

Symptoms reported by elderly patients with isolated systolic hypertension: baseline data from the SYST-EUR trial

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Abstract

Objectives: to determine the symptomatic well-being of elderly persons with isolated systolic hypertension.

Design and setting: well-being determined during the placebo run-in period prior to entry to the Systolic Hypertension in Europe (SYST-EUR) trial.

Subjects: 641 people, 60 years or older with an average sitting blood pressure of 173/86 mmHg.

Outcome measures: 33 symptomatic complaints determined by a standard interview.

Results: the 437 women complained of 25% of the symptoms and the 204 men 21% ($P < 0.001$). A markedly higher prevalence was observed in women compared with men for: pain in the joints of the hands (35% of women complained of this against 22% of men); 'racing heart' (33% against 17%); dry eyes (16% against 6%); blurring of vision (35% against 23%); cramps in the legs (43% against 31%); and a sore throat (15% against 7%). Nocturia was the most frequent complaint (68% in both sexes). Eight symptoms increased with age and one (rash) tended to decline. With increasing systolic pressure women also reported more headaches, unsteadiness, blurring of vision, irregular heart beat and 'racing heart' but, of these, only headaches increased with diastolic pressure. These observations were made after adjusting for age, blood sugar and body mass index (BMI) and were not observed in men. Higher blood sugars were associated with mouth ulcers, 'racing heart', blurring of vision and cramps in the legs. A higher BMI was associated with six symptoms, and a lower age of leaving education with eight. In men, alcohol consumption was related to 'racing heart', and smoking to wheezing and having a dry cough.

Conclusions: a high level of complaint was associated with female gender, increasing age, blood sugar and BMI and a low age of leaving education.

Keywords: gender differences, isolated systolic hypertension, quality of life

Introduction

When determining the benefit:risk ratio comparison of a treatment it is important to evaluate symptomatic well-being and quality of life. Isolated systolic hypertension

(ISH) affects many elderly people: the proportion aged over 65 varies from 6 to 18% of men and from 15 to 30% of women [1]. Sustained ISH occurs in about 30% of these subjects.

Elderly hypertensive subjects have most to gain

from prevention of cardiovascular deaths or morbid events, as these become common with advancing years. However, elderly people may be unwilling to suffer adverse effects (such as postural hypotension), which may prove more troublesome than in younger hypertensive subjects.

The Systolic Hypertension in the Elderly Program (SHEP) [2] trial reported treating ISH and showed a reduction in stroke and cardiac events from antihypertensive treatment. The results of the Systolic Hypertension in Europe (SYSTEUR) [3] trial and the SYST-CHINA [4] trial are similar. In previous trials of hypertension in older people (such as EWPHE [5], HEP [6], STOP [7] and the Medical Research Council trial [8]), the benefits of treatment outweighed the symptoms produced by treatment. Nevertheless, the one trial confined to patients with ISH, the SHEP trial, reported eight serious symptoms in the actively treated group: passing out, slow heart rate, chest pain, cold hands, ankle swelling, memory problems, joint pains and, in men, sexual dysfunction (all comparisons $P < 0.01$).

In the SYSTEUR trial we are evaluating both symptoms and quality of life to quantify the benefit and adverse effects of treatment [9]. A secondary objective is to learn more about the determinants of symptoms. The association between symptoms and gender, age, and blood pressure has been evaluated in mainly middle-aged hypertensive subjects [10] and the change in symptoms has also been investigated [11]. However, these relationships have not been investigated in elderly patients with ISH. We report the symptoms during the placebo run-in period and before entry to the SYSTEUR trial and examine associations between symptoms and obesity, fasting blood sugar, alcohol consumption, smoking habits and years of education.

