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Managing hypertension in general practice:

a cross-sectional study of treatment and ethnicity

Abstract

Background
NICE guidelines are the accepted standard for determining the management of hypertension in UK primary care.

Aim
To explore adherence and non-adherence to NICE hypertension guidelines, the extent to which this influences blood pressure control, and the role of ethnicity.

Design and setting
A cross-sectional study was conducted based on primary care data from Lambeth DataNet, a database of primary care records in one inner-city London borough.

Method
NICE guidelines were used to determine adherence to recommended treatment options for four groups of patients with hypertension: aged <55 years on monotherapy; aged ≥55 years on monotherapy; any age on dual therapy; any age and with comorbid diabetes. Blood pressure control was determined for each treatment category and ethnic group. The study controlled for age, sex, social deprivation, and clustering within general practices.

Results
A total of 32 183 patients were identified with a current diagnosis of hypertension. Ethnic coding was available for 28 320 (88.0%). Overall, 13 546 patients with ethnicity coding could be allocated to one of the four clinical categories of hypertension; 44% of these patients received non-guideline-adherent treatment; ethnicity was not a significant determinant. Mean arterial pressure did not differ significantly between those receiving 'correct' or 'incorrect' hypotensive therapy.

Discussion
Evidence-based guidelines for the management of hypertension were not followed in a relatively large proportion of patients included in this study. Nevertheless, no evidence was found that failure to follow treatment recommendations resulted in poorer blood pressure control. Further work is needed to determine the reasons for non-implementation of guideline recommendations in primary care.

Keywords
ethnicity; guidelines; hypertension; primary care.

INTRODUCTION

Hypertension is one of three major modifiable cardiovascular disease (CVD) risk factors, together with smoking and raised cholesterol. It accounts for 49% of the risk of coronary heart disease (CHD) and 62% of stroke risk.[1] CVD risk doubles for every 10 mmHg increase in diastolic blood pressure or for every 20 mmHg increase in systolic blood pressure.[1] The overall prevalence of hypertension in adults in England is 38%.[2] Viewed from another perspective, the prevalence of hypertension runs parallel to the age cohort, being approximately 40% for the over 40s, 50% for the over 50s, 60% for the over 60s, and so on.[3]

The black population in the UK has a higher mean blood pressure than the white population,[4] and a higher prevalence of hypertension by a factor of 2.6.[5] Other risk factors differ between the two ethnic groups: diabetes is 2.7 times as high but cholesterol levels and smoking rates are lower in the black population. These differences in risk factor profiles translate into a doubled prevalence of stroke in the black population.[6] Conversely, CHD prevalence is around half for black men and two-thirds for black women.[7,8]

Hypertension in the black population has been termed 'type 2 hypertension'.[9] This terminology focuses on the role of renin in raising blood pressure levels through its action promoting sodium retention. In type 1 hypertension, renin secretion is inappropriately high for the level of blood pressure, resulting in high sodium excretion. Type 2 hypertension is characterised by low renin levels, resulting in low sodium excretion. The distinction may be related to nephron mass, since black people have lower nephron mass (hence less sodium excretion and lower renin levels). Similarly, nephron numbers decline with age, resulting in an age-related fall in renin levels. On theoretical grounds, drugs that block the renin–angiotensin system would be expected to be more effective in type 1 hypertension. This is reflected in National Institute for Health and Clinical Excellence (NICE) guidelines for the management of hypertension (NICE CG34 and CG127),[10,11] which specifically recommend angiotensin-converting enzyme (ACE) inhibitors ('A') for younger white patients, in contrast to thiazide-like diuretics ('D') or calcium antagonists ('C') recommended for black patients; beta-blockers ('B') are no longer recommended as first-line treatment.

Controversy exists over distinctions between black and white populations and treatment recommendations according to ethnicity.[12] Given these uncertainties, it was decided to conduct an observational study of the primary care treatment of hypertension in an inner-city area with a notably large African Caribbean population. The research aimed to determine the extent to which UK hypertension guidelines are implemented in practice; ethnic differences in implementation; and the effectiveness

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Submitted: 1 February 2012; **Editor's response:** 28 February 2012; **final acceptance:** 1 May 2012.

