). Role of waist measures in characterizing the lipid and blood pressure assessment of adolescents classified by body mass index. Archives of Pediatrics & Adolescent Medicine, 166(8), 719–24. doi:10.1001/archpediatrics.2012.126 Mokha, J. S., Srinivasan, S. R., Dasmahapatra, P., Fernandez, C., Chen, W., Xu, J., & Berenson, G. S. (2010). Utility of waist-to-height ratio in assessing the status of central obesity and related cardiometabolic risk profile among normal weight and overweight/obese children: the Bogalusa Heart Study. BMC Pediatrics, 10, 73.

	Molarius, A., & Seidell, J. C. (1998). Selection of anthropometric indicators for classification of abdominal fatness--a critical review. International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity, 22(8), 719–27. Stevens, J., Couper, D., Pankow, J., Folsom, A. R., Duncan, B. B., Nieto, F. J., … Tyroler, H. A. (2001). Sensitivity and specificity of anthropometrics for the prediction of diabetes in a biracial cohort. Obesity Research, 9(11), 696–705. Taylor, A. E., Ebrahim, S., Ben-Shlomo, Y., Martin, R. M., Whincup, P. H., Yarnell, J. W., … Lawlor, D. A. (2010). Comparison of the associations of body mass index and measures of central adiposity and fat mass with coronary heart disease, diabetes, and all-cause mortality: a study using data from 4 UK cohorts. American Journal of Clinical Nutrition, 91(3), 547–556. Tulloch-Reid, M. K., Williams, D. E., Looker, H. C., Hanson, R. L., & Knowler, W. C. (2003). Do measures of body fat distribution provide information on the risk of type 2 diabetes in addition to measures of general obesity? Comparison of anthropometric predictors of type 2 diabetes in Pima Indians. Diabetes Care, 26(9), 2556–2561. Wannamethee, S. G., Shaper, A. G., Morris, R. W., & Whincup, P. H. (2005). Measures of adiposity in the identification of metabolic abnormalities in elderly men. American Journal of Clinical Nutrition, 81(6), 1313–1321. doi:81/6/1313 [pii] Wormser, D., Kaptoge, S., Di Angelantonio, E., Wood, A. M., Pennells, L., Thompson, A., … Danesh, J. (2011). Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet, 377(9771), 1085–95. doi:10.1016/S0140-6736(11)60105-0

REVIEWER	Savvas C Savva Research and Education Institute of Child Health, Cyprus
REVIEW RETURNED	27-Oct-2015

GENERAL COMMENTS	Ashwell M and Gibson S aim to compare the ability of a single anthropometric index (Waist-to-Height ratio, WHtR) to classify adults being at “increased health risk” compared to the National Institute for Health and Care Excellence (NICE) recommendations of using both BMI and waist circumference in identifying adults at “increased health risk”. Using data from the UK National Diet and Nutrition Survey (NDNS) they could identify a substantially higher proportion of adults as being at “early health risk” compared to the NICE guidelines. Moreover, projecting the results from the study to the whole UK population, the authors estimated that about 14% of the UK adult population (or 7 million adults) would be misclassified as at “no increased risk” using NICE guidelines but would be classified as at “early increased risk” using a WHtR boundary of >0.5. The authors clearly comment that “any anthropometric measure is only the first step in identifying people at risk”. Based on the above, I have two questions/suggestions for the

	authors. 1) The authors state that "We have unpublished data from this NDNS adult sample to show that triglycerides and total to HDL cholesterol ratio are raised in the group who would be misclassified by the NICE matrix . . .". I think that presenting these data and also other CVD risk factors would be in favour of the manuscript and perhaps would be more convincing in using WHtR instead of NICE guidelines for identifying at risk people. Moreover the discussion should include a cost-effect analysis if possible. 2) The Title of the manuscript is a little bit misleading. Indicating that WHtR is superior to current NICE matrix is not justified by the results. Unless if the authors can demonstrate that participants identified as at "increased risk" benefit in terms of CVD prevention.

