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A REVIEW OF THE METABOLIC SYNDROME

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SUMMARY

While the concept of this syndrome has been described more than 60 years ago, and more formally almost 20 years ago, the controversy continues as to its utility, which of the various syndrome definitions should be used and their ability to predict diabetes and/or cardiovascular disease. The metabolic syndrome, of cardiovascular risk factors, provides an early warning of at risk subjects and emphasises the need to treat more aggressively (by at least lifestyle modification) patients with multiple abnormalities even though the abnormalities might be slight. Further, the syndrome can be easily used in clinical practice and when it is assessed against the background of the patient's age, sex and smoking habits, it provides an evaluation of potential cardiovascular risk. Prospective intervention studies are the only means of definitively accepting or refuting the usefulness of the syndrome. The metabolic syndrome is an entity which merits attention from both the medical profession and public health authorities.

Key Words: Cardiovascular disease • Diabetes • Insulin resistance • Metabolic syndrome

RESUME

Voilà plus de 60 ans, le concept de syndrome métabolique a été identifié, et plus formellement décrit il y a une vingtaine d'années. La controverse continue quant à l'utilité d'un tel syndrome, quant à la définition utilisée et à la capacité des différentes définitions à prédire le diabète et/ou les maladies cardio-vasculaires. Le syndrome métabolique indique une alerte précoce pour traiter plus agressivement (au moins par des changements de comportement) les patients porteurs d'anomalies multiples, même si ces anomalies sont modérées. De plus, le syndrome est facile à utiliser en clinique et devrait être mis en parallèle avec l'âge, le sexe et le tabagisme du patient pour l'évaluation du risque cardio-vasculaire. Les études prospectives d'intervention sont les seules études qui fournissent la preuve de l'utilité du syndrome. Le syndrome métabolique mérite toute l'attention de la part du corps médical et des autorités de santé publique.

Mots Clés : Diabète • Insulino-résistance • Maladies cardiovasculaires • Syndrome métabolique

Introduction

The metabolic syndrome groups insulin resistance, hyperinsulinaemia, hyperglycaemia, dyslipidaemia (hypertriglyceridaemia and/or hypo HDL-cholesterolaemia), high arterial blood pressure and central adiposity. Other abnormalities are also associated with this constellation - and may well also be part of this syndrome. A variety of names have been associated with this condition: the pluri-metabolic syndrome, the insulin-resistance syndrome, syndrome X, the dysmetabolic syndrome, the metabolic syndrome ...

In itself insulin resistance is not a disease, but rather a risk factor for the syndrome abnormalities and it has yet to be demonstrated that it is a risk factor for later cardiovascular disease or for diabetes as there are few prospective studies that have measured insulin resistance by a validated method.

At the request of the American Association of Clinical Endocrinologists, in October 2001 the Centre for Disease Control created the code number 277.7 for the dysmetabolic syndrome X in the International Classification of Diseases (ICD-9). This code was recommended to be noted if a physician considered that the syndrome was present in a given individual. However, a report from the United States indicates that the code is little used [1].

History of the syndrome

In 1988 Gerald Reaven presented the Banting Lecture at the American Diabetes Association meeting. The title of his lecture was "The Role of Insulin Resistance in Human Disease", and the corresponding article was published in the same year [2]. He gave pathophysiological arguments for the existence of a "syndrome X", in which he included insulin resistance, hyperinsulinaemia, hyperglycaemia, dyslipidaemia, arterial hypertension. Several years later, during the Claude Bernard Lecture of the European Society for the Study of Diabetes (EASD), Reaven included central adiposity in the syndrome, and noted the importance of free fatty acids [3]. While Reaven's description was based on the pathophysiology of insulin resistance, the syndrome that he described was not precise and it was not possible to identify individuals as having the syndrome: the combination of abnormalities, the number of abnormalities, the thresholds defining the abnormalities were not given. The only abnormality Reaven quantified was insulin resistance, which he affirmed to be present in 25% of the adult population.

Reaven was not the first to propose such a syndrome. Kylin, in 1923, described the clustering of hypertension, hyperglycaemia and gout [4]. In France, Jean Vague, at the end of the 1940s, documented the association between central adiposity, diabetes, atherosclerosis and

gout [5,6]. Later, in 1967, Avogaro et al. described a metabolic syndrome [7] and in 1985 Michaela Modan proposed that hyperinsulinaemia was the link between hypertension, obesity and glucose intolerance [8].

Following the description of the syndrome by Reaven, it has become a major theme of research and of public health interest. The number of publications on the subject is ample evidence of the importance given to the syndrome by clinicians and researchers (over 18,000 citations to the "metabolic syndrome" in PubMed, December 2006 - with more than 3,000 citations in 2006 alone).

Arguments for the existence of a syndrome

The fact that this cluster of abnormalities exists has been well validated by epidemiological studies: the abnormalities cluster more frequently than what would be observed if they clustered by chance [9].

Definitions of the metabolic syndrome

In the absence of a diagnostic test, a number of definitions of the syndrome have been proposed (Appendix 1). They come from the World Health Organisation (WHO) [10], the European Group for the study of Insulin Resistance (EGIR) [11], J-P Després' group [12], the National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III) [13]. In 2003 the American Association of Clinical Endocrinologists and the American College of Endocrinologists provided a position statement of what they entitled the "insulin resistance syndrome" [14] but they did not give a precise definition, leaving it to a clinician to decide whether a given individual had the syndrome. They recognised that there was no experimental evidence to define diagnostic criteria for the syndrome and consequently their definition could not be precise. They conclude, that the more abnormalities, the more likely that an individual is insulin resistant.

These various definitions include different factors and different thresholds for them. For example the first definition, from the WHO, included microalbuminuria, which does not appear in the later definitions [10]. The EGIR definition [11] did not include diabetic patients, for two reasons - these patients should already be in the health care system, and have their health monitored so identification of the syndrome should not be necessary, and secondly, long standing diabetic patients have lower insulin levels, which do not reflect the level of insulin resistance, a key element of this definition. Finally the simple definition of the

"hypertriglyceridemic waist" was originally defined only for men, and it has not generally been used as a definition of the syndrome.

The most recent definitions, both in 2005, are from the International Diabetes Federation (IDF) [15, 16] and from the American Heart Association/National Heart, Lung, and Blood Institute AHA/NHLBI [17, 18].

The differences between these definitions are essentially the thresholds for the parameters to define a syndrome abnormality, the number of abnormalities before the syndrome is deemed to be present, and whether there is a compulsory abnormality which is required to be present.

Reavens' arguments were centred around insulin resistance, and the definitions proposed by the WHO, EGIR and the IDF have taken this into account - WHO because the presence of either insulin resistance or glucose dysregulation were required, EGIR because hyperinsulinaemia was a mandatory factor and for the IDF central obesity (as quantified by the waist circumference) is mandatory, because of the close association between insulin resistance and central adiposity.

The IDF definition, with its differing thresholds for waist circumference according to ethnic group, is likely to become the international norm, as it is supported by several international bodies, however, the more recent American definition will probably be used in the United States.

To define any diagnostic criteria is not easy (for diabetes, the criteria have changed over the years). For a syndrome it is even more complicated - what parameters, what thresholds, what combinations should be used to define it? In fact a score to evaluate the severity of the syndrome, using a combination of continuous variables would be more logical than a syndrome defined with arbitrary thresholds.

Frequency of the syndrome and of its abnormalities

The frequency of the syndrome differs according to the definition, country, sex, age, and even according to the region in France. From the French MONICA study, the frequency of the NCEP-ATP III defined syndrome, in men aged 35 to 65 years was 26% in Lille, 22% in Strasbourg and 16% in Toulouse; in women, the corresponding frequencies were 26%, 24% and 13% [19]. (The definition used included subjects treated by drugs for hypertension and/or for diabetes). In comparison, in the French D.E.S.I.R. Study, of men and women aged 30 to 64 years, the

corresponding frequencies were 9% and 6% and if treatment for diabetes and for hypertension were also included, the frequencies increased to 15% and to 10%, respectively [20].

Table 1 shows the means and standard deviations of syndrome parameters from a general French population, recruited in Preventive Health Examination Centres in the central western part of France. More details of the reference values, and centiles are given on www.sciencedirect.com. These data are for subjects aged 20 to 74 years, and are given by 5-year age classes and by sex; they are from a sample of 130,882 consultants at IRSA (an Institute which provides health screening examinations which are financed by the French social security system). In the tables, the column on the right gives the reference values in a population of 19,126 men and 19,874 women with the same age structure as the French population in the 1999 census, for subjects aged between 20 and 74 years.

In this French population, the frequency of the NCEP-ATP III defined syndrome was 10% in the men and 9% in the women, for the IDF definition 21% and 17% and for the AHA/NHBLI definition 18% and 14% respectively (Table 2).

Note that central adiposity is more common in women than in men - because of the choice of the thresholds (Table 2). The NCEP thresholds for the waist circumference $> 102/88$ for men/women were defined because of their relation with obesity, a BMI ≥ 30 kg/m² and/or a high waist-hip ratio $> 0.95/0.80$ men/women [21], and not in relation with the diseases associated with the syndrome, diabetes and cardiovascular disease. The IDF waist thresholds were chosen for the sensitivity/specificity to screen for a BMI ≥ 25 kg/m² [21].

Hypo HDL-cholesterolaemia was also defined according to sex, and is more frequent in women than in men.

It has already been noted that in the French D.E.S.I.R. study [20], high arterial blood pressure is more commonly present than in the United States, where the NCEP-ATP III definition was conceived: in men 67% vs 38% and in women 44% vs 29%. Such differences have been documented in a collaborative study where the prevalences of hypertension were 28% in North American countries in comparison to 44% in Europe [22].

