

# An Evidence-Based Review of the Resting Electrocardiogram as a Screening Technique for Heart Disease

Euan A. Ashley, Vinod Raxwal, and Victor Froelicher

---

Given renewed interest in the primary prevention of cardiovascular disease, we comprehensively reviewed the utility of the electrocardiogram (ECG) for screening considering the seminal epidemiologic studies. It appears that conventional risk factors relate to long-term risk, while ECG abnormalities are better predictors of short-term risk. For individual ECG abnormalities as well as for pooled categories of ECG abnormalities, the sensitivity of the ECG for future events was too low for it to be practical as a screening tool. This almost certainly relates to the low prevalence of these abnormalities. However, all ECG abnormalities increase with age and pre-test risk. Also screening with the ECG is of minimal cost and likely to decrease further as stand-alone machines are replaced by integration into personal computers (PC). Another potential impact on performing screening ECGs would be distribution and availability of digitized ECG data via the World Wide Web. For clinical utility of ECG data, comparison with previous ECGs can be critical but is currently limited. PC based ECG systems could very easily replace many of the ECG machines in use that only have paper output. PC-ECG systems would also permit interaction with computerized medical information systems, facilitate emailing and faxing of ECGs as well as storage at a centralized web-server. Web-enabled ECG recorders similar to the new generation of home appliances could follow this quick PC solution. A serious goal for the medical industry should be to end the morass of proprietary ECG digital formats and follow a standardized format. This could lead to a network of web-servers from which every patient's ECGs would be available. Such a situation could have a dramatic effect on the advisability of performing screening ECGs.

Copyright © 2001 by W.B. Saunders Company

---

**T**he landscape of secondary prevention in cardiovascular disease management is changing. Recent years have given us hard data on the

usefulness of cardiac rehabilitation, statins, beta-blockade, and angiotensin-converting enzyme (ACE) inhibitors for ischemic heart disease (IHD), and warfarin for atrial fibrillation (AF). Evidence-backed primary prevention is also available in the form of antihypertensives, statins, ACE inhibitors,<sup>1</sup> and risk factor management for stable coronary disease. As our armory increases, it is natural that the question of screening should arise. Some conditions such as myocardial infarction (MI), AF, or hypertension can be silent, whereas others, such as angina, are by definition not. If we can detect silent conditions with a screening test, and have tools available to reduce risk, then it is right to consider applying the test to large populations. At the extremes, the decision is obvious. It is reasonable to screen those middle-aged and above for hypertension with a blood pressure cuff; it is not reasonable to screen for IHD with angiography. However, in the middle lies a gray area.

The resting electrocardiogram (ECG) is the most widely used cardiovascular diagnostic test. Approximately 75 million are performed each year in the United States alone, and probably twice that number around the world. Approximately one half are performed by physicians without special training in cardiology. Payment rates for the technical and professional components amount to

---

From the Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, UK, and the Cardiology Division, Palo Alto Veterans Administration Health Care System and Stanford University, Palo Alto, CA.

Address reprint requests to Victor Froelicher, MD, Cardiology Division (111C), VA Palo Alto Health Care System, 3801 Miranda Ave, Palo Alto, CA 94304.

Copyright © 2001 by W.B. Saunders Company

0033-0620/01/4401-0005\$35.00/0

doi:10.1053/pcad.2001.24683

the equivalent of \$29 US, with most health insurances reimbursing at a similar rate. There are over 3,000 ECG reading and storage systems in use.

Remarkably, few investigators have approached the question of using the ECG as a screening test. In 1989, Sox et al<sup>2</sup> reviewed the literature to provide a clinical review.<sup>2</sup> In 1995, Whincup et al concluded that the prognostic importance of major ECG abnormalities was strongly influenced by the presence of symptomatic congestive heart disease (CHD), and that the ECG had little or no value as a screening tool in middle-aged men without symptomatic CHD.<sup>3</sup> However, these are the only 2 studies that assess the question directly.

In light of the paucity of work examining this issue and the recent advances in primary and secondary prevention, we undertook to assess the comprehensive epidemiologic literature in which the ECG has been used. The task proved significant, and we recently published a monograph detailing our general findings.<sup>4</sup> Here we look specifically at our original question, that of the role of the ECG in screening patients for cardiovascular disease.

