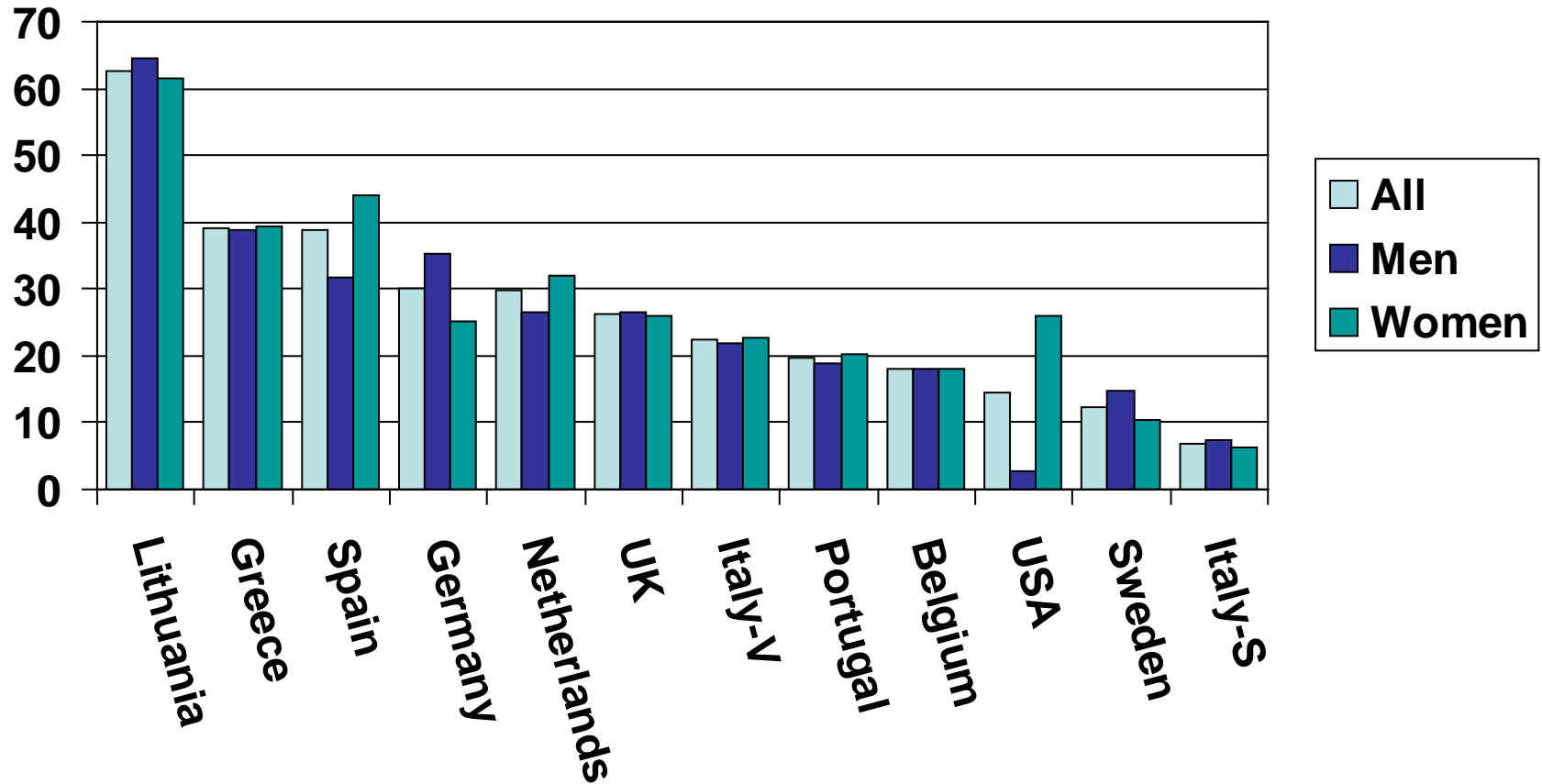