For the IDF definition of the metabolic syndrome, in comparison with the NCEP-ATP III definition, the definitions of all abnormalities are changed, with an increase in frequency for each abnormality, in comparison with the NCEP-ATP III definition (Table 2). The result is a doubling of the syndrome frequency. The most marked increases in frequency are associated with the waist circumference and fasting glucose (Table 2) where the thresholds have been lowered. For high blood pressure and dyslipidaemia, the changes in frequency are due only to

the inclusion of the corresponding treatments - little change for high blood pressure, and a close to doubling for both lipid abnormalities; it must be noted that all lipid treatments were included in this analysis, as there was no information as to whether the lipid-lowering therapy was prescribed for treatment of LDL-cholesterol or for triglycerides/HDL-cholesterol.

The AHA/NHLBI definition is similar to the NCEP-ATPIII, with the major difference being the lowering of the glucose threshold, and in consequence a more than three-fold increase in hyperglycaemia.

Consequences of the syndrome

Reaven described the consequences of the syndrome as cardiovascular disease and diabetes [2].

A meta-analysis of prospective studies quantified the risks of all cause mortality, of morbidity or mortality from cardiovascular diseases and of diabetes from the metabolic syndrome as defined by NCEP-ATP III [23]. The relative risks were estimated as: 1.3 (95% CI: 0.9-1.8), 1.6 (1.3-2.0) and 3.0 (1.9-4.6), respectively. These are certainly dependent on the subjects in the study, and if diabetic subjects are included, the risk associated with cardiovascular disease is higher than when they are excluded [24].

There are a number of more recent analyses, one from the Framingham Offspring Cohort showed age-adjusted relative risks for CVD, CHD and type 2 diabetes of 2.9, 2.5 and 6.9 for men, and 2.2, 1.5 and 6.9 for women [25]. In France the D.E.S.I.R. study has shown that the syndrome is predictive of both cardiovascular events and diabetes [26], and in the PRIME study of men from France and northern Ireland, the IDF defined syndrome carried a relative risk for coronary heart disease of 1.41, the WHO 1.40 and the NCEP 1.46 [27].

While these relative risks may be statistically significant, a risk equation for cardiovascular morbidity or mortality, for example the Framingham or the SCORE risk equations [28, 29], are better predictors [30]. However, in the European DECODE study, in men at low risk, with an estimated 10-year risk of cardiovascular mortality under 5%, the metabolic syndrome had a relative risk of cardiovascular mortality of 2.5 (1.2-5.0) [31,32]. Thus the syndrome provides additional predictive information on CVD risk, over and above that given by a CVD risk score, and involved 9% of the men. Of the men at high CVD risk (more than 5% over 10 years, and involving 41% of the men), the syndrome was present in only one third of them. The hazards ratios of men at high risk of CVD, whether they had the syndrome or not, and those at low risk *with the syndrome*, were very similar: 2.5, 2.2 and 2.5 respectively, after adjustment for age and the recruitment centre. For women there were fewer cardiovascular events, there

was no relation, and the relative risk was 1.3 (0.4-4.2). However, the waist alone, with the NCEP-ATP III thresholds, was associated with higher cardiovascular mortality: 2.2 (1.1-4.8) in men and 2.3 (0.8-6.7) in women, after adjustment for age and recruitment centre, and these two risks were not significantly different.

The metabolic syndrome carries a much higher risk for diabetes than for CVD. To predict incident diabetes, the traditional risk markers of diabetes, such as glucose concentrations perform better than the metabolic syndrome [30, 33]. But in the Framingham Offspring Study [25], while high fasting glucose carried a hazards ratio of 12.5 (9.1-17.3) for high glucose alone, the syndrome had a hazards ratio of 11.0 (8.1-14.9), and the hazards ratio was still high, 5.0 (3.7-6.8) if the syndrome was present, but the glucose level low < 6.1 mmol/l.

Other consequences of the syndrome are hypertension, polycystic ovary syndrome, non-alcoholic steatosis and chronic renal disease.

Treatment of the syndrome

As the syndrome does not have a known cause, the cause is not able to be treated.

To delay the appearance of the syndrome or its manifestations, insulin sensitivity could be targeted, by lifestyle modification - loss of weight, increase in physical activity, a healthy diet or by pharmacological intervention. There are several medications which target insulin sensitivity (Thiazolidinediones, Metformin, ...) and others which help in weight loss (Orlistat, Sibutramine, Rimonabant). In the future, there will be more evidence to elucidate whether these treatments are effective in delaying the appearance of the metabolic syndrome and in the patients with the syndrome, in preventing CVD and diabetes.

To treat the abnormalities of the metabolic syndrome, the first step is lifestyle modification and modest weight may be effective [34]. Drug treatment should be used for the specific abnormalities according to current guidelines, and a more aggressive approach may be appropriate when more than one abnormality is present.

Statement from the European Association for the Study of Diabetes and the American Diabetes Association, 2005

This joint statement gave a "critical appraisal" of the metabolic syndrome [35]. It concluded: "Until much-needed research is completed, clinicians should evaluate and treat all CVD risk factors without regard to whether a patient meets the criteria for diagnosis of the "metabolic

syndrome". The review aimed to argue four points, which are given below along with our responses, given in italics:

1. "the metabolic syndrome is not nearly as well defined and characterized as is often assumed"

RESPONSE:

The syndrome is certainly not well defined, and it was Reaven who was initially (perhaps deliberately) vague with his description of the syndrome [2]. The multiplicity of definitions for the syndrome has resulted in confusion and has led to a lack of credibility for the concept as a whole.

2. "the notion that it is a useful marker of CVD risk above and beyond the risk associated with its individual components is uncertain"

RESPONSE

That the individual components of the syndrome may carry a similar or even higher risk than the syndrome has been illustrated in the DECODE study [32]; these analyses also show that men at lower estimated risk of cardiovascular death (<5% in 10 years according to the SCORE risk equations), who have the syndrome, are at high risk of fatal CVD, of equivalent risk to those at higher risk of CVD death, according the European CVD Score equation. Thus, the syndrome - or at least the components in the syndrome that are not included in a classical CVD risk score (waist circumference in particular) - identifies a group of men at risk. This was not the case in the women, but waist circumference was a good marker of fatal CVD risk, in the women at low risk (< 5% in 10 years).

While CVD risk scores appear to be more closely related with CVD outcomes than the syndrome [30], they are rarely used in clinical practice. The syndrome is an easy concept enabling a physician to identify patients at risk, with routinely available measures. The thresholds of the various parameters enable a quick categorisation of patients, with a large waist circumference being a clear first step, which should prompt the search for the cluster of metabolic abnormalities. If age, sex and smoking are taken into account along with the syndrome abnormalities, the cardiovascular risk can be assessed. An evaluation needs to be made of the severity of the various abnormalities, and each one may not carry the same importance.

Further, the promotion of the concept of the metabolic syndrome has drawn attention to the fact that patients diagnosed with diabetes, hypertension or lipids, should be investigated for other abnormalities in the metabolic syndrome cluster.

3. "although certain CVD risk factors undoubtedly occur together more often than expected, the underlying pathophysiology of the syndrome is unclear"

RESPONSE

The clustering of the CVD risk factors, the syndrome abnormalities cannot be disputed - and research is needed to elucidate the reasons for this clustering. Given current knowledge, drug treatment can only be factor by factor, with appropriate care to choose the treatments which do not aggravate the other abnormalities. Research will provide more information, and may also provide new molecules to treat the syndrome as a cluster, rather than treating the individual abnormalities. In the meantime, the outcome is treated, without consideration of the physiology which has led to the condition. Treatment should target insulin sensitivity: increase in physical activity and weight loss, and possibly some drugs in the future.

4. "the list of risk factors comprising the cluster is not grounded by well-defined criteria"

They then state that "the manuscript is a cautionary reminder to practitioners, and an urgent call for further research."

RESPONSE

The abnormalities proposed for the definitions of the syndrome have been chosen following Reaven [2], and other components have been added or proposed because of their close correlation with insulin concentrations or insulin resistance indexes. As argued above, the choice of the components, their thresholds or the number of them required for the syndrome is all rather arbitrary. Each of the syndrome parameters has a continuous relation with cardiovascular disease incidence, thus it is difficult to define a threshold on this basis. The combination of abnormalities is also difficult to justify, as is the inclusion of other possible related abnormalities.

Other arguments pro- and con for the syndrome

In a similar vein, a recent article by Reaven is entitled "The Metabolic Syndrome: Requiescat in Pace" [36]. His arguments are targeted on insulin resistance and its relation with clinically significant disease with the aim of understanding the pathophysiology. Insulin resistance can exist without metabolic clustering. However, Reaven does argue that there is a benefit in diagnosing a syndrome to initiate lifestyle changes, but that the use of a precise definition,

given the arbitrary nature of the thresholds, may not be appropriate. The diagnosis of diabetes relies on somewhat arbitrary, consensual thresholds, and has long proved its usefulness.

Greenland poses the clinical question as to whether patient outcome is improved by identification of the syndrome - rather than by a classical global CVD risk score [37].

The American Heart Association, in particular Grundy et al. [17, 18, 38], and Eckel et al. [39], have argued both in scientific journals and in internet newsletters about the utility of the syndrome and provided guidelines for its management.

Conclusion.

While awaiting further knowledge on the causes of the abnormalities of the metabolic syndrome and of the metabolic syndrome itself, the metabolic syndrome should be recognized as an entity which deserves attention from the medical profession and public health authorities. The metabolic syndrome provides an early, simple and cheap warning of patients at risk of cardiovascular disease and diabetes, and emphasizes the need to treat more aggressively those with multiple abnormalities, even though individually these abnormalities may be slight. While there is no clinical trial evidence for the efficacy of such an approach, it is in line, for example, with recommendations for the more aggressive treatment of lipids and hypertension in diabetic patients. In all cases, the first-line treatment consists of lifestyle modification. Drug treatments should be used according to current recommendations for each individual risk factor. Additional research is needed to identify new targets for treatments to prevent cardiovascular disease, in particular other lipid goals, such as increasing HDL-cholesterol levels once the LDL-cholesterol goal is achieved.