REVIEWER	Lesley Gray University of Otago New Zealand
REVIEW RETURNED	28-Oct-2015

GENERAL COMMENTS	**Overall** this is an important study using existing data sources, focusing on measurement to inform risk and highlights limitations of BMI for sensitivity of metabolic risk indicators. I commend the authors for this important and timely comparison. I have followed closely the development and supporting evidence relating to WHtR and welcome evidence regarding its utility in order to confidently recommend WHtR as an evidence based tool to health professionals and individuals. The word count is 1561 (up to 4000 allowed) which allows for some expanded text to add clarity to this study. I detail below areas requiring minor revision in my opinion: ABSTRACT Line 17 and 18 – Suggest re-word e.g. Data from four years of the ………….(2008 to 2012) were utilised. Line 18 – Suggest add word - 19 <u>years</u> and over. Line 30 and 31 – Suggest re-word e.g. ….of the metabolic risks associated with central obesity. Lines 37 to 50 – consistency of bullet points – some with full stops and some without. Line 46 – typing error – been BACKGROUND Line 6, 7 and 8 – suggest re-word e.g. …metabolic risks [12-18]. As well as its close….. WHtR also has a clearer relationships with mortality compared to BMI [19]. Line 10 – suggest re-word e.g. We have previously shown that… Lines 17-19 – personally I would be inclined to delete reference to the reported actions by the NICE Director in this particular article. I would retain the last sentence (line 19-20). METHODS The methodology for this study is not clearly stated i.e. what sort of methodology/study design (e.g.. primary or secondary research, quantitative or qualitative, prospective or retrospective, cohort or case control). What permissions (if any) were required to access the NDNS data? How were the data accessed? Please add a new first

	paragraph to detail the methodology and what if any statistical calculations were to be undertaken. Is it possible to show the categories as a table? RESULTS Consider an overview sentence e.g. This analysis shows that… (see paragraph starting at line 51 for possible overview sentence) before moving into detail currently shown in first paragraph line 43 on. Line 43 – suggest add word – 41% of the NDNS adult population sampled. Lines 45-47 – can this data be added into Fig 1 or be shown as a new Fig 2? When referring to the Table can you please number the Table (Table1) and I suggest rather than attempting to explain which column, you label each column e.g. a,b,c,d. Can the data referred to as 'not shown' in the table be included in any way? Presumably the NDNS categorized participants as men and women? DISCUSSION Line 17 – suggest change word – We are unaware of any other UK study Line 18 – suggest delete word 'However' – The New Zealand Ministry…. Line 22 – Use of acronym NZ – not previously defined in article Line 23 – suggest re-word – …..increased risk' compared to the NICE matrix. Lines 27-32 – Unpublished data - do you mean NDNS data that was unpublished and if so, how did you access the data? Either include this in you methodology and results for later discussion or exclude from this article? Perhaps refer to the Singapore study in terms of implications and signal further analysis the researchers will/have conduct(ed) which is not included in this article. Line 32 – remove 'in both genders' (there are multiple domains defining gender and gender is not limited to two). Lines 34-43 – this paragraph concerns children who are not the subject of the NDNS survey – suggest limit this discussion to adult comparators for metabolic implications. Lines 45 – 48 – some explanation of what apples and pears mean in context would be useful. Line 50 - number the table (Table1) and if column's labelled this would read as ....of our data (Table 1, column f). CONCLUSIONS AND IMPLICATIONS Line 7 – suggest re-word – e.g. …risk factors should follow for those deemed… Lines 10 – 19 - this paragraph largely relates to children who are not the subject of the NDNS survey and therefore the results of this article. Suggest you limit concluding comments to the benefits to adults and risk assessments concerning adults and strengthen the concluding comments specifically in relation to WHtR and NICE matrix and associated recommendations, implications, next steps. REFERENCES Ref 6. Is first author MA Ashwell or M Ashwell? (shown as Ashwell MA) Delete ref 20 if reference to NICE Director removed in text (see comment above). Re-order remaining references. For references accessed via web link, please add "Retrieved from" and the web link e.g. ref 23.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: David S Freedman
Centers for Disease Control, USA