This is the full-length article (published online 1 Oct 2012) of an abridged version published in print. Cite this article as: **Br J Gen Pract 2012; DOI: 10.3399/bjgp12X656847**

How this fits in

Population studies have demonstrated that hypertension is more than twice as prevalent in the black compared to the white population. Current National Institute for Health and Clinical Excellence guidelines recommend ethnic-specific treatment for some black patients with hypertension. Using a large primary care database, it was found that almost half of patients with hypertension included in this study were prescribed 'non-recommended' treatments. Overall, prescription of non-recommended treatment was not associated with black or white ethnicity. No evidence was found that blood pressure was better controlled in patients given 'recommended' treatment.

of guideline-concordant and guideline-non-concordant treatment regimes in controlling hypertension.

METHOD

Study design

A cross-sectional population-based study was conducted using anonymised computerised general practice records from practices in Lambeth contributing to the Lambeth DataNet. Lambeth has the second highest proportion of 'Black or Black British' residents in the UK, at 25.8%; neighbouring Southwark has the highest proportion at 25.9%, based on the findings of the 2001 national census.

Lambeth DataNet is a database covering practices located in one inner-city London Borough. Clinical information and prescribing data from GP consultations are available at patient level, together with demographic details including age, sex, geographical location, and self-ascribed ethnicity. Data were extracted in March 2011, covering the previous 15 months. At the time of the study, 51 of 52 (98%) practices in Lambeth contributed to the Lambeth DataNet, providing data for a total of 367 422 patients. Guideline recommendations were based on those guidelines current at the time of the sample data extraction.

Patient sample

Primary analysis concerned the implementation of the ethnic-specific treatment guideline for hypertension in patients who were aged <55 years, and were prescribed just one drug for the treatment of hypertension (NICE CG34 and CG127).[10,11] For this group, the preferred treatment in black patients is a drug from either the 'C' or 'D' category, and in patients from all other ethnic groups, is a drug from the 'A' category. Patients aged 18–54 years with a coded diagnosis of hypertension were selected. Patients were excluded if they had other comorbidities, including chronic kidney disease, heart failure, stroke, and CHD, because some hypotensive agents may also be used as first-line treatment for these conditions. Three secondary analyses were conducted on patients with hypertension.

First, patients aged ≥55 years with no other recorded comorbidities and who were prescribed just one drug for their hypertension were selected. For these patients, NICE guidelines are not ethnic specific. Recommended treatment consists of medication from either the 'C' or 'D' category. The research aimed to determine if GP adherence to this recommendation differed between black and non-black patients.

Second, all patients aged 18 years or over, coded with hypertension, with no other recorded comorbidities, and treated with dual therapy were selected. For this group of patients the current recommendation is for treatment with 'A' plus 'C' or 'D'. Again, the research aimed to determine ethnic differences in the prescribing of recommended treatment.

Third, patients with comorbid diabetes were selected, as the treatment recommendations for these patients are also ethnic specific (NICE CG66): black patients should be offered both 'A' plus 'C' or 'D' (dual therapy), whereas patients of all other ethnicities who have diabetes should be treated with 'A' alone as monotherapy, regardless of age, or if they need dual therapy, both 'A' plus 'C' or 'D'.[13]

Patients were selected for the analyses according to age (as above). Ethnicity was allocated according to ethnicity codes corresponding to the 'five plus one' ethnic categories used in the 2001 UK national census.[14]

Outcome variables

Prescribing data were based on all hypotensive drugs prescribed in the 9 months preceding data extraction. Hypotensive agents were classified into four groups: ACE inhibitors and angiotensin receptor blockers (ARBs) ('A'), beta-blockers ('B'), calcium anagonists ('C'), and thiazide-like diuretics ('D'). Blood pressure readings were based on the most recent value recorded in the previous 6 months.

The mean arterial pressure (MAP) for the

Table 1. Ethnicity of patients with hypertension (*n* = 28 320)

Ethnicity	Frequency	%
White	13 909	49.1
Mixed	917	3.2
Asian or Asian British	1909	6.7
Black or Black British	10 746	37.9
Chinese or Other	839	3.0

sample was calculated, using the formula:

MAP = [(2 × d) + s]/3

where 'd' is diastolic and 's' is systolic blood pressure.

Differences in MAP between ethnic groups were adjusted for sex, age, and Index of Multiple Deprivation (IMD-2010) scores, based on linkage of residence to lower layer super output area.[15,16] For the regression analysis, standard errors were adjusted to account for the effect of clustering at practice level, using the Huber/White sandwich estimating procedure. To allow for multiple testing, the Bonnferoni transformation was used to set the standard for achieving statistical significance at $P<0.012$. All statistical analysis was performed using Stata (version 10).

