

Evaluation of Metabolic Syndrome in Adults of Talca City, Chile.

Verónica Mujica^{a,b}, Elba Leiva^b, Gloria Icaza^c, Nora Diaz^c, Miguel Arredondo^d, Rodrigo Moore-Carrasco^b, Roxana Orrego^b, Marcela Vásquez^b, Iván Palomo^b.

^a Diabetes and Cardiovascular Program, Maule Health Service, Talca, Chile.

^b Department of Clinical Biochemistry and Immunohematology, Health Sciences School, Universidad de Talca, Talca, Chile.

^c Institute of Mathematics and Physics, Universidad de Talca, Talca, Chile.

^d Institute of Nutrition and Food Technology, Universidad de Chile, Santiago, Chile

Running Title: Metabolic Syndrome in Chilean adults.

* To whom correspondence should be addressed:

Verónica Mujica, MD.

Department of Clinical Biochemistry and Immunohematology, School of Health Sciences, University of Talca, Talca City, Chile.

P.O. box: 747, Talca, Chile

E-mail: vmujica@utalca.cl

Phone: 56-71-200493

Fax: 56-71-200488

Word Count: 2.059

Tables: 3

Figures: 2

Key Word: Metabolic syndrome, Cardiovascular Diseases, Diabetes Mellitus.

Abstract

Background: Insulin resistance (IR) is an important risk factor for the type 2 Diabetes Mellitus (DM2) and cardiovascular disease (CVD). Metabolic Syndrome (MS) is a clustering of metabolic alterations associated to IR, however, there is no international consensus to define its diagnosis. Our objective was to evaluate the prevalence and characteristics of MS defined with the ATP III and IDF criteria in adults from Talca city.

Methods: We studied 1007 individuals, aged 18–74 years, and residents from Talca city. MS subjects were defined according ATP III (three altered factors) and IDF criteria (patients with waist circumference >80/90 cm (W/M) and two others altered factors).

Results: The prevalence of metabolic syndrome according to the IDF and ATP III criteria, after adjustment for age and sex, was 36.4% and 29.5%, respectively. The agreement for both criteria was 89%. The prevalence in men was higher than women in both MS definition, although not significant. MS probability increased with age, and the highest risk was in the 57-68 age group (ATP-MS) and 53-72 age group (IDF-MS). Hypertension, high triglycerides and abdominal obesity are the most frequent alterations in MS. MS prevalence in adults was higher diagnosed with IDF than ATP criterion, in both age is directly related with the MS presence. The MS subjects showed higher levels of blood pressure, waist circumference and plasma triglycerides.

Conclusion: It is preoccupant that one third of our population has a high risk of developing DM2 and CVD in the future.

Background

Insulin resistance (IR) is an important risk factor for the type 2 Diabetes Mellitus (DM2) and cardiovascular disease (CVD) [1]. It is characterized by a decrease on biologic insulin action, so plasmatic insulin levels are higher to keep normal glucose plasma levels [2].

Insulin sensitivity measurement is complex and expensive, so it has acquired importance the model proposed by Mathews et al. [3] that estimates the degree of IR at baseline by the homeostasis model assessment (HOMA-IR). Metabolic Syndrome (MS) is a clustering of metabolic alterations associated to IR, but conceptual differences exist between the currently available definitions [4]. Reaven [5] was the first that described this combination as a syndrome that he called IR syndrome or simply “X Syndrome”, later the World Health Organization (WHO) [6] named it as a Metabolic Syndrome. This definition based the diagnosis of MS on rather the presence of hypertension, hypertriglyceridemia, low HDL cholesterol (HDLc), hyperglycemia and/or, hyperinsulinism, but added the waist/hip ratio and urinary albumin excretion as components of this syndrome.

The progressive increase in obesity, CVD and MS prevalence motivated the National Education Cholesterol Program (NECP) on its third panel: *Treatment of High Blood Cholesterol in Adult (ATP III)* [7], to propose simple and clinic criteria to define the MS and by the presence of at least three altered factors: High blood pressure (BP), hypertriglyceridemia, low HDLc, high plasmatic glucose and abdominal obesity. This definition was simple, so various prospective studies incorporated this definition and determined its relation with CVD, but furthermore, the NCEP criteria have been criticized because the identification of those affected is strongly influenced by ethnicity [8], the thresholds were selected based on evidence from studies in Caucasian populations and

variability among ethnic groups was not taken into account since waist circumference and body composition are different in Asian and Hispanic populations [9].