### Screening

The value of any screening test depends critically on four key principles: (1) its cost; (2) the prevalence of the abnormalities detected in the population assessed; (3) the relationship of the abnormalities to morbidity and mortality; and (4) the possibility of reducing or avoiding future morbidity or mortality given the information provided by the test. In particular, to justify the additional expense, the ECG must add significantly to the ability of standard risk factors to identify asymptomatic individuals with subclinical disease.

### Methods

Using MEDLINE, we reviewed the literature over a period of 33 years, from 1966 to 1999. We attempted to identify studies in which a population of asymptomatic patients with no history of ischemic heart disease underwent resting 12-lead ECG before a follow-up of at least 5 years with respect to mortality. Very few studies exactly met these criteria, so several studies have been included in which symptomatic patients were not

**Table 1. The ECG Screening Studies**

---

The Framingham Heart Study <sup>44,50-52,61,66,74,85-92</sup>
The Seven Countries Study <sup>23</sup>
The US Pooling Project <sup>29</sup>
The Finnish Social Insurance Study <sup>72</sup>
The Manitoba Study <sup>8,93</sup>
The Busselton Health Studies, Busselton City, Australia <sup>17,94,95</sup>
Chicago Heart Association Detection Project in Industry <sup>25</sup>
Chicago Western Electric Study <sup>96</sup>
Copenhagen City Heart Study <sup>12,97</sup>
White Hall Study <sup>24</sup>
British Regional Heart Study <sup>14</sup>
Italian Risk Factors and Life Expectancy Pooling Project <sup>41</sup>
The Tecumseh Community Health Study <sup>98-100</sup>
Belgian Inter-University Research on Nutrition and Health <sup>15,38,40,101</sup>
The WHO European Study <sup>26</sup>
Multiple Risk Factor Intervention Trial (MRFIT) <sup>102-104</sup>
The Honolulu Heart Program <sup>11,63,105</sup>
Evans County Study <sup>9,106,107</sup>
Charleston Heart Study <sup>10,108</sup>
The Cardiovascular Health Study <sup>20</sup>
The Bronx Aging Study <sup>60</sup>
The ECG and Survival in the Very Old <sup>19,77</sup>

---

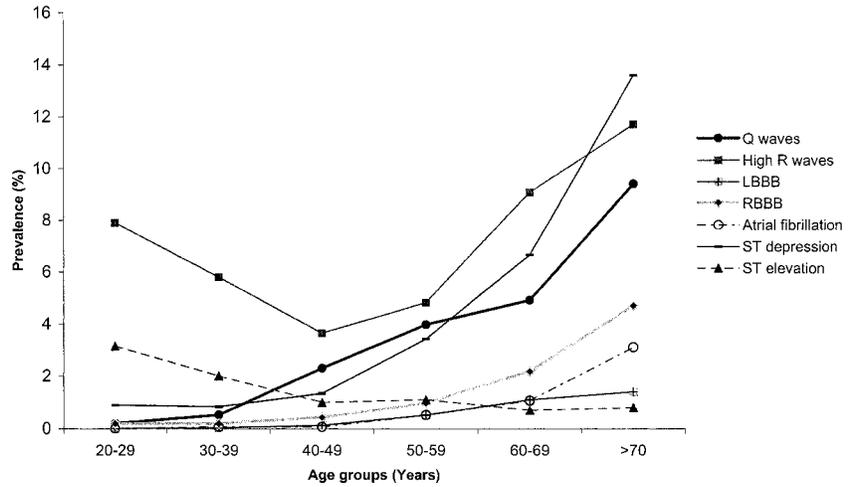
excluded, or where soft endpoints were used. All studies were critically assessed according to standard criteria.<sup>5</sup> The 22 identified studies are listed in Table 1.

### Demographics

The majority of subjects for whom ECG prevalence data are available are male. This is mostly attributable to 2 very large prevalence studies that screened 189,418 young fit men in the United States Air Force.<sup>6,7</sup> These 2 studies have not been included in Figures 1 and 2 for fear of biasing the estimates with a heavy weighting from populations prescreened to be eligible for military service. With some exceptions,<sup>8-11</sup> the ongoing epidemiologic trials now all include women in their cohorts.