In clinical practice either the NCEP-ATP III or the IDF or the AHA/NHBLI definitions of the syndrome could be used: the fact that the thresholds and the combinations of abnormalities might be arbitrary does not prevent the use of the concept. For epidemiological studies, it would be preferable to report frequencies and outcomes for all three definitions. The AHA/NHBLI definition, which retains the higher thresholds values for waist circumference is likely, to be adopted in the United States [17, 18]. Certainly, the recognition of a high waist circumference as a first abnormality, as in the IDF definition of the syndrome, will enable a quick screening of subjects at risk for cardiovascular disease and for diabetes.

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Table 1

Means and standard deviations (SD), according to age, of parameters included in the metabolic syndrome in a population of 130,882 consultants, 65,372 men and 65,510 women, in 2002-2004 at the "Institut inter Régional de la Santé", (IRSA) an Institute in central-western France which provides health examinations. The last column shows the reference values for a population aged 20-74 years with the same age structure as the French population in the 1999 census. More complete information with the distribution of the percentiles is available at www.xxxxxx.

MEN		Age (years)											20-74 n=19126
		20-24 n=3436	25-29 n=4812	30-34 n=7068	35-39 n=8850	40-44 n=8885	45-49 n=9077	50-54 n=9038	55-59 n=6474	60-64 n=3649	65-69 n=2684	70-74 n=1399	
WAIST (cm)	mean	79	83	86	88	89	91	93	94	95	96	97	89
	SD	9	10	10	10	10	10	10	10	10	10	10	11
GLUCOSE (g/l)	mean	0.91	0.92	0.94	0.96	0.98	1.00	1.02	1.04	1.03	1.04	1.05	0.98
	SD	0.11	0.10	0.11	0.12	0.14	0.16	0.19	0.21	0.21	0.22	0.25	0.17
TRIGLYCERIDES (g/l)	mean	0.84	0.93	1.01	1.06	1.11	1.14	1.15	1.14	1.12	1.09	1.10	1.06
	SD	0.47	0.56	0.64	0.63	0.67	0.66	0.66	0.65	0.59	0.53	0.53	0.62
HDL-CHOLESTEROL (g/l)	mean	0.51	0.53	0.53	0.54	0.55	0.56	0.56	0.56	0.56	0.56	0.56	0.55
	SD	0.12	0.13	0.13	0.13	0.14	0.14	0.14	0.13	0.14	0.13	0.14	0.13
SYSTOLIC BLOOD PRESSURE (mmHg)	mean	127	128	128	129	131	134	137	140	142	146	148	134
	SD	10	11	11	12	13	14	15	16	17	18	18	15
DIASTOLIC BLOOD PRESSURE (mmHg)	mean	73	75	76	78	80	82	83	84	84	84	83	80
	SD	8	8	8	9	9	10	10	10	10	10	10	10

WOMEN		Age (years)											
		20-24 n=5261	25-29 n=5398	30-34 n=7264	35-39 n=7368	40-44 n=8558	45-49 n=8879	50-54 n=8619	55-59 n=6655	60-64 n=3509	65-69 n=2580	70-74 n=1419	20-74 n=19874
WAIST (cm)	mean	72	74	76	77	78	79	81	83	84	85	86	79
	SD	10	11	11	11	11	12	12	12	12	12	12	12
GLUCOSE (g/l)	mean	0.87	0.87	0.89	0.90	0.92	0.94	0.95	0.96	0.97	0.97	0.99	0.93
	SD	0.10	0.10	0.10	0.11	0.12	0.15	0.15	0.16	0.17	0.19	0.20	0.15
TRIGLYCERIDES (g/l)	mean	0.83	0.80	0.79	0.78	0.79	0.82	0.85	0.93	0.97	0.98	1.02	0.85
	SD	0.36	0.38	0.38	0.39	0.40	0.45	0.44	0.47	0.48	0.46	0.51	0.43
HDL-CHOLESTEROL (g/l)	mean	0.59	0.61	0.61	0.63	0.64	0.65	0.67	0.67	0.67	0.67	0.66	0.64
	SD	0.14	0.15	0.14	0.15	0.15	0.15	0.16	0.16	0.16	0.16	0.16	0.15
SYSTOLIC BLOOD PRESSURE (mmHg)	mean	118	117	117	118	121	125	128	132	136	139	143	126
	SD	10	11	12	12	14	15	15	16	16	17	18	16
	mean	71	72	72	74	76	77	78	79	80	80	80	76

DIASTOLIC BLOOD	mean	71	72	72	74	76	77	78	79	80	80	80	76
PRESSURE (mmHg)	SD	8	8	9	9	9	10	9	9	9	9	9	10

Table 2

Frequency of the metabolic syndrome abnormalities and frequency of the syndrome defined according to the NCEP-ATP III, the IDF and the AHA/NHLBI definitions, in a sample of consultants from IRSA (French Health Examination Centres) in 2002-2004. These men and women, aged 20 to 74 years, had the same age structure as the French population in the 1999 census.

NCEP-ATP III defined metabolic syndrome.	MEN n = 19 126	WOMEN n = 19 874
Waist circumference > 102 / 88 cm	12%	20%
Fasting glucose \geq 1.10 g/l	12%	6%
Blood pressure \geq 130 / \geq 85 mmHg	66%	43%
Triglycerides \geq 1.50 g/l	17%	7%
HDL-cholesterol < 0.40/0.50 g/l	10%	18%
NCEP-ATP III syndrome present	10%	9%

IDF defined metabolic syndrome	MEN n = 19 126	WOMEN n = 19 874
Waist circumference \geq 94 / 80 cm	33%	40%
Fasting glucose \geq 1.00 g/l or previously diagnosed type 2 diabetes	35%	18%
Raised blood pressure: SBP \geq 130 or DBP \geq 85 mmHg or treatment of previously diagnosed hypertension	67%	44%
Raised triglycerides \geq 1.5 g/l or a specific treatment for this lipid abnormality*	23%	14%
Reduced HDL-cholesterol < 0.4/0.5 g/l (men/women) or a specific treatment for this lipid abnormality*	18%	24%
IDF syndrome present†	21%	17%

* any lipid treatment was included here

† if treated for lipids, only counted for the hypertriglyceridaemia abnormality

AHA/NHLBI defined metabolic syndrome	MEN n = 19 126	WOMEN n = 19 874
Waist circumference \geq 102 / 88 cm	14%	22%
Fasting glucose \geq 1.00 g/l or previously diagnosed type 2 diabetes	35%	18%
Raised blood pressure: SBP \geq 130 or DBP \geq 85 mmHg or drug treatment for hypertension	67%	44%
Raised triglycerides \geq 1.5 g/l or drug treatment for elevated triglycerides	23%	14%
Reduced HDL-cholesterol $<$ 0.4/0.5 g/l (men/women) or drug treatment for reduced HDL cholesterol	18%	24%
AHA/NHLBI syndrome present†	18%	14%

* any lipid treatment was included here

† if treated for lipids, only counted for the hypertriglyceridaemia abnormality

Appendix 1

DEFINITIONS OF THE SYNDROME

WHO definition of the metabolic syndrome, 1999 [10]

Glucose intolerance, IGT or diabetes mellitus and/or insulin resistance together with two or more of the other components listed below:

- Impaired glucose regulation or diabetes
- Insulin resistance (under hyperinsulinaemic, euglycaemic conditions, glucose uptake below lowest quartile for background population under investigation)
- Raised arterial pressure $\geq 140 / 90$ mm
- Raised plasma triglycerides (≥ 1.7 mmol/l (1.5 g/l) and/or low HDL-cholesterol (< 0.9 mmol/l (0.35 g/l) men: < 1.0 mmol/l (0.39 g/l) women)
- Central obesity: (men: waist to hip ratio > 0.90 ; women: waist to hip ratio > 0.85 and/or BMI > 30 kg/m²)
- Microalbuminuria (urinary albumin excretion rate ≥ 20 μ g/min or albumin:creatinine ratio ≥ 30 mg/g)

EGIR Syndrome d'Insulino-Résistance, 1999 [11]

Defined only for non-diabetic subjects.

Insulin-resistance (defined by hyperinsulinaemia - above the third quartile of the fasting insulin concentration in non-diabetic subjects, sexes and all ages combined) plus two abnormalities among:

- Central obesity: waist circumference $\geq 94 / 80$ cm (men / women)
- Dyslipidaemia: high triglycerides: ≥ 2.0 mmol/l (1.8 g/l) and/or low HDL-cholesterol: < 1.0 mmol/l (0.40 g/l) or treatment for dyslipidaemia
- Hyperglycaemia: fasting plasma glucose ≥ 6.1 mmol/l (1.1 g/l) but < 7.0 mmol/l (1.26 g/l)
- Hypertension: systolic/diastolic ≥ 140 and/or 90 mmHg or treatment for hypertension

Després' Group, the hypertriglyceridemic waist, 2000 [12]

Defined only for men

- Waist ≥ 90 cm
- Triglycerides ≥ 2.0 mmol/l (1.75 g/l)

NCEP-ATP III definition of the metabolic syndrome, 2001 [13]

Three or more of the following risk factors:

- Abdominal obesity: waist circumference $> 102 / 88$ cm (men/women)
- Triglycerides ≥ 1.50 g/l (1.69 mmol/l)
- HDL-cholesterol $< 0.40 / 0.50$ g/l (1.04 / 1.29 mmol/l) (men/women)
- Blood pressure $\geq 130 / \geq 85$ mmHg
- Fasting glucose ≥ 1.10 g/l (6.1 mmol/l)

American Association of Clinical Endocrinology, American College of Endocrinology (ACE) [14]

ACE Position Statement on the insulin resistance syndrome*, 2002

- Abnormalities of the insulin resistance syndrome
- Triglycerides ≥ 1.50 g/l (1.7 mmol/l)
- HDL-cholesterol $< 0.40 / 0.50$ g/l (1.04 / 1.29 mmol/l) (men/women)
- Blood pressure $> 130 / 85$ mmHg
- Glucose: fasting 1.10 - 1.25 g/l (6.1 - 6.9 mmol/l), 2 hours post-glucose challenge 1.40 - 2.00 g/l (7.8 - 11.1 mmol/l)

*The diagnosis of the insulin resistance syndrome must be based on the professional opinion of the physician.