F1 While it may be true that waist circumference (possibly divided by height) is a better indicator of health risk than is BMI, I feel the authors do not adequately address the difficulties in teasing out the relative importance of very highly correlated variables; I believe that the correlation between BMI and WHtR is ~0.80 to 0.95. Molarius and Seidell (Molarius & Seidell, 1998) emphasize the difficulties involved in attempting to determine the single best anthropometric indicator of disease risk
We thank the reviewer for making this important point We have now included discussion of this point in the revised text as follows:
Although BMI, WC and WHtR are, by their very nature, strongly correlated {Molarius, 1998 #184}{Ashwell, 2009 #77}, the most important question is to ask which anthropometric proxy measure is the simplest and most accurate in helping to indicate 'early health risk'?

F2 It's troubling that the 1st cited article (Mokha et al., 2010) appears to completely ignore this strong correlation. The analysis largely consists of contrasting CVD risk factor levels between children who have a WHtR of ≥ 0.5 and those < 0.5 within very broad categories of BMI. The authors appear not to realize that 'normal-BMI' children with a high WHtR almost certainly have higher BMI levels than do normal-BMI children who have a low WHtR. We have now omitted the Mokha reference at this point and included a better balance of papers in the background section on page 3. We have mentioned in our discussion that authors often do not adjust for BMI within WHtR categories and we cite Mokha as an example

F3 Interestingly another paper published 3 years earlier (Freedman et al., 2007) using the same data, found that BMI-for-age and WHtR did not differ in their abilities to identify children with adverse risk factor levels. Other papers in the literature that purportedly support the superiority of WHtR also suffer from residual confounding by BMI (Khoury et al., 2012)
This important point about residual confounding by BMI has motivated us on to include our unpublished data in this paper (also requested by the other reviewers) and we believe that the manuscript, in its revised form, is much better for this inclusion.
In revising our manuscript we have also checked that, even after adjusting for BMI, WHtR was still a significant predictor in regression for several cardiometabolic risk factors. Please see new Tables 2, 3 and Figure 3.This important point is also included in our discussion.

The new Tables 2 and 3 and the new figure 3 have lengthened our manuscript but, as all 3 reviewers asked us to include our, hitherto unpublished, analysis, we hope they and the Editor will appreciate the improvement in our revised manuscript .Our total word count is still well within the BMJ limit.

F4 It should also be realized that although WHtR may, in some studies, be found to be more accurate in the identification of adverse risk factor levels than is BMI, many of the observed differences have been very small (Bosy-Westphal et al., 2006). This can also be seen in the 3rd cited paper (Guasch-Ferré et al., 2012): for the most part, the C-statistics for BMI and WHtR were very similar, and BMI was actually a better predictor of hypertension than WHtR. The only outcome for which WHtR was appreciably better than BMI was for metabolic syndrome, but as one component of this syndrome is a high waist circumference, it is unsurprising that WHtR was a better predictor.

We concede that the differences are fairly small and have changed the revised text accordingly in our background and discussion sections.

We also recognise that one component of the metabolic syndrome is a high waist circumference so it is unsurprising that WHtR is a better predictor. In our analysis, we have put our focus on specific cardiometabolic risk factors and, we hope, avoided this pitfall.

F4 In contrast to the many studies that the authors cite in support of WHtR, the authors fail to cite any studies that have found BMI and WHtR to be equivalent in the assessment of risk factor levels or in the assessment of disease risk (Stevens et al., 2001; Taylor et al., 2010; Tulloch-Reid, Williams, Looker, Hanson, & Knowler, 2003; Wannamethee, Shaper, Morris, & Whincup, 2005; Wormser et al., 2011). Some of these papers should be cited to provide a more balanced view of the literature, and the authors should consider replacing 'overwhelming' in the Abstract with some other description of the evidence.
We thank the reviewer for suggesting these references and hope he will find that the revised text is more balanced with inclusion of some of these suggested references.