Although most studies included a wide age range of participants, most information is available about subjects 40 to 60 years old. Some studies stratified according to age.<sup>12-17</sup> A small number of studies focused particularly on the elder population.<sup>18-20</sup> One study took a young, fit population and followed them up for more than 35 years.<sup>8</sup>

**Fig 1. The median prevalence of ECG abnormalities in men from the available studies.**

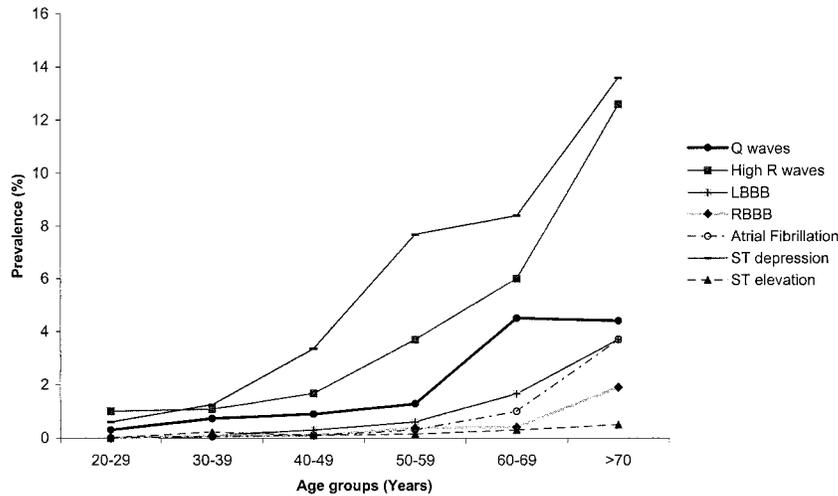


The largest portion of data available on young people is the above-mentioned prevalence data from US Air Force screening programs.<sup>6,7</sup>

As with much of the current literature, the data on ECG abnormalities are heavily biased toward a white population, although in some studies it was difficult to obtain detailed information on the ethnicity of the participant population. Fortunately, however, a small number of studies have specifically focused on groups with different racial backgrounds. The Strong Heart Study<sup>21</sup> looked at Native Americans, and the Evans County study<sup>9</sup> and the Charleston study<sup>10</sup> compared abnormalities in blacks and whites living in the United States. The Jamaican study<sup>22</sup> assessed prevalence among

blacks in Africa. Those of Japanese ancestry were examined both in Hawaii (the Honolulu Heart program<sup>11</sup>) and in Japan.<sup>23</sup> Two studies included pan-European cohorts.<sup>23,24</sup> It is clear that although the racial backgrounds of participants heavily favors whites, there is at least some information from each one of the five continents.

The socioeconomic status of participants was not always well documented. Several studies recruited from particular sections of industry,<sup>25</sup> business,<sup>26</sup> or even the British civil service.<sup>24</sup> Some reports specified if the community was predominantly rural.<sup>13,27</sup> However, many studies provided very little socioeconomic information at all.



**Fig 2. The median prevalence of ECG abnormalities in women from the available studies.**

### Exclusions

In assessing the value of the baseline ECG as a screening test, we were particularly interested in studies that excluded or analyzed separately those patients with a known history of cardiovascular disease or a current history of undiagnosed disease. There were a number of different approaches to this. Some studies made no exclusions.<sup>10,18-20,22</sup> The Manitoba study<sup>28</sup> followed an initially young and fit population over many years as they developed cardiovascular disease. Some studies made exclusions on the basis of ECG findings alone (evidence of MI<sup>25</sup>). The Pooling Project excluded all those with major Q waves.<sup>29</sup> However, many more excluded participants on the basis of more than one criterion, including physician history of MI or angina pectoris, medical examination, and ECG. Many studies used the Rose questionnaire<sup>30</sup> to assess current symptoms. Three studies analyzed symptomatic and asymptomatic participants separately,<sup>14,17,26</sup> although one did not present the separate data.<sup>17</sup>

### ECG Classification

The Minnesota Code was developed by the pioneering cardiovascular epidemiologists of the 1960s<sup>31</sup> as a tool to aid consistency and comparison in the use of the ECG in large clinical studies. The rules for its application were more closely defined in 1968,<sup>32</sup> but it was criticized by one of its originators<sup>33</sup> and a modified version was published in 1982. Despite the initial shortcomings, it rapidly became the de facto standard for the accurate and reproducible measurement of ECG abnormalities in epidemiologic trials. Perhaps its biggest contribution to mainstream cardiology, however, was its clarity and definitive guidance for ECG wave labeling and measurement. The classification itself is hierarchically based and represented by three numbers separated by dashes. The first number refers to the broad grouping (eg, Q waves = 1-x-x), and the second and third numbers indicate severity.

