Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass index and waist circumference in the Chilean population?

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Title: Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass index and waist circumference in the Chilean population?

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Keywords: Obesity; Morbidity; Risk Factors; Chronic disease; Cardiovascular diseases.

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Abstract: Objective - To identify which anthropometric measurements (body-mass-index [BMI], waist circumference [WC], and waist-to-height ratio [WHtR]) is a better predictor of type 2 diabetes and hypertension in the Chilean population.

Research Methods & Procedures - 13,044 participants (59.7% women) from the Chilean National Health Surveys conducted in 2003, 2009-2010, and 2016-2017 were included. BMI, WC, and WHtR were the anthropometric measurements evaluated. Hypertension was defined as systolic blood pressure  $\geq$  140 mmHg and diastolic blood pressure  $\geq$  90 mmHg or on medication for hypertension. Diabetes was defined as fasting glucose ≥7.0 mmol/L or on medication for diabetes. The Receiver Operating Characteristics (ROC) curve and the Area Under Curve (AUC) were computed to derive the specificity and sensitivity using a bootstrapping approach. Results - Compared to BMI and WC, WHtR was the anthropometric measurement with the highest AUC curve in both sexes for hypertension (AUC for women: 0.70 [95% CL: 0.67 to 0.73] and AUC for men: 0.71 [95% CI: 0.69 to 0.74]) and diabetes (AUC for women: 0.71 [95% CI: 0.66 to 0.77] and AUC for men: 0.71 [95% CI: 0.67 to 0.76]). The sex-specific cut-off points of WHtR to predict hypertension were 0.59 and 0.55 for women and men, respectively. Those to predict diabetes were 0.60 and 0.58 for women and men, respectively.

Conclusion - WHtR was a better predictor of hypertension and diabetes compared with BMI and WC in Chile. The definition of cut-off points specific for the Chilean population could be implemented in future screening programmes aiming to identify high risk individuals.



Dr Alessandro Laviano Editor in Chief *Nutrition* 9<sup>th</sup> June 2020

*Re: Response to the reviewers of the manuscript entitled* **"Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass index and waist circumference in the Chilean population?"** to *Nutrition.* 

Dear Dr Laviano,

Thank you very much for the feedback provided, which has helped us to improve the manuscript. We have addressed all issues raised by the reviewers.

On the online platform, three different files were uploaded: i) a revised manuscript, ii) revised manuscript with changes in red, and iii) rebuttal blinded letter.

Yours faithfully,

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#### Blinded response - NUT-D-20-00390

# Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass index and waist circumference in the Chilean population?

#### **Reviewers' comments**

1. It may be mentioned in the discussion that hip circumference was not measured.

**<u>Response</u>**: Thank you for this suggestion. This information was incorporated in the limitation section to read now:

"Finally, the CNHs did not count with other anthropometric measurements such as hip circumference. Therefore, further investigations considering a larger dataset and other anthropometric measurements should be carried out to generalise the obtained results."

Journal Rendon

#### Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass

#### index and waist circumference in the Chilean population?

- Waist-to-height ratio (WHtR) may be better predictors of cardiometabolic risk.
- In Chile, it is unclear if WHtR is a better predictor of hypertension and diabetes compared with BMI and WC.
- A bootstrapping approach was performed to determine which of these three anthropometric predicts the highest ROC and AUC.
- WHtR was a better predictor of hypertension and diabetes compared with BMI and WC in Chile.

Journal Preservoor

#### Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass

#### index and waist circumference in the Chilean population?

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#### **Conflict of interest**

None to declare.

#### Author contributions

FPR and AP generated the research question. FPR and AP planned the analysis. FPR performed the literature search. FPR and AP performed the analyses. FPR and AP wrote the first draft of the manuscript. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission. FPR is the guarantor.

#### **Ethical standard disclosure**

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The Chilean National Health Surveys were funded by the Chilean Ministry of Health and led by the Department of Public Health of the Pontificia Universidad Católica de Chile. The Chilean National Health Surveys were approved by the Ethics Research Committee of the Faculty of Medicine at the same university. All participants who participated provided written informed consent.

### Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass index and waist circumference in the Chilean population?

#### 3 Abstract

Objective – To identify which anthropometric measurements (body-mass-index [BMI], waist
circumference [WC], and waist-to-height ratio [WHtR]) is a better predictor of type 2 diabetes and
hypertension in the Chilean population.