International Diabetes Federation (IDF) [15, 16]

Consensus worldwide definition of the metabolic syndrome, 2005

Central obesity ^{*†} - ethnic specific

Europids $\geq 94 / 80$ cm (men / women) (*In the USA the ATP III (102 male, 88 female) are likely to be used for clinical purposes*)

South Asians $\geq 90 / 80$ cm (men / women)

Chinese $\geq 90 / 80$ cm (men / women)

Japan $\geq 85 / 90$ cm (men / women)

Ethnic Central and South Americans: use South Asians recommendations

Sub-Saharan Africans: use Europid recommendations

Eastern Mediterranean and Middle East (Arab): use Europid recommendations

plus any two of the following four factors:

- raised triglycerides level: ≥ 1.50 g/l (1.7 mmol/l) or a specific treatment for this lipid abnormality (given as > 1.50 g/d in [16])
- reduced HDL-cholesterol: $< 0.40/0.50$ g/l (1.03 / 1.29 mmol/l) (men/women) or a treatment specific for this lipid abnormality
- raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension
- raised fasting plasma glucose ≥ 1.00 g/l (5.6 mmol/l) or previously diagnosed type 2 diabetes.

American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) diagnostic criteria for Metabolic Syndrome 2005 [17, 18]

Three or more of the following risk factors:

- Elevated waist circumference: $\geq 102 / 88$ cm (men / women)
- Elevated triglycerides ≥ 1.50 g/l (1.7 mmol/l) or drug treatment for elevated triglycerides
- Reduced HDL-cholesterol $< 0.40 / 0.50$ g/l (1.04 / 1.29 mmol/l) (men/women) or drug treatment for reduced HDL-cholesterol (there is an incorrect conversion from mg/dl to mmol/l, and the correction conversion is 1.03 / 1.29 mmol/l)
- Elevated blood pressure ≥ 130 or ≥ 85 mmHg or drug treatment for hypertension
- Elevated fasting glucose ≥ 1.00 g/l (5.6 mmol/l) or drug treatment for elevated glucose

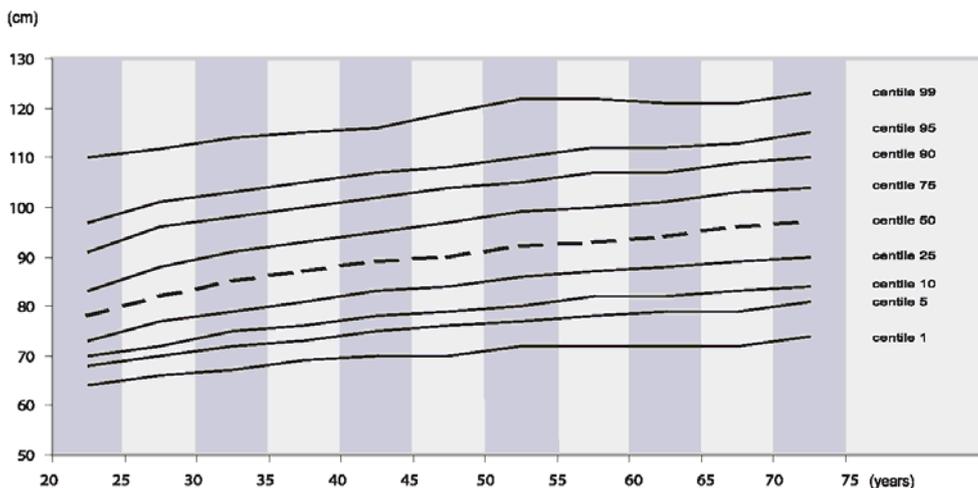
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Distribution of the centiles, means and standard deviations, according to age, of parameters included in the metabolic syndrome. Population is 130,882 consultants, 65,372 men and 65,510 women, examined in 2002-2004 at the "Institut inter Régional de la Santé", (IRSA) an Institute in central-western France which provides health examinations financed by the French social security system. The last column shows the reference values for a population aged 20-74 years with the same age structure as the French population according to the 1999 census.

Waist circumference (cm) : centiles by age class on 65,372 men from preventive health centers (IRSA, France)

	Age (years)											
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126
mean	79.2	83.2	85.8	87.5	89.3	90.9	92.7	94.0	94.6	96.0	97.4	89.1
standard deviation	9.2	9.5	9.7	9.7	9.8	10.0	10.1	10.3	10.0	10.4	10.3	11.1
centiles	99	110	112	114	115	116	119	122	122	121	121	118
	95	97	101	103	105	107	108	110	112	112	113	108
	90	91	96	98	100	102	104	105	107	107	109	104
	85	88	92	95	97	99	101	103	104	105	106	100
	80	85	90	93	95	97	98	100	102	103	104	98
	75	83	88	91	93	95	97	99	100	101	103	96
	70	82	87	90	92	93	95	97	99	99	101	94
	65	81	85	88	90	92	94	96	97	98	100	93
	60	80	84	87	89	91	93	94	96	97	98	91
	55	78	83	86	88	90	91	93	95	95	97	90
	50	78	82	85	87	89	90	92	93	94	96	88
	45	77	81	84	85	87	89	91	92	93	95	87
	40	76	80	83	84	86	88	90	91	92	93	86
	35	75	79	82	83	85	87	89	90	90	92	84
	30	74	78	80	82	84	85	87	88	89	91	83
	25	73	77	79	81	83	84	86	87	88	89	81
	20	72	75	78	79	81	83	84	85	86	88	80
15	71	74	76	78	80	81	83	84	85	86	78	
10	70	72	75	76	78	79	80	82	82	83	75	
5	68	70	72	73	75	76	77	78	79	79	72	
1	64	66	67	69	70	70	72	72	72	72	74	68

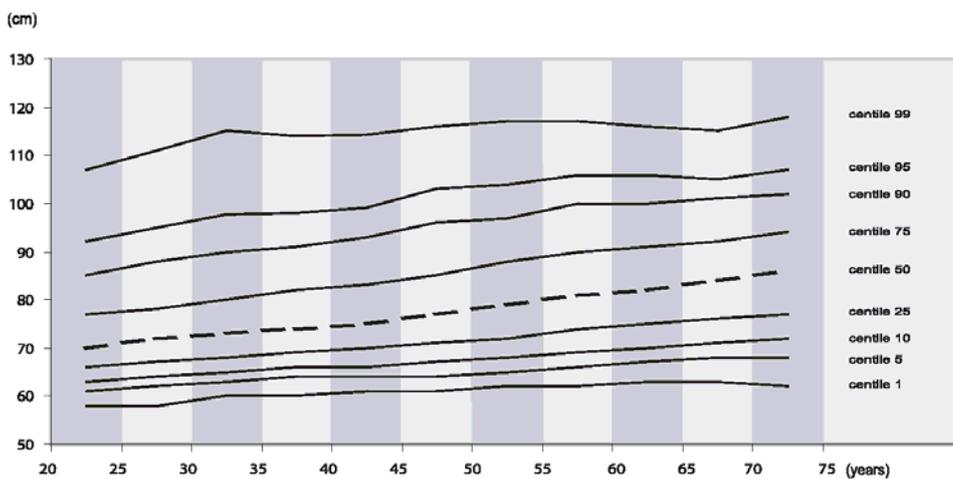
* population with the same age structure as the French men 1999 census population aged 20-74.



Waist circumference (cm) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)											
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874
mean	72.4	74.2	75.6	76.7	77.6	79.3	80.9	82.8	83.7	84.7	86.3	78.9
standard deviation	9.9	10.6	11.0	10.9	11.2	11.9	12.0	12.1	11.9	11.6	11.8	12.0
centiles	99	107	111	115	114	114	116	117	117	116	115	118
	95	92	95	98	98	99	103	104	106	106	105	107
	90	85	88	90	91	93	96	97	100	100	101	102
	85	81	84	86	87	89	91	93	95	96	97	98
	80	78	81	83	84	86	88	90	92	93	94	96
	75	77	78	80	82	83	85	88	90	91	92	94
	70	75	77	78	80	81	83	85	88	89	90	92
	65	73	76	77	78	79	81	84	86	87	88	91
	60	72	74	75	77	78	80	82	84	85	87	89
	55	71	73	74	75	76	78	80	82	84	85	87
	50	70	72	73	74	75	77	79	81	82	84	86
	45	69	71	72	73	74	75	77	79	81	82	84
	40	68	70	71	72	73	74	76	78	79	81	83
	35	68	69	70	71	72	73	75	77	78	80	81
	30	67	68	69	70	71	72	73	75	76	78	80
	25	66	67	68	69	70	71	72	74	75	76	77
	20	65	66	67	68	69	70	71	72	73	74	76
15	64	65	66	67	67	68	69	71	72	73	73	
10	63	64	65	66	66	67	68	69	70	71	72	
5	61	62	63	64	64	64	65	66	67	68	68	
1	58	58	60	60	61	61	62	62	63	63	62	

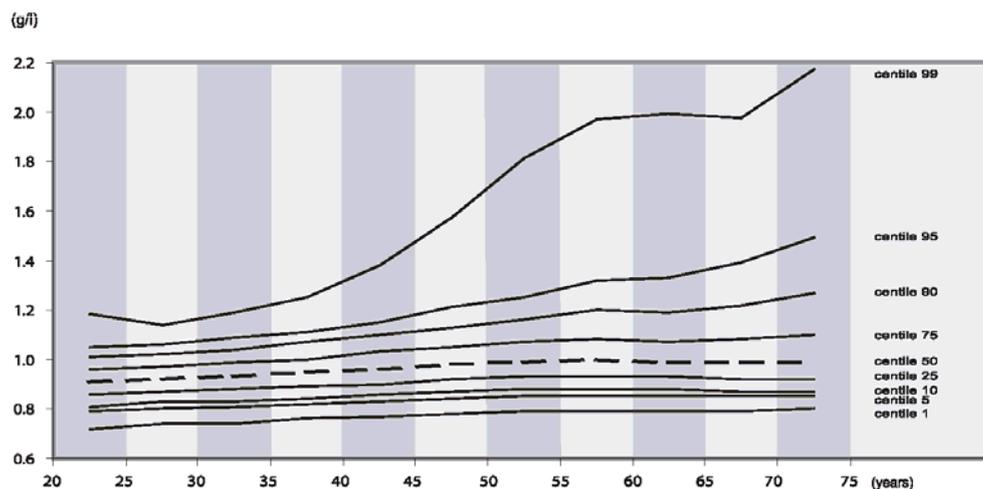
* population with the same age structure as the French women 1999 census population aged 20-74.