Methods

In the protocol for the SYSTEUR trial [3], eligible patients must be at least 60 years old with an average sitting blood pressure (mean of six measurements obtained at three visits, each 1 month apart, in the run-in period): 160–219 mmHg systolic and >95 mmHg diastolic, and an average standing systolic pressure ≥ 140 mmHg. Active treatment is nitrendipine (10–40 mg daily), if necessary combined with enalapril (5–20 mg daily) and finally hydrochlorothiazide (12.5–25 mg daily). The patients in the control group receive matching placebos. The active drugs are stepwise titrated to reach goal pressure (sitting systolic blood pressure <150 mmHg with a reduction from baseline of at least 20 mmHg).

Assessment of symptoms and quality of life

The questionnaire covers many aspects of quality of life. Section 1 is a short test of cognitive function: the Reitan trail-making test (A and B) [12]. Section 2 consists of the following sections of the Sickness

Impact Profile [13]: ambulation; homework; social interaction; and sleep and rest. Section 3 is the card version of the Brief Assessment Index to assess depression [14]. Section 4 consists of a check list of 33 symptoms, including the expected side effects of the antihypertensive drugs used in the trial. The patients are asked to rate these on a five-point scale according to whether they had the symptom in the past week and, if so, the extent to which it bothered them. The symptom questions have been validated [10, 11, 15] and are responsive to several antihypertensive agents in randomized controlled trials [16–22]. When translated into a different European language, the new questionnaire was back-translated by someone who had not seen the original English version and further changes to the translation were made until an acceptable match was achieved.

Administration of the quality of life questionnaire

The reasons for choosing to use a trained interviewer under standard conditions in the clinic rather than a self-completed questionnaire are:

1. The cognitive function test must be administered by trained personnel.
2. Self-completed data may not be reliable in elderly subjects due to lack of familiarity with checking of responses.
3. Patients who cannot read or write for educational or health reasons can be included.

The interviewers were trained to administer the trial tests and questionnaires at special training sessions organized by the project leaders of the side project (A.E.F., C.J.B.). A training booklet and video was provided. The questionnaires were administered before seeing the doctor or having the blood pressure taken, in a quiet room, without interruptions.

The questionnaires were administered: (i) at randomization in the placebo run-in period, (ii) after 6 months, (iii) after 1 year and (iv) every year thereafter. Where possible, patients who withdrew from the trial were interviewed as close to the time of withdrawal as possible, and were followed-up in the open part of the study. In a centre participating in the quality of life side project, a second log-book was kept of all patients in this project. All patients in that centre randomized into the double-blind part of the trial were invited to take part in the quality of life assessment. The nature of the questions and tests was explained and full confidentiality assured. Details of patients who did not complete the assessments, together with reasons, were entered into the log-book. The present report deals only with the information provided at randomization.

Statistical methods

Many of the explanatory variables were inter-related

and, to adjust for confounding variables, a symptom was categorized as absent (0) when it had bothered the subjects "not at all" during the last week. The symptom was categorized as present (1) when it had bothered the subject "a little", "moderately", "quite a bit" or "extremely". A logistic regression model was then performed on the explanatory variables to determine the odds ratio (OR) or the relative risk of developing the symptom for a 1-unit increase in the explanatory variable.

A complaint rate was computed as the sum of the number of symptoms present divided by the total number of symptom questions answered (maximum 33 for men, 32 for women). If eight or more questions were not answered, the complaint rate was not computed (this only occurred in one patient). The distribution of the complaint rate was sufficiently robust (mean 0.24, median 0.21, SD 0.10) to allow multiple regression techniques to be performed on the explanatory variables.

Results

By 1 March 1996, a symptomatic assessment had been made in 437 women and 204 men during the placebo run-in period. Sixty percent of the patients attending the centres involved in the quality of life study completed a baseline assessment. Their mean age was 70 years (range 60–100) and average sitting blood pressure was 173/86 mmHg (range 160–217 mmHg systolic, 62–94 mmHg diastolic). Blood sugar was measured fasting in 588 patients, non-fasting in 32 and with fasting status unknown in three; it was not determined in the remaining 18 subjects. Blood sugar concentration ranged from 3.4 to 16.1 mmol/l, mean (SD) 5.3 (1.3) mmol/l and body mass index (BMI) ranged from 17.9 kg/m² to 42.9 kg/m², mean 26.9 (3.9) kg/m². Age up to which patient attended full-time education averaged 15.6 (4.6) years, and 31.6% had been previously treated for hypertension. 4.7% were receiving oral hypoglycaemic drugs, 4.1% digoxin, 1.6% antidepressants and 10.8% sleeping tablets.