RESULTS

Study sample

A total of 32 183 patients with a diagnosis of hypertension were identified, giving a population prevalence of 8.9%, and a prevalence of 10.8% in those aged ≥18 years, and 48.6% in those aged ≥60 years.

Ethnicity coding was available for 88.0% of these patients (*n* = 28 320) (Table 1). Those with missing ethnicity were excluded from the analyses. Also excluded from the analysis were patients with blood pressure values considered implausible for routine clinic recordings (a systolic value ≥300 mmHg and a diastolic ≤30 mmHg). For the primary analysis, 2256 patients were aged <55 years and met the study criteria for hypertension treated with monotherapy (mean age 46.1 years; 44.8% male).

Details of the number of patients fulfilling each study criterion and their age and sex, are summarised in Table 2.

Table 1. Guideline adherence in four groups of patients with hypertension

				Prescribed non-recommended treatment	
Category of patients (aged ≥18 years)	*n*	Mean age, years	Sex, % male	Black, *n* (%)	Non-black, *n* (%)
Age <55 years; treatment: monotherapy	2256	46.1	44.8	118 (10.3)	596 (53.8)
Age ≥55 years; treatment: monotherapy	3570	68.4	42.4	123 (12)	898 (35.8)
Age: all ages; treatment: dual therapy	5355	61.5	42.0	1473 (66.7)	1614 (51.3)
Age: all ages; treatment: monotherapy or dual therapy, comorbidity: diabetes	2895	62.7	49.1	803 (62.0)	601 (37.6)

Hypotensive treatment and blood pressure control in patients aged <55 years on monotherapy

In the main sample of patients aged <55 years on monotherapy, 118 (10.3%) of the black patients with hypertension were prescribed treatment not recommended by NICE ('A' or 'B'), as were 596 (53.8%) of the non-black patients with hypertension (prescribed 'B', 'C', or 'D'). Non-recommended treatment was significantly more commonly prescribed to non-black patients, Pearson $\chi^2 = 494.8$; $P<0.001$.

Blood pressure outcomes for black patients on NICE-recommended monotherapy were compared with those for black patients on non-recommended monotherapy. MAP was 103.9 mmHg in the 'correct' treatment group and 102.9 mmHg in the 'incorrect' group. The difference, adjusted for age, sex, and practice clustering, was not significant: regression coefficient $B = 1.73$ (95% confidence interval [CI] = −0.94 to 4.4); $P = 0.20$.

For non-black patients, the MAP was 101.9 mmHg in the group taking 'correct' monotherapy and 103.6 mmHg in the group taking 'incorrect' monotherapy. After adjustment, this difference was not significant at the predetermined level for the study: $B = 1.92$ (95% CI = 0.41 to 3.42); $P = 0.014$.

Hypotensive treatment and blood pressure control in patients aged ≥55 years on monotherapy

The sample of older patients on monotherapy consisted of 123 (12.0%) black patients and 898 (35.8%) non-black patients who were prescribed one of the monotherapy options not recommended by NICE (that is, 'A' or 'B'). A larger proportion of non-black than black patients were prescribed the 'incorrect' treatment: Pearson $\chi^2 = 213.8$; $P<0.001$.

For black patients, there was no significant difference in MAP according to whether they received 'correct' (100.0 mmHg) or 'incorrect' treatment

(102.0 mmHg): adjusted *B* = 2.78 (95% CI = 0.13 to 5.43); *P* = 0.04.

For non-black patients, there was again no significant difference in MAP, regardless of whether they received 'correct' (99.0 mmHg) or 'incorrect' treatment (99.1 mmHg): adjusted *B* = –0.35 (95% CI = –1.09 to 0.38); *P* = 0.34.

Hypotensive treatment and blood pressure control in patients on dual therapy

In this analysis, 1473 (66.7%) black patients and 1614 (51.3%) non-black patients were prescribed one of the dual therapy combinations (as above) not recommended by NICE. Non-recommended treatment was more commonly prescribed in black patients: Pearson χ^2 = 126.4; *P*<0.001. Nevertheless, there was no significant association between the MAP and whether the patient was taking the 'correct' treatment combination (103.9 mmHg) or 'incorrect' treatment combination (101.6 mmHg): adjusted *B* = –0.44 (95% CI = –1.20 to 0.31); *P* = 0.25.