Overwhelming has been replaced with the word 'good' .
F5 There are also some changes that should be made in the Results and Discussion sections of the paper. The table and Figure 2 present exactly the same information, and the figure should be deleted
We would like to keep Figure 2, if we may, because we believe the graphic makes our point more succinctly than Table 1 (which includes full details).

F6 Page 4 states that the authors have unpublished data showing that levels of TG and the HDL ratio are elevated in the group who are would be misclassified by the NICE matrix. I think the authors are referring to subjects who have a higher WHtR category than NICE category in the table, and these data should be shown in the article. It should be clarified if the reason for this finding is that these misclassified subjects have a higher BMI (or other covariate) than subjects who are classified identically by the 2 systems.
Motivated by the reviewers' comments, we have progressed our analysis on cardiometabolic risk factors in this study population and have now included this extra data in our revised manuscript.
The new Tables 2 and 3 and the new figure 3 have lengthened our manuscript but, as all 3 reviewers asked us to include our hitherto unpublished analysis, we hope they and the Editor will appreciate the improvement in our revised manuscript .Our total word count is still well within the BMJ limit.

Our analysis was adjusted for BMI as well as for age and sex and it still showed that subjects with normal BMI but WHtR >0.5 had higher levels of all cardiometabolic risk factors and that for three out of four of these the differences were statistically significant. – see table 2 and fig 3.

F7 Please check reference #20 as there is not enough information in the citation to obtain this article/working paper. Is the information available on a website?

This reference has been expanded and a web reference given to make it easier for referral to the PHE slide set. Thank you.
Reviewer 2
Savvas C Savva
Research and Education Institute of Child Health, Cyprus

S1 Ashwell M and Gibson S aim to compare the ability of a single anthropometric index (Waist-to-Height ratio, WHtR) to classify adults being at “increased health risk” compared to the National Institute for Health and Care Excellence (NICE) recommendations of using both BMI and waist circumference in identifying adults at “increased health risk”.
Using data from the UK National Diet and Nutrition Survey (NDNS) they could identify a substantially higher proportion of adults as being at “early health risk” compared to the NICE guidelines. Moreover, projecting the results from the study to the whole UK population, the authors estimated that about 14% of the UK adult population (or 7 million adults) would be misclassified as at “no increased risk” using NICE guidelines but would be classified as at “early increased risk” using a WHtR boundary of >0.5 Thank you.
S2 The authors clearly comment that “any anthropometric measure is only the first step in identifying people at risk”.
Based on the above, I have two questions/suggestions for the authors. 1) The authors state that “We have unpublished data from this NDNS adult sample to show that triglycerides and total to HDL cholesterol ratio are raised in the group who would be misclassified by the NICE matrix . . .”. I think that presenting these data and also other CVD risk factors would be in favour of the manuscript and perhaps would be more convincing in using WHtR instead of NICE guidelines for identifying at risk people See F3
Motivated by the reviewers’ comments, we have completed our analysis on CVD risk factors in this study population and have now included this extra data in our revised manuscript.

Our analysis was adjusted for BMI as well as for age and sex and it still showed that subjects with normal BMI but WHtR >0.5 had higher levels of all cardiometabolic risk factors and that for three out of four of these the differences were still statistically significant.
The new Tables 2 and 3 and the new figure 3 have lengthened our manuscript but, as all 3 reviewers asked us to include our hitherto unpublished analysis, we hope they and the Editor will appreciate the improvement in our revised manuscript Our total word count is still well within the BMJ limit.