**Glucose (g/l) : centiles by age class on 65,372 men
from preventive health centers (IRSA, France)**

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126	
mean	0.91	0.92	0.94	0.96	0.98	1.00	1.02	1.04	1.03	1.04	1.05	0.98	
standard deviation	0.11	0.10	0.11	0.12	0.14	0.16	0.19	0.21	0.21	0.22	0.25	0.17	
centiles	99	1.19	1.14	1.19	1.25	1.38	1.57	1.81	1.97	1.99	1.97	2.17	1.66
	95	1.05	1.06	1.09	1.11	1.15	1.21	1.25	1.32	1.33	1.39	1.49	1.20
	90	1.01	1.02	1.04	1.07	1.10	1.13	1.16	1.2	1.19	1.22	1.27	1.12
	85	0.99	1.00	1.02	1.04	1.07	1.10	1.12	1.14	1.14	1.15	1.18	1.08
	80	0.98	0.98	1.00	1.02	1.04	1.07	1.09	1.11	1.10	1.11	1.13	1.05
	75	0.96	0.97	0.99	1.00	1.03	1.05	1.07	1.08	1.07	1.08	1.10	1.03
	70	0.95	0.96	0.97	0.99	1.01	1.03	1.05	1.06	1.05	1.06	1.07	1.01
	65	0.93	0.95	0.96	0.98	1.00	1.02	1.03	1.04	1.04	1.04	1.04	1.00
	60	0.92	0.94	0.95	0.97	0.99	1.01	1.02	1.03	1.02	1.02	1.03	0.98
	55	0.92	0.93	0.94	0.96	0.97	0.99	1.01	1.01	1.01	1.01	1.01	0.97
	50	0.91	0.92	0.93	0.95	0.96	0.98	0.99	1.00	0.99	0.99	0.99	0.96
	45	0.90	0.91	0.92	0.94	0.95	0.97	0.98	0.98	0.98	0.98	0.98	0.95
	40	0.89	0.90	0.91	0.92	0.94	0.96	0.97	0.97	0.97	0.96	0.97	0.93
	35	0.88	0.89	0.90	0.91	0.93	0.95	0.96	0.96	0.95	0.95	0.95	0.92
	30	0.87	0.88	0.89	0.90	0.92	0.93	0.94	0.95	0.94	0.94	0.94	0.91
	25	0.86	0.87	0.88	0.89	0.90	0.92	0.93	0.93	0.93	0.92	0.92	0.90
20	0.85	0.86	0.87	0.88	0.89	0.90	0.92	0.92	0.91	0.91	0.91	0.88	
15	0.83	0.85	0.85	0.86	0.88	0.89	0.90	0.90	0.90	0.89	0.89	0.87	
10	0.81	0.83	0.83	0.84	0.86	0.87	0.88	0.88	0.88	0.87	0.87	0.85	
5	0.79	0.80	0.81	0.82	0.83	0.84	0.85	0.85	0.85	0.85	0.85	0.82	
1	0.72	0.74	0.74	0.76	0.77	0.78	0.79	0.79	0.79	0.79	0.80	0.76	

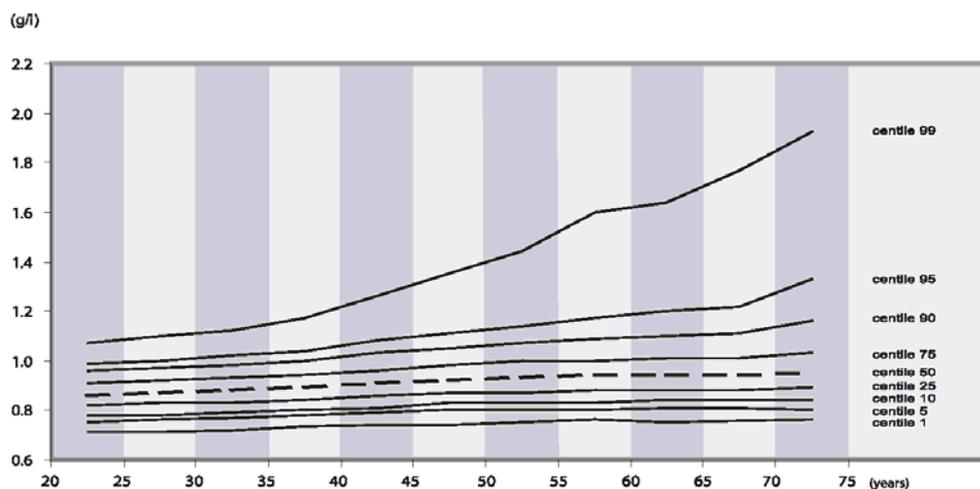
* population with the same age structure as the French men 1999 census population aged 20-74.



Glucose (g/l) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874	
mean	0.87	0.87	0.89	0.90	0.92	0.94	0.95	0.96	0.97	0.97	0.99	0.93	
standard deviation	0.10	0.10	0.10	0.11	0.12	0.15	0.15	0.16	0.17	0.19	0.20	0.15	
centiles	99	1.07	1.10	1.12	1.17	1.26	1.35	1.44	1.60	1.63	1.77	1.93	1.43
	95	0.99	1.00	1.02	1.04	1.08	1.11	1.14	1.17	1.20	1.22	1.33	1.11
	90	0.96	0.97	0.98	1.00	1.03	1.05	1.07	1.09	1.10	1.11	1.16	1.04
	85	0.94	0.95	0.96	0.98	1.00	1.02	1.04	1.05	1.06	1.06	1.08	1.01
	80	0.92	0.93	0.94	0.96	0.98	1.00	1.01	1.02	1.03	1.03	1.06	0.99
	75	0.91	0.92	0.93	0.94	0.96	0.98	1.00	1.00	1.01	1.01	1.03	0.97
	70	0.90	0.91	0.92	0.93	0.95	0.97	0.98	0.99	0.99	0.99	1.01	0.95
	65	0.89	0.89	0.91	0.92	0.94	0.95	0.96	0.97	0.97	0.97	0.98	0.94
	60	0.88	0.89	0.90	0.91	0.93	0.94	0.95	0.96	0.96	0.96	0.97	0.93
	55	0.87	0.88	0.89	0.9	0.92	0.93	0.94	0.95	0.95	0.95	0.96	0.92
	50	0.86	0.87	0.88	0.89	0.91	0.92	0.93	0.94	0.94	0.94	0.95	0.90
	45	0.85	0.86	0.87	0.88	0.90	0.91	0.92	0.92	0.92	0.93	0.94	0.89
	40	0.84	0.85	0.86	0.87	0.89	0.90	0.91	0.91	0.91	0.92	0.93	0.88
	35	0.84	0.84	0.85	0.86	0.88	0.89	0.90	0.90	0.90	0.91	0.91	0.87
	30	0.83	0.83	0.84	0.85	0.87	0.88	0.89	0.89	0.89	0.90	0.90	0.86
	25	0.82	0.83	0.83	0.84	0.86	0.87	0.87	0.88	0.88	0.88	0.89	0.85
	20	0.80	0.81	0.82	0.83	0.84	0.86	0.86	0.87	0.87	0.87	0.87	0.84
15	0.79	0.80	0.81	0.82	0.83	0.84	0.85	0.85	0.85	0.85	0.86	0.83	
10	0.78	0.78	0.79	0.8	0.81	0.83	0.83	0.83	0.84	0.84	0.84	0.81	
5	0.75	0.76	0.77	0.78	0.79	0.80	0.80	0.80	0.81	0.81	0.80	0.78	
1	0.71	0.71	0.72	0.74	0.74	0.74	0.75	0.76	0.75	0.76	0.76	0.73	

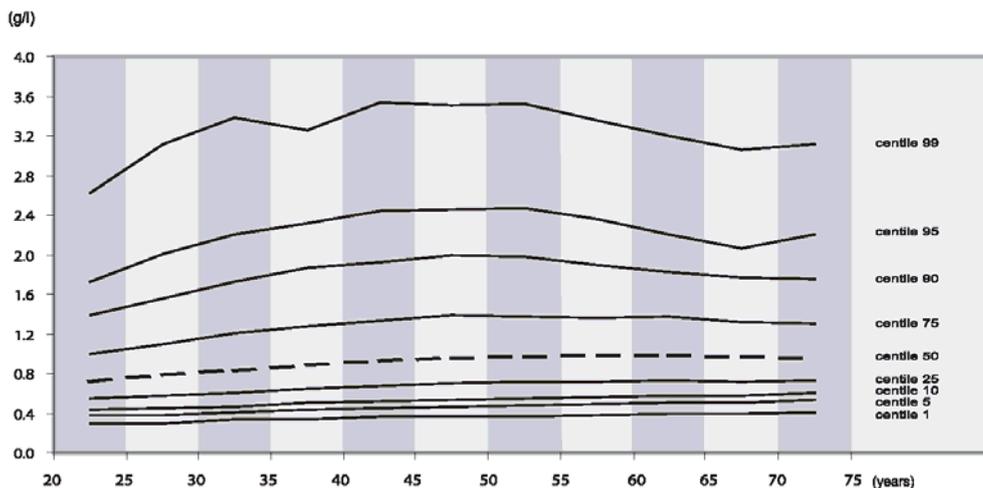
* population with the same age structure as the French women 1999 census population aged 20-74.