On average, women complained that 25% of the symptoms were present and men 21% ($P < 0.001$). Table 1 gives the percentage complaining of each symptom (irrespective of severity) according to gender. Nocturia, cramps in the legs, dry mouth, and cold hands and feet were mentioned by more than 30% of both men and women. Conversely, feeling as if your mouth had been burnt, having a mouth ulcer, feeling sick and diarrhoea were complained of by less than 10% of subjects. Women complained more frequently than men of pain in the joints of hands, 'racing heart', dry eyes, blurring of vision, cramps in the legs and sore throat. No symptom was statistically more prevalent in men.

Table 2 indicates that, although all subjects were

over the age of 60, age was still important for many symptoms. The most marked increases were seen in weakness of the limbs, unsteadiness, blurring of vision and cramps in the legs. The prevalence of rash tended to decrease with age ≥ 80 years, particularly in men.

The most common symptoms related to systolic pressure after adjustment for age, blood sugar and BMI are given in Table 3, together with the OR for an increase in systolic pressure of 1 mmHg. The positive relationships between headaches, unsteadiness, blurring of vision, 'heart thumps or misses a beat', 'racing heart' and systolic pressure were observed in women but not in men, although 'racing heart' had an adjusted OR of 1.018 in men. 'Light hurts eyes' achieved statistical significance in men but not in women.

For diastolic pressure the only important ORs in women were headaches (adjusted OR = 1.050, $P < 0.05$), sore throat (adjusted OR = 1.106, $P < 0.001$) and stomach pains (adjusted OR = 1.054, $P < 0.05$). No statistically significant positive associations between symptoms and diastolic pressure were observed in men.

In the remaining analyses, the results for men and women were pooled and the OR adjusted also for gender. Generally, only adjusted associations with a probability value of $< 1\%$ are reported, to reduce the number of potentially spurious associations. However, relationships expected on clinical grounds are reported with P values < 0.05 .

Table 4 indicates that both mouth ulcer and 'racing heart' were associated with increases in blood glucose concentration. Two symptoms suspected of an association with blood sugar—blurring of vision and cramps in the legs—had adjusted ORs of 1.177 ($P < 0.05$) and 1.153 ($P < 0.05$) respectively. Increasing BMI was associated with swollen ankles, weakness of the limbs and shortness of breath (Table 4). Unexpectedly, an increase in BMI was also associated with dry mouth [OR 1.056]. Anticipated associations with BMI were also observed for two symptoms with $P < 0.05$ adjusted ORs: these were wheezing (1.067) and itching (1.064).

Twenty-five percent of men drank one or more units of alcohol per day but only 7% of women. Similarly, 14% of men smoked, compared with 7% of women, so the association between these factors and symptoms was only examined in men. An increase in alcohol intake was associated with 'racing heart'. Few other symptoms were associated with either alcohol consumption or lack of consumption. The expected association with diarrhoea (at least for heavy beer drinkers) did not achieve statistical significance (adjusted OR = 1.455; $P = 0.08$). The smokers had more wheezing and dry cough than non-smokers. In addition, the adjusted ORs for shortness of breath and feeling sick were 2.51 ($P = 0.06$) and 3.85 ($P = 0.06$) respectively.