The International Diabetes Federation (IDF) proposed a new definition for MS [10] that is based on the importance of abdominal obesity as a condition that must be present in all subjects with the syndrome, and that the threshold for waist circumferences must be defined in each country for its own ethnic groups [11]. In Latin-American populations, since there are not epidemiologic studies to define the best waist circumference cut-off points, they suggested considering the same values of south-Asiatic populations who consider altered waists over 80 cm in women and 90 cm in men. So IDF-MS is defined as abdominal obesity with the presence of two altered factors, same as the ATP-MS. IDF considered abnormal glucose over 100 mg/dl as was suggested by the American Diabetes Association (ADA) [12]. Furthermore, the American Association of Clinical Endocrinologist (AACE) and the American Heart Association (AHA) agreed about the lower glucose level but decided to keep the ATP III diagnosis criteria [13] for MS. Although there is controversy for the diagnosis, most of the authors agree that the presence of MS is associated with higher risk to develop DM2 and CVD [14-15] and they include as important factors for the diagnosis, the alterations in waist circumference, BP, HDLc, triglycerides and glucose levels.

If we consider the high incidence of MS in Chile and in Talca city [16], we decided to study the prevalence and characteristics of the MS by the IDF and ATP diagnosis criteria and the relative importance from its individual components.

Methods

Patients and samples

We studied 1007 subjects, aged 18 to 74 years old, residents from Talca city, Chile. The study group was selected from a probabilistic polietapic sampling scheme. Anthropometric and arterial blood pressure measurements and blood extractions (for glucose and lipids) were performed at the Clinical Laboratory of the Health Sciences School from Universidad de Talca. Informed consent was signed by all participant subjects. The protocol was approved by the ethic committee from Universidad de Talca and Health Service of Maule, Chile.

Diagnosis criteria for Metabolic Syndrome

The diagnosis criteria used for MS were: **a) According to ATP definition (ATP-MS):** three or more of the following factors: 1) Blood pressure: Systolic ≥ 130 mmHg and/or diastolic ≥ 85 mmHg and/or subjects who received anti hypertension drug therapy. 2) Triglycerides: ≥ 150 mg/dl; 3) HDL cholesterol: < 40 in men and < 50 mg/dl in women; 4) Plasmatic glucose: ≥ 100 mg/dl, and/or subjects who received anti diabetic drug therapy and 5) Waist circumference: > 102 cm in men and > 88 cm in women; and **b) MS according to IDF definition (IDF-MS):** Waist circumference over 90 cm in men and over 80 cm in women, and the presence of any two altered factors described above for the ATP criteria.

Statistical methods

MS prevalence was adjusted by population of Talca city distribution by age and sex according to last 2002 census. Means differences between sexes were evaluated using Student t-test. Agreement analysis was performed to compare diagnosis criteria with Mc-

Nemar test and Kappa statistic (17). We adjusted a generalized additive model, to evaluate the probability of MS associated with age under both criteria. We used a SAS 9.1.3., software for statistical analysis.

Results

From the 1007 total subjects, 37.5% presented overweight and 32.6% obesity, with 41.1% of abdominal obesity; 37% had high BP and 26.3% impaired fasting glucose; 40.1% of the studied subjects had high triglycerides and 21.5% had low HDLc. The anthropometric and biochemistry characteristics by sex are showed in table 1. There was no difference in age and BMI between men and women; however, all the other parameters were significantly different.

Prevalence of Metabolic syndrome.

