

# The incidence and persistence of the NCEP (National Cholesterol Education Program) metabolic syndrome. The French D.E.S.I.R. study

B Balkau, M Vernay, L Mhamdi, M Novak, D Arondel, S Vol, J Tichet, E Eschwège  
The D.E.S.I.R. Study Group

## SUMMARY

**Context:** In 2001 the "National Cholesterol and Education Program Expert Panel" gave a clinical definition of the metabolic syndrome. The frequency of this syndrome at baseline and its incidence and persistence at three years is studied in a French population.

**Subjects:** 2109 men and 2184 women from the D.E.S.I.R. longitudinal cohort study (Data from an Epidemiological Study on the Insulin Resistance syndrome) in central-western France, aged 30 to 64 years, were examined at inclusion and three years later.

**Methods:** Evaluation of the frequencies, incidences and persistence of the metabolic syndrome and its abnormalities. This syndrome is defined by the presence of three or more of five abnormalities: waist circumference  $> 102/88$  cm (men/women); triglycerides  $\geq 1.69$  mmol/l, HDL-cholesterol  $< 1.04/1.29$  mmol/l (men/women); systolic/diastolic blood pressure  $\geq 130$  and/or 85 mmHg; fasting plasma glucose  $\geq 6.1$  mmol/l.

**Results:** At baseline, 10% of men and 7% of women had the metabolic syndrome. If the syndrome was defined to include a treatment in the abnormalities (for diabetes, hypertension, dyslipidemia), the syndrome frequencies increased to 16% and 11%. However only 12% and 8% respectively, had this syndrome both at inclusion and at three years. High blood pressure was the most frequent abnormality: 70% and 47% in men and women respectively, at inclusion. The most stable abnormality was high waist circumference (80% persisted), hyperglycaemia the least stable (60% persisted). Hyperinsulinaemia did not cluster closely with this syndrome.

**Conclusions:** The age-specific frequency of the syndrome is more than 2.5 times higher in the US than in this French cohort and this ratio increased with age. The higher frequencies of abdominal obesity and low HDL-cholesterol in women than in men suggest that these gender-specific thresholds may need to be refined.

**Key-words:** Insulin resistance · Metabolic syndrome X · Diabetes · Epidemiology · Prevalence · Incidence.

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INSERM U258, Villejuif, France.

## RÉSUMÉ

**L'incidence et persistance du syndrome métabolique défini par le NCEP (National Cholesterol Education Program). L'étude française D.E.S.I.R.**

**Contexte :** Le "National Cholesterol and Education Program Expert Panel" a publié, en 2001, une définition clinique du syndrome métabolique. Une évaluation a été faite, dans une population française, de la fréquence de ce syndrome et, après un suivi de 3 ans, de l'incidence et de la persistance de ce syndrome.

**Sujets :** 2109 hommes et 2184 femmes de l'étude "D.E.S.I.R.", (Données Épidémiologiques sur le Syndrome d'Insulino-Résistance) une cohorte longitudinale du centre-ouest de la France. Les sujets, âgés de 30 à 64 ans, ont tous été examinés à l'inclusion et après trois ans de suivi.

**Méthodes :** Evaluation de la fréquence, de l'incidences et de la persistance du syndrome métabolique et de ses anomalies. Ce syndrome est défini par la présence d'au moins anomalies trois de cinq anomalies suivantes : tour de taille  $> 102/88$  cm (hommes/femmes); triglycérides  $\geq 1,69$  mmol/l, HDL-cholestérol  $< 1,04/1,29$  mmol/l (hommes/femmes); pression artérielle systolique/diastolique  $\geq 130$  et/ou 85 mmHg; glycémie plasmatique à jeun  $\geq 6,1$  mmol/l.