Table 5 lists eight symptoms that were negatively related to years of education. For no symptom was

Table 1. Presence of symptoms according to gender (%)

Symptom ^a	Women (<i>n</i> = 437)	Men (<i>n</i> = 204)	<i>P</i> -value ^b
Getting up at night to pass urine	68	68	0.87
Cramps in leg	43	31	0.005
Dry mouth	42	35	0.09
Cold hands or feet	37	35	0.63
Head pains or headaches	35	27	0.05
Blurring of vision	35	23	0.002
Pain in joints of hands	35	22	<0.001
Blocked or runny nose	33	36	0.50
Weakness of limbs	33	34	0.84
Racing heart	33	17	<0.001
Heartburn	28	28	0.96
Sweating more than usual	28	23	0.14
Swollen ankles	28	16	<0.001
Light hurts your eyes	27	24	0.41
Shortness of breath	26	23	0.47
Heart thumps or misses a beat	26	18	0.03
Dry cough	25	25	0.96
Constipation	24	16	0.02
Bad taste in mouth	21	19	0.60
Itching	20	22	0.60
Unsteadiness	20	14	0.08
Stomach pain	19	13	0.06
Flushing of face	18	14	0.27
Wheezing	16	14	0.65
Dry eyes	16	6	<0.001
Sore throat	15	7	0.005
Rash on body	14	14	0.87
Shaking hands	14	13	0.92
Diarrhoea	9	7	0.63
Feeling sick	9	6	0.35
Mouth ulcer	7	4	0.17
Feeling of having burnt your mouth	5	5	0.93
Problems with erection	-	26	-

^aListed in order of frequency of complaints in women.^bFisher exact test.

Table 2. Presence of symptoms according to age (percentage present irrespective of severity)

Symptom	Women					Men				
	Age (years)					Age (years)				
	60-69 (<i>n</i> = 201)	70-79 (<i>n</i> = 202)	80+ (<i>n</i> = 34)	OR	95% CI	60-69 (<i>n</i> = 102)	70-79 (<i>n</i> = 80)	80+ (<i>n</i> = 22)	OR	95% CI
Weakness of limbs	23	39	62	1.091 ^c	1.05-1.13	25	35	73	1.084 ^c	1.04-1.14
Unsteadiness	14	22	41	1.076 ^c	1.04-1.12	12	14	27	1.044 ^c	0.99-1.10
Blurring of vision	28	38	62	1.068 ^c	1.03-1.10	23	20	38	1.025	0.98-1.08
Cramps in legs	34	49	65	1.059 ^c	1.03-1.10	26	35	41	1.051 ^a	1.01-1.10
Wheezing	11	18	26	1.072 ^b	1.03-1.12	11	18	18	1.053	1.00-1.11
Light hurts your eyes	20	31	35	1.050 ^b	1.01-1.08	24	21	32	1.005	0.96-1.05
Dry mouth	38	44	56	1.048 ^b	1.02-1.08	37	35	23	0.978	0.94-1.02
Shaking hands	9	16	21	1.046 ^a	1.00-1.09	8	19	18	1.080 ^b	1.02-1.14
Rash	11	17	9	1.027	0.98-1.07	16	15	5	0.904 ^b	0.84-0.97

^a*P* < 0.05; ^b*P* < 0.01; ^c*P* < 0.001.

OR, odds ratio (increase in odds for a 1 year increase in age); 95% CI, 95% confidence interval.

Table 3. Presence of symptoms according to entry systolic blood pressure in women and men (percentage present irrespective of severity), odds ratio (increase in odds for a 1 mmHg increase in pressure) and 95% confidence interval (CI)

Symptom	Gender	Systolic blood pressure (mmHg)			Odds ratios		
		160–169	170–179	≥180	Unadjusted	Adjusted ^a	95% CI ^b
Heart thumps or misses a beat	F	22	22	39	1.029 ^d	1.030 ^d	1.01–1.05
	M	19	15	20	0.991	0.991	0.95–1.03
Unsteadiness	F	15	19	30	1.033 ^d	1.026 ^c	1.00–1.05
	M	12	13	21	0.995	0.994	0.96–1.04
Blurring of vision	F	31	34	47	1.028 ^d	1.021 ^c	1.00–1.04
	M	22	24	25	1.003	0.999	0.97–1.03
Light hurts your eyes	F	24	22	40	1.024 ^c	1.020	1.00–1.04
	M	18	25	34	1.035 ^c	1.031 ^c	1.00–1.06
Racing heart	F	30	31	45	1.020 ^c	1.023 ^c	1.00–1.04
	M	14	20	20	1.020	1.018	0.98–1.05
Head pains or headaches	F	30	36	43	1.020 ^c	1.020 ^c	1.00–1.04
	M	30	20	29	1.000	1.000	0.97–1.03

^aFor age, blood sugar and body mass index.^bFor the adjusted odds ratio.^c $P < 0.05$; ^d $P < 0.01$.

there a statistically significant association with an increase in years of education. That this association was not negated by alcohol, smoking and BMI suggests that these factors do not account for this association.