Research Methods & Procedures – 13,044 participants (59.7% women) from the Chilean National
Health Surveys conducted in 2003, 2009-2010, and 2016-2017 were included. BMI, WC, and WHtR were
the anthropometric measurements evaluated. Hypertension was defined as systolic blood pressure ≥
10 140 mmHg and diastolic blood pressure ≥ 90 mmHg or on medication for hypertension. Diabetes was
defined as fasting glucose ≥7.0 mmol/L or on medication for diabetes. The Receiver Operating
Characteristics (ROC) curve and the Area Under Curve (AUC) were computed to derive the specificity
and sensitivity using a bootstrapping approach.

Results – Compared to BMI and WC, WHtR was the anthropometric measurement with the highest AUC curve in both sexes for hypertension (AUC for women: 0.70 [95% CI: 0.67 to 0.73] and AUC for men: 0.71 [95% CI: 0.69 to 0.74]) and diabetes (AUC for women: 0.71 [95% CI: 0.66 to 0.77] and AUC for men: 0.71 [95% CI: 0.67 to 0.76]). The sex-specific cut-off points of WHtR to predict hypertension were 0.59 and 0.55 for women and men, respectively. Those to predict diabetes were 0.60 and 0.58 for women and men, respectively.

Conclusion – WHtR was a better predictor of hypertension and diabetes compared with BMI and WC in
 Chile. The definition of cut-off points specific for the Chilean population could be implemented in future
 screening programmes aiming to identify high-risk individuals.

**Keywords:** Obesity; Morbidity; Risk Factors; Chronic disease; Cardiovascular diseases.

#### 24 Introduction

Obesity is an inflammatory, progressive, and chronic condition with a multifactorial aetiology and a huge physical, emotional and economic burden [1, 2]. More than 650 million people live with obesity worldwide and, in 2015, obesity was associated with 4 million deaths and 120 million disability-adjusted life-years worldwide [3]. Obesity is, therefore, one of the major risk factors for chronic diseases and cardiovascular risk factors, such as cardiovascular diseases (CVD), type 2 diabetes (hereafter called 'diabetes') and hypertension [1, 2].

Body mass index (BMI) - weight divided by height squared - is the most used measure to determine obesity in adults [2]. Quetelet was the first on proposing that the body mass in adults tends to vary with the square of height in 1835 [4]. Since that time, other anthropometric measurements have also been used to estimate not only the total body fat in the body (beyond the excess of body weight), but also to determine its visceral, abdominal and central distribution such as waist circumference (WC), waist-to-hip ratio and, more recently, waist-to-height ratio (WHtR) [5]. These measurements are not only effective indicators of abdominal obesity, but also more effective parameters predicting risk factors for CVD [6, 7].

In the last years, the use of BMI has been questioned because it does not consider the distribution of fat or the total muscle mass of the individuals. In fact, international cross-sectional and prospective studies have identified that WC or WHtR are better predictors of cardiometabolic risk than BMI [8]. Particular relevance has had WHtR in the last years since it has shown to be a better predictor of diabetes, hypertension and CVD than BMI and WC [8, 9].

Chile presents one of the highest prevalence of obesity and overweight in Latin America estimated by BMI (74.2%) [10, 11]. As a result, it is not surprising that the prevalence of cardiovascular risk factors associated with obesity, such as hypertension and diabetes, have increased in the country in the last twenty years [11-13]. Considering that is unclear which anthropometric measurement (BMI, WC or WHtR) is a better predictor of hypertension and diabetes in Chile, this study aimed to identify which of these three anthropometric measurements is a better predictor of diabetes and hypertension in the Chilean population.

#### 51 Methods

This study was based on participants aged  $\geq$  15 years from the three available Chilean National Health Surveys (CNHSs) conducted in 2003, 2009-2010, and 2016-2017. The CNHSs are a large, nationally representative population-based study of biological and lifestyle risk factors, dietary status, and health conducted every six years in both urban and rural zones [11-13]. Data for each survey were collected by trained staff where participants were administered guestionnaires, and anthropometrical and physiological measures, as well as biological samples, were obtained. A total of 15,145 participants (59.6% women) completed one of the three surveys (3,619; 5,293; and 6,233 in 2003, 2009-2010, and 2016-2017, respectively). Of them, 13,044 (59.7% women) had available information for all anthropometric markers, diabetes and hypertension. More information about each survey can be found elsewhere [11-13].

