ΣΥΓΚΡΙΤΙΚΗ ΜΕΛΕΤΗ ΠΡΟΓΝΩΣΤΙΚΗΣ ΑΞΙΑΣ ΚΑΡΔΙΑΓΓΕΙΑΚΟΥ ΚΙΝΔΥΝΟΥ:

FRAMINGHAM RISK SCORE

VS

ΚΡΙΤΗΡΙΑ ΜΕΤΑΒΟΛΙΚΟΥ ΣΥΝΔΡΟΜΟΥ

Π. Τσατραφύλλιας, Δ. Θεοδωράκης, Ευδοξία Μπουτμπάρα, Δήμητρα Κεσίδου, Θ. Γεωργιάδης, Σ. Παραστατίδης, Γεωργία Θεοδωροπούλου, Χριστίνα Διδασκάλου

Ιατρείο Υπέρτασης, Κέντρο Υγείας Πολυκάστρου

ΕΙΣΑΓΩΓΗ

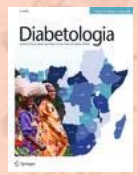
Mancia, Giuseppe; Bombelli, Michele; Corrao, Giovanni; Facchetti, Rita; Madotto, Fabiana; Giannattasio, Cristina; Trevano, Fosca Quarti; Grassi, Guido; Zanchetti, Alberto; Sega, Roberto
Metabolic Syndrome in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) Study: Daily Life Blood Pressure, Cardiac Damage, and Prognosis
Hypertension:Volume 49(1)January 2007pp 40-47

D. Mozaffarian, A. Kamineni, R. J. Prineas, and D. S. Siscovick
Metabolic Syndrome and Mortality in Older Adults: The Cardiovascular Health Study
Arch Intern Med, May 12, 2008; 168(9): 969 - 978.

Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes.
Diabetes Care. 2005.28:2289-2304.

J. Wang, S. Ruotsalainen, L. Moilanen, P. Lepisto, M. Laakso, and J. Kuusisto
The Metabolic Syndrome Predicts Incident Stroke: A 14-Year Follow-Up Study in Elderly People in Finland
Stroke, April 1, 2008; 39(4): 1078 - 1083.

T. Ninomiya, M. Kubo, Y. Doi, K. Yonemoto, Y. Tanizaki, M. Rahman, H. Arima, K. Tsuryuya, M. Iida, and Y. Kiyohara
Impact of Metabolic Syndrome on the Development of Cardiovascular Disease in a General Japanese Population: The Hisayama Study
Stroke, July 1, 2007; 38(7): 2063 - 2069.



Gale E: The myth of the metabolic syndrome. *Diabetologia 2005*: *48: 1679-1683*,2005

J.-P. Empana, P. Duciemetiere, B. Balkau, and X. Jouven
Contribution of the metabolic syndrome to sudden death risk in asymptomatic men: the Paris Prospective Study I
Eur. Heart J., May 1, 2007; 28(9): 1149 - 1154.

C. Lorenzo, K. Williams, K. J. Hunt, and S. M. Haffner
The National Cholesterol Education Program-Adult Treatment Panel III, International Diabetes Federation, and World Health Organization Definitions of the Metabolic Syndrome as Predictors of Incident Cardiovascular Disease and Diabetes
Diabetes Care, January 1, 2007; 30(1): 8 - 13.

ΕΙΣΑΓΩΓΗ

Should we dump the metabolic syndrome?