**Résultats :** A l'inclusion, 10 % des hommes et 7 % des femmes ont eu un syndrome métabolique. Quand les traitements médicamenteux sont inclus dans la définition des anomalies correspondantes mentionnés ci-dessus (pour le diabète, l'hypertension, la dyslipidémie) la fréquence du syndrome atteint 16 % et 11 %. Cependant, seuls 12 % et 8 %, respectivement, ont eu ce syndrome à la fois à l'inclusion et à trois ans. Une pression artérielle élevée a été l'anomalie la plus fréquente : 70 % et 47 % chez les hommes et les femmes respectivement, à l'examen d'inclusion. L'anomalie la plus stable dans le temps a été un tour de taille élevé (80 % ont persisté), la moins stable étant l'hyperglycémie (60 % ont persisté). Une hyperinsulinémie n'a pas été bien liée à ce syndrome.

**Conclusions :** La fréquence, par classe d'âge, du syndrome métabolique est 2,5 fois plus élevée aux États-Unis que dans cette population française. La fréquence de l'obésité abdominale et du cholestérol-HDL bas est plus élevée chez les femmes que chez les hommes, ce qui suggère que ces seuils, qui sont définis par sexe, devraient être affinés.

**Mots-clés :** Insulino-résistance · Syndrome métabolique · Syndrome X · Diabète · Épidémiologie · Prévalence · incidence.

Address correspondence and reprint requests to:

B Balkau, INSERM U258, 16 Avenue Paul Vaillant-Couturier, 94807 Villejuif Cedex, France.  
balkau@vjf.inserm.fr

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**F**ollowing the work of Reaven and his arguments for the existence of a syndrome X associated with cardiovascular disease and diabetes [1] there have been other names attributed to this syndrome and the most cited are the metabolic syndrome, the pluri-metabolic syndrome, the insulin-resistance syndrome. A multitude of epidemiological papers have shown that the abnormalities are indeed all inter-correlated, that they correlate with other cardiovascular disease risk factors and that the syndrome is predictive of cardiovascular events [2, 3]. However, there had been no common definition of the abnormalities included in this syndrome nor of the thresholds defining an abnormality. The World Health Organization (WHO) Expert Committee were the first to give an official definition of the syndrome. The cornerstone of this definition was that the subjects must have impaired glucose regulation (includes diabetes) and/or insulin-resistance: the 25% of subjects with the lowest insulin sensitivity (measured directly) in the "background" population were defined as insulin-resistant [4]. This definition has been criticised by the European Group for the Study of Insulin Resistance [5]. The National Cholesterol Education Program (NCEP) Adult Treatment Panel has recently defined a syndrome based on clinical and biological measures that are routinely available [6]; neither insulin-resistance nor insulin concentrations were considered in this definition of the syndrome.

The prevalence of the metabolic syndrome using this NCEP definition was evaluated in US adults from the Third Nutritional Health and Nutrition Examination Survey (NHANES III) [7]. However, they also included those subjects treated for hypertension and/or diabetes as having the corresponding abnormalities. More than 20% of the adult population were found to have this syndrome.

The aim of this article is to evaluate the frequency of the NCEP metabolic syndrome in a French population, and to analyse the persistence and incidence of this syndrome after three years of follow-up.

## Subjects and methods

### Subjects

The data were from 2109 men and 2184 women, aged between 30 and 64 years, participating in the D.E.S.I.R. Study (Data from an Epidemiological Study on the Insulin Resistance syndrome). The subjects were examined in 1994-1996, and three years later 87% returned for a follow-up examination. They were volunteers from among the consultants of ten Health Examination Centres (Centres d'Examens de Santé) of the French Social Security in the centre-west of France. At inclusion the men and the women were equally divided over five-year age classes. The study was approved by the CCPPRB (Comité Consultatif de Protection des Personnes pour la Recherche Biomédicale) of

Bicêtre, Kremlin Bicêtre, by the CNIL (Commission Nationale Informatique et Libertés) and INSERM (Institut National de la Santé et de la Recherche Médicale) is the promoter. Participants signed a statement of informed consent.