Hypotensive treatment and blood pressure control in patients with diabetes

Of the patients with hypertension and diabetes, 803 (62.0%) black patients were prescribed treatment not recommended by NICE (that is, any monotherapy or any of the following dual therapy combinations: 'A' + 'B'; 'B' + 'C'; 'B' + 'D'; 'C' + 'D'). A lower percentage of non-black patients, 601 (37.6%), with hypertension and diabetes were prescribed treatment not recommended by NICE (that is, any monotherapy apart from 'A', or any of the dual therapy combinations as for black patients). The proportion of black patients receiving 'incorrect' treatment was significantly greater: Pearson χ^2 = 170.3; *P*<0.001.

There were no significant differences in MAP for black patients receiving 'incorrect' (98.0 mmHg) compared to 'correct' treatment (99.3 mmHg) (adjusted *B* = 1.32 [95% CI = 0.14 to 2.51]; *P* = 0.03) nor for non-black patients receiving either alternative (96.7 mmHg compared to 97.0 mmHg respectively): *P* = 0.49.

Pooled analysis

Both primary and secondary analyses were pooled to compare patients treated with 'correct' and 'incorrect' treatments and the associated MAPs in both groups (*n* = 13 546).

Comparing values for all ethnic groups, there was no significant difference in MAP between those prescribed 'correct' treatment (MAP = 100.4 mmHg; *n* = 7850 [55.8%]) or 'incorrect' treatment (MAP = 99.9 mmHg; *n* = 6226 [44.2%]), adjusted *B* = –0.34 (95% CI = –0.73 to 0.04), *P* = 0.08.

Comparing ethnic differences between those prescribed 'incorrect' treatments, 2517 (44.1%) black and 3709 (44.4%) non-black patients received treatments that were not aligned to NICE recommendations: odds ratio 0.99 (95% CI = 0.92 to 1.07); *P* = 0.81.

DISCUSSION

Summary

The principal study analysis has provided evidence that a small minority (10.3%) of younger black patients with hypertension were prescribed ACE inhibitors or ARBs as the sole treatment for their hypertension, in spite of theoretical and trial evidence of the reduced effectiveness of this class of medication in black patients who have 'low-renin' hypertension.

It is not just black patients who were given treatments that fell outside NICE guideline recommendations. Just over half of younger non-black patients (53.8%) were prescribed 'incorrect' single hypotensive agents.

Although there were significant differences between black and non-black ethnic groups in terms of the proportions prescribed non-recommended treatments, the differences were not consistent. Black patients were significantly more likely to receive non-recommended hypotensive treatment if they had diabetes, or if they required dual therapy. Conversely, non-black patients were significantly more likely to receive non-recommended treatment if they were taking monotherapy, regardless of age. Overall, when findings from all categories were pooled, ethnicity ceased to remain a significant determinant of 'incorrect' hypotensive treatment.

In the pooled analysis, it was found that nearly half (44%) of all patients were prescribed 'incorrect' treatments. In practice, adherence to the recommendations of nationally accepted guidelines in this inner-city population was relatively low.

In spite of this evidence of guideline non-adherence, no evidence was found of significantly poorer blood pressure control in patients on any of the 'incorrect' treatments.

Limitations of the study

The distinction between 'correct' and 'incorrect' hypotensive treatment is often less

clear-cut than the categories on which this analysis was based. For example, although beta-blocker monotherapy is no longer recommended as first-line treatment, NICE guidelines suggest that if blood pressure control is adequate on beta-blockers, then treatment should not be amended. Similarly, ACE inhibitors, although the preferred first-line option for non-black patients aged <55 years, are contraindicated in women who may become pregnant but it was not possible to control for this contraindication using the study dataset.

Some patients on 'incorrect' treatment categories may have been unable to tolerate medication in the 'correct' category, or the correct treatment may have been contraindicated. The researchers did not have access to data on contraindications to the main hypotensive drug classes. Since this was a cross-sectional study, there was no information available on previous hypotensive treatment categories. It is therefore not possible to interpret, for example, the proportion of black patients taking ACE inhibitors, previously treated with other hypotensive drugs but who had expressed a preference for the 'incorrect' treatment.