**Triglycerides (g/l) : centiles by age class on 65,372 men
from preventive health centers (IRSA, France)**

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126	
mean	0.84	0.93	1.01	1.06	1.11	1.14	1.15	1.14	1.12	1.09	1.10	1.06	
standard deviation	0.47	0.56	0.64	0.63	0.67	0.66	0.66	0.65	0.59	0.53	0.53	0.62	
centiles	99	2.62	3.11	3.38	3.26	3.53	3.51	3.53	3.35	3.20	3.06	3.12	3.28
	95	1.72	2.01	2.20	2.32	2.44	2.45	2.47	2.36	2.20	2.06	2.20	2.26
	90	1.39	1.56	1.73	1.86	1.92	1.99	1.98	1.90	1.83	1.78	1.75	1.81
	85	1.19	1.34	1.49	1.58	1.67	1.71	1.70	1.66	1.62	1.57	1.56	1.57
	80	1.09	1.21	1.33	1.41	1.49	1.53	1.53	1.49	1.48	1.44	1.41	1.40
	75	1.00	1.10	1.21	1.28	1.34	1.39	1.38	1.36	1.37	1.32	1.30	1.27
	70	0.92	1.02	1.11	1.18	1.23	1.28	1.28	1.27	1.26	1.24	1.20	1.17
	65	0.86	0.95	1.02	1.09	1.14	1.18	1.18	1.18	1.18	1.16	1.14	1.09
	60	0.80	0.88	0.95	1.01	1.07	1.09	1.10	1.10	1.10	1.08	1.09	1.02
	55	0.76	0.83	0.88	0.94	0.99	1.02	1.04	1.04	1.04	1.02	1.01	0.96
	50	0.72	0.78	0.83	0.89	0.93	0.96	0.97	0.98	0.98	0.97	0.96	0.90
	45	0.68	0.73	0.78	0.83	0.87	0.90	0.91	0.92	0.92	0.92	0.92	0.84
	40	0.65	0.69	0.73	0.78	0.82	0.85	0.86	0.87	0.87	0.87	0.87	0.79
	35	0.61	0.65	0.69	0.73	0.76	0.80	0.80	0.82	0.82	0.82	0.82	0.74
	30	0.58	0.61	0.65	0.68	0.72	0.75	0.76	0.77	0.78	0.78	0.78	0.70
	25	0.55	0.57	0.61	0.64	0.67	0.70	0.71	0.72	0.73	0.72	0.73	0.65
	20	0.51	0.53	0.57	0.60	0.63	0.65	0.66	0.67	0.69	0.68	0.69	0.61
15	0.47	0.49	0.52	0.55	0.57	0.60	0.61	0.62	0.63	0.63	0.65	0.56	
10	0.43	0.45	0.47	0.50	0.52	0.54	0.55	0.56	0.58	0.58	0.60	0.51	
5	0.38	0.38	0.41	0.44	0.45	0.47	0.48	0.49	0.50	0.50	0.53	0.44	
1	0.30	0.30	0.33	0.33	0.36	0.37	0.37	0.38	0.40	0.40	0.41	0.34	

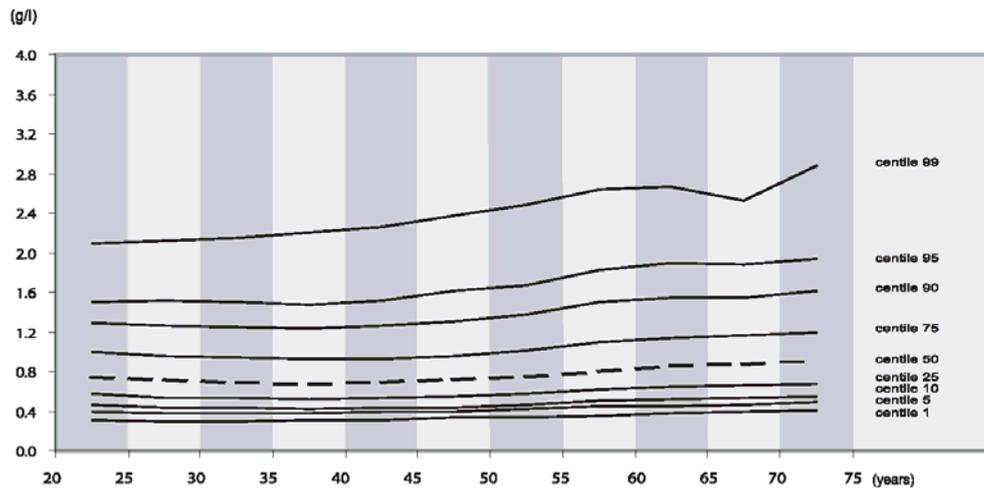
* population with the same age structure as the French men 1999 census population aged 20-74.



Triglycerides (g/l) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874	
mean	0.83	0.80	0.79	0.78	0.79	0.82	0.85	0.93	0.97	0.98	1.02	0.85	
standard deviation	0.36	0.38	0.38	0.39	0.40	0.45	0.44	0.47	0.48	0.46	0.51	0.43	
centiles	99	2.09	2.12	2.15	2.20	2.26	2.37	2.49	2.64	2.67	2.53	2.88	2.41
	95	1.50	1.51	1.50	1.48	1.52	1.62	1.67	1.83	1.89	1.88	1.93	1.65
	90	1.29	1.27	1.25	1.23	1.26	1.31	1.37	1.50	1.55	1.54	1.61	1.35
	85	1.18	1.14	1.10	1.09	1.11	1.15	1.20	1.31	1.37	1.39	1.41	1.21
	80	1.07	1.03	1.01	1.00	1.01	1.04	1.09	1.19	1.24	1.26	1.29	1.10
	75	1.00	0.96	0.94	0.93	0.93	0.96	1.01	1.09	1.14	1.16	1.20	1.02
	70	0.94	0.90	0.87	0.86	0.86	0.89	0.93	1.02	1.07	1.09	1.12	0.95
	65	0.88	0.84	0.83	0.81	0.81	0.83	0.87	0.96	1.01	1.03	1.06	0.89
	60	0.83	0.80	0.78	0.77	0.77	0.79	0.82	0.90	0.95	0.97	1.01	0.84
	55	0.79	0.75	0.74	0.73	0.73	0.74	0.78	0.85	0.89	0.91	0.96	0.79
	50	0.75	0.71	0.69	0.68	0.69	0.71	0.74	0.80	0.85	0.87	0.91	0.75
	45	0.72	0.68	0.66	0.65	0.65	0.67	0.70	0.76	0.81	0.83	0.86	0.71
	40	0.68	0.64	0.63	0.61	0.62	0.64	0.67	0.72	0.76	0.79	0.82	0.67
	35	0.65	0.61	0.60	0.58	0.59	0.61	0.63	0.68	0.72	0.75	0.77	0.64
	30	0.62	0.58	0.56	0.55	0.56	0.58	0.60	0.65	0.68	0.70	0.72	0.60
	25	0.58	0.54	0.53	0.52	0.53	0.55	0.57	0.62	0.65	0.66	0.68	0.57
	20	0.55	0.51	0.50	0.49	0.50	0.52	0.53	0.58	0.61	0.62	0.65	0.54
	15	0.50	0.47	0.46	0.46	0.47	0.48	0.5	0.54	0.57	0.57	0.6	0.50
	10	0.46	0.43	0.43	0.42	0.43	0.44	0.46	0.50	0.52	0.53	0.55	0.46
	5	0.40	0.38	0.38	0.38	0.39	0.40	0.42	0.45	0.45	0.47	0.49	0.40
	1	0.31	0.30	0.30	0.31	0.31	0.33	0.34	0.36	0.38	0.39	0.41	0.32

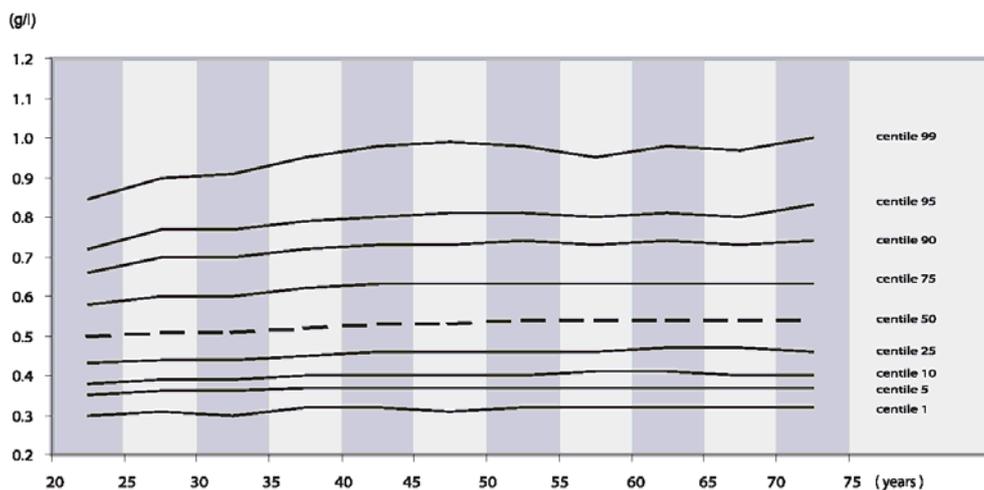
* population with the same age structure as the French women 1999 census population aged 20-74.