The number of people with the metabolic syndrome is rising alongside obesity. Nevertheless, **Edwin Gale** believes the diagnosis has little practical value. **George Alberti** and **P Z Zimmet,** however, think it increases the detection of people at high risk of diabetes and heart disease

Edwin A M Gale professor of diabetes, Diabetes and Metabolism, University of Bristol, Medical School Unit, Southmead Hospital, Bristol BS10 5NB
Edwin.Gale@bristol.ac.uk

YES Type 2 diabetes and lesser degrees of glucose intolerance are associated with insulin resistance, central obesity, hypertension, and dyslipidaemia. The term metabolic syndrome describes the same constellation, with or without glucose intolerance. Although these associations are well established, their pathophysiological basis remains unclear, and no unifying feature has emerged. Attempts have been made to assemble the various features of the metabolic syndrome into a single all-purpose definition, for which diagnostic, prognostic, and therapeutic value has been claimed. Diagnosis of the metabolic syndrome is redundant in those who already have diabetes and adds nothing to the management of those who do not.

Unclear definition

A cluster of clinical features constitutes a syndrome, but attempts to define the metabolic syndrome as a clinical entity have been hampered by the lack of an agreed unifying feature. The grouping was first described in patients with type 2 diabetes,[1] and the wider concept of a "metabolic" syndrome arose when Gerald Reaven suggested that the common factor was insulin resistance rather than diabetes.[2] Insulin resistance is, however, unsatisfactory as a core feature, for it cannot be defined or measured easily and is inconsistently related to the individual features of the syndrome.[3]

International Diabetes Federation definition of metabolic syndrome[4]

Presence of central obesity—Waist circumference varies with ethnicity (see bmj.com). If body mass index is >30 central obesity can be assumed
Plus any two of the following:
Triglyceride concentration ≥1.7 mmol/l or specific treatment for this lipid abnormality
High density lipoprotein cholesterol <1.03 mmol/l in men, <1.29 mmol/l in women, or specific treatment for hypercholesterolaemia
Systolic blood pressure ≥130 mm Hg or diastolic ≥85 mmol/l, or treatment for hypertension
Fasting plasma glucose ≥5.6 mmol/l or previously diagnosed glucose type 2 diabetes. If ≥5.6 mmol/l, oral glucose tolerance test is strongly recommended but is not necessary to diagnose the syndrome

Expert panels have made various attempts to establish a working definition using different scoring systems.[4 5] The endeavour was complicated by uncertainty about which associated features to include, what thresholds to set, and what exactly the experts were trying to achieve. The schemes that emerged have proved useful for statistical analysis and epidemiological comparison, but not for clinicians, who hardly ever record the diagnosis.[6]

The most recent definition, proposed by an expert committee of the International Diabetes Federation, bases the syndrome around a new core feature, central obesity, and is intended for clinical use (box).[4] Representatives of the American Diabetes Association and the European Association for the Study of Diabetes have, however, argued that any such attempt is premature.[5] This is not a turf war: the confrontation reflects perplexity within the diabetes community. One party maintains that a working definition is needed to resolve existing confusion; the other party argues that an inadequate definition merely adds to it.

The metabolic syndrome is a handy clinical label that lacks a useful definition

The proposed definition of the metabolic syndrome embraces overt diabetes and people with established cardiovascular disease, yet also purports to predict these as outcomes.[2] The "now you see it, now you don't" approach to diabetes means that it can be included when estimating the apparent health consequences of the syndrome in population studies, yet becomes an end point in predictive analyses. From a more practical point of view, energetic screening and treatment for obesity, hypertension, and dyslipidaemia already form the basis of managing diabetes. Diagnosis of the metabolic syndrome adds nothing to the understanding or management of people with known diabetes and is therefore redundant. Future consideration of the syndrome should exclude diabetes and known cardiovascular disease.[3]

Clinical value

The quest for a worldwide index of the health implications of central obesity is praiseworthy but problematic, given the limitations of waist circumference as a surrogate.[3] Clinical measures do not need to be perfect, but they do need to be consistent, and the relation between girth and fat distribution varies from one population to another. Different waist measures are needed for different ethnic groups, and race—for which no good definition exists—thus enters the equation (table).[4] Use of a sliding scale for waist circumference has the further consequence that an independent yardstick—cardiovascular risk—is then needed to calibrate one population with the next. The result is a circular definition, for vascular risk defines the syndrome and the syndrome defines vascular risk.