### Study Design

Weight, height and waist circumference (smallest trunk circumference) were measured by trained personnel. Blood pressures were determined after at least 5 minutes of rest, with subjects in a supine position. Fasting venous blood samples were analysed in one of four laboratories (IRSA (Institut inter Régional pour la Santé) at La Riche, Health Examination Centre laboratories at Blois, Orleans and Chartres) and all laboratories participated in a national quality control program. Plasma glucose was assayed by the glucose-oxidase method applied to fluoro-oxalated plasma using a Technicon RA 1000 or a KONE; HDL-cholesterol and triglycerides were determined with a DAX24 Technicon or with a KONE; serum insulin was centrally assayed at IRSA by a specific enzyme-immunoassay with an IMX.

Treatments for dyslipidaemia and diabetes were determined from the medications the subjects were taking and treatment for arterial hypertension from the questions posed by the examining physician, as medication is not specific for hypertension.

### Statistical Analysis

The NCEP metabolic syndrome is present in subjects who have three or more of the following abnormalities [6]:

- waist circumference > 102/88 cm (men/women);
- triglycerides  $\geq$  1.69 mmol/l;
- HDL-cholesterol < 1.04/1.29 mmol/l (men/women);
- systolic/diastolic blood pressure  $\geq$  130/85 mmHg;
- fasting glucose  $\geq$  6.1 mmol/l.

We have also investigated the effect of including treatment for dyslipidaemia, hypertension and diabetes as part of the corresponding abnormalities. The persistence and incidence of the syndrome after a three-year follow-up is also studied.

The sex-specific upper quartile of the insulin concentration was used to estimate the percentage of subjects with both the metabolic syndrome and hyperinsulinaemia; hyperinsulinaemia is a surrogate measure of insulin-resistance [5] and this threshold was chosen in accordance with the WHO recommendation which classified subjects as insulin-resistant if their insulin sensitivity (measured by a direct method) was in the lower quarter of the distribution [4].

The frequency of the syndrome abnormalities has been age-standardised to the age distribution of the French 1999 census population aged 30 to 64 years, to provide a more realistic comparison with the frequencies in the NHANES Study.

Analyses used the SAS software, version 8.

## Results

Of the 4293 men and women studied, 8.1% had the metabolic syndrome at inclusion, compared to 10.9% of the 921 subjects who were either not present at the three-year examination (26 had died) or who did not have data available. Although the subjects studied in this analysis were on average, three years older, the syndrome was less frequent ( $p < 0.01$ ).

The frequency of the syndrome increased with age and was higher in men than in women (Tab I). Excepting for low HDL-cholesterol, the frequency of each syndrome abnormality tended to increase with age in both sexes. The individual abnormalities were more frequent in men, excepting for the two abnormalities with sex-specific thresholds, abdominal obesity and low HDL-cholesterol. Almost twice as many women as men were classed as having abdominal obesity, with the frequencies being closest between the sexes in the oldest subjects. The younger women particularly, had a high frequency of low HDL-cholesterol. Overall, the frequency of the metabolic syndrome in this population was 9.7% in men and 6.6% in women. The syndrome lipid abnormalities are included as two components of the syndrome and in total 4.1% of men had both abnormalities and 22.7% had at least one lipid abnormality; the corresponding frequencies for women were 2.5% and 15.4%. Two thirds of the subjects with the metabolic syndrome had a fasting insulin concentration in the top 25% of the sex-

specific insulin distribution, as 6.0% of the men and 4.5% of the women had both the syndrome and a high insulin concentration.

Overall, 9.2% of the men and 7.0% of the women were treated for dyslipidaemia, 9.2% and 8.9% for hypertension and 1.3% and 0.5% for diabetes (Tab II). In the 60 to 64 year old subjects, more than 24% were treated for dyslipidaemia, more than 20% for hypertension and 5.5% of men, 1.3% of women for diabetes.