S3 . Moreover the discussion should include a cost-effect analysis if possible We have revised the text to make the cost effectiveness clearer.
S4 2) The Title of the manuscript is a little bit misleading. Indicating that WHtR is superior to current NICE matrix is not justified by the results. Unless if the authors can demonstrate that participants identified as at “increased risk” benefit in terms of CVD prevention.
Motivated by the reviewers’ comments, we have completed our analysis on CVD risk factors in this study population and have now included this extra data in our revised manuscript.

Our analysis was adjusted for BMI as well as for age and sex and it still showed that subjects with normal BMI but WHtR >0.5 had higher levels of cardiometabolic risk factors and that for three of these the differences was statistically significant.

We have changed the title in line with the reviewer's wishes and removed ‘superior’ . Because we have presented the extra analysis , we feel our revised title is justified:
Waist to height ratio as an indicator of ‘early health risk’: simpler and more predictive than using a ‘matrix’ based on BMI and waist circumference

Reviewer 3 Lesley Gray University Otago
G1 Overall this is an important study using existing data sources, focusing on measurement to inform risk and highlights limitations of BMI for sensitivity of metabolic risk indicators. I commend the authors for this important and timely comparison. I have followed closely the development and supporting evidence relating to WHtR and welcome evidence regarding its utility in order to confidently recommend WHtR as an evidence based tool to health professionals and individuals.
Thank you
G2 The word count is 1561 (up to 4000 allowed) which allows for some expanded text to add clarity to this study. I detail below areas requiring minor revision in my opinion:
We have added further text to help clarify the very good points made by the reviewers.
G3 ABSTRACT
Line 17 and 18 – Suggest re-word e.g. Data from four years of the …………..(2008 to 2012) were utilised.
Line 18 – Suggest add word - 19 years and over.
Line 30 and 31 – Suggest re-word e.g. ….of the metabolic risks associated with central obesity.
Lines 37 to 50 – consistency of bullet points – some with full stops and some without.
Line 46 – typing error – been Corrections made to the revised manuscript.
Thank you.
G4 BACKGROUND
Line 6, 7 and 8 – suggest re-word e.g. …metabolic risks [12-18]. As well as its close….. WHtR also has a clearer relationships with mortality compared to BMI [19].
Line 10 – suggest re-word e.g. We have previously shown that…
Lines 17-19 – personally I would be inclined to delete reference to the reported actions by the NICE Director in this particular article. I would retain the last sentence (line 19-20).
Corrections made to the revised manuscript.
Thank you.

This sentence has been rephrased to de- personalise it in line with the reviewer's wishes.
G5 METHODS
The methodology for this study is not clearly stated i.e. what sort of methodology/study design (e.g.. primary or secondary research, quantitative or qualitative, prospective or retrospective, cohort or case control). What permissions (if any) were required to access the NDNS data? How were the data accessed? Please add a new first paragraph to detail the methodology and what if any statistical calculations were to be undertaken.
We have added details on the methods of the original survey and this secondary analysis and data access.
G6
Is it possible to show the categories as a table?
We considered showing the 'matrix' in full but instead have put more detail into the revised manuscript about how the 'matrix' categories were defined.
We have also taken the opportunity to refer to the matrix as the 'matrix' because, strictly speaking, the 'matrix' was published by Public Health England as an adaptation and extension of the NICE Guidance and we felt it would be too unwieldy to call it the PHE/NICE matrix each time we referred to it. This has all been explained in the revised text
G7 RESULTS
Consider an overview sentence e.g. This analysis shows that… (see paragraph starting at line 51 for possible overview sentence) before moving into detail currently shown in first paragraph line 43 on.
We did consider this – but we could not find the correct words which did not pre-empt the results.