Diagnosis of the metabolic syndrome enhances prediction of diabetes and cardiovascular disease, if these are not already present, but impaired glucose tolerance alone is better than the combined features of the syndrome in predicting diabetes,[3,5] and it is unsurprising that combining known cardiovascular risk factors enhances cardiovascular risk. The metabolic syndrome is consistently outperformed by scoring systems that incorporate age, sex, and smoking together with personal and family history of heart disease. These have the further advantage of treating continuous variables as continuous, whereas the metabolic syndrome treats them as dichotomous.[3,5]

In sum, the metabolic syndrome is a handy clinical label that lacks a useful definition. The latest attempt is characterised by an elastic measure of the proposed unifying feature—central obesity—and has no agreed pathophysiological basis. A flourishing academic industry has been founded on a diagnostic artefact with little prognostic or therapeutic value. Reaven himself bids farewell to his syndrome, in so far as clinical value is concerned, with the words *requiescat in pace* (rest in peace).[3] To which we may add, Amen.

Competing interests: None declared.

People with metabolic syndrome have been characterised as being apple shaped rather than pear shaped

K G M M Alberti senior research investigator, Department of Endocrinology and Metabolism, St Mary's Hospital and Imperial College, London
george.alberti@gmail.co.uk
P Z Zimmet director International Diabetes Institute, Melbourne, Australia

NO The clustering of several disorders associated with increased risk of cardiovascular disease has been recognised for over 80 years,[1] making claims that the drug industry invented the syndrome lack credibility. However, the modern concept of the metabolic syndrome started in 1988 with Reaven describing the clustering of insulin resistance, hyperinsulinaemia, glucose intolerance, hypertension, raised triglyceride concentration, and low high density lipoprotein cholesterol concentration.[2]

Over the next decade other features, most notably central obesity, were found to be associated with this cluster. There was little argument about the existence of the clustering but confusion about its diagnosis. Different criteria abounded, the most widely used coming from the World Health Organization[3] and the National Cholesterol Education Programme (adult treatment panel III).[4] The International Diabetes Federation then brought the various groups together recommending a diagnostic set[5] which was similar to the updated version of adult treatment panel III.[6]

Recognising that the syndrome provides a simple public health strategy to define those at higher risk, the federation's definition provided a stepwise approach, with measurement of waist as a simple initial screening test followed by assessment of the other components (hyperglycaemia, hypertension, raised triglyceride concentration, low high density lipoprotein cholesterol concentration).

Several other factors are associated with this cluster but the federation felt that a practical set of measurements was needed that could be used in most primary care and hospital settings worldwide. Thus it did not include insulin resistance because it cannot easily be measured.

The syndrome is becoming increasingly prevalent because of the current epidemic of obesity and sedentary lifestyle.[7 8] It highlights the form of obesity that is associated with increased risk of diabetes and cardiovascular disease and pinpoints those at risk allowing targeted therapy.

Importance of a name

Recently the American Diabetes Association and the European Association for the Study of Diabetes questioned both the existence and usefulness of the metabolic syndrome.[9] It was a comprehensive and thought provoking review which may have heightened interest in the syndrome but missed the point.

The review started by asking whether it was a syndrome at all. At its simplest syndrome means a collection of things. Our definition of metabolic syndrome is stronger: a cluster of inter-related risk factors for cardiovascular disease and diabetes with association greater than by chance alone. This has been shown repeatedly.[10 11]

Focus on the syndrome has brought diabetologists and cardiologists together

Although the aetiology of the syndrome is uncertain, strong hypotheses implicate central adiposity, insulin resistance, and low grade inflammation.[10] Aetiology is unknown for many other conditions whose existence is accepted, including type 2 diabetes. The syndrome is not creating a new disease but identifies a risk state, like pre-diabetes (which was created by the American Diabetes Association) or dyslipidaemia.