More recently, computerization has solved many of the problems that the Minnesota code was designed to address.<sup>34</sup> The most commonly used computer coding system in epidemiologic trials has been the NOVACODE system,<sup>35</sup> and the Minnesota Code has recently been computerized

as the MEANS program from the Netherlands and operates on a personal computer under the Windows operating system.<sup>36,37</sup>

The US Pooling Project categorized individual ECG findings into major and minor groupings. The clinical utility of this is clear: clinicians screen for several abnormalities at once, not just one. In addition, the statistical barrier that is low prevalence of individual abnormalities can be overcome by grouping abnormalities together. In fact, the final report of the Pooling Project<sup>29</sup> does not make it clear why these particular abnormalities were chosen, or indeed why they chose to categorize at all. Despite this, the categorization proved popular and was used in numerous trials.<sup>9,10,12,25,38,39</sup> An important note is that the Pooling Project categorization does not include major Q waves because this finding was an exclusion criterion for entry into the study.

## Results and Discussion

Our major results are presented in Figures 1 and 2. The median of the prevalences of the major ECG abnormalities in the studies reviewed were calculated and plotted. Caveats to be considered when interpreting these figures are the differences in criteria applied by the studies and the wide range of prevalences among the studies.

A critical factor in the adoption of any screening test is the prevalence of an abnormal test in the asymptomatic, apparently healthy population. Few studies were identified that presented ECG data from participants in whom the signs or symptoms of heart disease were entirely excluded.<sup>9,14,26,29,40-42</sup> In addition, exclusion criteria for cardiac disease varied in those studies that did. However, despite the wide interpopulation variation in prevalence, and despite some studies finding no intrapopulation difference in prevalence of ECG abnormalities between those with a diagnosis of heart disease and those without,<sup>25</sup> findings from 18,403 British men in the Whitehall study suggest caution in the combination of these 2 groups for analytical purposes.

### Left Ventricular Hypertrophy

Electrocardiographic left ventricular hypertrophy (LVH) has been recognized as a risk factor for

cardiac death for some time. Most of the seminal data comes from the Framingham study,<sup>43,44</sup> but as these researchers have pointed out, assessment of the actual impact of LVH has been confounded by the use of different definitions. Recent work has focused on improving the classification (or prognostic value) of different ECG criteria for LVH. However, most of the studies reported in this article, antedating these modifications, used either the simple high-R-wave criterion of Minnesota Code 3.1, or the more inclusive criterion, which includes ST depression (code 4.1–4.4).

*Prevalence of ECG LVH.* The prevalence of ECG LVH varies widely. All studies showed increasing prevalence with increasing age. The high values seen in the young men can be readily explained by physical fitness and ventricular hypertrophy associated with testosterone (see High R wave, Fig 1). With aging, men are less physically active and have correspondingly lower-voltage R waves, whereas with increasing age in both men and women (Fig 2), pathologic processes set in, and the size of the R wave increases again. In fact, recent studies in both humans and animals have emphasized gender differences in the response to pressure overload. Although the degree of hypertrophy seems to be similar,<sup>45,46</sup> male animals show earlier transition to heart failure, with cavity dilatation, loss of concentric remodeling, and diastolic dysfunction. This corresponds to human echocardiographic studies that show that for obesity and hypertension, relative increases in left ventricular mass are similar<sup>47</sup> among men and women, but that overall, other factors, including risk,<sup>48</sup> are not.<sup>49</sup>

*Finnish Populations and LVH.* The most surprising finding from these studies is the high prevalence of LVH in the Finnish populations assessed both as part of the Finnish cohort of the Seven Countries study and the Finnish Social Insurance Institution study. For the 50- to 59-year-old men, the Finnish cohort of the Seven Countries study had a mean prevalence of LVH (Minnesota Code 3-1) of 19%; the Finnish Social Insurance study had a mean prevalence of 27.3% and this relatively high prevalence even extended to women (mean, 13.5%). These values are extreme outliers. Of all of the other countries with predominant Caucasian populations, only Copenhagen (LVH prevalence of 12%) and the Moscow cohort of the Eu-

ropean study (18.7%) approached these figures. Prevalence was also high in black populations, both from the Jamaica study (29.9% in the 40 to 49 age group) and 19.8% of LVH in Evans County. The wide variation is shown well by studies such as the Whitehall study, which found a prevalence of less than 1% in British civil servants aged 50 to 59, and the age-pooled white male cohort of the Charleston study.