449 (44.6%) subjects presented MS including both criteria ATP and/or IDF. 75% of them present the MS by both criteria. The average age in these patients was 51.6 ± 11.8 years old in patient diagnosis with ATP criteria and 51.1 ± 12.0 years old in individual diagnosis with IDF. The IDF criteria detected more prevalence of MS than ATP criteria (Table 2). 357 subjects (35.5%) were diagnostic as a MS by ATP criteria and 430 patients (42.7%) by IDF criteria. After adjusting for age and sex, the prevalence of MS by IDF was 36.4%, which is significantly higher than the prevalence found by ATP criteria (29.5%) ($p = 0.001$). Men showed higher MS prevalence, however, these differences were not significant (IDF: 39.0% y 34.0%, $p=0.138$; ATP: 30.1% y 29.0%, $p=0.786$ in men and women, respectively). The MS risk for age according both criteria is show in Figure 1A and 1B. MS probability increased with age, with the highest risk in the 57-68 age group (ATP-MS) and 53-72 age group (IDF-MS).

In relationship to the distribution of the involved factors, we observed a similar behavior for ATP and IDF MS that is expected if we consider that it exist an important over position between the subjects. High blood pressure, high triglycerides and increased waist circumference were the major components found in subjects with MS, independently of the criteria (Figure 2).

Analysis of the concordance from the different syndrome status

When we compare the concordance between both diagnosis criteria, the Kappa statistic was 0.77 (95% CI 0.73-0.81), that suggests a good concordance between the ATP and the IDF diagnosis for MS (Table 3). We evaluated the discrepancies in the diagnosis and we observed that IDF criteria was more likely to diagnose MS positive than ATP criteria (McNemar test: $p < 0.001$); 9.1% is considered with MS only by IDF, and 1.9% is considered with MS only by ATP criteria.

Discussion

MS presents a high prevalence in the world and in Chile [14]. In Latin America there are no other published studies about MS-IDF with the present waist circumference cut-off points. Park et al. [18] reported in Korean population, a MS-IDF prevalence of 13.5% in men and 15.0% in female, remarkably lower than our prevalence. Boehm et al. [19] studies in older German people (over 55 years old), showed an important discordance between both diagnosis criteria: in females a prevalence of 24% with ATP and 46% with IDF and in men 28% y 57%, respectively. These differ from our results that found 75% of concordance for both criteria.

The MS prevalence vary depending the diagnosis criteria, most are higher with IDF than ATP. Also there is marked disagreement if we consider the geographic regions and the ethnic origin, so it would be interesting to compare our findings with similar populations. The Chilean National Health Report showed a 27% of MS in Maule Region, results that are similar to the 31% reported for Americans of Hispanic origin [20]. Both groups used ATP criteria with glycaemia over 110 mg/dl so the criteria is not exactly the same, however, those prevalence are similar to the 29% found by our group for ATP-SM.

Other groups have reported important differences in the prevalence of MS by sex. The Americans did not find differences in the NECP study [20], neither did the Philippines [21], the Spanish in the Canary Islands [22] or Koreans [18]. We did not found significant difference by sex, even though with IDF criteria women present a tendency to show a higher prevalence. Nevertheless, there are many populations where there are marked differences by sex, as the Iranians in the Teheran study; they found a prevalence of 42% in women and 24% in men [23], something similar to the Hindu's study that reported 46.5% in women and 36.4% in men [24]. A Lithuania study, by IDF criteria, found a prevalence of 28.1% in men and 16.6% in women [25], similar to the San Antonio Heart Study that had 28.9% in men, and 20.8% in women [26]. Also, a similar prevalence was reported by Magi in Italians [27], but they found greater MS-ATP in women (27%) than men (22%).

The most frequent individual factor is the high blood pressure in most of the populations studied, for instance, Koreans [18], Philippines [21], Lithuanians [27], and Americans [28], and also in our MS subjects IDF as much as ATP, in both sex. Finally we think that cumulative evidence continues showing controversies about definition and the relationship of MS and CVD, so the best diagnosis criteria and its significance require more studies.

Author's contributions

VM and EL designed the research plan; GI and ND performed statistical analysis; RMC, RO and MV provided and analyzed specimens, VM, EL, MA and IP analyzed data and wrote the paper. All the authors read and approved the final manuscript.

Acknowledgements

Supported by Cardiovascular Diseases Factors Research Program (PIFRECV) (<http://pifrecv.usalca.cl>).

