

- 6 Pediatric Eye Disease Investigator Group. Treatment of anisometropic amblyopia in children with refractive correction. *Ophthalmology* 2006;113:895-903.
- 7 Moseley MJ, Neufield M, McCarty B, Chamock A, McNamara R, Rice T. Remediation of refractive amblyopia by optical correction alone. *Ophthalmic Physiol Opt* 2002;22:296-9.
- 8 Stewart CE, Moseley MJ, Stephens DA, Fielder AR, on behalf of the MOTAS cooperative. Refractive adaptation in amblyopia: quantification of effect and implications for practice. *Br J Ophthalmol* 2004;88:1552-6.
- 9 Stewart CE, Moseley MJ, Fielder AR. Defining and measuring treatment outcome for unilateral amblyopia *Br J Ophthalmol* 2003;87:1229-31.
- 10 Fielder AR, Irwin M, Auld R, Cocker KD, Jones HS, Moseley MJ. Compliance monitoring in amblyopia therapy: objective monitoring of occlusion. *Br J Ophthalmol* 1995;79:585-9.
- 11 Stewart CE, Fielder AR, Stephens DA, Moseley MJ. Design of the monitored occlusion treatment of amblyopia study (MOTAS). *Br J Ophthalmol* 2002;86:915-9.
- 12 Stewart CE, Stephens DA, Fielder AR, Moseley MJ, MOT AS Cooperative. Modelling dose-response in amblyopia: toward a child-specific treatment plan. *Invest Ophthalmol Vis Sci* 2007;48:2589-94.
- 13 Hrisos S, Clarke MP, Wright CM. The emotional impact of amblyopia treatment in preschool children. *Ophthalmology* 2004;111:1550-6.
- 14 Searle A, Norman P, Harrad R, Vedhara K. Psychosocial and clinical determinants of compliance with occlusion therapy for amblyopic children. *Eye* 2002;16:150-5.
- 15 Kushner BJ. Patching regimens for amblyopia. *Ophthalmology* 2004;112:736.
- 16 Newsham D. A randomised controlled trial of written information: the effect on parental non-compliance with occlusion therapy. *Br J Ophthalmol* 1997;86:787-91.
- 17 Massie H. Fixing eye for occlusion: survey of 1,000 cases of patients receiving occlusion of the fixing eye. *Trans Ophthalmol Soc Aust* 1965;24:39-46.
- 18 Hiscox FN, Strong N, Thompson JR, Minshull C, Woodruff G. Occlusion for amblyopia: a comprehensive survey of outcome. *Eye* 1992;6:300-4.
- 19 Lea HSJ, Rubenstein JLM. The sensitive period for anisometropic amblyopia. *Eye* 1989;3:783-90.
- 20 Kutschke PJ, Scott WE, Keech RV. Anisometropic amblyopia. *Ophthalmology* 1991;98:259-63.
- 21 Cobb CJ, Russell K, Cox A, MacEwan CJ. Factors influencing visual outcome in anisometropic amblyopes. *Br J Ophthalmol* 2002;86:1278-81.
- 22 Flynn JT, Woodruff G, Thompson JR, Hiscox F, Fever W, Shiftman J. The therapy of amblyopia: an analysis comparing the results of amblyopia therapy utilizing two pooled sets. *Trans Am Ophthalmol Soc* 1999;97:373-90.
- 23 Fulton AB, Mayer DL. Esotropic children with amblyopia: effects of patching on acuity. *Graefes Arch Clin Exp Ophthalmol* 1988;226:309-12.