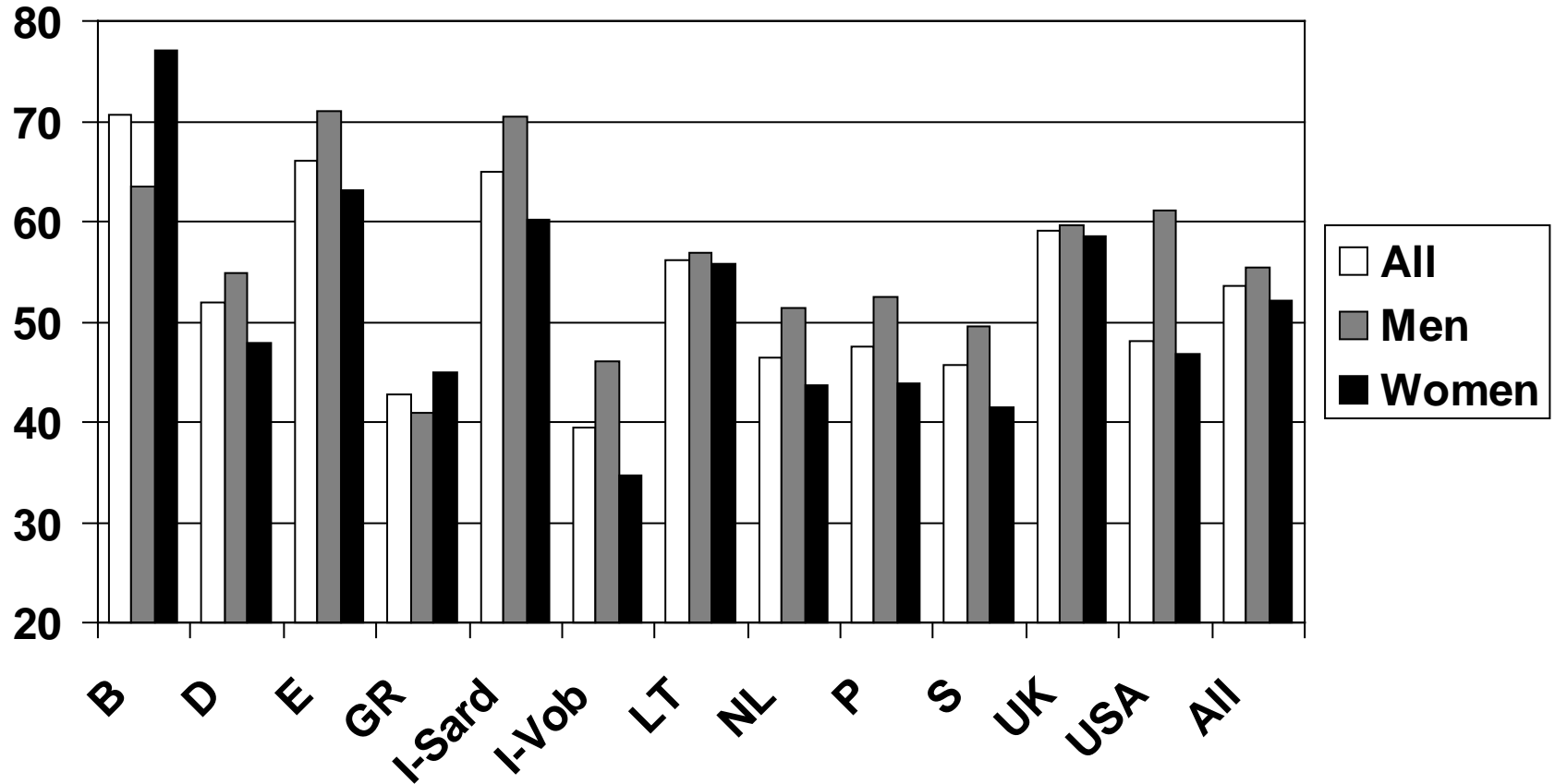


