Quality control of the blood pressure phenotype in the European Project on Genes in Hypertension

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Objectives In the European Project on Genes in Hypertension (EPOGH) standardized epidemiological methods were used to determine complex phenotypes consisting of blood pressure (BP) in combination with other traits. In this report, we present the quality control of one of the BP phenotypes.

Methods In seven European countries eight different research groups recruited random samples of nuclear families. Trained observers measured the BP five times consecutively with the participants in the seated position at each of two separate home visits, 1 to 3 weeks apart, according to the guidelines of the British Hypertension Society. Quality assurance and quality control of this BP phenotype were implemented according to detailed instructions defined in the protocol of the EPOGH study.

Results On 31 August 2001, BP measurements of 2476 subjects were available for analysis. Fewer BP readings than the five planned per visit occurred in one of the eight centres, but only in 0.4% of the home visits. Across centres the relative frequency of identical consecutive readings for systolic or diastolic blood pressure varied from 0 to 6%. The occurrence of odd readings ranged from 0 to 0.1%. Of the 49 488 systolic and diastolic BP readings, 24.0% ended on a zero (expected 20%). In most EPOGH centres there was a progressive decline in the BP from the first to the second home visit. Overall, these decreases averaged 2.36 mmHg [95% confidence interval (CI): 1.98–2.74, $P < 0.001$] for systolic BP and 1.74 mmHg (95% CI: 1.46–2.02, $P < 0.001$) for diastolic BP.

Conclusions Quality assurance and control should be planned at the design stage of a project involving BP measurement and implemented from its very beginnings until the end. The procedures of quality assurance set up in the EPOGH study for the BP measurements resulted in a well-defined BP phenotype, which was consistent across centres. *Blood Press Monit* **7**: 215–224 © 2002 Lippincott Williams & Wilkins.

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Introduction

Accurate measurement of the blood pressure phenotype is of paramount importance in studies on the genetic determination of hypertension [1]. In most studies in humans, the blood pressure phenotype is the mean of three to five readings obtained in a single occasion. A number of automated electronic devices have become available for blood pressure measurement under static or ambulatory conditions [2–4]. However, until now auscultatory blood pressure measurement using the Riva-Rocci/Korotkoff technique remains the standard in clinical and epidemiological research.

The European Project on Genes in Hypertension (EPOGH) involves eight centres in seven European countries. Its main objective is to identify genetic polymorphisms that are significantly associated with blood pressure as a continuous or dichotomous trait. In addition to ambulatory blood pressure monitoring and measurement of the clinic blood pressure, the blood pressure phenotype

in the EPOGH study also consists of five consecutive blood pressure readings obtained with the subjects seated at each of two separate home visits. Intra- and inter-observer variability in blood pressure measurements may already be large in single-centre studies and may even further increase in large-scale epidemiological projects, involving multiple centres. In this article we present the initial progress of the EPOGH study together with the results of the quality control programme of the blood pressure phenotype measured at the participants' homes.

Methods

Fieldwork

Random samples of nuclear families were recruited in Hechtel-Eksel [Belgium (B)], Sofia [Bulgaria (BU)], Pilsen and Prague [Czech Republic (CZ)], Mirano [Padova, Italy (I)], Cracow [Poland (PL)], Bucharest [Romania (RO)], and Novosibirsk [Russian Federation (RF)]. To increase the number of hypertensive patients, four groups (those of Padova, Cracow, Bucharest, and Novosibirsk) also recruited approximately 30% of the required number of nuclear families via specialized clinics for hypertensive patients.

Nuclear families had to include at least one parent and two siblings. The minimum age for participation was 10 years. Family members had to live within a distance of no more than approximately 10 km to make repeated home visits feasible.

Trained observers measured blood pressure with a standard mercury sphygmomanometer five times consecutively during each of two home visits. The guidelines of the British Society of Hypertension [5] were applied. Standard cuffs had a 12×24 cm inflatable bladder, but, if upper arm circumference exceeded 31 cm, larger cuffs with 15×35 cm bladder were used. After at least 10 min rest, five consecutive blood pressure readings were obtained in the sitting position with an interval of 30 to 60 s between readings. The cuff was deflated at approximately 2 mmHg per second, and systolic and phase V diastolic blood pressure were recorded to the nearest 2 mmHg. Each subject's conventional blood pressure was the mean of the 10 readings obtained at home.

Quality assurance procedures

Quality assurance refers to the procedures set up at all centres to ensure high quality blood pressure measurements throughout the project. At the start of the EPOGH study (November 1998), we organized a 1-week workshop at the Coordinating Office in Leuven, Belgium. Subsequently, during the course of the study, investigators of four centres requested further training and visited the Coordinating Office, respectively, in June 1999, June 2000, October 2000, and February 2001. On each occasion, the investigators took a refresher course on the procedures of blood pressure measurement.