Accepted: 16 July 2007

## Accuracy of electrocardiography in diagnosis of left ventricular hypertrophy in arterial hypertension: systematic review

Daniel Pewsner,<sup>1</sup> Peter Jüni,<sup>2</sup> Matthias Egger,<sup>3</sup> Markus Battaglia,<sup>1</sup> Johan Sundström,<sup>4</sup> Lucas M Bachmann<sup>5</sup>

**EDITORIAL** by Nielsen and Sajadieh

<sup>1</sup>Institute of Social and Preventive Medicine (ISPM), University of Bern, Finkenhubelweg 11, CH-3012 Berne, Switzerland; and Medix General Practice Network, Bern, Switzerland

<sup>2</sup>Institute of Social and Preventive Medicine (ISPM), University of Bern

<sup>3</sup>Institute of Social and Preventive Medicine (ISPM), University of Bern; and Department of Social Medicine, University of Bristol, Bristol

<sup>4</sup>Department of Medical Sciences, Uppsala University Hospital, Uppsala, Sweden

<sup>5</sup>Horten Centre, University of Zurich, Zurich, Switzerland

Correspondence to: M Egger [egger@ispm.unibe.ch](mailto:egger@ispm.unibe.ch)

BMJ 2007;335:711-4

doi:10.1136/bmj.39276.636354.AE

This article is an abridged version of a paper that was published on [bmj.com](http://bmj.com) on 28 August 2007. Cite this version as: *BMJ* 28 August 2007, doi: 10.1136/bmj.39276.636354.AE (abridged text, in print: *BMJ* 2007;335:711-4)

### ABSTRACT

**Objective** To review the accuracy of electrocardiography in screening for left ventricular hypertrophy in patients with hypertension.

**Design** Systematic review of studies of test accuracy of six electrocardiographic indexes: the Sokolow-Lyon index, Cornell voltage index, Cornell product index, Gubner index, and Romhilt-Estes scores with thresholds for a positive test of  $\geq 4$  points or  $\geq 5$  points.

**Data sources** Electronic databases ((Pre-)Medline, Embase), reference lists of relevant studies and previous reviews, and experts.

**Study selection** Two reviewers scrutinised abstracts and examined potentially eligible studies. Studies comparing the electrocardiographic index with echocardiography in hypertensive patients and reporting sufficient data were included.

**Data extraction** Data on study populations, echocardiographic criteria, and methodological quality of studies were extracted.

**Data synthesis** Negative likelihood ratios, which indicate to what extent the posterior odds of left ventricular hypertrophy is reduced by a negative test, were calculated.

**Results** 21 studies and data on 5608 patients were analysed. The median prevalence of left ventricular hypertrophy was 33% (interquartile range 23-41%) in primary care settings (10 studies) and 65% (37-81%) in secondary care settings (11 studies). The median negative likelihood ratio was similar across

electrocardiographic indexes, ranging from 0.85 (range 0.34-1.03) for the Romhilt-Estes score (with threshold  $\geq 4$  points) to 0.91 (0.70-1.01) for the Gubner index. Using the Romhilt-Estes score in primary care, a negative electrocardiogram result would reduce the typical pre-test probability from 33% to 31%. In secondary care the typical pre-test probability of 65% would be reduced to 63%.

**Conclusion** Electrocardiographic criteria should not be used to rule out left ventricular hypertrophy in patients with hypertension.

### INTRODUCTION

Left ventricular hypertrophy is an important risk factor in patients with hypertension, leading to a fivefold to 10-fold increase in cardiovascular risk.<sup>1-5</sup> Decisions about treatment should be based on assessments of hypertensive target organ damage and overall cardiovascular risk. The appropriate diagnostic work-up of suspected left ventricular hypertrophy in patients with hypertension is less clear, however. More than 30 electrocardiographic indexes for the diagnosis of left ventricular hypertrophy have been described. Many of the proposed indexes have remained anecdotal, but others are commonly used.<sup>6-10</sup> Debate about their comparative diagnostic value continues.<sup>11-13</sup> We did a systematic review to clarify the accuracy of different electrocardiographic indexes.