Identifying risk

Although the syndrome has had several definitions during its evolution, today there are two main closely related definitions, as described above.[5 6] Both use specific cut-off points for continuous variables, which allows them to be used in all clinical settings.

The use of cut-off points is common throughout medicine where yes or no answers are the norm, including in the diagnosis of hypertension or diabetes. The decision to use different waist cut-off values for different ethnic groups is supported by available data that relate waist circumference to risk of diabetes and cardiovascular disease. For example, the prevalence of type 2 diabetes is consistently higher among Asians than Europids at any level of excess abdominal fat.[4 12]

The syndrome is not intended to give an absolute risk of cardiovascular disease or diabetes but to highlight people at increased relative risk on whom doctors can then focus. Absolute risk would require information on other factors such as low density lipoprotein cholesterol concentration, family history, age, and smoking. The question also arises whether the risk associated with the syndrome is greater than the sum of the parts. The evidence is equivocal, but again it is irrelevant—risk increases with the number of abnormal components.

We believe the syndrome has clinical value. In the specialised academic world of the syndrome's critics, every person may automatically have all known risk factors checked routinely but in the "real world" of primary health care, this definition helps identify people at high risk without the need for sophisticated technology. The federation's[4] recommendations provide a simple approach that allows the identification of most people who are at risk. Other measurements can then be made and preventive steps taken to reduce the long term burden of disease. Although lifestyle measures are of prime importance, sometimes drug treatment is needed.

Focus on the syndrome has brought diabetologists and cardiologists together, ensuring better appreciation of risk of diabetes among cardiologists and cardiovascular disease among diabetologists. This results in better management of people with type 2 diabetes, given that over 70% of them may die from cardiovascular disease. The outcome is that clinicians are focused on high risk patients.

The increased prevalence of the underlying causes of the metabolic syndrome (obesity and sedentary lifestyle) portends an enormous increase in cardiovascular disease and type 2 diabetes worldwide.[4] The diagnosis of the metabolic syndrome provides a focus on the cluster of cardiovascular disease and diabetes risk factors that require attention and emphasises the multifactorial nature of the risk for these diseases. So the syndrome has an important role in public health and individual care.

Competing interests: None declared.

The table and all references are in the version on bmj.com

WHERE DO YOU STAND ON THE ISSUE? Tell us on bmj.com

BMJ MARCH 2008, vol 336

ΣΚΟΠΟΣ

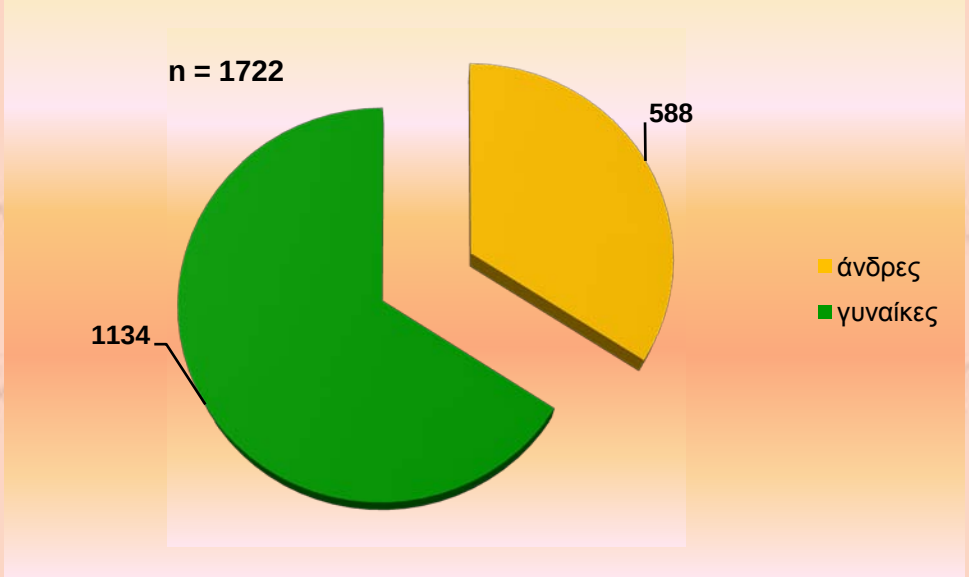
Εκτίμηση των διαγνωστικών εργαλείων της ΠΦΥ

Framingham Risk Score και **MetS**

στην εκδήλωση Στεφανιαίας Νόσου.