If the treatments were included in the definitions of dyslipidaemia, hypertension and hyperglycaemia, the frequencies of the corresponding abnormalities were higher (Tab III). This increase in frequencies corresponded to the treated subjects who no longer had the corresponding abnormalities; 6.6% of the men and 6.3% of the women were treated for dyslipidaemia and had low triglyceride concentrations; 8.3% of the men and 6.4% of the women were treated for dyslipidaemia and had high HDL-concentrations; 0.7% and 1.0% were treated for high blood pressure and controlled below the given threshold values; 0.1% of men and 0.0% of women were treated for diabetes and had a fasting glucose concentration controlled to below 6.1mmol/l. Overall, after including treatment, the syndrome frequency increased from 9.7% to 16.3% in men and from 6.6% to 11.4% in women. If lipid treatment was ignored, the syndrome frequency decreased to frequencies similar to those when treatment was not included at all, 9.8% in men

**Table I**

Frequency (%) of the NCEP metabolic syndrome abnormalities and of the metabolic syndrome, at the inclusion examination, according to sex and to age; the age standardised frequency $\pm$ SE is for the French 1999 population. The D.E.S.I.R. Study.

	Age	Number	Abdominal adiposity	High triglycerides	Low HDL-cholesterol	High blood pressure	High fasting glucose	NCEP metabolic syndrome	
			Waist $\geq$ 102/88 cm (m/w)	$\geq$ 1.69 mmol/l	$<$ 1.04/1.29 mmol/l (m/w)	$\geq$ 130/85mmHg	$\geq$ 6.1mmol/l	AND insulin $>$ 8.03/7.43mU/l (m/w)	
Men	30-39	647	3.4	16.9	8.2	58.7	7.6	5.6	3.4
	40-49	555	6.5	21.8	6.0	66.5	13.7	8.1	5.2
	50-59	599	10.5	18.9	6.0	77.1	19.7	11.5	6.8
	60-64	308	20.4	24.4	7.8	79.9	25.0	17.5	11.0
	Overall	2109	8.7	19.8	6.9	69.1	15.2	9.7	6.0
		Age standardised frequency $\pm$ SE	7.9 $\pm$ 0.1	19.7 $\pm$ 0.1	6.9 $\pm$ 0.1	68.0 $\pm$ 0.2	14.4 $\pm$ 0.1	9.1 $\pm$ 0.1	5.6 $\pm$ 0.1
Women	30-39	653	7.4	5.4	11.8	24.7	1.5	4.0	3.4
	40-49	583	11.2	6.5	9.8	38.8	5.0	4.8	4.0
	50-59	632	19.2	10.1	6.5	63.3	5.9	8.4	4.9
	60-64	316	24.4	15.2	9.8	69.6	10.8	12.0	7.3
	Overall	2184	14.2	8.5	9.4	46.1	5.0	6.6	4.5
		Age standardised frequency $\pm$ SE	13.3 $\pm$ 0.1	8.0 $\pm$ 0.1	9.6 $\pm$ 0.1	43.7 $\pm$ 0.1	4.7 $\pm$ 0.1	6.2 $\pm$ 0.1	4.4 $\pm$ 0.1

**Table II**

Frequency (%) of treatment for dyslipidaemia, hypertension and diabetes at the inclusion examination. The D.E.S.I.R. Study.

	Age	Number	Drug treatment		
			Dyslipidaemia	Hypertension	Diabetes
Men	30-39	647	2.6	1.6	0.0
	40-49	555	6.0	5.6	0.5
	50-59	599	11.7	14.7	1.3
	60-64	308	24.0	21.4	5.5
	Overall	2109	9.2	9.2	1.3
Women	30-39	653	0.8	1.1	0.2
	40-49	583	1.9	4.1	0.5
	50-59	632	9.3	14.7	0.5
	60-64	316	24.4	22.5	1.3
	Overall	2184	7.0	8.9	0.5

and 6.6% in women, indicating that the subjects treated for dyslipidaemia often had triglycerides and HDL-cholesterol concentrations within the "normal" range, whereas subjects

treated for hypertension and/or for diabetes were not controlled to the low thresholds used for the definition of the syndrome.