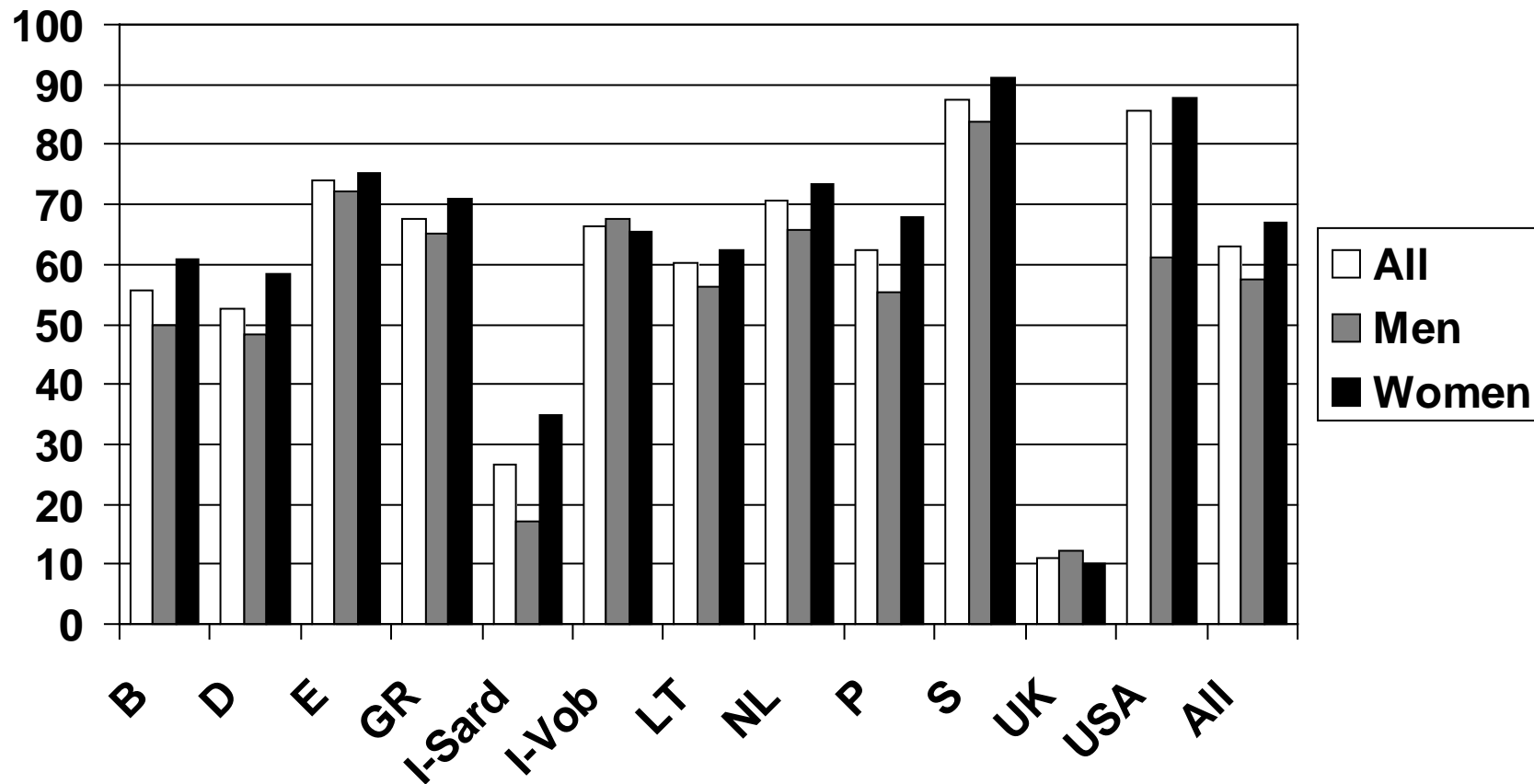
# MetS prevalence



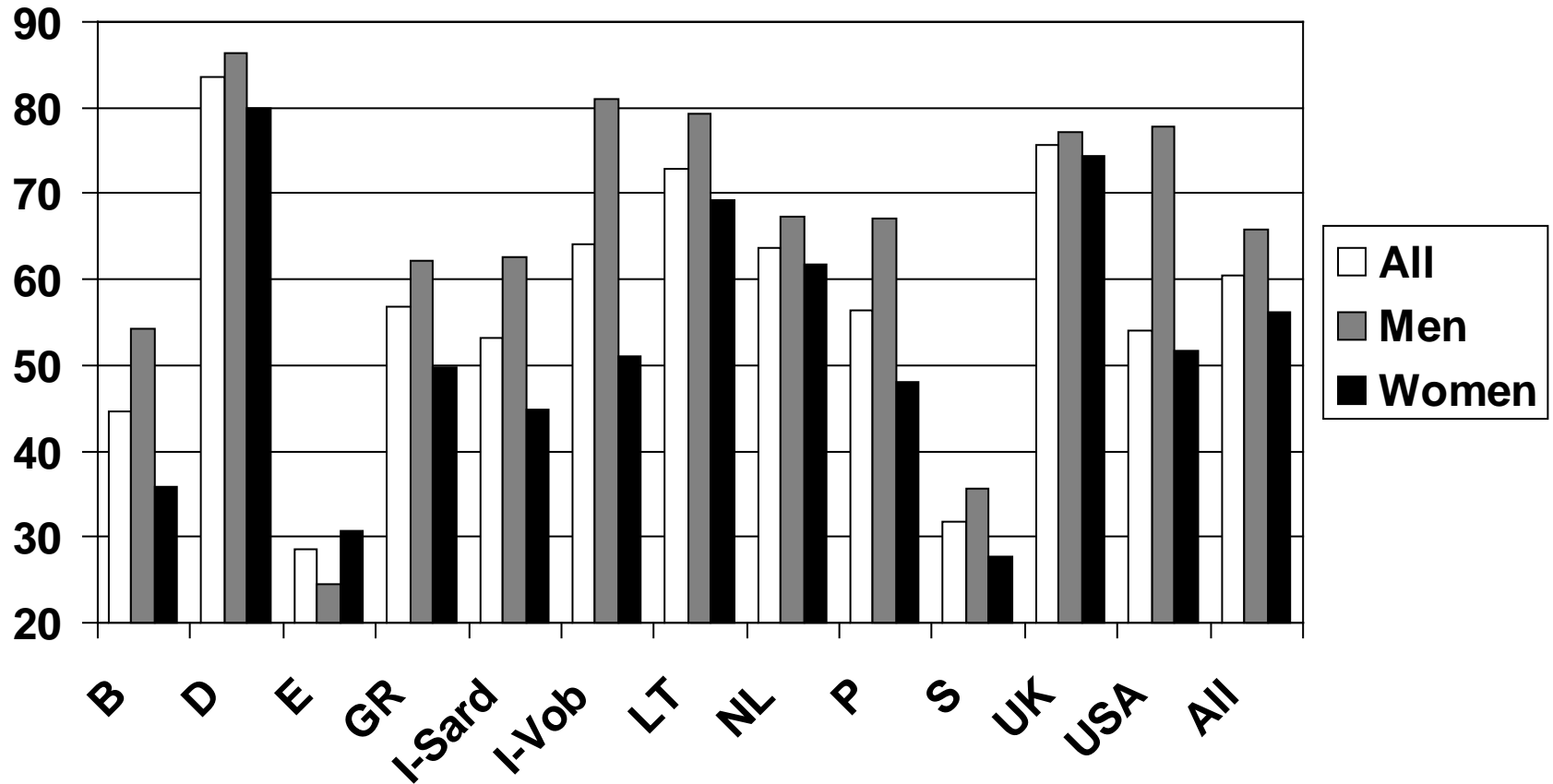
# High Glucose



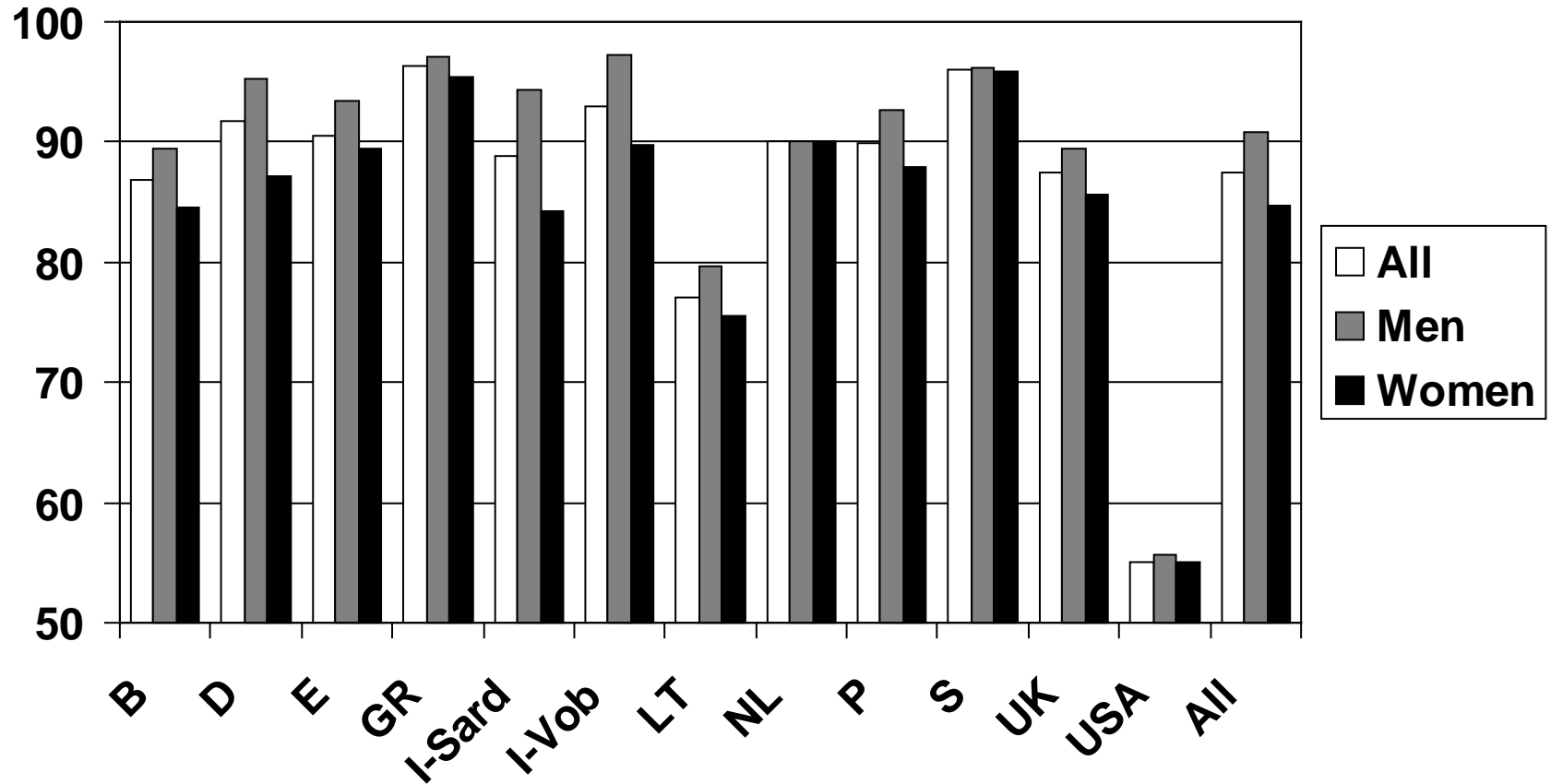
# Low HDL Cholesterol



# High Triglycerides

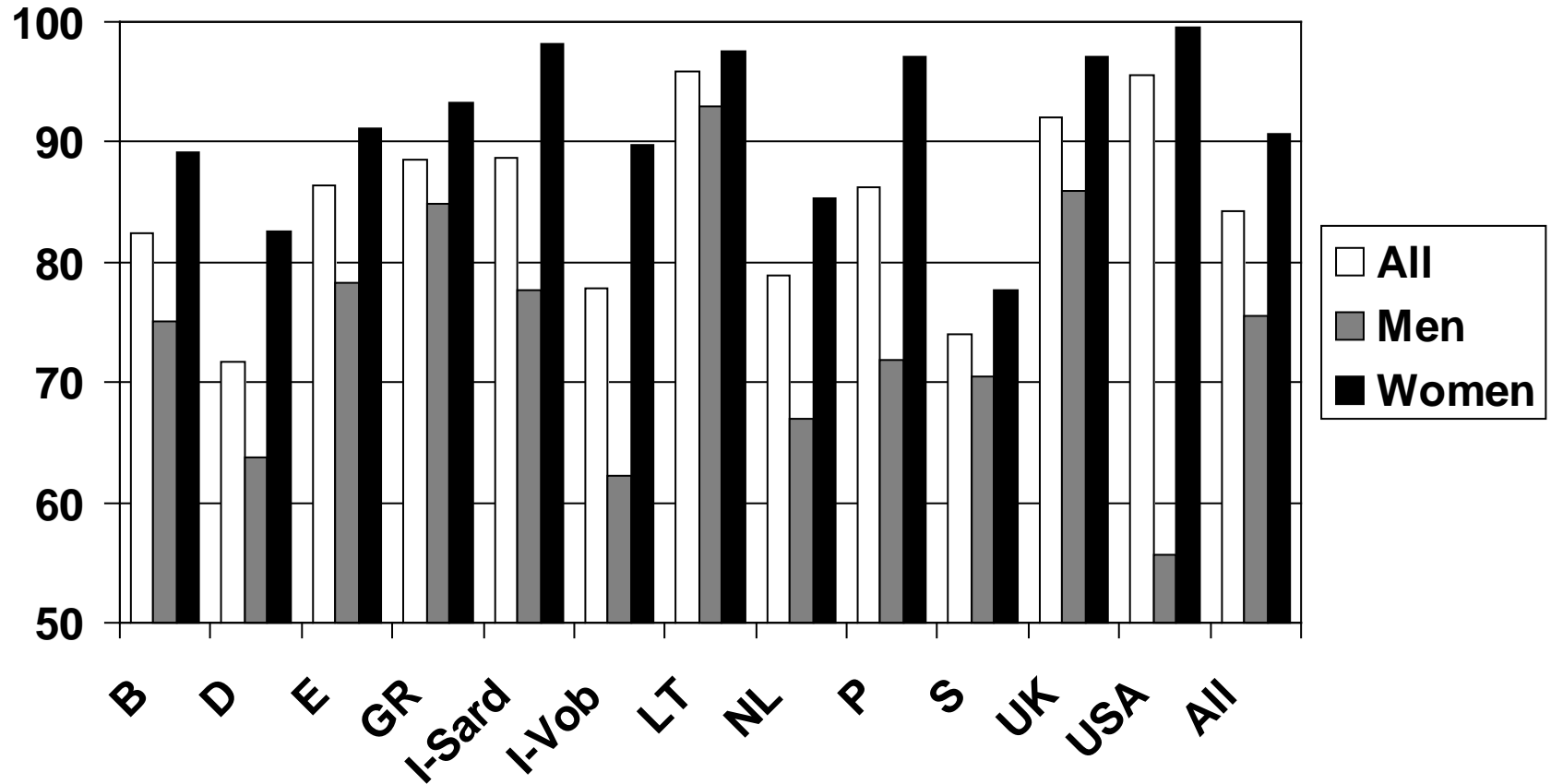


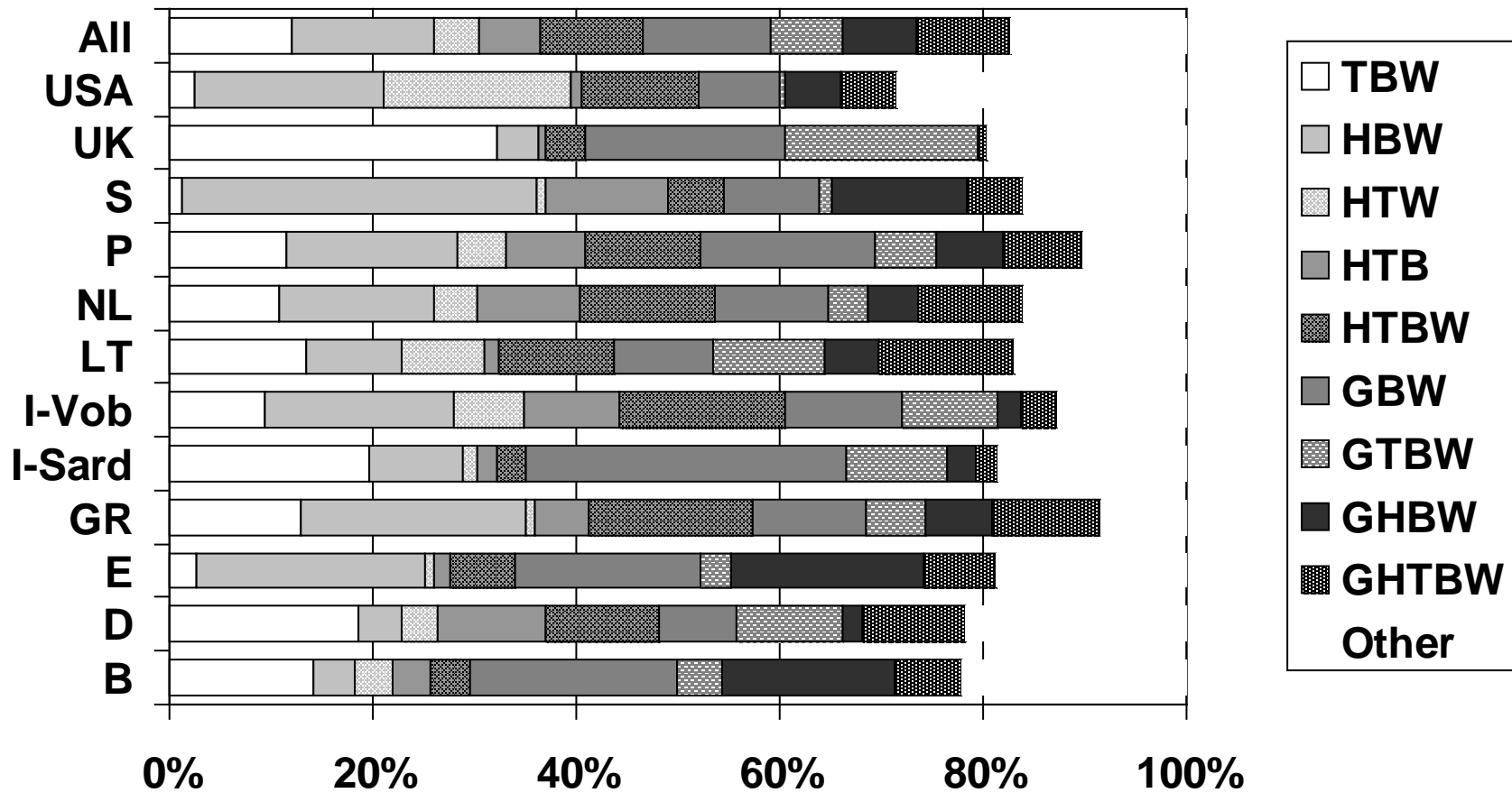
# Elevated Blood Pressure





# Abdominal Obesity





## **BRIEF DESCRIPTION OF THE PARTICIPATING COHORTS**

### **Asklepios Study**

The Asklepios Study is an extensively phenotyped population-representative random sample of Belgian volunteers free from clinically overt CV disease at baseline. An in-depth description of the Asklepios study protocol has been published (1). The population participating this study consisted of 2524 volunteers, aged 31 to 103 years, of which 52.6% were women,. Their data were collected between 2002 and 2004.

### **The Baltimore Longitudinal Study of Aging (BLSA)**

The Baltimore Longitudinal Study of Aging (BLSA) is a prospective study of community-dwelling, healthy volunteers conducted by the National Institute on Aging since 1958. Participants returned to the National Institute on Aging Clinical Unit in Baltimore, Maryland, at regular intervals for 2–3 days of medical, physiological, and psychological examinations (2-3). The population participating this study consisted of 1389 volunteers, aged 31 to 103 years, of which 50.1% were women,. Their data were collected between 1958 and 2012.