At each field centre, quality assurance sessions were organized at three to six monthly intervals to reinforce the theoretical concepts and to rehearse the practical procedures of sphygmomanometric blood pressure measurement. At each session the observers had to pass a test requiring them to read blood pressures from videotape featuring a falling mercury column with simultaneous Korotkoff sounds (Measuring Blood Pressure; British Medical Association, London, 1990). For each session a specific standard was computed which reflected the acoustic conditions under which the test had taken place, and which was computed by averaging the film readings of experienced senior clinical researchers. All readings from each observer had to be within 5 mmHg of the standard. If an observer failed to pass the test, she/he did not participate in blood pressure measurement until re-tested successfully at a later session. The intra-observer reproducibility was studied by comparing 10 pairs of identical video simulations of blood pressure measurements and was calculated as twice the standard deviation of the differences between duplicate readings. Moreover, the reproducibility coefficient was expressed as a percentage of the mean of the identical readings. Digit preference was not evaluated at the training sessions, but computed from the blood pressure measurements in study participants.

All observers involved in the study completed a questionnaire providing information on their gender, age, and qualification (paramedic, nurse, or medical doctor). In addition, in the same questionnaire, the observers provided information on the technical characteristics of the sphygmomanometers used for blood pressure measurement at subjects' homes (aneroid versus mercury; cuff size).

Quality control

The present analysis includes the blood pressure readings obtained at the participants' homes and made available to the Coordinating Office before 31 August 2001. From published guidelines [5,6] and six previous studies [7–12] we selected six criteria applicable to the design and the multicentre character of the EPOGH study:

1. In each participant, the blood pressure measurements were considered as complete if all five systolic and diastolic blood pressure readings at each of the two separate home visits were available in the database.
2. Five consecutive blood pressure readings obtained in a subject were considered as identical, if there was no single difference between any of the systolic or diastolic blood pressure values among the five readings. The frequency of consecutive five identical readings was determined.

3. The proportion of odd blood pressure readings with as terminal digit 1, 3, 5, 7, or 9 was determined for systolic and diastolic measurements separately.
4. Digit preference, i.e., the distribution of the last digits of all single systolic and diastolic blood pressure readings was monitored at three-monthly intervals throughout the EPOGH project.
5. To assess the consistency between centres, we evaluated the blood pressure changes from the first to the second home visit and across the ten readings obtained at the two home visits.
6. To investigate the pattern of variation between observers, the mean for each individual observer's blood pressure readings was computed and compared with the overall within-centre mean.

Statistical analysis

We used the SAS software package, version 6.12. (SAS Institute, Cary, North Carolina, USA) for database management and statistical analysis. Comparison of means and proportions were performed with the standard normal z-test and the χ^2-statistic, respectively. To assess intra-observer variability, Bland and Altman's technique [13] was applied. We used analysis of covariance to compare blood pressure measurements between observers with adjustment for sex, age, body mass index, antihypertensive treatment, smoking, alcohol intake, and the use of oral contraceptives. To compare trends in the consecutive blood pressure measurements between centres we used repeated measures analysis of variance and we determined the significance of the interaction terms between centre and the order of the blood pressure readings.

Results

Characteristics of the study population

The 2476 participants included 1173 men (47.4%) and 605 hypertensive patients (24.4%) of whom 328 were on antihypertensive drug treatment (Table 1). The subjects ranged in age from 10 to 84 years. Among the men, 32.5% ($n = 374$) were current smokers, and 57.8% ($n = 661$) reported intake of alcohol. In women, these proportions were 21.4% ($n = 273$) and 36.1% ($n = 460$), respectively. Among women, 20.0% ($n = 261$) used oral contraceptives.

Characteristics of the observers

The number of observers employed per centre ranged from one to six (Table 2). The observers' age ranged from 25 to 62 years. Most observers (84%) were female and/or medical doctors (77%). Two centres employed only nurses for measuring blood pressure during the study (Table 2). The number of blood pressure readings per observer ranged from 60 to 4560. All centres used standard mercury sphygmomanometers and adjusted cuff size according to arm circumference.

Video test

Table 3 summarizes the results of all training sessions by centre and gives for each centre the distribution of the differences between the observers' film readings and the standard (20 differences per observer during one training session) and the intra-observer reproducibility. Overall, 88% of the observers' systolic pressure readings were within ± 5 mmHg of the standard. For diastolic pressure this proportion was 87.4%. The repeatability coefficient across seven centres and 29 observers was 5.4% for systolic pressure and 6.4% for diastolic pressure.

Quality control according to six predefined criteria

Fewer blood pressure readings than the five projected per visit occurred in one of the eight centres, but only in 0.4%. of the home visits (Table 4). The frequency of identical consecutive readings for systolic or diastolic blood pressure varied across the centres from 0 to 6%. The occurrence of odd readings which represented a deviation from the study protocol, ranged from 0 to 0.1%. Of 49 488 systolic and diastolic blood pressure readings, 24.0% ended on a zero (Fig. 1). The difference with the expected frequency of 20% was statistically significant ($\chi^2 = 390.5$; $P < 0.001$).