#### 62 Anthropometric measures

Weight was measured by a digital scale and height with a height rod in their home, with participants not wearing shoes and in light clothing through standardised methods and by trained nurses or midwives, as described elsewhere [11-13]. BMI was calculated as weight/height<sup>2</sup>. WC was measured at the midaxillary line at the midpoint between the costal margin and the iliac crest by an ergonomic circumference measuring tape. WHtR was computed as WC/height both in centimetres [11-13].

#### 68 Hypertension and diabetes

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90
mmHg or on medication for hypertension. On the other hand, diabetes was defined as fasting glucose
≥7.0 mmol/L or on medication for diabetes [11-13].

#### 72 Statistical analyses

All analyses were performed in Matlab R2019a. Descriptive characteristics, broken down by sex, are
 presented as means with standard deviations (SD) for quantitative variables or as percentages for
 categorical variables.

Linear binary classification seeks to divide the dataset into two different classes (hypertension vs. no hypertension and diabetes vs. no diabetes) using a continuous predictor variable that was defined, in this study, as: i) WC in cm; ii) WHtR (dimensionless quantity); and, iii) BMI in kg/m<sup>2</sup>. Performance evaluation required the computation of true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN) predicted for each anthropometric measurement. Identification of errors and correct predictions were carried out by the following measures:

 

•	Sensitivity (or true positive rate) defined as: Sensitivity =	$=\frac{TP}{TP+FN};$
		TP+FN'

- Specificity (or true negative rate) defined as: Specificity =  $\frac{TN}{TN+FP}$ ;
  - Error type I (or false positive rate) defined as:  $R_{FP} = \frac{FP}{TN+FP} = 1 Specificity$ ;
    - Error type II (or false negative rate) defined as:  $R_{FN} = \frac{FN}{TP+FN} = 1 Sensitivity$ .

The optimal value for each anthropometric measurement was computed minimising the sum of the errors ( $R_{FP} + R_{FN}$ ). We decided to use this approach, rather than other methods (e.g. Youden index, LR+, LR-), because we think it is important to balance between the numbers of false-positive and false-negative. The performances have been compared by means of the Receiver Operating Characteristics (ROC) curve and the Area Under Curve (AUC).

Ten thousand subsamples from the original dataset were randomly chosen with replacement to compute the ROC curve, its associated AUC value, and the corresponding confidence intervals using bootstrapping. Each bootstrap contained a sample size of 3,000 participants randomly chosen following a uniform distribution. In consequence, it covered between the 40 and 60% of the original dataset by sex. This method allowed the computation of 10,000 ROC curves and their respective AUC values. ROC curves and their associated AUC values were estimated for each anthropometric measure by sex and disease (hypertension and diabetes). Additionally, the optimal cut-off points and their 95% confidence intervals (95% CI) were calculated for each anthropometric measurement, sex, and disease. The 95% CI were empirically estimated following the same bootstrapping approach.

#### 100 Results

Table 1 describes the general characteristics of participants by sex. In summary, women and men had a
similar average age (48.7 versus 47.3 years); however, men had a higher body weight, height and WC
whilst women showed a higher BMI and WHtR. Furthermore, women were more likely to have diabetes
(14.0% versus 12.2%) while men hypertension (35.1% versus 39.6%).

Figure 1 and Table 2 present the ROC and AUC analyses for hypertension and diabetes by the different anthropometric measurements and sex. Employing the bootstrapping methodology, WHtR was the anthropometric measurement with the highest AUC for hypertension (AUC for women: 0.70 [95% CI: 0.67 to 0.73] and AUC for men: 0.71 [95% CI: 0.69 to 0.74]. Figure A1/A2) and diabetes (AUC for women: 0.71 [95% CI: 0.66 to 0.77] and AUC for men: 0.71 [95% CI: 0.67 to 0.76]. Figure B1/B2). In contrast, BMI showed the lowest AUC both in hypertension and diabetes for both sexes (hypertension= AUC for women: 0.63 [95% CI: 0.59 to 0.66] and AUC for men: 0.63 [95% CI: 0.61 to 0.66]; Diabetes= AUC for women: 0.66 [95% CI: 0.61 to 0.71] and AUC for men: 0.64 [95% CI: 0.59 to 0.69]). The aforementioned behaviour, in terms of differences of ROC curves, was even more marked for hypertension, where ROCcurves were more distanced among each other.