Average complaint rate

To summarize the influence of the above factors on the number of symptoms, the increase in average

complaint rate was calculated for increases in systolic and diastolic blood pressure, smoking *versus* non-smoking, a unit increase in daily alcohol intake, and a unit increase in blood sugar, BMI and age at leaving education.

In men, a 15 mmHg excess in systolic blood pressure (adjusted for age, blood sugar and BMI) was required for an increase of one complaint (non-significant, $P = 0.82$) whereas a 7 mmHg increase in

Table 4. Presence of symptoms according to blood sugar (mmol/l), body mass index (BMI, kg/m²), alcohol intake (units/day) and current smoking habit (yes/no): the odds ratios give the increase in odds for 1 mmol/l blood sugar, 1 kg/m² BMI, 1 unit/day alcohol and smoking *versus* not smoking

		Odds ratio		
Symptom	Variable	Unadjusted	Adjusted ^a	95% CI ^b
All subjects				
Mouth ulcers	Blood sugar	1.268	1.289 ^d	1.06–1.56
Racing heart	Blood sugar	1.247	1.263 ^d	1.10–1.45
Blurring of vision	Blood sugar	1.178	1.177 ^c	1.03–1.35
Cramps in legs	Blood sugar	1.118	1.153 ^c	1.01–1.32
Swollen ankles	BMI	1.128	1.153 ^c	1.10–1.22
Weakness of limbs	BMI	1.064	1.105 ^c	1.05–1.16
Shortness of breath	BMI	1.083	1.116 ^c	1.06–1.17
Dry mouth	BMI	1.053	1.056 ^d	1.01–1.11
Wheezing	BMI	1.050	1.067 ^c	1.01–1.13
Itching	BMI	1.038	1.064 ^c	1.01–1.12
Men only				
Racing heart	Alcohol	1.482	1.542 ^d	1.12–2.13
Wheezing	Smoking	3.488	4.025 ^d	1.45–11.20
Dry cough	Smoking	2.929	3.748 ^c	1.53–9.17

^aFor blood sugar and BMI, adjusted for gender, age, systolic pressure and BMI/blood sugar. For alcohol and smoking, adjusted for age, BMI and smoking/alcohol.^b95% confidence interval for the adjusted odds ratio.^c $P < 0.05$; ^d $P < 0.01$; ^e $P < 0.001$.

Table 5. Presence of symptoms according to years of education for all subjects: the odds ratio gives the change in odds for one additional year of education

Symptom	Odds ratio		
	Unadjusted	Adjusted ^a	95% CI ^b
Bad taste in mouth	0.880 ^d	0.890 ^c	0.84–0.94
Wheezing	0.896 ^d	0.913 ^d	0.86–0.97
Blurring vision	0.914 ^d	0.927 ^c	0.89–0.97
Weakness of limbs	0.915 ^d	0.934 ^d	0.90–0.97
Constipation	0.915 ^d	0.925 ^d	0.88–0.97
Shortness of breath	0.929 ^d	0.943 ^c	0.90–0.99
Light hurts your eyes	0.935 ^d	0.946 ^c	0.91–0.99
Dry mouth	0.953 ^d	0.958 ^c	0.92–0.99

^aFor gender, age, smoking, alcohol intake and body mass index.

^b95% confidence intervals for the adjusted odds ratio.

^c $P < 0.05$; ^d $P < 0.01$; ^e $P < 0.001$.

adjusted diastolic pressure reduced the number of complaints by one ($P = 0.02$). In women, the complaint rate was not statistically related to either systolic or diastolic blood pressure.