Many overview sentences are elsewhere in the manuscript.
G8 Line 43 – suggest add word – 41% of the NDNS adult population sampled.
Done

G9 Lines 45-47 – can this data be added into Fig 1 or be shown as a new Fig 2?
This data is already in Figure 1

G10 When referring to the Table can you please number the Table (Table1) and I suggest rather than attempting to explain which column, you label each column e.g. a,b,c,d.
Corrections made to the revised manuscript

G11 Can the data referred to as 'not shown' in the table be included in any way? Presumably the NDNS categorized participants as men and women?
We have preferred to put the extra data on men and women in the text. Their inclusion in Table 1 would have made it too unwieldy.

G12 DISCUSSION
Line 17 – suggest change word – We are unaware of any other UK study
Line 18 – suggest delete word 'However' – The New Zealand Ministry….
Line 22 – Use of acronym NZ – not previously defined in article
Line 23 – suggest re-word – …..increased risk' compared to the NICE matrix.
Corrections made to the revised manuscript

G13 Lines 27-32 – Unpublished data - do you mean NDNS data that was unpublished and if so, how did you access the data? Either include this in you methodology and results for later discussion or exclude from this article? Perhaps refer to the Singapore study in terms of implications and signal further analysis the researchers will/have conduct(ed) which is not included in this article.
Motivated by the reviewers' comments, we have completed our analysis on CVD risk factors in this study population and have now included this extra data in our revised manuscript.

Our analysis was adjusted for BMI as well as for age and sex and it still showed that subjects with normal BMI but WHtR >0.5 had higher levels of cardiometabolic risk factors and that for three out of four of these the differences were statistically significant.

G14 Line 32 – remove 'in both genders' (there are multiple domains defining gender and gender is not limited to two).
Done. (I have a friend who is doing her PhD thesis on the numbers of gender and I think it's at least 24!
G15 Lines 34-43 – this paragraph concerns children who are not the subject of the NDNS survey – suggest limit this discussion to adult comparators for metabolic implications Discussion about children is reduced in revised text but we would still like to make this point because so many of the papers supporting WHtR have used data from children. Also because the most critical use of WHtR is to use it in prevention in children.
G16 Lines 45 – 48 – some explanation of what apples and pears mean in context would be useful.
Corrections made to the revised manuscript.
We have omitted reference to apples and pears in this manuscript.
G17 Line 50 - number the table (Table1) and if column's labelled this would read as ....of our data (Table 1,column f).

Done

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G18 CONCLUSIONS AND IMPLICATIONS
Line 7 – suggest re-word – e.g. …risk factors should follow for those deemed Corrections made to the revised manuscript

G19 Lines 10 – 19 - this paragraph largely relates to children who are not the subject of the NDNS survey and therefore the results of this article. Suggest you limit concluding comments to the benefits to adults and risk assessments concerning adults and strengthen the concluding comments specifically in relation to WHtR and NICE matrix and associated recommendations, implications, next steps See above
G20 REFERENCES
Ref 6. Is first author MA Ashwell or M Ashwell? (shown as Ashwell MA)
Done. Thank you for pointing out my inconsistency.
G21 Delete ref 20 if reference to NICE Director removed in text (see comment above). Re-order remaining references.
Have kept reference but have 'depersonalised' in revised text
G22 For references accessed via web link, please add "Retrieved from" and the web link e.g. ref 23.
done

VERSION 2 – REVIEW

REVIEWER	David Freedman Centers for Disease Control, US
REVIEW RETURNED	13-Dec-2015

GENERAL COMMENTS	The paper has been improved, but I have a few additional concerns. The revised paper includes analyses from the NDNS, a national survey. In the analyses, the authors make use of the sample weights (line 17), but there is no mention of the sample design variables (PSUs and strata). I'd like to see a justification of why the authors feel it's appropriate to treat this survey as if it were a simple random sample (SRS). This might be appropriate for the NDNS, but most national survey utilize a complex sampling design which if ignored, will result in SEs (and p-values) that are very likely to be too small. For example, information on the U.S. NHANES studies state that, "... the use of sampling weights and sample design variables is recommended for all analyses because the sample design is a clustered design and incorporates differential probabilities of selection. Accounting for the complex sampling design of NHANES is especially critical when calculating statistical estimates and estimating standard errors ... " http://www.cdc.gov/nchs/tutorials/nhanes/faqs.htm I was also able to find this information concerning the NDNS: "The statistical analysis of data generated from this complex survey design requires taking the sample design (i.e. sample stratification, clustering and weighting) into account to yield valid estimates of the population parameters. http://www.foodstandards.gov.scot/sites/default/files/ndns-scotland-appendix-y.pdf