The reason for the wide variation in ECG LVH prevalence from studies performed in different populations using the same criteria is not clear. Many studies were rigorous in their training of coders and use of independent assessments. In particular, the Finnish Social Insurance study used 2 independent coders, and multiple independent medical readers at the University of Minnesota read all ECGs from the Seven Countries participating centers. It seems then that the differences noted are real: black populations and the Finnish population actually have higher mean R wave amplitude than many others. As discussed above, this may not necessarily correspond to a greater prevalence of echocardiographic LVH, although comparison of the relative weight and skin fold thickness measurements from the Seven Countries study suggests no difference between the Finnish population and the others (Finnish relative weight: 92.5%, others: 92%; Finnish skin fold: 15, others: 17.7). Notably, Finland had the highest rates of hypertension and CHD death.

It seems therefore that in at least some populations LVH is found at a sufficiently high percentage of prevalence to make it a candidate for screening. The important point, however, is its accompanying risk and the possibility of reversing that risk with appropriate intervention. In these terms, the Framingham study has provided the essential data.<sup>43,50-52</sup> It has been clear for some time that electrocardiographic ST-depression-inclusive LVH has a significantly higher risk than high-R-wave LVH alone. The Framingham data suggest that the 5-year mortality rate for the former condition is 33% for men and 21% for women. Further, the risk of sudden death is comparable to that of CHD or cardiac failure. To put this in perspective, the mortality risk of ST-depression-inclusive LVH is higher than that after overt CHD in the form of MI or angina,<sup>43</sup> yet is silent. In comparison, when adjusted for hyper-

tension, the risk associated with high-R-wave LVH is virtually nil.<sup>43</sup> In one sense, this is not surprising because resting ST depression has for some time been known to be associated with latent CHD in asymptomatic men.<sup>53</sup>

Equally strong is the evidence for improving prognosis. It is now clear from several trials, meta-analyses,<sup>54</sup> and one review of meta-analyses<sup>55</sup> that there is a strong relationship between control of blood pressure and regression of at least echocardiographic LVH. Population data also support this.<sup>56</sup> Most importantly, data from the Framingham study have shown that reduction of electrocardiographic LVH is associated with a decrease in risk.<sup>57</sup>

It would seem then that there is a case to be made for screening for ST-depression-inclusive LVH. Although high-R-wave LVH may simply be a marker of physiologic response to hypertension, ST-depression-inclusive LVH is associated with up to 15 times the risk of cardiac death, which makes it a more potent risk factor even than smoking (risk ratio of 7x).<sup>58</sup> However, although convincing, these data remain circumstantial and cannot directly answer the question posed. The only study that presented ST-depression-inclusive LVH prevalence data on individuals with no history of cardiovascular disease pooled the prevalences from participants ages 25 to 74 years and found it to be low (0.8%). What remains absolutely clear, however, is that as clinicians, we should have a low threshold for performing a screening ECG in patients with known predisposing conditions (age, hypertension, obesity, stature, and glucose intolerance<sup>52</sup>).

### Q Waves

The prevalence of both major and minor Q waves is low in the asymptomatic population (about 1%), but as with LVH, it increases with age. In fact, in middle age, when the increase in prevalence is most marked, this review offers some support for the concept that women lag approximately 10 years behind men regarding the prevalence of cardiovascular disease (compare Q wave prevalence in Fig 1 to Fig 2). At all ages, women have a lower prevalence than men.

Q waves noted on screening ECGs are important as markers for unrecognized cardiac disease. In fact, the syndrome of painless MI has been

recognized for some time.<sup>59</sup> Estimates vary regarding the proportion of actual infarctions that go unrecognized, but the average seems to be between 15% and 30%,<sup>60</sup> and this increases with age.

Of 708 MIs among the 5,127 participants in the Framingham study,<sup>61</sup> more than 25% were recognized only at screening ECG (half of these were truly silent and half were associated with atypical symptoms—a finding consistent with those of the Israel study<sup>62</sup>). Risk estimate comparisons between recognized and unrecognized MI suggested that unrecognized infarctions were as likely as recognized ones to cause death, heart failure, or stroke. This finding corresponds with data from the Honolulu Heart study,<sup>63</sup> in which the 10-year prognosis of unrecognized infarction was in fact (nonsignificantly) worse than recognized infarction (relative risks of all cause, coronary heart disease and cardiovascular mortality on the order 1.5 to 1.7). The Reykjavik study also looked at this<sup>64</sup> and found 10 and 15 year survival probabilities of 51% and 45%, similar to those for patients with recognized MI.