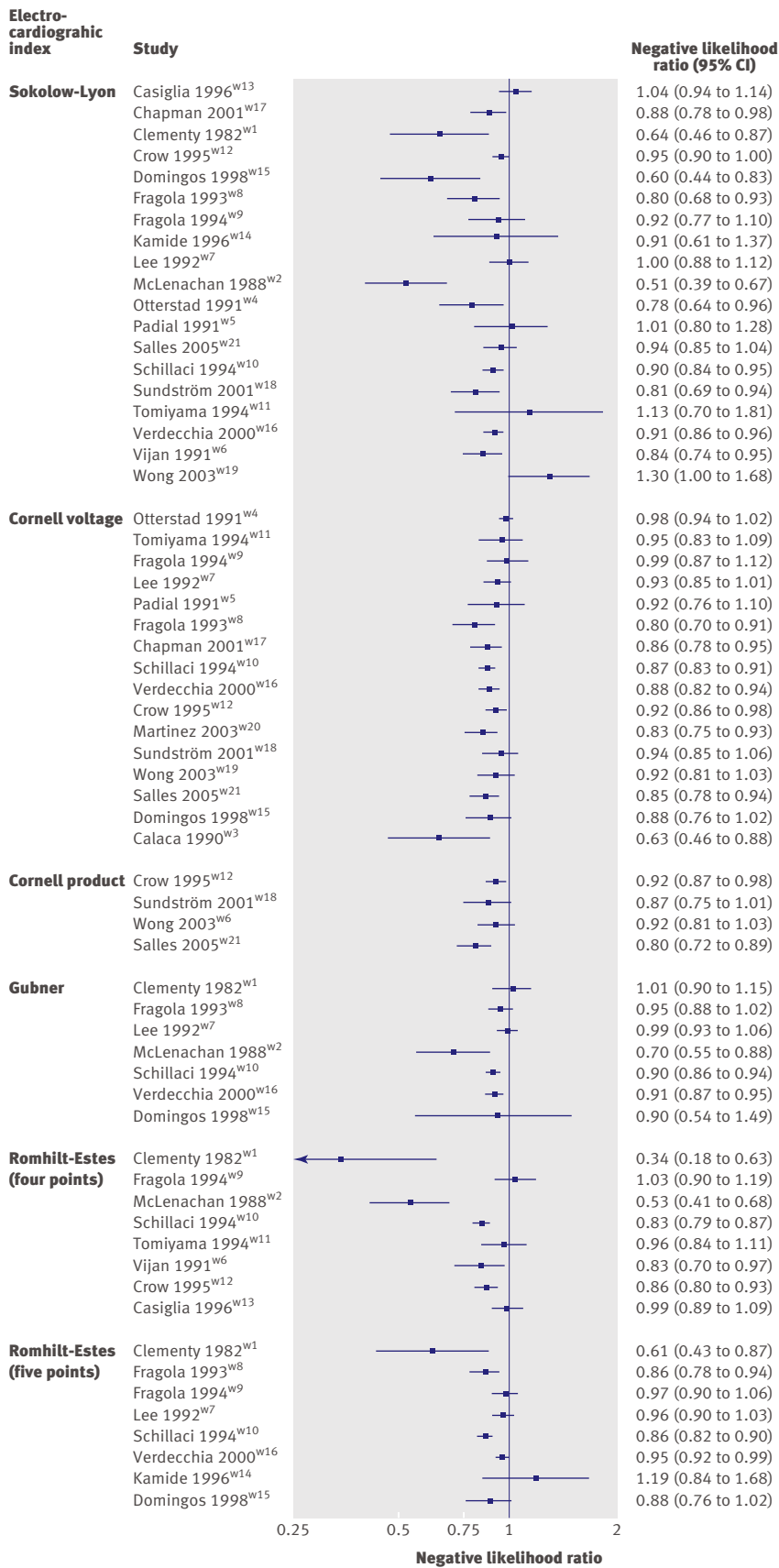


Fig 1 | Forest plots of negative likelihood ratio from test accuracy studies of six electrocardiographic indexes in diagnosis of left ventricular hypertrophy. Points represent estimates of likelihood ratio; lines represent 95% confidence intervals

METHODS

**Identification of studies**—We searched Medline from 1966 to December 2005 and Embase from 1980 to December 2005 to identify observational studies that evaluated the accuracy of electrocardiographic indexes for the diagnosis of left ventricular hypertrophy and established the presence or absence of left ventricular hypertrophy with echocardiography. We checked reference lists of relevant studies and contacted experts to complement electronic searches.