Table 1 Characteristics of the participants

Characteristics	Hechtel-Eksel (B)	Sofia (BU)	Pilsen (CZ)	Prague (CZ)	Mirano (I)	Cracow (PL)	Bucharest (RO)	Novosibirsk (RF)	Total
Number[†]	1024	40	190	42	346	325	193	316	2476
Female (%)	513 (50.1)	21 (52.5)	101 (53.2)	17 (40.5)	187 (54.0)	176 (54.2)	111 (57.5)	177 (56.0)	1303 (52.6)
Age (years)	37.4 ± 16.8	37.1 ± 14.5	37.4 ± 13.5	39.2 ± 13.8	41.1 ± 14.0	35.5 ± 13.9	39.4 ± 16.0	38.9 ± 15.0	38.1 ± 15.5
Body mass index (kg/m^2)	24.6 ± 4.5	23.7 ± 4.1	26.2 ± 4.9	24.3 ± 4.2	25.3 ± 4.3	25.5 ± 4.9	24.8 ± 5.5	25.3 ± 5.0	25.0 ± 4.8
Systolic pressure (mmHg)[‡]	121.4 ± 14.4	123.7 ± 17.6	123.5 ± 15.5	116.9 ± 10.9	126.5 ± 16.1	129.3 ± 18.1	124.6 ± 21.5	124.6 ± 17.6	123.9 ± 16.5
Diastolic pressure (mmHg)[‡]	74.8 ± 10.7	79.6 ± 10.9	77.9 ± 10.1	74.7 ± 8.0	80.6 ± 9.8	80.8 ± 11.5	79.3 ± 13.5	79.4 ± 11.3	77.7 ± 11.2
Heart rate (beats/min)	66.8 ± 8.2	76.0 ± 10.6	70.7 ± 8.6	73.8 ± 8.9	73.2 ± 8.8	73.8 ± 9.0	75.6 ± 8.2	74.1 ± 7.4	70.7 ± 9.1
Hypertensive (%)	189 (18.5)	11 (27.5)	46 (24.2)	4 (9.8)	106 (30.6)	112 (34.5)	52 (26.9)	85 (26.9)	605 (24.4)
Taking antihypertensive drugs (%)	106 (56.1)	7 (63.6)	35 (76.1)	2 (50.0)	50 (47.2)	63 (56.3)	20 (38.5)	45 (52.9)	328 (54.1)

Values are arithmetic means (SD), or number of subjects (%). [†]Number of subjects with data available at the Coordinating Office. [‡]Average of 10 readings at the first and second home visit.

Table 2   **Characteristics of observers**

Centre	Age group (years)		Gender		Qualification	
	25–35	> 35	Male	Female	Nurse	Doctor
Hechtel-Eksel (B) $n = 4$	2 (50%)	2 (50%)	–	4 (100%)	4 (100%)	–
Sofia (BU) $n = 2$	2 (100%)	–	1 (50%)	1 (50%)	–	2 (100%)
Pilsen (CZ) $n = 3$	2 (67%)	1 (33%)	–	3 (100%)	1 (33%)	2 (67%)
Prague (CZ) $n = 1$	–	1		1	1	–
Mirano (I) $n = 6$	4 (67%)	2 (33%)	2 (33%)	4 (67%)	–	6 (100%)
Cracow (PL) $n = 6$	4 (67%)	2 (33%)	1 (17%)	5 (83%)	1 (17%)	5 (83%)
Bucharest (RO) $n = 6$	2 (33%)	4 (67%)	1 (17%)	5 (83%)	–	6 (100%)
Novosibirsk (RF) $n = 3$	2 (67%)	1 (33%)	–	3 (100%)	–	3 (100%)
Total $n = 31$	18 (58%)	13 (42%)	5 (16%)	26 (84%)	7 (23%)	24 (77%)

Table 3   **Results of training sessions for observers**

Centre	Hechtel-Eksel (B)		Sofia (BU)[†]		Pilsen (CZ)		Prague (CZ)		Mirano (I)		Cracow (PL)		Bucharest (RO)		Novosibirsk (RF)	
Number of sessions	5		1		1		1		7		5		2		5	
	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)	SBP (%)	DBP (%)
Deviation of observers' readings *vs.* reference																
> 10 mmHg	1.5	0.5	0	0	0	0	0	0	3.3	3.3	1.3	3.0	1.9	4.4	0	0
8–10 mmHg	1.8	2.8	5.0	5.0	0	0	0	0	0	1.3	2.5	0	3.8	3.7	0	0
5–7 mmHg	5.5	3.5	5.0	0	0	0	0	0	1.5	0.8	4.3	1.8	5.6	7.5	0	0
2–4 mmHg	31.5	30.8	5.0	20.0	16.7	30.0	10.0	25.0	4.8	11.9	12.2	15.0	25.0	21.3	25.0	16.0
−1 to 1 mmHg	39.3	38.3	80.0	65.0	53.3	45.0	35.0	45.0	62.7	45.8	51.2	50.7	47.5	35.0	65.0	68.0
−2 to −4 mmHg	14.8	21.3	5.0	10.0	30.0	25.0	50.0	30.0	20.8	27.1	23.7	23.2	11.8	13.1	10.0	14.0
−5 to −7 mmHg	0.8	0.8	0	0	0	0	5.0	0	5.0	8.1	1.8	4.0	1.9	4.4	0	2.0
−8 to −10 mmHg	2.3	0.8	0	0	0	0	0	0	1.3	1.0	1.5	1.2	1.3	3.1	0	0
< −10 mmHg	2.8	1.5	0	0	0	0	0	0	0.6	0.6	1.5	1.2	1.2	7.5	0	0
Reproducibility[‡]	5.2	6.8	4.0	9.5	2.7	3.6	2.8	2.8	8.8	6.6	13.7	5.7	9.4	10.9	2.2	3.0
	(3.3)	(6.3)	(2.4)	(8.7)	(1.6)	(3.4)	(1.9)	(2.6)	(5.3)	(6.0)	(8.1)	(5.3)	(5.3)	(10.4)	(1.4)	(2.9)