References

- 1 Alexander CM, Landsman PB, Teutsch SM, Haffner SM: **NCEP-Defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III Participants Age 50 Years and Older.** *Diabetes* 2003, **52**:1210-14.
- 2 Hollenbeck C, Reaven GM: **Variations in insulin stimulated glucose uptake in healthy individuals with glucose intolerance.** *J Clin Endocrinol Metab* 1987, **64**:1169-73.
- 3 Mathews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: **Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentration in man.** *Diabetologia* 1985, **28**:412-419.
- 4 Alberti KG, Zimmet PZ: **Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation.** *Diabet Med* 1998, **15**:539–553.

- 5 Raven GM: **Insulin resistance, cardiovascular disease and the metabolic syndrome: how well do the emperor's clothes fit?** *Diabetes Care* 2004, **27**:1011-1012.
- 6 WHO consultation: **Definition, diagnosis and classification of diabetes mellitus and its complication.** *WHO/NCD/XXXX*, **99**.2:31-33.
- 7 Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults: **Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and treatment of High Cholesterol.** *JAMA* 2001, **285**:2486–2497.
- 8 Palaniappan LP, Carnethon MR, Fortmann SP: **Heterogeneity in the relationship between ethnicity, BMI, and fasting insulin.** *Diabetes Care* 2002, **25**:1351–1357.
- 9 Rush E, Plank L, Chandu V, Laulu M, Simmons D, Yajnik C: **Body size, body composition, and fat distribution: a comparison of young New Zealand men of European, Pacific Island, and Asian Indian ethnicities.** *N Z Med J* 2004, **117**: U1218.
- 10 Alberti KG, Zimmet P, Shaw J: IDF Epidemiology Task Force Consensus Group: The metabolic syndrome -a worldwide definition. *Lancet* 2005, **366**:1059–1062.
- 11 Katzmarzyk PT, Janssen I, Ross R, Church TS, and Blair SN: **The Importance of Waist Circumference in the Definition of Metabolic Syndrome: Prospective analyses of mortality in men.** *Diabetes Care* 2006, **29**(2): 404-409.
- 12 Shaw JE, Zimmet PZ, Alberti KG: **Point: Impaired Fasting Glucose: The Case for the New American Diabetes Association Criterion.** *Diabetes Care* 2006, **29**:1170-1172.
- 13 Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC, Lenfant C: **Definition of metabolic syndrome: report of the National Heart, Lung, and Blood.**

- Institute/American Heart Association conference on scientific issues related to definition.** *Circulation* 2004, **109**:433-438.
- 14 Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB, Wilson PW: **Insulin resistance, the metabolic syndrome, and incident cardiovascular events in the Framingham Offspring Study.** *Diabetes* 2005, **54**: 3252–3257.
 - 15 Sierra-Johnson J, Johnson BD, Allison TG, Bailey KR, Schwartz GL, Turner ST: **Correspondence between the adult treatment panel III criteria for metabolic syndrome and insulin.** *Diabetes Care* 2006, **29**:668–672.
 - 16 Ministerio de Salud de Chile. **Encuesta Nacional de Salud 2003.** Departamento de Salud Pública de la Pontificia Universidad Católica de Chile: *Informe Técnico.* 2003
 - 17 Pfeiffer R, Castle P: **With or without a gold standard.** *Epidemiology* 2005, **16**:595-97.
 - 18 Park HS, Lee SY, Kim SM, Han JH, Kim DJ: **Prevalence of the metabolic syndrome among Korean adults according to the criteria of the International Diabetes Federation.** *Diabetes Care* 2006, **29**: 933-934.
 - 19 Boehm BO, Claudi-Boehm S, Yildirim S: **Prevalence of the Metabolic Syndrome in Southwest Germany.** *Scand J Clin Lab Invest Suppl.* 2005, **240**:122–128.
 - 20 Ford ES, Giles WH, Dietz WH: **Prevalence of the Metabolic Syndrome among US Adults Findings From the Third National Health and Nutrition Examination Survey.** *JAMA* 2002, **287**:356-359.
 - 21 Tanchoco CC, Cruz AJ, Duante CA, Litonjua AD: **Prevalence of metabolic syndrome among Filipino adults aged 20 years and over.** *Asia Pac J Clin Nutr* 2003, **12(3)**:271-6.
 - 22 Cordero A, Alegría E and Leon M. **Prevalencia de Síndrome Metabólico.** *Rev Esp Cardiol* 2005, **5**:11D–15D.