HDL-Cholesterol (g/l) : centiles by age class on 65,372 men from preventive health centers (IRSA, France)

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126	
mean	0.51	0.53	0.53	0.54	0.55	0.56	0.56	0.56	0.56	0.56	0.56	0.55	
standard deviation	0.12	0.13	0.13	0.13	0.14	0.14	0.14	0.13	0.14	0.13	0.14	0.13	
centiles	99	0.85	0.90	0.91	0.95	0.98	0.99	0.98	0.95	0.98	0.97	1.00	0.95
	95	0.72	0.77	0.77	0.79	0.80	0.81	0.81	0.80	0.81	0.80	0.83	0.79
	90	0.66	0.70	0.70	0.72	0.73	0.73	0.74	0.73	0.74	0.73	0.74	0.72
	85	0.63	0.66	0.65	0.67	0.69	0.69	0.69	0.69	0.69	0.69	0.70	0.68
	80	0.60	0.62	0.63	0.64	0.65	0.66	0.66	0.66	0.66	0.66	0.66	0.64
	75	0.58	0.60	0.60	0.62	0.63	0.63	0.63	0.63	0.63	0.63	0.63	0.62
	70	0.56	0.58	0.58	0.59	0.60	0.61	0.61	0.61	0.61	0.61	0.61	0.60
	65	0.54	0.56	0.56	0.57	0.58	0.59	0.59	0.59	0.59	0.59	0.59	0.58
	60	0.53	0.54	0.54	0.56	0.57	0.57	0.57	0.57	0.57	0.57	0.57	0.56
	55	0.51	0.53	0.53	0.54	0.55	0.55	0.55	0.55	0.55	0.55	0.56	0.54
	50	0.50	0.51	0.51	0.52	0.53	0.53	0.54	0.54	0.54	0.54	0.54	0.53
	45	0.48	0.50	0.50	0.51	0.52	0.52	0.52	0.52	0.53	0.53	0.52	0.51
	40	0.47	0.48	0.48	0.49	0.50	0.50	0.51	0.51	0.51	0.51	0.51	0.50
	35	0.46	0.47	0.47	0.48	0.49	0.49	0.49	0.49	0.50	0.50	0.49	0.48
	30	0.44	0.45	0.46	0.47	0.47	0.47	0.48	0.48	0.48	0.48	0.48	0.47
	25	0.43	0.44	0.44	0.45	0.46	0.46	0.46	0.46	0.47	0.47	0.46	0.45
	20	0.41	0.42	0.43	0.43	0.44	0.44	0.44	0.45	0.45	0.45	0.45	0.44
	15	0.40	0.40	0.41	0.42	0.42	0.43	0.43	0.43	0.43	0.43	0.42	0.42
	10	0.38	0.39	0.39	0.40	0.40	0.40	0.40	0.41	0.41	0.40	0.40	0.40
5	0.35	0.36	0.36	0.37	0.37	0.37	0.37	0.37	0.37	0.37	0.37	0.37	
1	0.30	0.31	0.30	0.32	0.32	0.31	0.32	0.32	0.32	0.32	0.32	0.31	

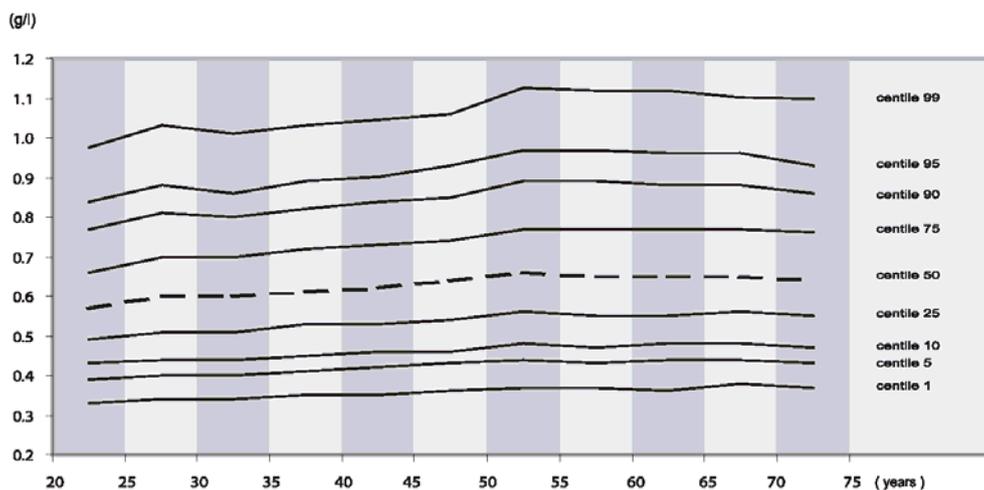
* population with the same age structure as the French men 1999 census population aged 20-74.



HDL-Cholesterol (g/l) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)											
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874
mean	0.59	0.61	0.61	0.63	0.64	0.65	0.67	0.67	0.67	0.67	0.66	0.64
standard deviation	0.14	0.15	0.14	0.15	0.15	0.15	0.16	0.16	0.16	0.16	0.16	0.15
centiles	99	0.97	1.03	1.01	1.03	1.04	1.06	1.13	1.12	1.12	1.10	1.10
	95	0.84	0.88	0.86	0.89	0.90	0.93	0.97	0.97	0.96	0.96	0.93
	90	0.77	0.81	0.80	0.82	0.84	0.85	0.89	0.89	0.88	0.88	0.86
	85	0.73	0.76	0.76	0.78	0.80	0.81	0.84	0.84	0.84	0.83	0.82
	80	0.69	0.73	0.73	0.74	0.76	0.77	0.80	0.80	0.80	0.80	0.78
	75	0.66	0.70	0.70	0.72	0.73	0.74	0.77	0.77	0.77	0.77	0.76
	70	0.64	0.67	0.67	0.69	0.71	0.72	0.75	0.74	0.74	0.74	0.73
	65	0.62	0.65	0.65	0.67	0.68	0.70	0.72	0.72	0.71	0.71	0.70
	60	0.60	0.63	0.63	0.65	0.66	0.67	0.70	0.69	0.69	0.69	0.68
	55	0.58	0.61	0.61	0.63	0.64	0.65	0.68	0.67	0.67	0.67	0.66
	50	0.57	0.60	0.60	0.61	0.62	0.64	0.66	0.65	0.65	0.65	0.64
	45	0.55	0.58	0.58	0.60	0.61	0.62	0.64	0.63	0.63	0.63	0.62
	40	0.54	0.56	0.56	0.58	0.59	0.60	0.62	0.61	0.61	0.61	0.60
	35	0.52	0.54	0.54	0.56	0.57	0.58	0.60	0.59	0.59	0.59	0.59
	30	0.51	0.53	0.53	0.54	0.55	0.56	0.58	0.57	0.57	0.57	0.57
	25	0.49	0.51	0.51	0.53	0.53	0.54	0.56	0.55	0.55	0.56	0.55
	20	0.47	0.49	0.49	0.50	0.51	0.52	0.54	0.53	0.53	0.53	0.52
15	0.45	0.46	0.47	0.48	0.49	0.49	0.51	0.50	0.50	0.51	0.50	
10	0.43	0.44	0.44	0.45	0.46	0.46	0.48	0.47	0.48	0.48	0.47	
5	0.39	0.40	0.40	0.41	0.42	0.43	0.44	0.43	0.44	0.44	0.43	
1	0.33	0.34	0.34	0.35	0.35	0.36	0.37	0.37	0.36	0.38	0.37	

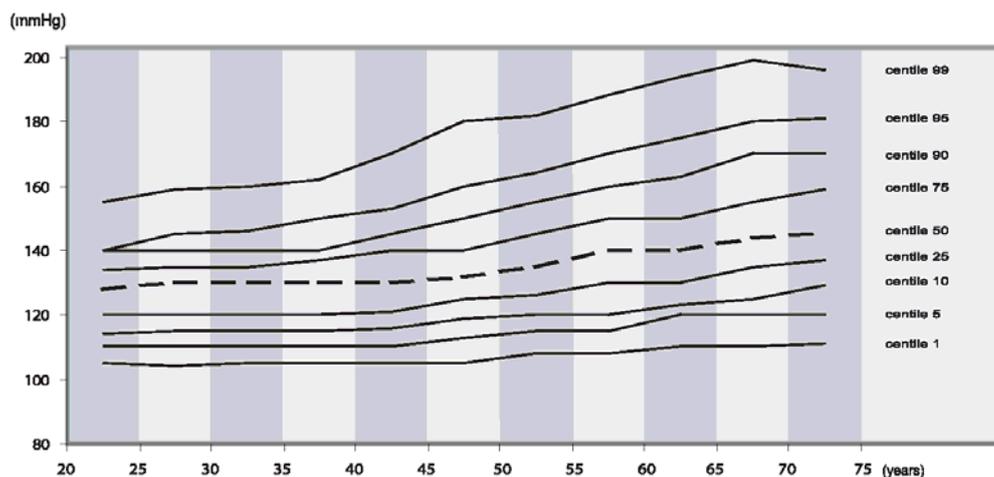
* population with the same age structure as the French women 1999 census population aged 20-74.