**Study selection**—We included studies in asymptomatic patients with primary arterial hypertension in any healthcare setting. Studies included patients taking anti-hypertensive treatment, those being evaluated for treatment, and patients in whom treatment was withdrawn shortly before evaluation. Two reviewers independently assessed the abstracts of all retrieved studies. We included all studies that assessed the electrocardiographic criteria in hypertensive adults against echocardiography.

**Data extraction**—We extracted data in duplicate, including the number and characteristics of patients, the healthcare setting, the prevalence of echocardiographically confirmed left ventricular hypertrophy, the electrocardiographic indexes evaluated, and the definition of the echocardiography threshold.

**Assessment of study quality**—We assessed the methodological quality of papers. We examined the methods of patient selection and data collection, completeness of descriptions of index and reference tests, completeness of blinding, and the likelihood of verification bias.<sup>14-16</sup> We ranked the quality of studies on the basis of the following criteria: description of setting; prospective data collection, with enrolment of consecutive patients and follow-up of all patients; and provision of details on echocardiography and blinding.

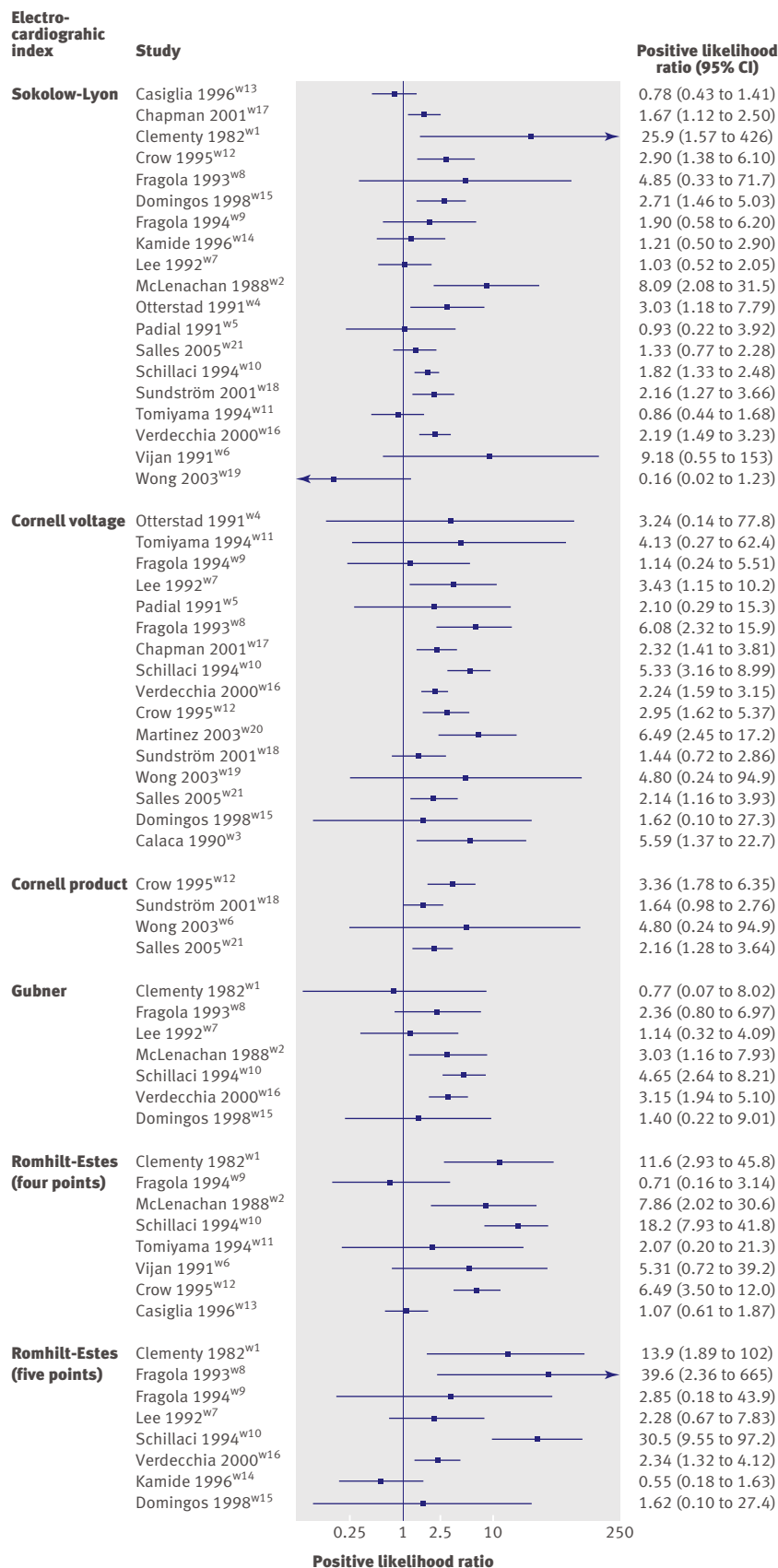
**Statistical analysis**—We calculated sensitivities, specificities, and likelihood ratios with their confidence intervals. As the electrocardiogram will mainly be used to rule out the diagnosis of left ventricular hypertrophy, we were particularly interested in the sensitivity and the likelihood ratio of a negative electrocardiogram result. The likelihood ratio of a negative test indicates how likely it is to find a negative result among people with left ventricular hypertrophy compared with those without.<sup>17</sup> We summarised results by plotting sensitivities and specificities in the receiver operating curve space and by calculating medians, ranges, and interquartile ranges.