Defining the syndrome abnormalities by both the threshold values and treatment (for dyslipidaemia, hypertension, diabetes), when the subjects were examined three years later, more than one quarter of those who had the syndrome at inclusion, were no longer classed as having the syndrome three years later and one third did not have a syndrome with the same abnormalities (*Tab IV, V*). High fasting glucose was the abnormality, which "normalised" more frequently than the other abnormalities, with 40% becoming "normal", in comparison to the most stable abnormality, abdominal obesity, for which about 20% became "normal".

The frequency of the syndrome and its abnormalities increased over the three-year period as this population aged (*Tab V*). High blood pressure remained the most frequent abnormality and had the highest incidence.

## Comment

In a French population of men and women 30 to 64 years, if the syndrome definition does not include treatment, the age-standardised frequencies of the syndrome were 9.1%

**Table III**

Frequency (%) of the NCEP metabolic syndrome abnormalities when treatment was included as an abnormality and of the resulting metabolic syndrome at the inclusion examination, according to sex and age; the age standardised frequency $\pm$ SE is for the French 1999 population. The D.E.S.I.R. Study.

	Age	Number	Abdominal adiposity	High triglycerides	Low HDL-cholesterol	High blood pressure	High fasting glucose	NCEP metabolic syndrome		
			Waist $\geq$ 102/88 cm (m/w)	$\geq$ 1.69 mmol/l or treatment	$<$ 1.04/1.29 mmol/l (m/w) or treatment	$\geq$ 130/85mmHg or treatment	$\geq$ 6.1 mmol/l or treatment	Including treatment for hypertension and diabetes	Including treatment for dyslipidaemia, hypertension, diabetes	AND insulin $>$ 8.03/7.43 mU/l (m/w)
Men	30-39	647	3.4	18.2	10.5	59.0	7.6	5.6	7.6	4.0
	40-49	555	6.5	26.8	11.5	66.7	13.7	8.1	12.8	6.8
	50-59	599	10.5	27.7	16.5	78.1	19.9	11.5	19.9	8.8
	60-64	308	20.4	40.3	28.9	81.5	25.3	18.2	33.8	15.9
	Overall	2109	8.7	26.4	15.2	69.8	15.3	9.8	16.3	7.9
	Age standardised frequency $\pm$ SE		7.9 $\pm$ 0.1	25.6 $\pm$ 0.1	14.2 $\pm$ 0.1	68.6 $\pm$ 0.2	14.4 $\pm$ 0.1	9.2 $\pm$ 0.1	15.0 $\pm$ 0.1	7.3 $\pm$ 0.1
Women	30-39	653	7.4	6.1	12.4	25.0	1.5	4.0	4.3	3.5
	40-49	583	11.2	8.4	11.3	39.6	5.0	4.8	6.2	4.6
	50-59	632	19.2	18.7	15.5	65.0	5.8	8.4	14.9	7.1
	60-64	316	24.4	36.7	32.0	70.9	10.8	12.0	28.5	11.1
	Overall	2184	14.2	14.8	15.8	47.1	5.0	6.6	11.4	6.0
	Age standardised frequency $\pm$ SE		13.3 $\pm$ 0.1	13.2 $\pm$ 0.1	14.9 $\pm$ 0.1	44.6 $\pm$ 0.1	4.7 $\pm$ 0.1	6.2 $\pm$ 0.1	10.1 $\pm$ 0.1	5.6 $\pm$ 0.1

**Table IV**

Frequency (%) of the NCEP metabolic syndrome abnormalities and of the metabolic syndrome present both at baseline and after three years of follow-up, according to sex and to age at inclusion in the study; the age standardised frequency $\pm$ SE is for the French 1999 population. The D.E.S.I.R. Study.