ΥΛΙΚΟ - ΜΕΘΟΔΟΣ

Αναδρομική μελέτη



- Ηλικία: 58±8 χρόνια
- BMI: 29,7±4,4
- Διάρκεια υπέρτασης: 4±6 έτη

ΥΛΙΚΟ - ΜΕΘΟΔΟΣ

Framingham Risk Score

10ετής απόλυτος θεωρητικός ΚΑ κίνδυνος > 20%

Φύλο

Ηλικία

Συστολική ΑΠ

Ολική χοληστερόλη

HDL χοληστερόλη

ΣΔ

Κάπνισμα

Υπερτροφία (ΑΡ) κοιλίας

MetS κατά NCEP-ATPIII

3 ή περισσοτέρων από:

περίμετρος μέσης (άνδρες> 102cm και γυναίκες > 88cm)

υπερτριγλυκεριδαιμία (>150mg/dl),

χαμηλά επίπεδα HDL (<40mg/dl στους άνδρες και <50mg/dl στις γυναίκες),

αρτηριακή υπέρταση (ΣΑΠ>130mmHg και/ή ΔΑΠ>85mmHg ή λήψη αντιϋπερτασικής αγωγής)

υψηλό **σάκχαρο νηστείας** (ή λήψη αντιδιαβητικής αγωγής)

Στο ιστορικό των ασθενών αναζητήθηκε η χρήση καπνού και το οικογενειακό ιστορικό ΚΑΝ ή/και ΣΔ.

ΥΛΙΚΟ - ΜΕΘΟΔΟΣ

Υπόθεση: σε άνδρες >45 ετών και σε γυναίκες >55 ετών, που έχουν μεγαλύτερο κίνδυνο ανάπτυξης ΚΑΝ, το MetS θα αποτελούσε επίσης έναν καλό δείκτη προσδιορισμού της ανάπτυξης ΚΑΝ σε σχέση με το Framingham Risk Chart.

ΥΛΙΚΟ - ΜΕΘΟΔΟΣ

Τελικό σημείο: η εμφάνιση καρδιαγγειακής νόσου

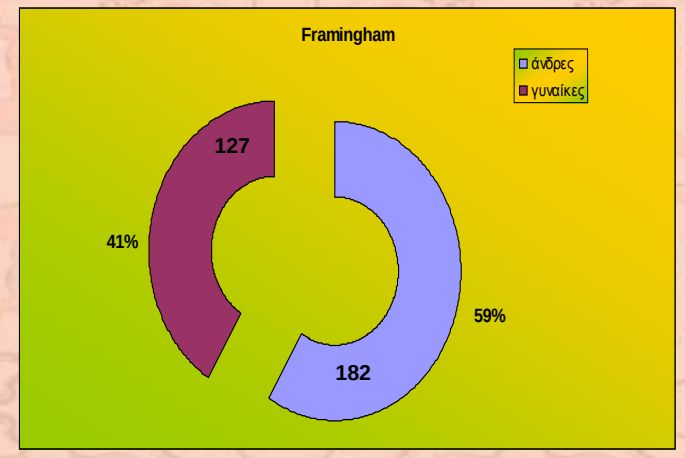
- Έμφραγμα μυοκαρδίου
- Στηθάγχη
- Αορτοστεφανιαία παράκαμψη
- ΑΕΕ

Ασθενείς που πριν την μελέτη υπέστησαν στεφανιαίο ή εγκεφαλικό επεισόδιο ή απεβίωσαν κατά την διάρκεια της δεκαετίας από άλλη αιτία διαγράφτηκαν.