Given the relation of silent MI to age, particularly interesting data come from the Bronx aging study,<sup>60</sup> which assessed unrecognized MI in participants 75 years and over in an 8-year prospective investigation. They found no difference in mortality and morbidity between subjects with recognized and unrecognized MI. In fact, the mortality rate per 100 person-years was 7.1 for ECG diagnosis and 8.4 for ECG and history diagnosis. The only study to find a lower risk for unrecognized MI was the Israel study<sup>62,65</sup> (in which the risk was about half in 5-year follow-up of 10,000 participants [122 MIs]).

In summary, unrecognized MI is a common and high-risk condition. Secondary prevention measures for recognized infarction are widely recommended and often represent significant life changes for individuals who can drastically cut their risk factor profiles. We know from the studies discussed above that the long-term risk of infarction is likely to be similar whether recognized or not. It may be that we should be making more effort to detect those with silent infarcts to allow them the same chance at secondary prevention. Our data suggest that for the age group 40 to 59, we might expect to pick up 1 silent MI per 100 patients from routine screening.

### *ST Segment Abnormalities*

That ST depression is a negative prognostic marker for cardiovascular disease is clear from all the studies cited in this article in which this feature was related to mortality. In the Framingham study,<sup>66</sup> the prevalence of nonspecific ECG abnormality (defined as “greater than 1 mm ST depression and/or T wave flattening or inversion where this should not occur”) over 30 years was 8.5% for men and 7.7% for women. It was clearly related to age and blood pressure. The age-adjusted CHD morbidity and mortality occurred at about twice the rate in those with this abnormality. The Manitoba study<sup>67</sup> found the prevalence of electrocardiographic abnormalities pre-empting sudden death to be 71.4%, and among these, found the frequency of major ST-T abnormalities to be 31.4%—greater than any other ECG abnormality.

Although ST segment depression is known to be associated with digitalis therapy, hyperventilation, electrolyte abnormalities, and even recent food ingestion,<sup>68</sup> it is also clearly associated with considerable cardiovascular risk. The Framingham study predicts long- and short-term risk of sudden death in the presence of ST depression in the range 1.3 to 3, whereas estimates from other studies ranged as high as 11.4 (Finnish Social) and 6.2 (Honolulu). Ischemic changes can also be silent, and the Reykjavik study calculates a risk of 2 for silent ST-T change. Despite a lack of specificity for CHD, the association of ST segment depression with poor cardiovascular prognosis is stable, reproducible, related to the frequency with which the abnormality is present, found in both men and women,<sup>15</sup> and shown by both mortality and morbidity<sup>69</sup> data including that for the very old.<sup>19</sup> Further, as a marker of ischemic disease, the primary prevention literature can be brought to bear on its reversal.<sup>70</sup> Data from asymptomatic individuals suggest that 2% of the male population age 50 to 59 years would be expected to show ST depression on a screening ECG.

### *Bundle Branch Block*

It is clear from a number of studies that left bundle branch block (LBBB) is associated with a significant increase in risk.<sup>8,12,14,26,71,72</sup> Of the 55 people who developed LBBB over 18 years of observation in the Framingham study, most had antecedent

hypertension, cardiac enlargement, or coronary heart disease. The appearance of LBBB was an independent contributor to increased risk of cardiovascular disease mortality. The British Regional study<sup>14</sup> and the Copenhagen Heart study<sup>12</sup> both calculated relative risks for all-cause mortality above 4, whereas the Manitoba study reported 29 cases of LBBB without clinical evidence of ischemic heart disease in their cohort of 3,983 men.<sup>73</sup> On follow up, the most frequent cardiovascular event observed was sudden death, and they report a 5-year incidence for this as “the first manifestation of heart disease” 10 times greater for those with LBBB than for those without.