### **Guinaraes Study**

It is a population based study conducted in two adjacent cities (Guimarães and Vizela) of the region of Alto Minho (Portugal), characterized by one of the highest incidence of stroke in Europe. The cohort included randomly selected subjects. Each subject underwent a detailed medical history, blood pressure and anthropometric measurements, a 12-lead resting EKG, blood and urine analysis, measurements of arterial stiffness and central blood pressure, and (for subjects older than 50 years) cognitive testing. The population participating this study consisted of 2124 volunteers, aged 18 to 94 years, of which 55.7% were women,. Their data were collected between 2010 and 2011.

### **HYGEIA (Hippokration hYpertension, aGEIng and Arterial function)**

It is a cohort of 1225 naïve hypertensive subjects recruited in Athens, Greece, of broad age range (19-84 years) (HYGEIA-HTN) and a cohort of 466 subjects from the community-dwelling population of the Greek island of Ikaria (HYGEIA-AGE) (4). The population participating this study consisted of 1691 volunteers, aged 19 to 99, of which 42.6% were women,. Their data were collected between 2000 and 2005.

## **LitHiR**

LitHiR is a prospective study conducted in Lithuania. Caucasian subjects with metabolic syndrome (originally defined according to the updated NCEP definition) with no previous CV disease underwent full medical examination, which included a 12-lead resting ECG, exercise tolerance test, echocardiogram, blood tests for metabolic and lipid profile, and measurements of arterial structure and function. The population participating in this study consisted of 2948 volunteers, aged 22 to 78, of which 65.3% were women. Their data were collected between 2007 and 2012.

## **Malmö Diet and Cancer – Cardiovascular Cohort**

The Malmö Diet and Cancer (MDC-CC) study is a population-based, prospective epidemiologic cohort of 28 449 persons enrolled between 1991 and 1996 aged 45 to 69 years. From this cohort, 6103 persons were randomly selected to participate in the MDC cardiovascular cohort, which was designed to investigate the epidemiology of carotid artery disease (5). The population participating in this study consisted of 5533 volunteers, aged 46 to 66 years, of which 65.3% were women. Their data were collected between 1992 and 1996.

## **Rotterdam Study**

The Rotterdam Study (RS) is a prospective population-based cohort study comprising 7,983 subjects (78% response rate) aged 55 years or older. Baseline data (RS-I) were collected between 1990 and 1993. In 1999, inhabitants who turned 55 years of age or moved into the study district since the start of the study were invited to participate in an extension of the RS (RS-II) of whom 3,011 participated (67% response rate). The rationale and design of the RS have been described in detail elsewhere (6). The population participating in this study consisted of 4796 volunteers, aged 61 to 106 years, of which 59.9% were women. During the third examination phase from the RS-I (1997-1999) and the first examination phase from the RS-II (1999-2001), measurements of arterial stiffness were performed.

## **SardiNIA Study**

The SardiNIA Study investigates the genetics and epidemiology of complex traits / phenotypes, including CV risk factors and arterial properties, in a Sardinian founder population (7-8). Study design and measurements have been described previously (7-8). Follow-up visits occurred every 3 years. The population participating in this study consisted of 6123 volunteers, aged 14 to 101 years, of which 57.5% were women. Their data were collected between 2001 and 2004.