The optimal cut-off points for the three anthropometric measurements are also presented in Table 2. For hypertension, 0.59, 89.1 cm and 27.9 kg/m<sup>2</sup>, were the optimal cut-off points identified for WHtR, WC, and BMI, respectively, in women. On the other hand, for men, these cut-off points were 0.55, 93.0 cm and 26.9 kg/m<sup>2</sup>, respectively. In terms of diabetes, the optimal cut-off points identified for WHtR, WC, and BMI were 0.60, 92.5 cm and 29.1 kg/m<sup>2</sup>, respectively, for women. In men, in turn, the optimal cut-off points for diabetes were 0.58, 97.1 cm and 28.5 kg/m<sup>2</sup>, respectively (see Table 2 for the 95% Cl of each cut-off point).

#### 122 Discussion

The main finding of this study highlights that WHtR had a better predictive ability, based on AUC values, for hypertension and diabetes compared to BMI and WC for Chilean men and women. The sex-specific cut-off points for WHtR, based on the highest sensitivity and specificity, were 0.59 and 0.55 for hypertension in women and men, respectively. Those for predicting diabetes were 0.60 and 0.58 for women and men, respectively.

WHtR was first proposed in the middle of 1990s [5, 14]. At that time, a threshold of 0.50 was introduced as a first cut-off point for WHtR along with the simple message "keep your waist to less than half your height"[9, 15]. From that point onwards, different cut-off points for children, adolescents and adults have been proposed for different populations and countries worldwide [8, 9, 16-18]. These studies also concluded that WHtR is a better anthropometric approach than WC or BMI [8, 9]. As the measure of WHtR does not require weight scale - an instrument that could be costly and require a constant calibration - is a cost-effective alternative since for its evaluation is necessary a tape and a stadiometer only. Nevertheless, as the measure of WC requires trained professional, more people should be skilled on how to do a correct evaluation. 

Earlier studies have shown similar outcomes in terms of WHtR as a predictor for hypertension and diabetes, both internationally [8, 9, 16-18] as in Chile [19-24]. Ashwell et al. - in a systematic review and meta-analysis of 123,231 individuals from Europe, the Middle East, Australia, Asia, South America and the Caribbean from 31 studies- identified that WHtR had the highest AUC for hypertension and diabetes both in men (AUC for hypertension: 0.690 and AUC for diabetes: 0.711) and women (AUC for hypertension: 0.732 and AUC for diabetes: 0.753) in comparison to BMI and WC [8]. Nevertheless, in this meta-analysis, the studies were not necessarily representative of their respective national population. In Brazil, Castanheira et al. showed that WHtR was better than other anthropometric measurements to predict cardiometabolic risk outcomes [16]. In the Spanish population, this index showed the best ability

to determine both diabetes and CVD [17]. However, Battie et al. did not find a difference in the ability to
 predict hypertension or diabetes among WC, BMI and WHtR in Filipino-American women [18].

In Chile, few studies have used WHtR as a predictor of metabolic syndrome in children and adolescents [19-22], and as a predictor of cardiometabolic risk and obesity in adults [23, 24]. In fact, Koch et al., using data from 11,600 Chilean participants from the "San Francisco study", also demonstrated that WHtR was the measurement with the highest AUC value in the prediction of diabetes in women (AUC: 0.71) and hypertension both in men (AUC: 0.70) and women (AUC: 0.66) [24]. Though, this study was realised in one city of Chile only and did not use a representative sample of the Chilean population like this study. This limitation has also been identified in other studies conducted in Latin America [16].

Previous studies have highlighted why measurements of abdominal obesity are better than BMI in predicting cardiometabolic risk. For instance, BMI is unable to differentiate between lean mass and fat mass [25]. In addition, the metabolic and inflammatory activity of visceral fat, in comparison to other fat deposits in the body, cannot be determined by BMI [26]. However, why should WHtR be a better predictor than WC alone? The evidence points stature as a key component. Indeed, short stature has been associated with impaired  $\beta$ -Cell function, insulin resistance, diabetes, and coronary disease [27, 28]. A systematic review and meta-analysis conducted in 3,012,747 individuals, demonstrated that adults in the shortest category of height had a 50% higher risk of coronary heart disease morbidity and mortality than taller individuals [28]. Therefore, the combination of WC and height seems to be stronger when it is associated with morbidity and mortality. 