Ανάλυση με τη χρησιμοποίηση του κριτηρίου x^2, με σημαντική πιθανότητα λάθους 5% ($p< 0.05$)

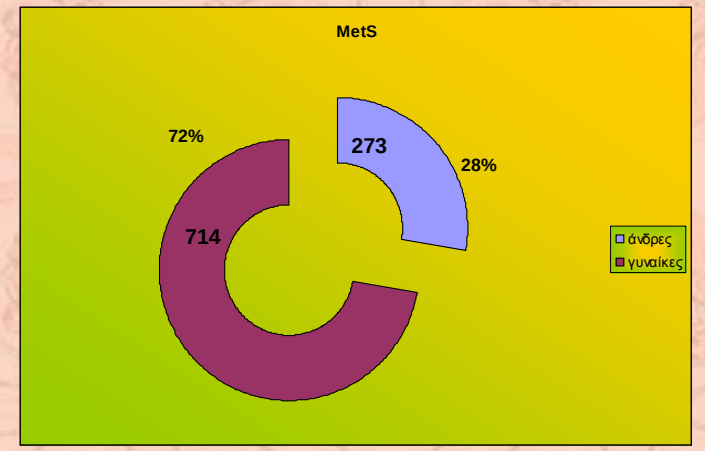
ΥΛΙΚΟ - ΜΕΘΟΔΟΣ

n= 309



y= 62 ± 5

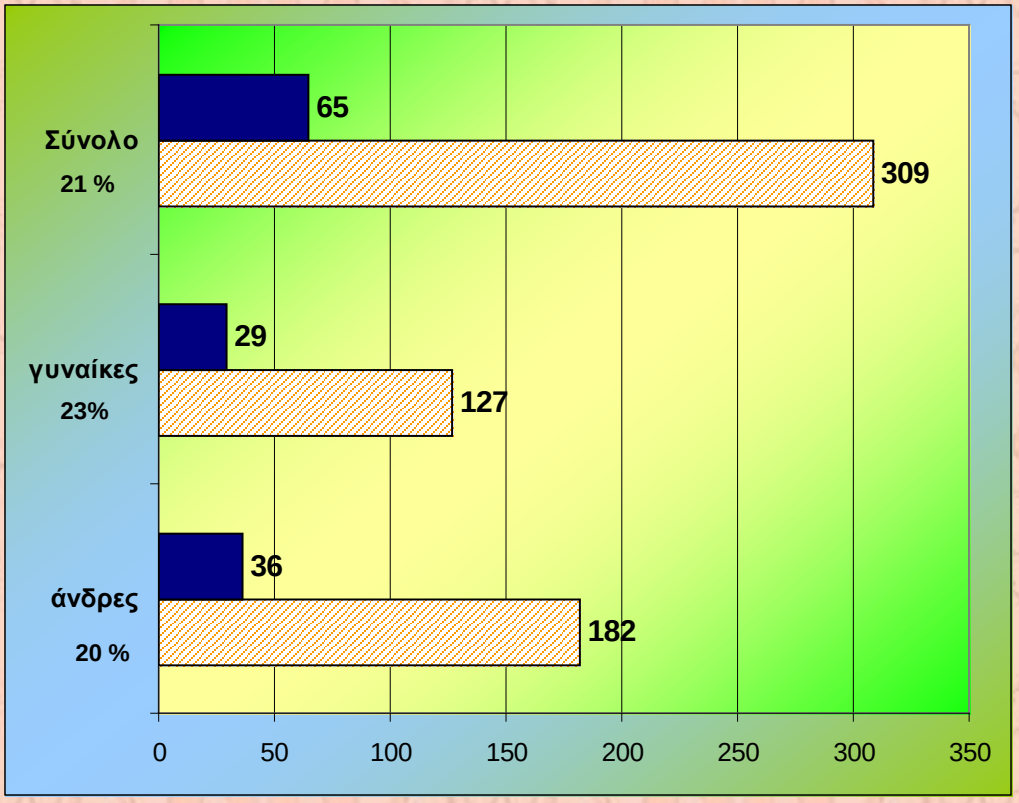
n= 987



y= 58 ± 8

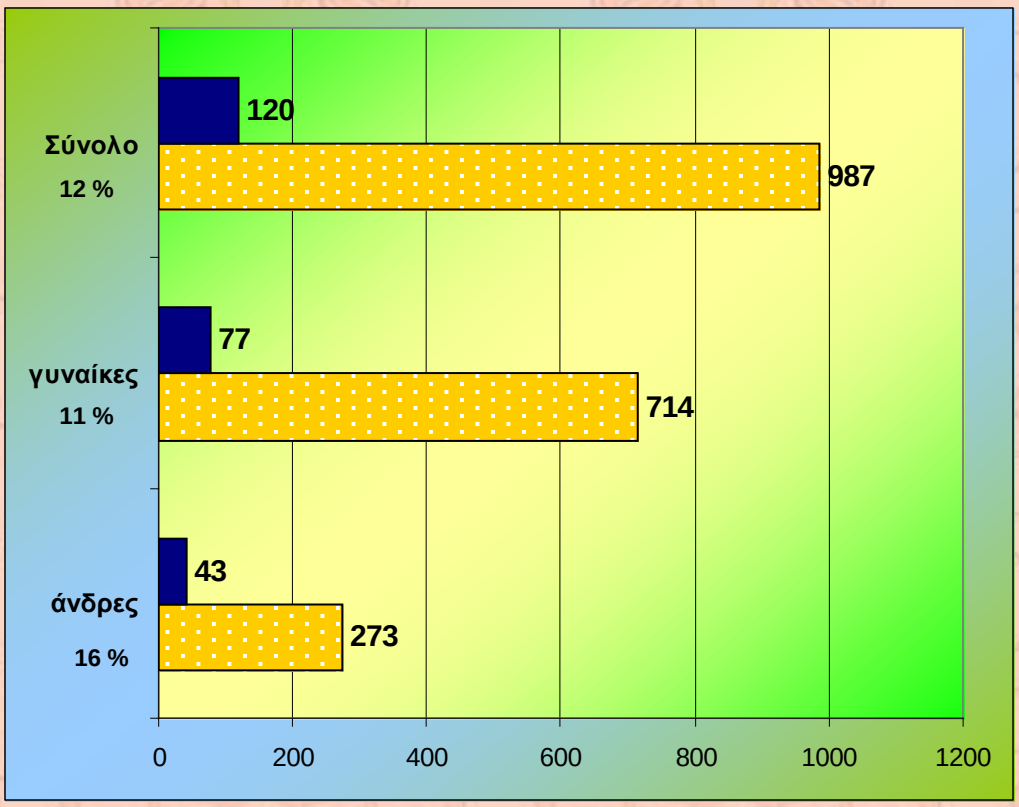
ΑΠΟΤΕΛΕΣΜΑΤΑ

Framingham risk score