## **Study of Health in Pomerania (SHIP)**

It is a population-based project in West Pomerania, the north-east area of Germany. Samples are drawn from population registries. The original SHIP cohort was established in 1997 and comprised 4308 subjects aged 20 to 79 years having participated in the baseline examinations (response 68.8%) (9). All cohorts are comprehensively characterized. Fasting glucose and triglycerides were estimated from non-fasting sample according to the method suggested by Lidfield et al (9). The population participating this study consisted of 4308 volunteers, aged 20 to 79 years, of which 50.9% were women,. Their data were collected between 1997 and 2001

## **SMART Study**

The SMART Study was designed to investigate the effect of individual risk factors in isolation and clustered on arterial properties and CV events. The cardiovascular risk was also assessed using the ESC Heartscore tool. Subjects undergo periodical follow-up in order to look at outcome data. The population participating this study consisted of 484 volunteers, aged 34 to 85 years, of which 55.1% were women,

## **Toledo Study of Healthy Aging (TSHA)**

Toledo Study of Healthy Aging is a longitudinal study that comprises 2,488 subjects. At baseline, subjects were interviewed at home. Information on socio-demographic characteristics, social support, independence in activities of daily living, health-related quality of life, physical activity, diet, alcohol use, and depressive symptoms were recorded. In addition, an extensive neuropsychological evaluation was performed for each subject. Furthermore in 1972 individuals from the cohort heart rate, blood pressure, anthropometric variables and the ankle-brachial index were measured during a physical exam.. Blood samples were centrifuged and serum fraction taken to the laboratory within two hours, using containers at a temperature between 2 and 4°C, and then divided in aliquots and stored at -80°C. Study participants gave a signed informed consent, and the study protocol was approved by the Clinical Research Ethics Committee of the Complejo Hospitalario de Toledo, Spain (10). The population participating this study consisted of 1957 volunteers, aged 65 to 99, of which 55.7% were women,. Their data were collected between 2006 and 2009.

## **Vobarno Study**

The Vobarno Study was conducted in Vobarno, a small town in Northern Italy. Subjects were selected from the electoral rolls of the town (response rate 66%) (11). The population participating this study consisted of 385 volunteers, aged 43 to 74, of which 56.1% were women,. Their data were collected between 2004 and 2007.

## REFERENCES

- 1- Rietzschel, E. R., De Buyzere, M. L., Bekaert, S., Segers, P., De Bacquer, D., Cooman, L., et al (2007). Rationale, design, methods and baseline characteristics of the Asklepios Study. *European Journal of Cardiovascular Prevention & Rehabilitation*; 14: 179–191. doi:10.1097/HJR.0b013e328012c380
- 2- Shock NW, Greulich RC, Andres RA, et al. 1984. *Normal Human Aging: The Baltimore Longitudinal Study of Aging* NIH. Washington, DC: U.S. Government Printing Office. Publication no. 84-2450.
- 3- Scuteri A, Morrell CH, Najjar SS, et al (2009). Longitudinal paths to the metabolic syndrome: can the incidence of the metabolic syndrome be predicted? *The Baltimore Longitudinal Study of Aging. J Gerontol A Biol Sci Med Sci.*; 64: 590–598. doi:10.1093/gerona/glp004.
- 4- Vlachopoulos C, Xaplanteris P, Vyssoulis G, Bratsas A, Baou K, Tzamouris V, Aznaouridis K, Dima I, Lazaros G, Stefanadis C (2011). Association of serum uric acid level with aortic stiffness and arterial wave reflections in newly diagnosed, never-treated hypertension. *Am J Hypertens*; 24: 33-9.
- 5- Hedblad B, Nilsson P, Janzon L, Berglund G (2000). Relation between insulin resistance and carotid intima-media thickness and stenosis in non-diabetic subjects. Results from a cross-sectional study in Malmö, Sweden. *Diabet Med*; 17:299-307
- 6- Hofman A, Breteler MM, van Duijn CM, Janssen HL, Krestin GP, Kuipers EJ, Stricker BH, Tiemeier H, Uitterlinden AG, Vingerling JR, Witteman JC (2009). The Rotterdam Study: 2010 objectives and design update. *Eur J Epidemiol*; 24:553-572.
- 7- Pilia G, Chen WM, Scuteri A, Orru M, Albai G, Dei M, Lai S, Usala G, Lai M, Loi P, Mameli C, Vacca L, Deiana M, Olla N, Masala M, Cao A, Najjar SS, Terracciano A, Nedorezov T, Sharov A, Zonderman AB, Abecasis GR, Costa P, Lakatta E, Schlessinger D (2006). Heritability of cardiovascular and personality traits in 6,148 Sardinians. *PLoS Genet*; 2: e132.
- 8- Scuteri A, Najjar SS, Orru' M, Albai G, Strait J, Tarasov KV, Piras MG, Cao A, Schlessinger D, Uda M, Lakatta EG (2009). Age- and gender-specific awareness, treatment, and control of cardiovascular risk factors and subclinical vascular lesions in a founder population: The SardiNIA Study. *Nutr Metab Cardiovasc Dis*; 19: 532-4
- 9- Völzke H, Alte D, Schmidt CO, Radke D, Lorbeer R, Friedrich N, Aumann N, Lau K, Piontek M, Born G, Havemann C, Ittermann T, Schipf S, Haring R, Baumeister SE, Wallaschofski H, Nauck M, Frick S, Arnold A, Jünger M, Mayerle J, Kraft M, Lerch MM, Dörr M, Reffelmann T, Empen K, Felix SB, Obst A, Koch B, Gläser S, Ewert R, Fietze I, Penzel T, Dören M, Rathmann W, Haerting J, Hannemann M, Röpcke J, Schminke U, Jürgens C, Tost F, Rettig R, Kors JA, Ungerer S, Hegenscheid K, Kühn JP, Kühn J, Hosten N, Puls R, Henke J, Gloger O, Teumer A, Homuth G, Völker U, Schwahn C, Holtfreter B, Polzer I, Kohlmann T, Grabe HJ, Roskopf D, Kroemer HK, Kocher T, Biffar R, John U, Hoffmann W (2011). Cohort profile: the study of health in Pomerania. *Int J Epidemiol*; 40: 294-307
- 10- Garcia-Garcia FJ, Gutierrez Avila G, Alfaro-Acha A, Amor Andres MS, De Los Angeles De La Torre Lanza M, Escribano Aparicio MV, et al (2011). The prevalence of frailty syndrome in an older population from Spain. *The Toledo Study for Healthy Aging. J Nutr Health Aging*; 15: 852-6
- 11- Muiesan ML, Salvetti M, Zulli R, Pasini GF, Bettoni G, Monteduro C, Rizzoni D, Castellano M, Agabiti-Rosei E (1998). Structural association between the carotid artery and the left ventricle in a general population in Northern Italy: the Vobarno study. *J Hypertens*; 16(12 Pt 1):1805-1812.