Observers read 20 blood pressures per session from a video movie showing a falling mercury column with Korotkoff sounds. [†]One observer's result not yet available at the Coordinating Office at the time of writing of this article. [‡]2SD of the changes between identical blood pressures from a video movie. See Methods for further explanations. SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 4   **Qualitative indicators for control of blood pressure measurement**

	Hechtel-Eksel (B)	Sofia (BU)	Pilsen (CZ)	Prague (CZ)	Mirano (I)	Cracow (PL)	Bucharest (RO)	Novosibirsk (RF)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of home visits	2103	80	380	84	692	650	398	632
Incomplete BP measurements[†]	8 (0.4%)	0	0	0	0	0	0	0
Number of five consecutive BP readings[‡]	4206	160	760	168	1384	1300	796	1264
Identical readings	66 (1.6%)	1 (0.6%)	0	10 (6.0%)	41 (3.0%)	1 (0.1%)	1 (0.1%)	0
Total number of BP readings[‡]	21018	800	3800	840	6920	6500	3980	6320
Odd readings	7 (0.03%)	1 (0.1%)	0	1 (0.1%)	6 (0.08%)	6 (0.09%)	0	0

[†]Less than five systolic or five diastolic measurements per home visit. [‡]Systolic and diastolic readings were counted as separate measurements.

Among individual observers the proportion of blood pressure readings with a terminal zero ranged from 15.5 to 47.6% (Table 5). Five observers in three centres were found to record blood pressure values with a terminal zero in excess of 30% (47.6, 32.9, 31.8, 31.5 and 31.4%).
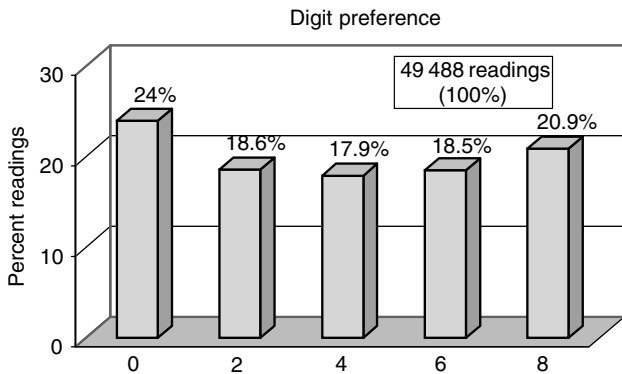
In most EPOGH centres there was a significant and progressive decline in the conventional blood pressure from the first to the second home visit (Fig. 2). Across all centres, blood pressure decreased by 2.36 mmHg (95% confidence interval (CI): 1.98–2.74, $P < 0.001$) systolic and by 1.74 mmHg (95% CI: 1.46–2.02, $P < 0.001$) diastolic. However, as illustrated in Figure 3, there were significant trend differences between the EPOGH centres in the blood pressure changes across the ten readings of systolic ($F = 5.32$, $P < 0.001$) and diastolic blood pressure ($F = 3.71$, $P < 0.001$). Moreover, the decline of blood pressure on repeat measurement depended on the level of pressure (Figs 2 and 3). For instance, in comparison with other EPOGH centres, we observed more prominent

decreases in systolic (5.25; 95% CI: 3.91–6.59) and diastolic (3.24; 95% CI: 2.32–4.16) blood pressures from the first to the second home visit in Cracow. In this centre blood

pressure at initial home visit was higher then in all other centres.