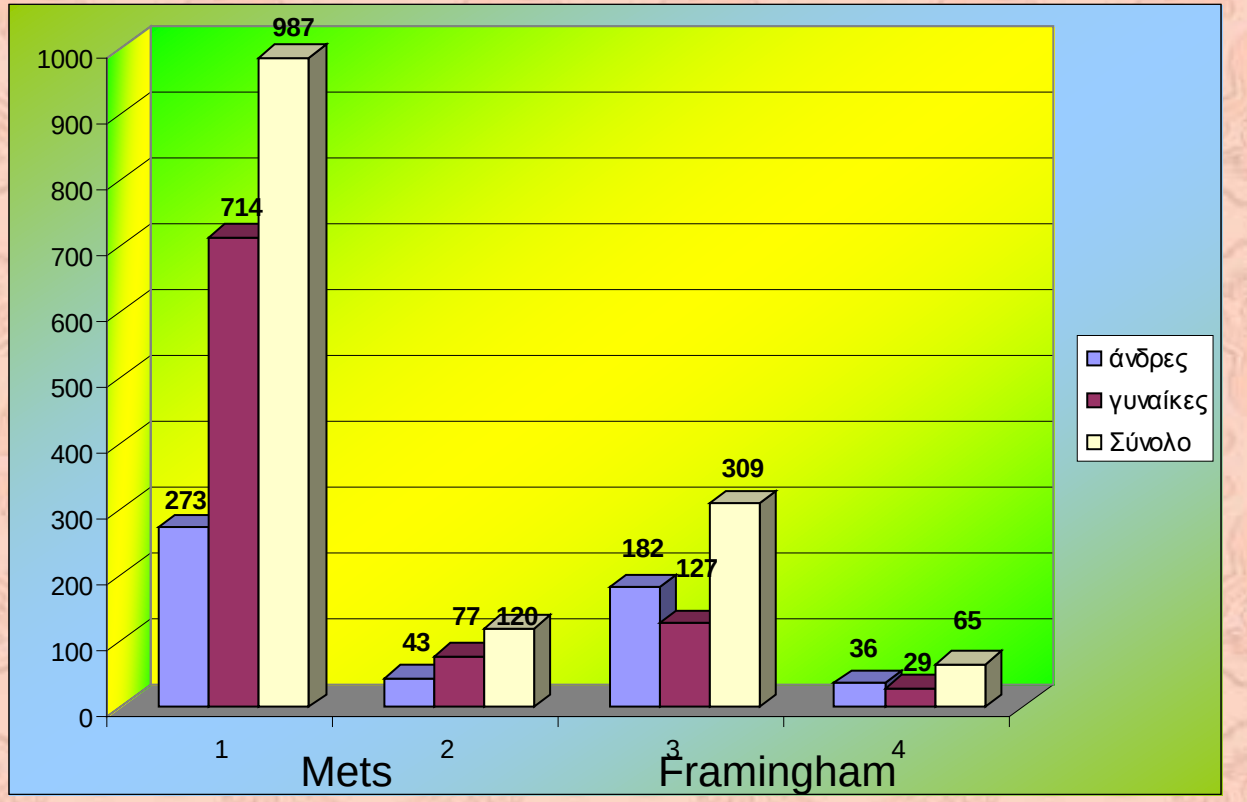


ΑΠΟΤΕΛΕΣΜΑΤΑ

MetS



ΑΠΟΤΕΛΕΣΜΑΤΑ



Σύνολο	**p < 0.005**
Άνδρες	**p = NS**
Γυναίκες	**p < 0.005**

ΣΥΜΠΕΡΑΣΜΑΤΑ

Η εκδήλωση ΚΑΝ στους ασθενείς με δείκτη Framingham Risk Chart > 20 % ήταν αυξημένη σε σχέση με αυτούς που πληρούσαν τα κριτήρια του MetS,στο σύνολο των ασθενών και στις γυναίκες, αλλά όχι και στο ανδρικό φύλο.

ΣΥΜΠΕΡΑΣΜΑΤΑ

Επομένως, η εξίσωση του Anderson από τη μελέτη Framingham μπορεί γενικά να χρησιμοποιηθεί καλύτερα σαν αδρός δείκτης κατηγοριοποίησης καρδιαγγειακού κινδύνου στην ΠΦΥ, χρήζει όμως περαιτέρω διερεύνησης η διαφοροποίηση ανάμεσα στα φύλα.

ΕΥΧΑΡΙΣΤΩ