- 23 Azizi F, Salehi P, Zahedi-Asl S: **Prevalence of metabolic syndrome in an urban population: Tehran lipid and glucose study.** *Diabetes Res Clin Pract* 2003, **61**:29-37.
- 24 Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V: **Metabolic syndrome in urban Asian Indian adults: a population study using modified ATP III criteria.** *Diabetes Res Clin Pract* 2003, **60**:199-204.
- 25 Gustiene O, Slapikas R, Klumbiene J, Sakalauskiene G, Kubilius R, Zaliūnas R. **The prevalence of Metabolic Syndrome.** *Medicine Kaunas*, 2005, **41**:867-76.
- 26 Lorenzo C, Williams K, Hunt KJ, Haffner SM: **Trend in the prevalence of the metabolic syndrome and its impact on cardiovascular disease incidence: the San Antonio Heart Study.** *Diabetes Care* 2006, **29**:625–630.
- 27 Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F: **Prevalence of the metabolic syndrome among Italian adults according to ATP III definition.** *Nutr Metab Cardiovasc Dis.* 2005, **15(4)**:250-4.
- 28 Hanley AJ, Williams K, Stern MP, Haffner SM: **Homeostasis model assessment of insulin resistance in relation to the incidence of cardiovascular disease: the San Antonio Heart Study.** *Diabetes Care* 2002, **25**:1177–1184.

Figure Legend

Figure 1: Prevalence of Metabolic Syndrome according age with IDF and ATP criteria.

Figure 2: Distribution of altered factors in MS subjects according ATP and IDF criteria.

Table 1: Characteristics of studied subjects by sex (n=1007).

	Men	Women
	Mean \pm SD	Mean \pm SD
N	339 (%)	668 (%)
Age (years)	44,3 \pm 15,1	45,6 \pm 13,5
BMI (Kg/m ²)	28,3 \pm 4,5	28,5 \pm 5,8
Waist circumference (cms)	96,3 \pm 12,0	89,2 \pm 13,0*
Systolic blood pressure (mmHg)	133,8 \pm 19,6	124,5 \pm 20,8*
Diastolic blood pressure (mmHg)	80,7 \pm 12,4	75,8 \pm 11,0*
Triglycerides (mg/dl)	190,4 \pm 175,2	147,6 \pm 95,4*
HDLc (mg/dl)	45,8 \pm 12,3	55,0 \pm 15,3*
Glucose (mg/dl)	100,2 \pm 29,2	93,7 \pm 24,1*

HDLc: HDL cholesterol

* Student t-test: $p < 0.05$

Table 2:**Characteristics of subjects with Metabolic Syndrome ATP and IDF definition**

	Male		Female	
	ATP	IDF	ATP	IDF
N	117	155	240	275
BMI (Kg/mt ²)	31,0 ± 4,3	30,5 ± 3,9	32,5 ± 5,8	31,9 ± 5,6
Waist circumference (cms)	104,5 ± 11,2	103,0 ± 9,9	99,2 ± 11,0	97,7 ± 10,9
Systolic blood pressure (mmHg)	143,7 ± 18,9	141,1 ± 19,3	136,5 ± 21,8	135,3 ± 22,0
Diastolic blood pressure (mmHg)	86,8 ± 12,0	85,9 ± 12,4	81,5 ± 11,1	80,8 ± 11,1
Triglycerides (mg/dl)	282,1 ± 250,9	260,9 ± 227,8	201,3 ± 115,1	201,9 ± 117,2
HDLc (mg/dl)	40,7 ± 11,4	40,4 ± 10,3	46,7 ± 11,6	47,5 ± 12,5
Glucose (mg/dl)	115,6 ± 39,1	111,9 ± 38,3	106,0 ± 33,1	104,5 ± 32,3

Data are means ± SD unless other was indicated.