The complaint rate was not statistically related to smoking, alcohol intake or blood sugar in either sex. However, after adjustment for age, for each 6-unit increase in BMI a woman had one additional complaint ($P = 0.01$) and for each 4-unit increase in BMI a man had one additional complaint ($P = 0.01$). A woman had to have six extra years of education to reduce her complaints by one ($P = 0.005$) and men tended to need eight extra years to reduce complaints by one ($P = 0.06$) [both calculations after adjustment for current age].

Discussion

Many untreated hypertensive subjects report symptoms in an interviewer-administered questionnaire [11, 17–22]. However only unsteadiness, nocturia and waking headache occur in excess in *untreated* hypertensives in comparison with the normal population [11]. The excess of complaints for *treated* hypertensive subjects has also been examined in comparison with controls. Marked increases in nocturia, dry mouth and swollen ankles have been observed, but no increase in headache, blurred vision, blocked nose or shortness of breath [10, 23].

All patients in the SYST-EUR trial are over 60. The total number of complaints in hypertensive patients may not increase over this age and may even fall [12]. This may be partly due to the expectation that increasing age will bring problems and therefore a reluctance to report trivial matters. Nevertheless, we have identified eight symptoms that 'increase' from the seventh to the ninth decade in subjects with ISH and one complaint (rash) which 'decreases'. The increases

might be expected with ageing and a reduction in skin problems may be due to changes in the immune system.

Four symptoms had positive associations with systolic blood pressure in women but not in men. These were 'heart thumps or misses a beat', unsteadiness, blurring of vision and headaches. Men and women agreed on the positive associations with 'light hurts eyes' and 'racing heart'. Headaches are a recognized association with higher levels of pressure, as are unsteadiness, weakness of the limbs and nocturia [10]. 'Heart thumps', 'racing heart' and 'light hurts eyes' are new observations that require confirmation. As the patients had low diastolic pressures it is not surprising that no positive association was observed between diastolic pressure and an individual symptom in men. However a positive association between diastolic pressure and headaches, sore throat and stomach pain was reported in women and requires confirmation.

Few patients in SYST-EUR have clinical diabetes mellitus and only 6% are receiving oral hypoglycaemic drugs, so we did not expect to detect the symptoms of hyperglycaemia. Nevertheless, cramps in the legs and blurring of vision were positively associated with fasting blood sugar and are recognized problems in diabetes mellitus. The association with mouth ulcers and 'racing heart' needs to be confirmed.

The symptoms associated with obesity are little researched on a quantitative basis. A 1-unit increase in BMI increased the complaint of swollen ankles, weakness of limbs and shortness of breath by over 10% and dry mouth, wheezing, itching and nocturia by over 5%. A similar analysis of untreated patients with non-insulin dependent diabetes mellitus confirmed the relationship for shortness of breath, swollen ankles, wheezing and nocturia [24].

Owing to the low rates of smoking and drinking alcohol in women, the association between these social habits and symptoms was only investigated in men. The clinical association between alcohol intake and tachycardia was illustrated by the positive association with 'racing heart'. Smoking was associated with an excess of wheezing and dry cough.

After adjusting for smoking, alcohol intake and BMI, eight miscellaneous symptoms were associated with a shorter period in education (Table 5). The association was marked and presumably not due to life style differences. However, the association may have been because those with a higher education were more physically fit, or that they may be more selective in the symptoms they report. Perhaps good social circumstances make the more educated less depressed and consequently less liable to experience symptomatic complaints. All symptomatic complaints increased in prevalence with the Brief Assessment Index score [14]. Whatever the reason, the less-educated rate their health lower [25–27].