#### 165 <u>Strengths and limitations</u>

This study was performed employing all the available data from the CNHSs that are a nationally representative sample of the Chilean adult population. Furthermore, all the anthropometric measures were obtained following standardised protocols [11-13]. Although these data were collected during three different periods and on various participants, the bootstrapping methodology allowed us to model our data by resampling and performing inference from all the possible cases. Finally, the CNHs did not count with other anthropometric measurements such as hip circumference. Therefore, further investigations considering a larger dataset and other anthropometric measurements should be carried out to generalise the obtained results. 

174 Conclusion

WHtR was the anthropometric measure with the highest AUC for both hypertension and diabetes in
Chilean men and women. Defining country-specific cut-off points to identify high-risk individuals based
on WHtR could facilitate the future implementation of this measure in primary care.

#### 179 Acknowledgements

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#### 258 Table 1. Characteristics of the Chilean population by sex

			_
Variable	Women	Men	
Total, n	7,791	5,243	
Age (years), mean (SD)	48.7 (18.6)	47.3 (18.9)	
Weight (kg), mean (SD)	68.7 (14.2)	77.8 (14.3)	
Height (m), mean (SD)	1.55 (0.07)	1.68 (0.07)	
BMI (kg/m²), mean (SD)	28.7 (5.7)	27.5 (4.7)	
Waist circumference (cm), mean (SD)	90.9 (13.7)	94.2 (12.2)	\$
WHtR, mean (SD)	0.59 (0.09)	0.56 (0.08)	C
Hypertension, n (%)	2,732 (35.1)	2,079 (39.6)	0
Diabetes, n (%)	1,089 (14.0)	637 (12.2)	

260 BMI: body mass index; WHtR: waist-to-height ratio; SD: standard deviation.

Jonulua

49

AUC

**Cut-off points** 

Diabetes

0.71 (0.66; 0.77)

0.60 (0.58; 0.62)

Data presented as mean and their 95% CI using the bootstrapping methodology.

Johna

1

261	Table 2. Area u	inder the curve	(AUC) and cut-off	points for the anthro	opometric measureme	nts by sex				
262	and disease.									
				Women		Men				
	Variables		WHtR (95% CI)	WC cm (95% CI)	BMI kg/m <sup>2</sup> (95% CI)	WHtR (95% CI)	WC cm (95% CI)	BMI kg/m <sup>2</sup> (95% CI)		
	Hypertension	AUC	0.70 (0.67; 0.73)	0.66 (0.63; 0.70)	0.63 (0.59; 0.66)	0.71 (0.69; 0.74)	0.68 (0.65; 0.70)	0.63 (0.61; 0.66)		
	,	Cut-off points	0.59 (0.58; 0.60)	89.1 (87.5; 91.3)	27.9 (26.0; 29.7)	0.55 (0.53; 0.57)	93.0 (89.1; 96.1)	26.9 (26.2; 27.5)		

0.70 (0.65;0.75)

92.5 (89.0; 96.2)

0.66 (0.61; 0.71)

29.1 (27.0; 31.0)

0.71 (0.67; 0.76)

0.58 (0.57; 0.58)

0.69 (0.65; 0.74)

97.1 (91.0; 100)

0.64 (0.59; 0.69)

28.5 (26.5; 30.0)

1	265	Figure 1. ROC analyses for hypertension and diabetes by different anthropometric measures and sex
2	266	Figures A1 and A2 show the ROC for hypertension by women and men, respectively. Figures B1 and B2 show the
3	267	same information for diabetes.
5	268	ROC: Receiver Operating Characteristic; WHtR: waist-to-height ratio; WC: waist circumference; BMI: body mass
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#### Is waist-to-height ratio a better predictor of hypertension and type 2 diabetes than body mass

#### index and waist circumference in the Chilean population?

#### Author contributions

FPR and AP generated the research question. FPR and AP planned the analysis. FPR performed the literature search. FPR and AP performed the analyses. FPR and AP wrote the first draft of the manuscript. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission. FPR is the guarantor.

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