In contrast, there is some debate over whether right bundle branch block (RBBB) exerts a negative prognostic effect. Some studies found that it did,<sup>11,14,26</sup> and others found the reverse. The Framingham study<sup>74</sup> showed an excess of cardiovascular disease mortality, related primarily to the high prevalence of associated cardiovascular abnormalities, in all 70 people who developed complete RBBB during 18 years of follow-up. Although the initial appearance of RBBB was usually unaccompanied by overt clinical events, the subsequent incidence of coronary heart disease was 2.5 times greater than that in matched control subjects. Data from the Finnish population<sup>71,72</sup> also suggest an increase in risk in those manifesting RBBB. The Manitoba study found an increase in cardiovascular mortality but no increase in all-cause mortality. Some insight into pathology can be gained from the study of Froelicher et al<sup>53</sup> who carried out angiography on 325 air crewmen with the US Air Force. In the 41 who manifested RBBB, only 8 were found to have significant coronary artery disease on later angiography.

The increasing prevalence of BBB with age makes the prognostic character of the abnormality in the elderly population of interest. Rajala et al<sup>19</sup> found no increased risk of death associated with either LBBB or RBBB in a population of 559 people over the age of 85 years, a finding that confirms the earlier finding of Kitchin and Milne<sup>75</sup> but contradicts the findings of Caird et al.<sup>76</sup>

In summary, the picture is more clear for LBBB rather than RBBB and more clear in the middle-aged rather than the elderly population. Again, we have established the possibility of potentially reversible asymptomatic ischemic risk. The low

prevalence of these abnormalities would, however, seem to argue against screening for them.

### Atrial Fibrillation

Atrial fibrillation is clearly associated with risk in asymptomatic individuals. In comparison with LVH, Q waves, and ST abnormalities, the prevalence of atrial fibrillation is low. Further, it can be seen in the figures that the prevalence remains fairly low in both men and women until 70 years of age, when it increases markedly. Some studies suggest that this steep increase continues. Rajala et al<sup>77</sup> reported prevalence as high as 19.2% and 17% in men and women over the age of 85 years, whereas other studies<sup>78-80</sup> also found values above 10%. The pathophysiologic mechanism for the increase in prevalence of AF with age is not entirely certain. Most cases seem to be related to coronary or hypertensive heart disease, whereas no cause is found in about 15%.<sup>81</sup>

As before, the critical questions are what proportion of atrial fibrillation goes unrecognized and what strategies are available to reduce risk. The prevalence in asymptomatic individuals seems to be low (our pooled data suggest a prevalence of approximately 1% in the 50- to 59-year-old asymptomatic population), but we can only guess what percentage of the increasing number of elderly people with AF go unrecognized. In contrast, there is little doubt from prospective randomized trials that anticoagulation can cut the stroke rate in half.<sup>82</sup> Although the risk/benefit balance of anticoagulation must be individual in elderly people, the very high prevalence rates and

dramatic effects of treatment argue for screening those above 70 years.

### Sensitivity and Specificity Estimates

Any test considered as a screening test for the asymptomatic population should be considered in terms of its sensitivity, specificity, and predictive value. If we are to assess the prognostic value of a screening ECG, we need to compare the test characteristics to the ultimate end point: mortality. Only one report could be found that has previously attempted to do this.<sup>14</sup> Our calculations are displayed in Table 2. As is clearly seen, the sensitivity estimates of individual ECG abnormalities are very low. This is explained by the fact that attributable risk relates to population prevalence and that low prevalence will result in low sensitivity. The data are calculated only from those studies with stringent exclusion criteria for cardiovascular disease so that we could be certain of assessing the true screening qualities of the test. The sensitivity values are highest for ST-inclusive ECG LVH, and this almost certainly relates to the higher prevalence of this abnormality and its greater attendant risk.

It is simplistic to consider only individual ECG abnormalities in isolation, however. The clinician carrying out a screening ECG will look for several abnormalities, and it is in just such a situation that the Pooling Project classification proves helpful. Accordingly, we have included estimates based on these data. As shown, the sensitivity values are higher when abnormalities are pooled but still do not reach levels at which we might consider the ECG

**Table 2. Sensitivity and Specificity of ECG Abnormalities as Predictors of Mortality**

Study	Q Waves		ST Depression		BBB		Atrial Fibrillation		Minor Abnormality		Major Abnormality		ST Depression—LVH	
	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
Framingham	19	98	18	98			24	65					37	94
BIRNH			12	98	5.2	99			25	86	16	96		
Tunstall-Pedoe	4	99	8	98										
British Regional*	21	96			5	98	3	99					2	99
Chicago Industries									12	89	32	87		

Abbreviations: BBB, bundle branch block; sens, sensitivity; spec, specificity.