In the SHEP trial, a pilot evaluation of quality of life suggested some impairment of cognitive functioning in those treated actively, where the Reitan trail-making test was prolonged by 3 s [28]. Nine out of 29 symptoms also increased in the actively treated group compared to the placebo group ($P < 0.01$ for each symptom) [2]. However the final report of the trial on behavioural variables [29] concluded that "medical treatment of isolated systolic hypertension does not cause deterioration in measures of cognition, emotional state, physical function or leisure activities". It is important to confirm that quality of life is maintained during active treatment of ISH. The SYST-EUR trial will provide valuable information on the benefit: risk evaluation for this condition and may clarify the association of symptoms with blood pressure, blood sugar and BMI.

Key points

- Untreated female patients with isolated systolic hypertension have complaints of headache, unsteadiness, blurred vision, irregular heart beat and 'racing heart' that increase with systolic blood pressure.
- Higher blood sugar concentrations were associated with mouth ulcers, 'racing heart', blurring of vision and leg cramps.
- Increasing obesity was associated with swollen ankles, weakness of limbs, shortness of breath, dry mouth, wheezing and itching.
- In men, alcohol consumption was related to 'racing heart' and smoking to wheezing and a dry cough.

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Appendix: study participants

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In Belgium: R. Fagard (Leuven), W. Pelemans (Leuven), *in Slovakia:* Z. Gerova (Bratislava), *in Finland:* O. Vänska (Joensuu), E. Lehtomäki (Tampere), R. Tilvis, H. Vanhanen (Helsinki), P. Kivinen (Kuopio), M. Jääskivi (Vantaa), P. Kuusisto (Ilomantsi), A. Lehtonen, T. Hakamäki

(Turku), R. Antikainen (Oulu), E. Ruotsalainen (Liperi), K. Halonen (Kuusankoski), M. Alaluoto (Pori), E. Lehmus (Hämeenlinna), *in Italy:* L. Terzoli (Milano), C. Pasotti (Voghera), A. Pirrelli (Bari), A. Bossini (Roma), G. Maiorano (Bari), P. Palatini (Padova), R. Rappelli (Ancona), *in Spain:* B. Gil-Extremuera, A. Maldonado-Martin (Granada), *in Poland:* J. Kocemba, K. Kawecka-Jaszcz (Krakow), *in the UK:* A. O'Brien (London), P. R. Wilkinson (Ashford), C. Davidson (Brighton), *in the Russian Federation:* V. Moissseyev (Moscow), *In Ireland:* J. Duggan, E. O'Brien, F. Mee (Dublin), *in Romania:* S. Babeanu, D. Dumitrascu.

Committees and co-ordination

Data monitoring committee: C. J. Bulpitt, A. E. Fletcher, J. A. Staessen, L. Thijs; *Endpoint committee:* P. De Leeuw, R. Fagard, G. Leonetti, J. Petrie; *Ethics committee:* W. Birkenhäger, C. T. Dollery, R. Fagard; *EU SYSTEUR liaison committee:* W. Birkenhäger, F. de Padua, C. T. Dollery, A. Efstratoulos, R. Fagard, F. Forette, D. Ganten, E. O'Brien, K. O'Malley, J. Rodicio, T. Strasser, J. Tuomilehto, C. Van Ypersele, A. Zanchetti; *Steering committee:* G. Abrabidze, P. De Cort, R. Fagard, F. Forette, K. Kawecka-Jaszcz, G. Leonetti, C. Nachev, E. O'Brien, J. Rodico, J. Rosenfeld, J. Tuomilehto, J. Webster, Y. Yodfat; *Trial co-ordinators:* R. Fagard, J. A. Staessen; *Co-ordinators of the side-project on ambulatory blood pressure monitoring:* D. Clement, E. O'Brien, G. Mancina, G. Parati, J. Staessen, L. Thijs; *Co-ordinator of the side-project on vascular dementia:* F. Forette; *Co-ordinators of the side project on quality of life:* C. J. Bulpitt, A. E. Fletcher; *Co-ordination of the general practitioners:* H. Celis; *Co-ordinating office:* H. Celis, L. De Pauw, P. Drent, R. Fagard, H. Fan, J. Staessen, L. Thijs, Y. Toremans, R. Vanhoof, J. Polfliet, R. Wolfs