GPs may have agreed with their patients to continue 'incorrect' treatment because of adequate blood pressure control. Thus, patients remaining on 'incorrect' treatments may have been selected according to treatment response, resulting in an overestimate of treatment effect in those on 'incorrect' treatment.

Estimates of adherence suggest that between 50% and 80% of patients with hypertension do not take all their hypotensive medication.[17,18] Bias may have influenced this study if differential treatment adherence rates applied to any of the study groups. It was not possible to obtain information on the frequency of repeat prescription requests, which might have provided confirmatory evidence of treatment adherence.

The study conclusion that blood pressure control was largely independent of treatment category needs to be viewed with caution. Again, since this study was cross-sectional, the end-point was successful control of blood pressure rather than the reduction achieved in blood pressure over time. It is possible that the study findings were influenced by bias arising from GP prescribing behaviour. GPs may have favoured prescriptions for 'correct' treatments when the blood pressure was substantially higher than treatment thresholds but may have considered non-recommended treatments when the blood pressure was less severely raised.

Comparison with existing literature

Blood pressure in black patients is better controlled on treatment with 'C' or 'D' hypotensive agents than with 'B'[19] or 'A' drugs.[20,21] Differential responsiveness to drug classes is reflected in differing rates of cardiovascular end-points. The ALLHAT study (Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) was the first trial to demonstrate ethnic differences in stroke and coronary heart disease outcomes in black patients according to the class of hypotensive agent.[22,23] Those randomised to treatment with diuretics (chlortalidone) had fewer cardiovascular events compared to those treated with ACE inhibitors (lisinopril). No difference was observed in those randomised to treatment with 'D' or 'C' drugs.

After 2 years of treatment, the ALLHAT study demonstrated blood pressure reductions in black patients that were 5/2 mmHg greater in those treated with 'D' than with 'A' drugs; at 4 years, the gap had narrowed to 4/1 mmHg. The findings of the present study show smaller, non-significant blood pressure differences between black patients treated with 'correct' compared to 'incorrect' treatment options. However, this study was observational and not conducted within the context of a randomised controlled trial, and treatment selection bias may well have contributed to the non-significance of the findings.

The prevalence of hypertension was somewhat lower in the present study than in many other epidemiological studies.[2,3] However, the prevalence value was based on the total registered population rather than a selected sample. Moreover, the definition of hypertension used necessarily relied on GP coding. If GPs were to follow NICE diagnostic guidelines, then these give a narrower definition of hypertension than that used by the Health Survey for England, which set the definition as ≥140 mmHg systolic or 90 mmHg diastolic, thus increasing their reported prevalence.

Implications for practice and research

Current guidance for the management of hypertension, introduced in August 2011, is more complex than the guidance that applied at the time of the study, and consists of 41 new or updated recommendations.[11] This complexity may further increase the current high rates of guideline non-adherence. Although the findings of this study provided no evidence that non-adherence translates into poorer blood pressure control, it is likely that over the longer term, blood pressure control and

Funding
Not applicable.

Ethical approval
Provided by the South East Research Ethics Cimmittee (07/MREOI/26).

Provenance
Freely submitted; externally peer reviewed.

Competing interests
The authors have declared no competing interests.

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the complications of hypertension would be improved through the adoption of guideline recommendations.[11]

This study was based on an anonymised database, which meant that it was not possible to interview either GPs or patients. Further work is needed to determine the reasons for non-adherence to guidelines. Is this simply a case of GPs failing to implement evidence-based medicine? Or does treatment choice involve several other factors related to patient preference, side-effect profile, comorbidity and drug interactions, all of which may have resulted in the use of non-recommended treatments.

The findings of this study have implications for the role of guidelines in primary care. NICE guidelines are the accepted standard for determining the management of hypertension in UK primary care. Nevertheless, almost half of all patients included in this study were given medication that did not adhere to the recommended 'A, B, C, D' treatment categories.

NICE guidelines for the management of hypertension are unique in making different treatment recommendations according to ethnicity. Nevertheless, no consistent evidence was found that ethnicity was a factor determining whether patients received prescriptions for 'correct' or 'incorrect' treatment regimes.