Systolic blood pressure (mmHg) : centiles by age class on 65,372 men from preventive health centers (IRSA, France)

	Age (years)												
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *	
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126	
mean	126.9	127.9	128.5	129.3	131.0	133.7	136.6	139.8	142.5	145.7	147.9	134.0	
standard deviation	10.5	10.9	11.2	11.7	12.8	14.2	15.1	16.4	16.9	17.9	17.7	15.3	
centiles	99	155	159	160	162	170	180	182	188	194	199	196	183
	95	140	145	146	150	153	160	164	170	175	180	181	160
	90	140	140	140	140	145	150	155	160	163	170	170	152
	85	139	140	140	140	140	146	150	155	159	161	165	148
	80	135	136	139	140	140	143	147	150	154	160	160	144
	75	134	135	135	137	140	140	145	150	150	155	159	140
	70	131	133	134	135	137	140	140	145	150	150	155	140
	65	130	130	131	133	135	139	140	144	146	150	151	139
	60	130	130	130	130	133	136	140	140	145	149	150	135
	55	130	130	130	130	130	135	138	140	141	145	149	134
	50	128	130	130	130	130	132	135	140	140	144	145	131
	45	125	127	128	130	130	130	134	138	140	140	144	130
	40	124	125	125	126	129	130	130	135	139	140	140	130
	35	121	123	124	125	125	130	130	132	135	140	140	129
	30	120	120	120	122	125	126	130	130	134	137	140	125
	25	120	120	120	120	121	125	126	130	130	135	137	123
	20	120	120	120	120	120	120	125	128	130	130	135	120
	15	117	118	119	120	120	120	120	124	127	130	130	120
	10	114	115	115	115	116	119	120	120	123	125	129	118
5	110	110	110	110	110	113	115	115	120	120	120	112	
1	105	104	105	105	105	105	108	108	110	110	111	105	

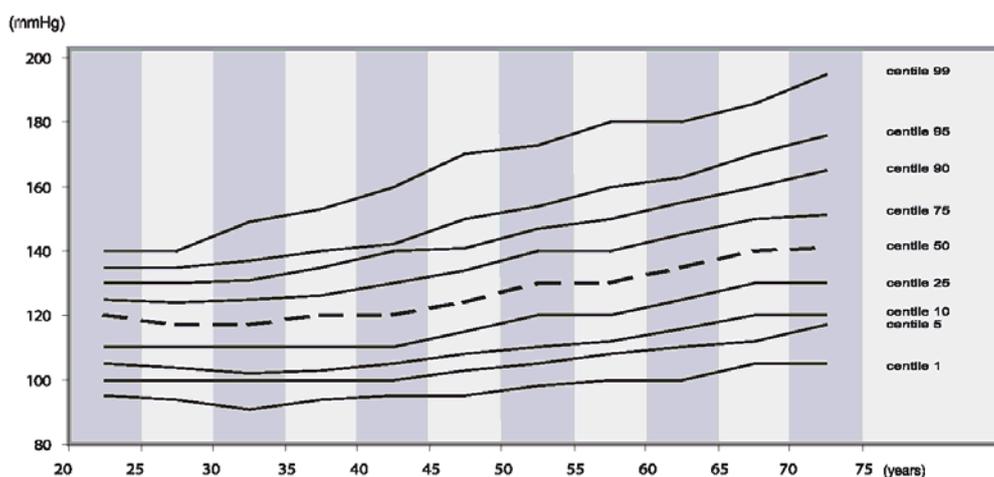
* population with the same age structure as the French men 1999 census population aged 20-74.



Systolic blood pressure (mmHg) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)											20-74 *	
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74		
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874	
mean	117.8	116.9	117.2	118.5	121.4	125.0	128.5	132.4	135.8	139.2	143.2	125.5	
standard deviation	10.5	10.9	11.8	12.4	13.7	14.7	15.3	16.0	16.2	16.7	17.6	16.4	
centiles	99	140	140	149	153	160	170	173	180	180	186	195	175
	95	135	135	137	140	142	150	154	160	163	170	176	155
	90	130	130	131	135	140	141	147	150	155	160	165	146
	85	130	130	130	130	135	140	142	148	150	155	160	140
	80	127	125	127	130	131	136	140	144	148	150	155	140
	75	125	124	125	126	130	134	140	140	145	150	151	135
	70	122	121	121	125	130	130	135	140	142	146	150	131
	65	120	120	120	121	125	130	133	139	140	144	149	130
	60	120	120	120	120	124	130	130	135	140	140	145	130
	55	120	120	120	120	120	125	130	134	139	140	144	125
	50	120	117	117	120	120	124	130	130	135	140	141	123
	45	117	115	115	116	120	120	126	130	133	138	140	120
	40	115	114	114	115	119	120	124	130	130	135	140	120
	35	114	111	111	113	115	120	120	126	130	132	136	120
	30	110	110	110	110	114	117	120	124	129	130	134	116
	25	110	110	110	110	110	115	120	120	125	130	130	114
	20	110	108	108	110	110	112	115	120	120	125	130	110
	15	107	105	105	105	108	110	112	116	120	120	128	110
	10	105	104	102	103	105	108	110	112	116	120	120	106
	5	100	100	100	100	100	103	105	108	110	112	117	102
	1	95	94	91	94	95	95	98	100	100	105	105	95

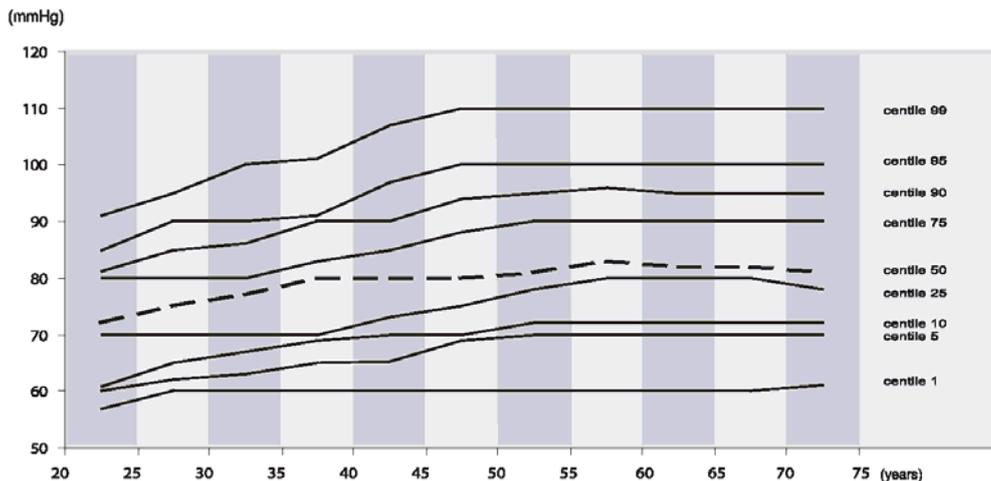
* population with the same age structure as the French women 1999 census population aged 20-74.



Diastolic blood pressure (mmHg) : centiles by age class on 65,372 men from preventive health centers (IRSA, France)

	Age (years)											
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *
n	3,436	4,812	7,068	8,850	8,885	9,077	9,038	6,474	3,649	2,684	1,399	19,126
mean	73.0	75.4	76.5	78.1	80.0	81.6	83.0	83.9	83.8	83.7	83.1	79.7
standard deviation	8.0	8.1	8.3	8.7	9.4	9.8	9.8	9.9	9.7	9.5	9.5	9.8
centiles	99	91	95	100	101	107	110	110	110	110	110	107
	95	85	90	90	91	97	100	100	100	100	100	97
	90	81	85	86	90	90	94	95	96	95	95	90
	85	80	82	85	86	90	90	91	93	92	92	90
	80	80	80	82	85	87	90	90	90	90	90	88
	75	80	80	80	83	85	88	90	90	90	90	85
	70	80	80	80	81	84	85	88	90	89	89	84
	65	77	80	80	80	82	85	85	87	87	87	81
	60	75	79	80	80	80	82	85	85	85	85	80
	55	74	77	80	80	80	80	83	85	84	84	80
	50	72	75	77	80	80	80	81	83	82	82	80
	45	70	75	75	79	80	80	80	80	80	80	80
	40	70	72	75	77	80	80	80	80	80	80	79
	35	70	70	72	75	77	80	80	80	80	80	76
	30	70	70	70	73	75	78	80	80	80	80	75
	25	70	70	70	70	73	75	78	80	80	80	72
	20	67	70	70	70	70	73	75	77	77	77	70
	15	65	69	70	70	70	70	72	74	75	75	70
	10	61	65	67	69	70	70	70	70	70	70	70
	5	60	60	61	65	65	69	70	70	70	70	65
	1	57	60	60	60	60	60	60	60	60	61	60

* population with the same age structure as the French men 1999 census population aged 20-74.



Diastolic blood pressure (mmHg) : centiles by age class on 65,510 women from preventive health centers (IRSA, France)

	Age (years)													
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	20-74 *		
n	5,261	5,398	7,264	7,368	8,558	8,879	8,619	6,655	3,509	2,580	1,419	19,874		
mean	71.0	71.8	72.5	73.8	75.5	76.8	78.3	79.3	79.7	80.1	80.5	75.8		
standard deviation	8.0	8.3	8.7	8.9	9.3	9.6	9.4	9.3	9.3	9.4	9.3	9.6		
centiles	99	90	90	95	100	100	101	102	102	105	104	105	100	
	95	84	85	87	90	90	92	94	95	95	95	95	90	
	90	80	81	83	85	87	90	90	90	90	90	91	88	
	85	80	80	80	81	85	86	88	90	90	90	90	85	
	80	80	80	80	80	82	84	85	86	87	88	88	83	
	75	77	79	80	80	80	81	84	85	85	85	86	80	
	70	75	76	78	80	80	80	82	83	84	85	85	80	
	65	74	75	76	78	80	80	80	81	82	82	83	80	
	60	71	73	75	76	80	80	80	80	80	80	80	81	80
	55	70	71	72	75	77	80	80	80	80	80	80	78	
	50	70	70	70	73	75	78	80	80	80	80	80	76	
	45	70	70	70	71	74	75	79	80	80	80	80	74	
	40	70	70	70	70	71	74	76	79	80	80	80	72	
	35	70	70	70	70	70	71	75	76	77	78	79	70	
	30	68	69	70	70	70	70	72	75	75	76	76	70	
	25	65	67	68	70	70	70	70	72	73	74	75	70	
	20	64	65	65	67	70	70	70	70	70	70	70	72	70
15	60	62	63	65	66	69	70	70	70	70	70	66		
10	61	61	61	61	64	65	68	70	70	70	70	63		
5	60	60	60	60	60	61	61	65	65	65	65	60		
1	55	55	55	58	59	60	60	60	60	60	60	57		

* population with the same age structure as the French women 1999 census population aged 20-74.