Figure 4 shows the deviations between the mean of each individual observer's blood pressure readings and the overall within-centre mean for the eight EPOGH centres. These deviations were adjusted for sex, age, body mass index, antihypertensive treatment, smoking, alcohol intake, and the use of oral contraceptives. For systolic blood pressure, the deviations ranged from -1.48 to $+2.07$ mmHg in Hechtel-Eksel (Belgium), from -0.50 to $+0.50$ mmHg in Sofia (Bulgaria), from -1.17 to $+0.99$ mmHg in Pilsen (Czech Republic), from -4.86 to $+7.33$ mmHg in Mirano (Italy), from -1.46 to $+3.19$ mmHg in Cracow (Poland), from -1.80 to $+2.79$ mmHg in Bucharest (Romania), and from -2.86 to $+2.01$ mmHg in Novosibirsk (Russia). For diastolic blood pressure, the deviations ranged from -3.00 to $+2.90$ mmHg in Hechtel-Eksel (Belgium), from -0.33 to $+0.33$ mmHg in Sofia (Bulgaria), from -1.45 to $+1.03$ mmHg in Pilsen (Czech Republic), from -2.04 to $+4.33$ mmHg in Mirano (Italy), from -1.11 to $+0.62$ mmHg in Cracow (Poland), from -4.80 to

Fig. 1

Digit preference

49 488 readings (100%)

Digit preference in the blood pressure readings across six EPOGH centres. The proportion of systolic or diastolic blood pressure readings with an even terminal digit is presented.

Table 5 Digit preference

Observer	0		2		4		6		8		Total number of BP readings
	n	%	n	%	n	%	n	%	n	%	
Hechtel-Eksel (B)											
1	743	47.6	162	10.4	261	16.7	197	12.6	197	12.6	1560
2	2687	31.8	1436	17.0	1107	13.1	1623	19.2	1595	18.9	8448
3	1416	15.5	1667	18.3	1963	21.5	2021	22.2	2047	22.4	9120
4	415	22.0	342	18.1	344	18.2	353	18.7	431	23.0	1890
Pilsen (CZ)											
1	420	20.8	414	20.5	428	21.2	368	18.2	390	19.3	2020
2	200	20.4	184	18.8	186	19.0	185	18.9	225	23.0	980
3	189	23.6	143	17.9	149	18.6	148	18.5	171	21.4	800
Prague (CZ)											
1	246	31.4	166	19.8	119	14.2	105	12.5	185	22.0	840
Sofia (BU)											
1	68	17.0	97	24.3	94	23.5	72	18.0	69	17.3	400
2	87	21.8	60	15.0	59	14.8	86	21.5	107	26.8	400
Mirano (I)											
1	435	25.3	331	19.2	316	18.4	239	13.9	398	23.1	1720
2	60	27.3	42	19.1	40	18.2	29	13.2	48	21.8	220
3	666	18.8	768	21.7	719	20.3	732	20.7	652	18.4	3540
4	30	25.0	24	20.0	22	18.3	23	19.2	21	17.5	120
5	100	17.9	134	23.9	109	19.5	93	16.6	123	22.0	560
6	134	19.1	116	16.6	157	22.4	146	20.9	147	21.0	700
Cracow (Poland)											
1	288	24.8	213	18.4	202	17.4	188	16.2	268	23.1	1160
2	288	18.9	272	17.9	293	19.3	304	20.0	362	23.8	1520
3	200	29.4	101	14.9	146	21.5	89	13.1	143	21.0	680
4	170	31.5	85	15.7	86	15.9	92	17.0	107	19.8	540
5	306	17.2	426	23.9	339	19.0	277	15.6	432	24.3	1780
6	270	32.9	129	15.7	130	15.9	98	12.0	190	23.2	820
Bucharest (RO)											
1	40	28.6	34	24.3	25	17.9	20	14.3	21	15.0	140
2	201	22.3	187	20.8	142	15.8	148	16.4	222	24.7	900
3	378	27.4	256	18.6	205	14.9	254	18.4	287	20.8	1380
4	338	21.7	307	19.7	266	17.1	309	19.8	340	21.8	1560
Novosibirsk (RF)											
1	808	26.2	566	18.4	524	17.0	525	17.0	657	21.3	3080
2	36	22.5	34	21.3	36	22.5	31	19.4	23	14.4	160
3	827	26.9	602	19.5	514	16.7	508	16.5	629	20.4	3080