REFERENCES

1. Mackay J, Mensah GA, Mendis S, Greenlund K. *The atlas of heart disease and stroke*. Geneva: World Health Organization, 2004.
2. Colhoun HM, Dong W, Poulter NR. Blood pressure screening, management and control in England; results from the Health Survey for England 1994. *J Hypertens* 1998; **16(6):** 747–753.
3. Primatesta P, Brookes M, Poulter NR. Improved hypertension management and control. Results from the Health Survey for England, 1998. *Hypertension* 2001; **38(4):** 827–832.
4. Chaturvedi N, McKeigue PM, Marmot MG. Resting and ambulatory blood pressure differences in Afro-Caribbeans and Europeans. *Hypertension* 1993; **22(1):** 90–96.
5. Cappucio FP, Cook DG, Atkinson RW, Strazzullo P. Prevalence, detection, and management of cardiovascular risk factors in different ethnic groups in south London. *Heart* 1997; **78(6):** 555–563.
6. Stewart JA, Dundas R, Howard RS, *et al*. Ethnic differences in incidence of stroke: prospective study with stroke register. *BMJ* 1999; **318(7189):** 967–971.
7. Balarajan R. Ethnic differences in mortality from ischaemic heart disease and cerebrovascular disease in England and Wales. *BMJ* 1991; **302(6776):** 560–564.
8. Wild S, McKeigue P. Cross sectional analysis of mortality by country of birth in England and Wales. *BMJ* 1997; **314(7082):** 705–710.
9. Brown MJ. Hypertension and ethnic group. *BMJ* 2006; **332(7545):** 833–836.
10. National Institute for Health and Clinical Excellence. *Hypertension: management in adults in primary care: pharmacological update*. Clinical Guideline 34. London: NICE, 2006. http://www.nice.org.uk/nicemedia/live/13561/56682/56682.pdf (accessed 28 Aug 2012).
11. National Institute for Health and Clinical Excellence. *Hypertension: clinical management of primary hypertension in adults*. Clinical Guideline 127. London: NICE, 2011. http://www.nice.org.uk/nicemedia/live/13561/56008/56008.pdf (accessed 28 Aug 2012).
12. Williams B. Recent hypertension trials: implications and controversies. *J Am Coll Cardiol* 2005; **45(6):** 813–827.
13. National Institute for Health and Clinical Excellence. *Type 2 diabetes: the management of type 2 diabetes*. Clinical Guideline 66. London: NICE, 2008. http://www.nice.org.uk/nicemedia/pdf/CG66NICEGuideline.pdf (accessed 28 Aug 2012).
14. White A (ed.). *Social focus in brief: ethnicity 2002*. London: Office for National Statistics, 2002.
15. Department of Communities and Local Government. *The English indices of deprivation 2010*. http://www.communities.gov.uk/documents/statistics/pdf/1871208.pdf (accessed 28 Aug 2012).
16. Office for National Statistics. *Super Output Areas (SOAs)*. http://www.ons.gov.uk/ons/guide-method/geography/beginner-s-guide/census/super-output-areas--soas-/index.html (accessed 28 Aug 2012).
17. Royal Pharmaceutical Society of Great Britain Working Party. *Partnership in medicine taking: a consultative document*. London: Royal Pharmaceutical Society of Great Britain and Mercke Sharpe and Dohme, 1996.
18. Luscher TF, Vetter H, Siegenthaler W, Vetter W. Compliance in hypertension: facts and concepts. *J Hypertens Suppl* 1985; **3(1):** S3–S9.
19. Materson BJ, Reda DJ, Cushman WC, *et al*, for the Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. Single-drug therapy for hypertension in men. A comparison of six antihypertensive agents with placebo. *N Engl J Med* 1993; **328(13):** 914–921.
20. Brown MJ, Palmer CR, Castaigne A, *et al*. Morbidity and mortality in patients randomised to double-blind treament with long-acting calcium channel blocker or diuretic in the International Nifedpine GITS study: intervention as a goal in hypertension treatment (INSIGHT). *Lancet* 2000; **356(9228):** 366–372.
21. Hansson L, Hedner T, Lund-Johansen P, *et al*. Randomised trial of effects of CCBs compared to diuretics and β-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diliazem (NORDIL) study. *Lancet* 2000; **356(9227):** 359–365.
22. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the antihypertensive and lipid lowering treatment to prevent heart attack trial (ALLHAT). *JAMA* 2002; **288(23):** 2981–2997.
23. Wright JT Jr, Dunn JK, Cutler JA, *et al;* ALLHAT Collaborative Research Group. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. *JAMA* 2005; **293(13):** 1595–1608.