	Please note that it may be appropriate to analyze data from the NDNS as if it was a simple random sample, but a justification needs to be provided. (Note that it isn't enough to simply state that other investigators have also treated the data in this manner.). As many of the p-values (particularly those that are adjusted for BMI) in Table 3 are very close to the magical 0.05 cut-point, I think that it's possible that a statistical analyses that accounts for the sample design could result in many of the differences becoming non-significant. There are also some minor points that need to be addressed: 1) Please show the Ns for each cell in Table 1. 2) The PDF that I was able to access did not have any of the figures included 3) In the PDF that I accessed, the references are in landscape orientation

REVIEWER	Savvas C Savva Research and Education Institute of Child Health Cyprus
REVIEW RETURNED	23-Dec-2015

GENERAL COMMENTS	The authors have made drastic changes/improvements in the manuscript based on reviewers' comments. There are a couple of concerns: 1) The authors state that "We have revised the text to make the cost effectiveness clearer" after a suggestion was made. However there is no such discussion! 2) The legend of the vertical axis in the new Figure 3 states 'mmol/l.' Although this is the case for HDL cholesterol, this does not apply for the second column (Total cholesterol/HDL cholesterol ratio).

REVIEWER	Lesley Gray University of Otago, Wellington, New Zealand
REVIEW RETURNED	29-Dec-2015

GENERAL COMMENTS	The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1: David S Freedman ***Centers for Disease Control, USA***		
F1	*The revised paper includes analyses from the NDNS, a national survey. In the analyses, the authors make use of the sample weights (line 17), but there is no mention of the sample design variables (PSUs and strata). I'd like to see a justification of why the authors feel it's*	We are grateful to Dr Freedman for his comments and referring to the NDNS methods report for FSA Scotland. This is largely derived from Appendix B in the main survey report whose guidance we have followed

	appropriate to treat this survey as if it were a simple random sample (SRS). This might be appropriate for the NDNS, but most national survey utilize a complex sampling design which if ignored, will result in SEs (and p-values) that are very likely to be too small. For example, information on the U.S. NHANES studies state that, "... the use of sampling weights and sample design variables is recommended for all analyses because the sample design is a clustered design and incorporates differential probabilities of selection. Accounting for the complex sampling design of NHANES is especially critical when calculating statistical estimates and estimating standard errors ... " http://www.cdc.gov/nchs/tutorials/nhanes/faqs.htm *I was also able to find this information concerning the NDNS: "The statistical analysis of data generated from this complex survey design requires taking the sample design (i.e. sample stratification, clustering and weighting) into account to yield valid estimates of the population parameters. http://www.foodstandards.gov.scot/sites/default/files/ndns-scotland-appendix-y.pdf* *Please note that it may be appropriate to analyze data from the NDNS as if it was a simple random sample, but a justification needs to be provided. (Note that it isn't enough to simply state that other investigators have also treated the data in this manner.). As many of the p-values (particularly those that are adjusted for BMI) in Table 3 are very close to the magical 0.05 cut-point, I think that it's possible that a statistical analyses that accounts for the sample design could result in many of the differences becoming non-significant.*	We have not gone into details because the sample weights we use in our analysis already take account of the sample design as well as non-response. To quote from Appendix B: "The NDNS Rolling Programme (RP) requires weights to adjust for differences in sample selection and response. The weights adjust for differential selection probabilities of addresses, households and individuals … • non-response to the individual questionnaire • non-response to the nurse visit and • non-response of participants aged 16 years and older to the physical activity self-completion questionnaire (the RPAQ). Weights have also been generated to adjust for non-response to providing a blood sample, a 24-hour urine sample and wearing an ActiGraph. Non-response weights were generated using a combination of logistic regression modelling and calibration." We have added more detail and references to the Methods section and hope this reassures.
F2	*Please show the Ns for each cell in Table 1.*	
F3	*The PDF that I was able to access did not have any of the figures included*	The figures were included so we are sorry you could not view them. They are included in this revised submission
F4	*In the PDF that I accessed, the references are in landscape orientation*	They are in portrait in the latest version