Fig. 2
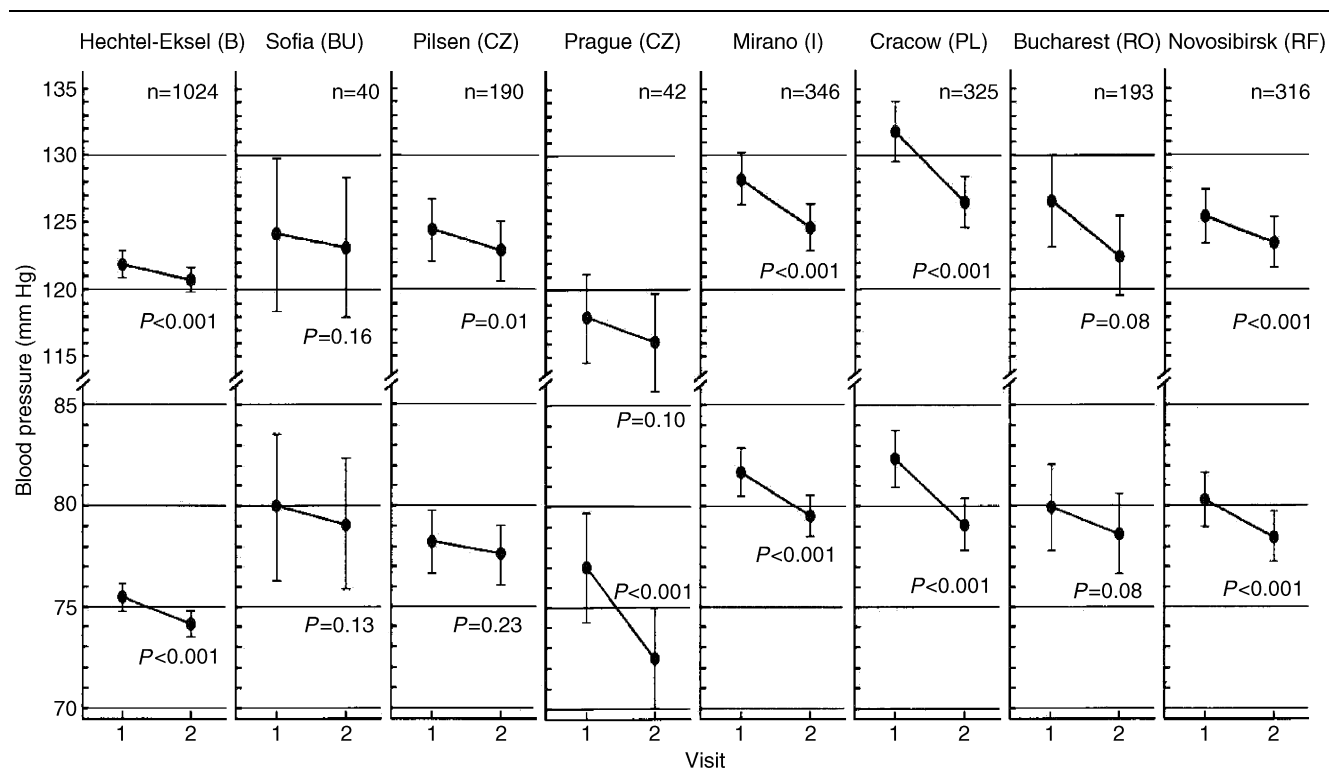
Mean systolic and diastolic blood pressure values at the first and second home visits. *P* values for the differences between the two visits are given.

+2.64 mmHg in Bucharest (Romania), and from −0.35 to +0.22 mmHg in Novosibirsk (Russia). The significance of these systolic and diastolic deviations increased with the number of subjects examined by each observer, with the amount that an observer's readings deviated from the overall within-centre population mean, and with the total number of subjects per centre.

Discussion

The main objective of the EPOGH study was to investigate a well-standardized blood pressure phenotype in relation to genetic polymorphism. This report focuses on the quality assurance and quality control procedures, which were an essential and intricate part of the EPOGH protocol.

Accurate determination of the blood pressure levels in large-scale surveys or multicentre studies requires central coordination and the implementation of a standardized protocol. The measurement of blood pressure according to Riva-Rocci/Korotkoff technique [14] is dependent on the accurate transmission and interpretation of a signal (Korotkoff sound or pulse wave) from a subject via a device (the sphygmomanometer) to an observer [15,16].

The successful outcome of this complex interaction requires that the observer is competent in performing the technique of blood pressure measurement, that the subject is examined in basal and standardized conditions, that the equipment used for the measurement is well maintained and calibrated, and that the blood pressure readings are archived accurately. This procedure is fraught with sources of potential error, which may arise in the observer, the subject, the sphygmomanometer or in the overall application of the technique [4,15,17,18]. The quality assurance and the quality control in our study focused on these potential sources of inaccuracy.

In our study, subjects were visited at home on two separate occasions and trained observers, either doctors or nurses, measured blood pressure in the relaxed home environment. This procedure of blood pressure measurement tends to increase the participation rate and has been validated in several epidemiological studies in Belgium. Blood pressure, measured this way, shows the expected associations with gender, age, body mass index, social class, and physical activity [19,20].

Our quality assurance programme was based on published guidelines [5,6]. Its objective was to ensure high quality