RESULTS

Our search identified 1761 citations. We considered 142 as potentially eligible, and after scrutinising the full text articles we included 21 studies.<sup>w1-w21</sup>

Study characteristics

The 21 studies included a total of 5608 (range 30-947) patients. Ten studies were done in primary care and 11 in secondary care. The median prevalence of left ventricular hypertrophy was 33% (interquartile range 23-41%) in primary care settings and 65% (37-81%) in



**Fig 2 | Forest plots of positive likelihood ratio from test accuracy studies of six electrocardiographic indexes in diagnosis of left ventricular hypertrophy. Points represent estimates of likelihood ratio; lines represent 95% confidence intervals**

secondary care. Three studies met all six methodological criteria and were ranked as high quality. Another 11 studies met four or five criteria and were ranked as intermediate quality, whereas seven studies met two or three quality criteria and were considered of low quality.

### Electrocardiographic indexes

The 21 articles reported on 12 different electrocardiographic criteria. We analysed in detail the six most commonly used indexes, including the Sokolow-Lyon voltage index,<sup>6</sup> the Cornell voltage and Cornell product indexes,<sup>7,8</sup> the Gubner index,<sup>9</sup> and the Romhilt-Estes score with thresholds for a positive test of  $\geq 4$  points or  $\geq 5$  points.<sup>10</sup>

### Sensitivity, specificity, and likelihood ratios

For all indexes, most studies showed low sensitivity and high specificity (see [bmj.com](http://bmj.com)). The median sensitivity ranged from 10.5% (range 0-39%) for the Gubner index to 21% (4-52%) for the Sokolow-Lyon index. Median specificity ranged from 89% (53-100%) for the Sokolow-Lyon index to 99% (71-100%) for the Romhilt-Estes (five points) score.