Supplemental Table 1: Characteristic of cohorts participating the MARE Consortium

	Asklepios	BLSA	Guimaraes	HYGEIA	LitHiR	MDC-CV	Rotterdam	SardiNIA	SHIP	SMART	Toledo	Vobarno
N	3055	1389	2123	1691	2948	5533	4797	6123	4308	512	1957	385
Age (years)	51.0 ± 12.5	65.4 ± 13.7	47.3 ± 19.6	54.6 ± 13.0	54.4 ± 6.1	57.6 ± 5.9	73.3 ± 7.7	43.7 ± 17.6	49.8 ± 16.4	62.2 ± 11.2	75.3 ± 6.2	56.5 ± 9.7
Men (%)	52.6	50.1	55.7	42.6	65.3	58.6	59.9	57.5	50.9	55.1	55.7	56.1
Waist (cm)	88.9 ± 13.4	91.3 ± 12.5	93.7 ± 11.8	97.1 ± 13.0	105.2±10.9	84.0 ± 12.9	93.5 ± 11.6	84.8 ± 13.1	89.4 ± 13.9	96.0 ± 13.8	100.8±12.1	89.8 ± 11.8
BMI (Kg/m <sup>2</sup> )	26.3 ± 4.5	27.2 ± 4.8	26.7 ± 4.6	28.4 ± 4.6	31.7 ± 5.0	25.7 ± 4.0	26.8 ± 4.0	25.4 ± 4.7	27.3 ± 4.8	28.1 ± 5.1	29.3 ± 5.1	25.7 ± 3.9
Glucose (mg/dl)	93.7 ± 16.9	92.8 ± 16.6	83.9 ± 23.7	98.7 ± 19.7	111.5±24.6	93.2 ± 24.9	106.8±26.6	90.1 ± 23.6	102.1±32.2	101.2±20.7	106.3±26.9	99.0 ± 20.8
Tot Cholesterol (mg/dl)	213.3±37.6	191.7±37.3	193.1±37.7	208.6±38.2	264.2±58.6	238.1±42.3	225.0±38.1	208.6±42.2	225.2±48.5	195.5±41.9	193.9±37.8	214.5±34.5
LDL Cholesterol (mg/dl)	129.2±34.4	112.7±33.4	116.6±33.2	135.0±33.9	171.6±50.6	160.8±38.1	N/A	127.0±35.0	139.5±45.3	110.4±41.7	118.2±33.7	135.3±33.2
HDLCholesterol (mg/dl)	62.3 ± 17.3	58.6 ± 16.8	54.5 ± 14.4	48.9 ± 12.1	50.3 ± 12.5	53.2 ± 14.4	53.9 ± 15.4	64.2 ± 14.9	56.6 ± 17.2	52.1±19.5	53.0 ± 14.4	57.1 ± 14.4
Triglycerides (mg/dl)	111.4 79.7	103.8±58.5	110.8±70.8	124.9±70.0	214.3±232.3	70.6 ± 41.1	134.7±67.0	85.2 ± 52.7	165.0±129.2	142.9±85.0	113.9±63.4	127.3±90.0
SBP (mmHg)	129.9±17.3	119.9±15.5	131.9±20.8	156.9±18.3	139.6±16.1	141.5±19.1	143.6±21.3	125.9±18.5	137.1±21.5	133.4±22.6	148.5±23.0	137.3±14.8
DBP (mmHg)	79.8 ± 10.3	66.6 ± 9.1	77.1 ± 10.5	95.2 ± 12.4	85.8 ± 9.5	87.0 ± 9.4	75.3 ± 11.2	77.6 ± 10.5	83.8 ± 11.3	77.0 ± 8.3	78.5 ± 12.2	85.9 ± 7.3
Hypertension (%)	32.4	36.3	43.0	81.9	93.7	37.8	N/A	25.5	40.8	47.0	49.1	62.9
Diabetes mellitus (%)	4.7	8.0	10.7	7.6	21.8	8.5	15.4	4.9	8.0		19.6	4.5
Antihypertensive medication (%)	10.5	4.1	28.9	7.2	N/A	36.5	39.6	9.7	63.1	N/A	40.7	33.6



Supplemental Figures 1-9: Overall and gender-specific occurrence of clusters of MetS components with an overall prevalence  $\geq 5\%$