Table 3: ATP and IDF agreement analysis

	ATP	
IDF	Positive	Negative
Positive	338 (33.6%)	92 (9.1%)
Negative	19 (1.9%)	558 (55.4%)

Figure 1

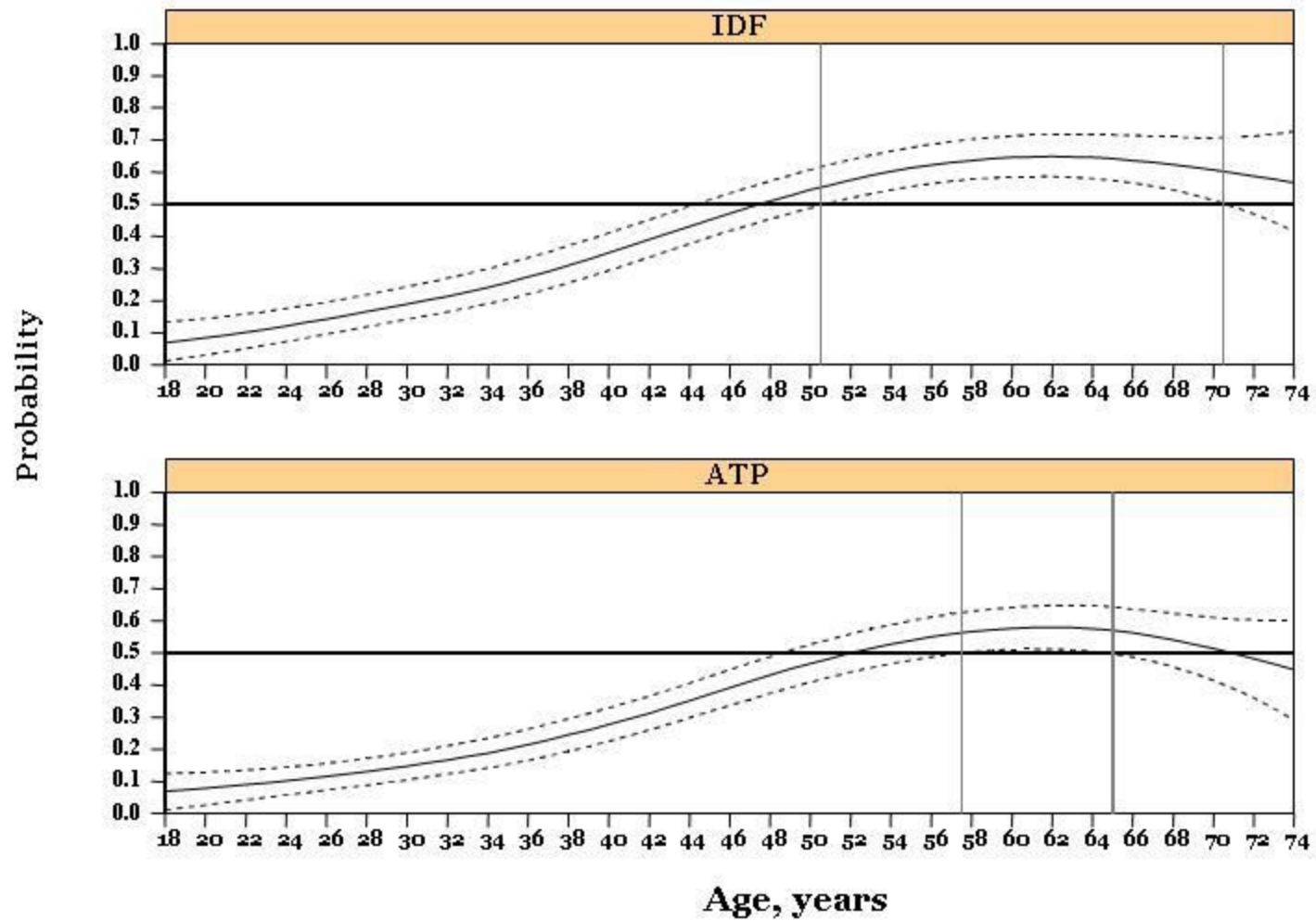


Figure 2