Figures 1 and 2 show forest plots of the negative and positive likelihood ratios. The median negative likelihood ratio was similar across electrocardiographic indexes, ranging from 0.85 (range 0.34-1.03) for the Romhilt-Estes score (four points) to 0.91 (0.70-1.01) for the Gubner index. More variation existed in the positive likelihood ratio, which ranged from 1.90 (0.16-25.9) for the Sokolow-Lyon index to 5.90 (0.71-18.2) for the Romhilt-Estes score (four points). Using the median likelihood ratios from the Romhilt-Estes score (four points) in primary care, a negative electrocardiogram result would reduce the typical pre-test probability of 33% to 31%, whereas a positive electrocardiogram would increase it to 74%. In secondary care, the typical pre-test probability of 65% would be reduced to 63% or increased to 92%.

### DISCUSSION

This systematic review of studies of the accuracy of diagnostic tests found that the accuracy of electrocardiographic indexes in the diagnosis of left ventricular hypertrophy is unsatisfactory. Irrespective of the index used, the electrocardiogram is a poor screening tool to exclude left ventricular hypertrophy in hypertensive patients. Of note, specificity was reasonably high in most studies, but because sensitivity was low the power to rule in left ventricular hypertrophy was also unsatisfactory.

### Strengths and limitations

We did a comprehensive literature search, selected studies according to pre-defined criteria, and appraised the methodological quality of studies. We excluded diagnostic case-control studies, which are known to overestimate accuracy,<sup>14,15</sup> as well as studies that did not index ventricular mass for body surface area. We also excluded studies that evaluated patients with concomitant left anterior fascicular block and left bundle

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Left ventricular hypertrophy leads to a fivefold to 10-fold increase in cardiovascular risk in hypertensive patients

Several indexes calculated from standard 12 lead electrocardiograms are used in the diagnostic work-up of patients with hypertension

**WHAT THIS STUDY ADDS**

The accuracy of the more commonly used electrocardiographic criteria for ruling out left ventricular hypertrophy is unsatisfactory in both primary and secondary care.

Echocardiography is needed for a comprehensive assessment of cardiovascular risk in hypertensive patients

branch block, because these patients usually need further examinations and referral irrespective of left ventricular hypertrophy. We summarised the evidence by calculating medians, rather than combining data in meta-analysis. We believe that a formal meta-analysis would have added little in this situation. We felt that further exploration of potential sources of heterogeneity was not warranted. The published data did not allow direct comparisons of test accuracy between the different indexes. More importantly, we did not identify any randomised comparisons of diagnostic and treatment strategies and assessed clinical end points.

**Implications for clinical practice**

Electrocardiograms should not be done specifically to exclude left ventricular hypertrophy in patients with hypertension. Referral for specialist examinations is often based on high cardiovascular risk scores, but echocardiography may be more informative in hypertensive patients who, on the basis of age, sex, smoking history, and blood lipids, are at low or intermediate risk. In patients known to be at high risk, echocardiographic findings will often not affect clinical management, because interventions to reduce risk are already in place.

The evidence on the capacity of various anti-hypertensive agents to decrease left ventricular hypertrophy is limited. Preventing cardiovascular disease through modifications of other risk factors such as smoking cessation, lifestyle change, or lipid lowering treatment is the most promising approach.<sup>18 19</sup>

**Future research**

Further research is needed to identify cost effective diagnostic strategies in primary care settings. Such research could inform the development of algorithms to identify patients who should be referred for echocardiography. In the absence of accurate and inexpensive screening tests for left ventricular hypertrophy, research into new diagnostic technologies is also warranted. Further studies are needed to better define the pathophysiological mechanisms and outcomes in patients with echocardiographically confirmed left ventricular hypertrophy but negative electrocardiograms. Similarly, more data are needed on patients with positive electrocardiographic tests but negative echocardiography.

**Conclusions**

The power of some of the more commonly used electrocardiographic criteria to rule out the diagnosis of left ventricular hypertrophy in patients with hypertension is poor. Further research is needed to assess the cost effectiveness of different diagnostic and treatment strategies of left ventricular hypertrophy in primary care.