	Age	Number	Abdominal adiposity	High triglycerides	Low HDL-cholesterol	High blood pressure	High fasting glucose	NCEP metabolic syndrome including treatment for dyslipidaemia, hypertension, diabetes		
			Waist $\geq$ 102/88 cm (m/w)	$\geq$ 1.69 mmol/l or treatment	$<$ 1.04/1.29 mmol/l (m/w) or treatment	$\geq$ 130/85 mmHg or treatment	$\geq$ 6.1 mmol/l or treatment	Any three abnormalities	Same three abnormalities	AND insulin $>$ 8.03/7.43 mU/l (m/w)
Men	30-39	647	2.5	12.5	6.6	34.8	3.1	3.3	2.6	1.1
	40-49	555	5.2	20.0	9.7	47.4	7.6	9.4	8.6	4.7
	50-59	599	8.8	21.4	13.5	64.3	13.2	15.4	14.7	6.5
	60-64	308	14.6	30.2	23.4	72.4	17.9	25.7	24.0	13.6
	Overall	2109	6.8	19.6	11.8	52.0	9.3	11.6	10.8	5.4
	Age standardised frequency $\pm$ SE			6.2 $\pm$ 0.1	18.9 $\pm$ 0.1	11.0 $\pm$ 0.1	50.1 $\pm$ 0.2	8.6 $\pm$ 0.1	10.6 $\pm$ 0.1	9.8 $\pm$ 0.1
Women	30-39	653	5.7	2.6	8.0	11.3	0.8	2.5	2.4	2.4
	40-49	583	8.7	5.0	9.1	28.1	2.9	5.2	4.6	3.6
	50-59	632	15.8	13.6	11.5	48.3	3.3	10.4	9.2	4.6
	60-64	316	19.3	31.6	28.2	57.3	7.3	22.5	20.9	8.9
	Overall	2184	11.4	10.6	12.2	33.1	3.0	8.4	7.6	4.3
	Age standardised frequency $\pm$ SE			10.6 $\pm$ 0.1	9.2 $\pm$ 0.1	11.4 $\pm$ 0.1	30.8 $\pm$ 0.1	2.8 $\pm$ 0.1	7.5 $\pm$ 0.1	6.8 $\pm$ 0.1

and 6.2%; if treatment for hypertension and diabetes only were included, the frequencies were 9.2% and 6.2% respectively; if treatment for dyslipidaemia was also included, the frequencies were 15.0% and 10.1% respectively.

The NHANES III study of the metabolic syndrome was based on 4265 men and 4549 women [7]. The syndrome frequencies were 24.0% and 23.4% in men and women respectively, in comparison to 9.2% and 6.2% in France, using the same definition for the syndrome; however, the French study had an age range 30 to 64 years in contrast to over 20 years in the US. The frequencies in the two countries were closer in the younger men and women aged 30 to 39 years, France: 6% and 4%, US: 12% and 14% than in the older subjects 50 to 59 years, France had lower frequencies: 12% and 8% than the US: 34% and 33%.

Using age-standardised frequencies, abdominal adiposity was three times more frequent in the US than in the France, 29.8% and 46.3% in comparison to 7.9% and 13.3% for French men and women respectively. Hypertriglyceridaemia (not including lipid treatment in the definition) was two to three times more frequent in the US, 35.1% and 24.7% in men and women compared to 19.7% and 8.0%; low HDL-cholesterol (not including lipid treatment) had frequencies of 35.2% and 39.3% compared to 6.9% and 9.6%, again, a

four to five-fold difference. In contrast, hypertension (high blood pressure or treatment) was almost two-fold lower in the US than in France, with overall age-standardised frequencies of 38.2% in men and 29.3% in women the US compared to 68.6% and 44.6% in France. In the MONICA project surveys, French men and women also had relatively high mean arterial blood pressures [8]. For the last abnormality, high fasting glucose or treatment for diabetes, the frequencies were similar for men in the two studies 15.6% in the NHANES III study and 14.4% in France but for women the frequencies were quite different, 10.0% and 4.7% respectively.

The D.E.S.I.R. cohort is not strictly representative of the French population: the participants were from the centre-western part of France, they were all insured by the French Social Security (which covers more than 80% of the French population), they had enrolled for a regular health check up to which all such insured individuals have the right, they agreed to participate in a 9-year study. In these analyses we study the 87% of subjects who participated at baseline and at the three-year follow-up and for whom data were available. The NHANES III study has a complex stratified multi-stage probability designed sampling scheme to be representative of the US population, and 80% of the subjects sampled

**Table V**

Frequency (%) at year three, incidence and returns to "normality" of the NCEP metabolic syndrome abnormalities and the metabolic syndrome, over 3-years follow-up. The D.E.S.I.R. Study.