Fig. 3
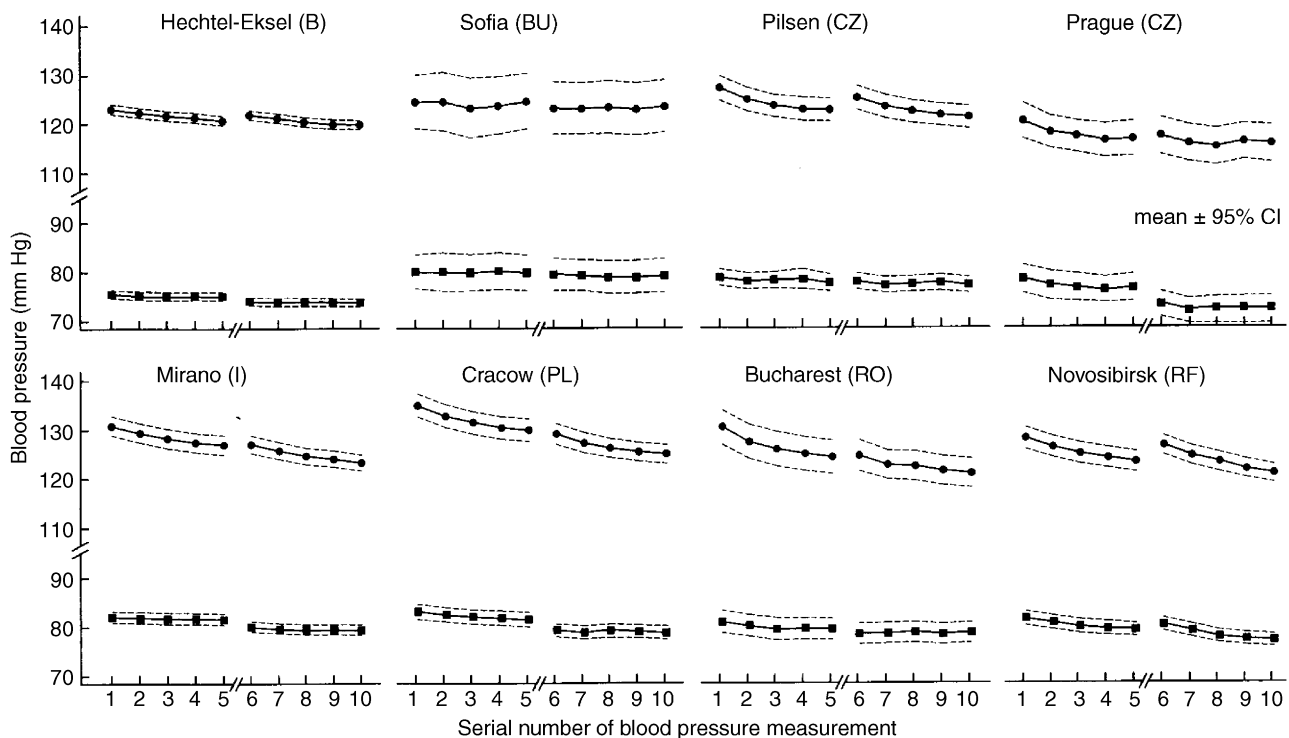
Systolic and diastolic blood pressure values for five consecutive readings at two separate home visits. Values are mean with 95% confidence intervals.

blood pressure measurements throughout the whole project, in which eight different researches groups and 27 observers participated. Various training programmes have been developed to minimize observer error [5,6,21], most of which use a film or a video showing a falling mercury column with Korotkoff sounds as the main component of training and quality assessment. The film allows quantifying inter- and intra-observer variability. In our study quality assurance was set up via repeated training sessions. The observers always received the results of their tests, so that they remained aware of their performance and were encouraged to improve their measurement technique.

In our quality control programme we used six criteria, because they reflect different problems that may occur during blood pressure measurement. Some of these items are conceived as qualitative rather than quantitative indicators of the accuracy of blood pressure measurement. The proportion of incomplete measurements is a strong indicator of validity problems in terms of population representativeness [7]. The occurrence of odd digits is likely to reflect forgetfulness of the protocol or a desire for extra accuracy by the observer [10]. It might also indicate a loss of accuracy. The frequency of identical blood pressure readings in series of repeated blood pressure readings might influence the overall shape of the blood pressure

distribution and the prevalence of diagnostic categories based on blood pressure thresholds [10,22]. It is well known from clinical and epidemiological studies [9,15,22] that repeated blood pressure measurements in the same subject are in most instances non-identical. The degree, to which the frequency of identical readings can be considered normal or at least acceptable, is not clearly defined. All eight EPOGH centres appeared to have complied well with these predefined quality criteria (Table 4).

Owing to habitation and regression to the mean, blood pressure usually falls when repeated measurements are obtained during a single visit or at consecutive visits over the course of a study. In all centres we noticed a progressive and significant decline in blood pressure when the readings were repeated by the observer at the subjects' homes. This observation underscores the need for multiple assessments of blood pressure over a time in order to avoid over-diagnosis of hypertension among individuals with high initial blood pressure values [2,23].

The maximal between-centre differences in blood pressure were 12.4 mmHg systolic and 6.1 mmHg diastolic (Prague centre versus Cracow centre). The maximal difference in pulse rate was between the Hechtel-Eksel and Sofia centres (9.2 beats per minute). These between-centre