We thank Marc Gertsch, Richard S Crow, Benedict Martina, Fritz Grossenbacher, and Heiner C Bucher for valuable input and for commenting on an earlier draft.

**Contributors:** See bmj.com.

**Funding:** Krankenfürsorgestiftung der Gesellschaft für das Gute und Gemeinnützige (GGG), Basel, Switzerland, Swiss National Science Foundation (grant 3233BO-103182 and 3200BO-103183).

**Competing interests:** None declared.

**Ethical approval:** Not needed.

**Provenance and peer review:** Non-commissioned; externally peer reviewed.

- 1 Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram: prevalence, incidence, and mortality in the Framingham study. *Ann Intern Med* 1969;71:89-105.
- 2 Kannel WB, Gordon T, Castelli WP, Margolis JR. Electrocardiographic left ventricular hypertrophy and risk of coronary heart disease: the Framingham study. *Ann Intern Med* 1970;72:813-22.
- 3 Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *J Am Coll Cardiol* 1998;32:1454-9.
- 4 Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Gattobigio R, Zampi I, et al. Prognostic value of a new electrocardiographic method for diagnosis of left ventricular hypertrophy in essential hypertension. *J Am Coll Cardiol* 1998;31:383-90.
- 5 Sundström J, Lind L, Amlöv J, Zethelius B, Andrén B, Lithell HO. Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. *Circulation* 2001;103:2346-51.
- 6 Sokolow M, Lyon TP. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *Am Heart J* 1949;37:161-86.
- 7 Casale PN, Devereux RB, Kligfield P, Eisenberg RR, Miller DH, Chaudhary BS, et al. Electrocardiographic detection of left ventricular hypertrophy: development and prospective validation of improved criteria. *J Am Coll Cardiol* 1985;6:572-80.
- 8 Norman JE Jr, Levy D. Adjustment of ECG left ventricular hypertrophy criteria for body mass index and age improves classification accuracy: the effects of hypertension and obesity. *J Electrocardiol* 1996;29(suppl):241-7.
- 9 Gubner R, Ungerleider HE. Electrocardiographic criteria of left ventricular hypertrophy. *Arch Intern Med* 1943;72:196-206.
- 10 Romhilt DW, Estes EH Jr. A point-score system for the ECG diagnosis of left ventricular hypertrophy. *Am Heart J* 1968;75:752-8.
- 11 Schillaci G, Verdecchia P, Pede S, Porcellati C. Electrocardiography for left ventricular hypertrophy in hypertension: time for re-evaluation? *G Ital Cardiol* 1998;28:706-13.
- 12 Verdecchia P, Dovellini EV, Gorini M, Gozzelino G, Lucci D, Millettich A, et al. Comparison of electrocardiographic criteria for diagnosis of left ventricular hypertrophy in hypertension: the MAVI study. *Ital Heart J* 2000;1:207-15.
- 13 Conway D, Lip GY. The ECG and left ventricular hypertrophy in primary care hypertensives. *J Hum Hypertens* 2001;15:215-7.
- 14 Lijmer JG, Mol BW, Heisterkamp S, Bossel GJ, Prins MH, van der Meulen JH, et al. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;282:1061-6.
- 15 Whiting P, Rutjes AW, Reitsma JB, Glas AS, Bossuyt PM, Kleijnen J. Sources of variation and bias in studies of diagnostic accuracy: a systematic review. *Ann Intern Med* 2004;140:189-202.
- 16 Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? *JAMA* 1994;271:389-91.
- 17 Pewsner D, Battaglia M, Minder C, Marx A, Bucher HC, Egger M. Ruling a diagnosis in or out with "SpPin" and "SnNOut": a note of caution. *BMJ* 2004;329:209-13.
- 18 Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA* 2003;289:2083-93.
- 19 Svetkey LP, Erlinger TP, Vollmer WM, Feldstein A, Cooper LS, Appel LJ, et al. Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age. *J Hum Hypertens* 2005;19:21-31.

**Accepted:** 11 July 2007