	<b>Abdominal adiposity</b>	<b>High triglycerides</b>	<b>Low HDL-cholesterol</b>	<b>High blood pressure</b>	<b>High fasting glucose</b>	<b>NCEP metabolic syndrome including treatment for dyslipidaemia, hypertension, diabetes</b>
	<b>waist <math>\geq</math> 102/88 cm (m/w)</b>	<b><math>\geq</math> 1.69 mmol/l or treatment</b>	<b>&lt; 1.04/1.29 mmol/l (m/w) or treatment</b>	<b><math>\geq</math> 130/85 mmHg or treatment</b>	<b><math>\geq</math> 6.1 mmol/l or treatment</b>	
Frequencies at the three year follow-up						
Men	11.3	32.6	22.0	58.5	15.5	19.2
Women	17.0	18.3	23.3	40.1	6.0	13.8
Incidence over three years of follow-up						
Men	4.4	14.0	13.4	24.3	7.9	10.5
Women	7.4	11.1	14.6	16.9	3.6	8.0
Return to "normality" at the three year follow-up						
Men	21.8	25.8	22.4	25.5	39.2	28.8
Women	19.7	28.4	22.8	29.7	40.0	33.3

participated in the study [9]. Thus while the frequencies of the syndrome and its abnormalities in the French study may not be true prevalences, even in this area of France, the results concerning the persistence and the incidence of the syndrome are more likely to be able to be generalised.

It is debateable whether the lipid abnormalities should be included as two separate factors; in the WHO definition of the syndrome [4], there was a combined lipid abnormality: triglycerides  $\geq$  1.69 mmol/l and/or HDL-cholesterol  $<$  1.04/1.29 mmol/l (men/women). The NCEP definition comes from experts in lipidology, thus an emphasis on the lipid abnormalities might be expected.

The original NCEP definition of the abnormalities of the metabolic syndrome did not include treatment by anti-dyslipidaemic, anti-hypertensive or anti-diabetic medications [6]. It does seem reasonable to consider treatment as part of an abnormality when evaluating the frequency of the syndrome, and particularly when evaluating its persistence and incidence over a time period. In contrast to the NHANES III study, we additionally included lipid treatment. This concerns 8% of our population and of those treated, 6.6% had triglycerides  $<$  1.69 mmol/l and 7.4% had HDL-cholesterol  $\geq$  1.04/1.29 mmol/l, so that they were treated and controlled. However, lipid treatment is usually instituted for the control of total and LDL-cholesterol, not for HDL-cholesterol or triglycerides, the dyslipidaemia associated with the metabolic syndrome, even though these lipid treatments may have an effect on both HDL-cholesterol and triglyceride concentrations.

The NCEP defined syndrome does not cluster closely with hyperinsulinaemia: by definition, 25% of all subjects had hyperinsulinaemia but only one half of those with the metabolic syndrome (including treatment) were hyperinsulinaemic. However, insulin-resistance and hyperinsulinaemia were the key factors in the physiological arguments used by Reaven in defining the syndrome [1]. This lack of clustering may be due to the fact that the abnormalities were defined with low thresholds, thus including subjects who would be considered to have just slightly high normal values.

In both this study and in the NHANES III study, abdominal adiposity had a higher frequency in men than in women, in contrast with the other risk factors. As the risks of cardiovascular disease and of cardiovascular risk factors tend to increase with central adiposity, independently of sex [10, 11], it may be more appropriate to choose the same threshold for men and for women. Similarly the NCEP thresholds for men and women differ for HDL-cholesterol, but not all guidelines propose gender-specific thresholds for classification of low HDL-cholesterol [6].