Reviewer 2
Savvas C Savva
Research and Education Institute of Child Health, Cyprus

S1	*The authors have made drastic changes/improvements in the manuscript based on reviewers' comments.*	Thank you for your appreciation of the improvements to our paper
S2	*The authors state that "We have revised the text to make the cost effectiveness clearer" after a suggestion was made. However there is no such discussion!*	Cost-effectiveness analysis is a form of economic analysis that compares the relative costs and outcomes (effects) of two or more courses of

		action. We assume the reviewer would like us to compare the cost of detecting early health risk with waist-to-height ratio compared to that of detecting early health risk with BMI. Unfortunately we are not in a position to do such a detailed analysis. We can only make the comment that measuring BMI requires weighing scales as well as stadiometer for measuring height and that waist-to-height ratio requires a tape measure and stadiometer. Since a tape measure is cheaper and more portable than weighing scales, we assume that the use of waist-to-height ratio will be more cost effective. We have also mentioned that a simple piece of string can be used in place of a tape if the assessor only wishes to know if the subject has a waist-to-height ratio at or below 0.5. We were pleased to see the publication from Thailand which showed how this very simple measure can be used in practice (Thaikruea L, Yavichai S. Proposed Waist Circumference Measurement for Waist-to-Height Ratio as a Cardiovascular Disease Risk Indicator: Self-Assessment Feasibility. Jacobs Journal of Obesity. 2015;1(2):1-7.). There can be no doubt that a piece of string alone must be more cost effective than weighing scales and a stadiometer. . We have moved this complete section into the Discussion and developed our argument along these lines in accordance with reviewer's suggestion
S3	*The legend of the vertical axis in the new Figure 3 states 'mmol/l.' Although this is the case for HDL cholesterol, this does not apply for the second column (Total cholesterol/HDL cholesterol ratio).*	Corrected in accordance with reviewer's suggestion in the Legends to figures and removed from Figure itself to save confusion.
S4		
	Reviewer 3 ***Lesley Gray University Otago***	
G1	Abstract	We prefer to say *using* a boundary value of 0.5 and not *with* a boundary value of 0.5
G2	Abstract results	Corrected in accordance with reviewer's suggestion
G3	Background	Corrected in accordance with reviewer's suggestion
G4	Classification of respondents by anthropometric indices (BMI, WC, WHtR)	This is a sub heading

G5	Discussion	The risk factors which retained significance were HDL cholesterol. total cholesterol: HDL cholesterol and SBP Added to text in accordance with reviewer's suggestion
G6	Conclusions and implications	Data from adults. Corrected in accordance with reviewer's suggestion
G7	Add references for studies in children	Added refs [33-35] in accordance with reviewer's suggestion

VERSION 3 - REVIEW

REVIEWER	Lesley Gray University of Otago, New Zealand
REVIEW RETURNED	26-Jan-2016

GENERAL COMMENTS	Thank you for the opportunity to further review this paper. The paper is much improved as a result of previous reviewers feedback. I append a marked up version with some minor improvements noted. I would like the sentence on page 6 (line 43-44) to be removed or amended as I do not feel this last sentence adds additional value to what is already stated in this paragraph. Please restrict observation to these studies and do not make inference to ' many others' not cited. I look forward to referring to this paper when it is published. The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.