Fig. 4
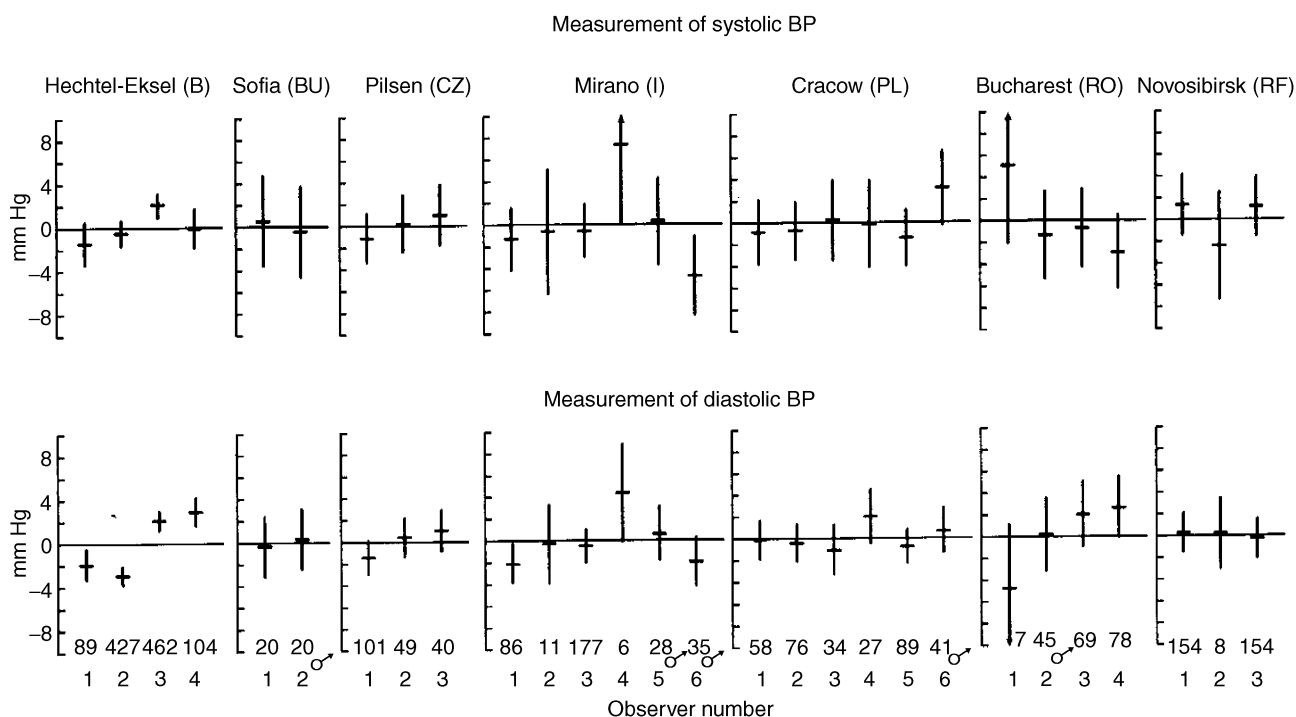
Mean systolic and diastolic differences between each observer's blood pressure (BP) readings and the overall within-centre population means. Values for each observer are point estimates with 95% confidence interval adjusted for sex, age, body mass index, antihypertensive treatment, smoking, alcohol intake, and the use of oral contraceptives. Along with the observer identification number, gender of the observer (♂ if male) and the number of subjects examined by each observer are presented.

differences may be expected on the basis of random variability, small sample size (for instance, in Sofia and Prague), and inclusion of varying proportions of hypertensive subjects.

Another common manifestation of measurement error in epidemiological studies is digit preference for a terminal zero [9,10,24–26]. Because this means that the precision of the measurements is 10 mmHg instead of 2 mmHg, this may result in considerable bias. Digit preference affects the shape of the blood pressure distribution [24] and reduces the power of statistical tests thereby making it more difficult to assess associations between potential risk factors and blood pressure [10,26]. In our report preference for a terminal zero was statistically significant, but of minor importance from a clinical point of view.

The present analysis not only focused on the centres as units of observation, but also included an evaluation of the performance of individual observers. Only a few studies [6,8,10,21,27] have reported data on inter- or intra-observer variability. In our study, we assessed inter-observer variability using the blood pressure readings of expert clinical observers as the standard. Overall, 88% of the observers' systolic pressure readings were within

± 5 mmHg of the standard. For diastolic pressure, this proportion was 87.4%. To assess intra-observer variability, we used Bland and Altman's technique. The repeatability coefficient across seven centres and 29 observers was 5.4% for systolic pressure and 6.4% for diastolic pressure. Higher repeatability coefficients indicate worse reproducibility. Furthermore, we also evaluated differences between observers, which could not be explained by confounding by gender, age, body mass index, antihypertensive treatment, use of oral contraceptives, smoking, and drinking habits. Differences between observers, over and beyond confounding, might be due to systematic error, prejudice for or against certain blood pressure values, the subjective and emotional interaction between subject and observer, the white-coat effect, and/or random variability [4,8,18].

As opposed, for instance, to biochemical measurements, external quality control cannot be easily mounted for blood pressure readings. However, quality assurance and control should be planned at the design stage of a project involving BP measurement and implemented from its very beginnings until the end. In our opinion, the procedures of quality assurance and control set up for the blood pressure measurement in the frame of the EPOGH study resulted

in a well-defined blood pressure phenotype, which was consistent across centres.

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Appendix
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