For the syndrome as a whole, more than one-quarter returned to the no-syndrome status, which may indicate that the threshold values are too liberal and too many subjects are included. There was a very high frequency of hyperglycaemic subjects returning to a normal glycaemia ( $<$  6.1 mmol/l) after three years, higher than for the other factors, indicating the higher intra-individual variability for fasting glucose

concentrations, particularly for this threshold, a phenomenon well recognised for glucose concentrations in general [12].

It remains to be seen whether this NCEP definition of the metabolic syndrome proves useful in clinical practice, even if it is shown that subjects with this syndrome are at a higher risk of cardiovascular events and all cause mortality.

*Author affiliations* – INSERM U258-IFR69, Université Paris XI, Villejuif (Balkau, Vernay, Eschwège, Mhamdi); IRSA, Châteauroux (Novak); Centre d'Examens de Santé, Chartres (Arondel); IRSA, La Riche, (Vol, Tichet) France. The D.E.S.I.R. Study Group: INSERM U258: B Balkau, P Ducimetière, E Eschwège; INSERM U367: F Alhenc-Gelas; CHU D'ANGERS: Y Gallois, A Girault; Hôpital Bichat: M MARRE; ASSOCIATION DE CARDIOLOGIE DU CENTRE, VAL DE LOIRE: M Brochier; CENTRES D'EXAMENS DE SANTÉ DU RÉSEAU 9: Alençon — MC Chesnier; Angers — F Rabouin; Blois — S Balland-Desprès, JP Sigalas; Caen — A Caradec, C Geslain; Chartres — D Arondel, ; Chateauroux — M Novak; Cholet — A Petrella; Le Mans — A D'Hour; Orléans — P Lépinay, E Wilpart; Tours — B Royer; INSTITUT DE RECHERCHE EN MÉDECINE GÉNÉRALE: J Cogneau, G Henry, P Ouvrard, F Paré, C Rougeron; MEDECINS GÉNÉRALISTES des Départements; INSTITUT RÉGIONAL POUR LA SANTÉ: C Born, E Cacès, M Cailleau, JM Jacquelin, JG Moreau, F Rakotozafy, J Tichet, S Vol.

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## References

1. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*, 1988, 37, 1595-607.
2. Pyorala M, Miettinen H, Halonen P, Laakso M, Pyorala K. Insulin resistance syndrome predicts the risk of coronary heart disease and stroke in healthy middle-aged men: the 22-year follow-up results of the Helsinki Policemen Study. *Arterioscler Thromb Vasc Biol*, 2000, 20, 538-44.
3. Isomaa B, Almgren P, Tuomi T, *et al.* Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*, 2001, 24, 683-9.
4. World Health Organisation Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Report of a WHO Consultation. Geneva, Switzerland, 1999.
5. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR) *Diabet Med*, 1999, 16, 442-3.
6. 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 the detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA*, 2001, 285, 2486-97.
7. Ford ES, Giles WH, Dietz. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*, 2002, 287, 356-9.
8. World Health Organisation. World Health Statistics Annual. Geneva, World Health Organisation, 1989, 27-149.
9. Alter MJ, Kruszon-Moran D, Nainan OV, *et al.* The prevalence of hepatitis C virus infection in the United States 1988 through 1994. *NEJM*, 1999, 341, 556-62.
10. Larsson B, Bengtsson C, Bjorntorp P, *et al.* Is abdominal body fat distribution a major explanation for the sex difference in the incidence of myocardial infarction? The study of men born in 1913 and the study of women, Goteborg, Sweden. *Am J Epidemiol*, 1992, 135, 266-73.
11. Bertrais S, Balkau B, Vol S, *et al.* Relationships between abdominal body fat distribution and cardiovascular risk factors: an explanation for women's healthier cardiovascular risk profile. The D.E.S.I.R. Study. *Int J Obes Relat Metab Disord*, 1999, 23, 1085-94.
12. Mooy JM, Grootenhuys PA, de Vries H, *et al.* Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general Caucasian population: the Hoorn Study. *Diabetologia*, 1996, 39, 298-305.