\*Sensitivity and specificity of ECG abnormalities as predictors of all-cause mortality over 8- to 10-year follow-up in initially asymptomatic populations.

useful as a screening tool in asymptomatic people (for the ultimate gold standard of mortality).

The only other investigators who performed similar analyses for ECG screening were Whincup et al.<sup>14</sup> Two important ECG abnormalities (definite myocardial ischemia and definite myocardial infarction) were analyzed separately in the presence or absence of symptomatic coronary disease. They noted that the prevalence of these abnormalities was low in their asymptomatic population, especially below 50 years of age, and that these abnormalities in combination identified only about 10% of patients with major CHD events in a 10-year follow up. Finally, they noted that the rate of major coronary disease events occurring in men identified by the test was low and of the order 14/1,000 per year. The fact that these 2 ECG abnormalities were able to identify only 10% of major events over 10 years agrees with our sensitivity estimates. However, as observed above, to consider 2 abnormalities alone (especially when neither is the extremely high-risk ST-depression-inclusive LVH) is to do injustice to the screening clinician who can account for many conditions in a single sweep of the ECG tracing.

### Conclusion

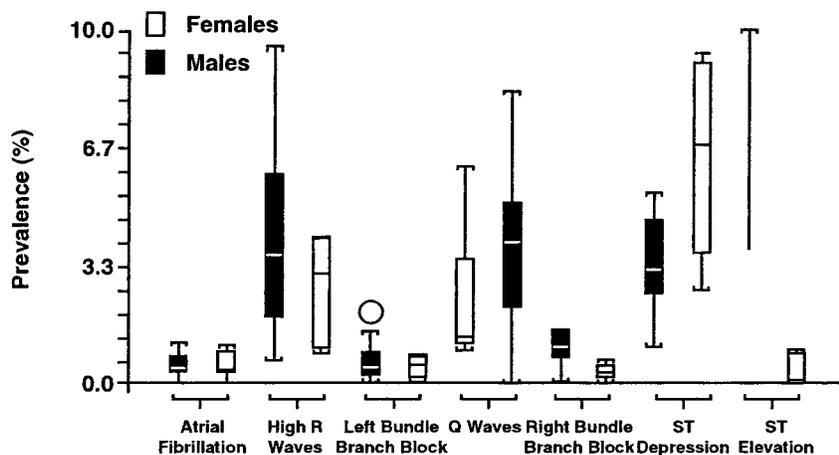
It is remarkable that so few investigators have attempted to synthesise the current data on the use of the ECG as a screening tool. Such an analysis is demanded even more by the significant recent advances in primary and secondary preven-

tion of cardiovascular disease. Perhaps one reason is the difficulty of pulling together a varied but full epidemiologic literature, which has more than answered many of those questions asked. While the epidemiologic studies were never designed to respond to the question of screening, they remain the best evidence we have.

What is clear is that (1) some risk-laden elements of cardiovascular disease can be silent, (2) we can pick these up with the ECG, and (3) we have a significant primary and secondary prevention armory that can reduce the attendant risk. What is less clear is at what stage the underlying prevalence of these conditions reaches the point at which we might consider screening worthwhile. Our sensitivity/specificity estimates and the calculations of Whincup et al.<sup>3</sup> suggest that this is not in middle age. However, prevalence increases steeply in the following decades, and there may be an argument for carrying out electrocardiography on all of those over the age of 50 who have not already had it. Figure 3 presents the prevalence data from the studies reviewed for the age group at highest risk for heart disease and appropriate for screening.

A further reason to consider carrying out ECGs on asymptomatic individuals is to acquire a baseline trace. Every clinician has at some point benefited from the availability of a past ECG for comparison. The large variance within the normal predicts this. However, we could find only 2 studies that have looked at this question specifically.<sup>83,84</sup> In the study of Rubenstein and

Fig 3. Box plots of the prevalence of ECG abnormalities among 50- to 59-year-old men and women from the available studies.



Greenfield,<sup>83</sup> the investigators reviewed the records of 236 patients presenting acutely with chest pain. Eighty-three percent had clinical or ECG findings sufficiently diagnostic that the baseline ECG could not have affected the decision to hospitalize or discharge. For 5% with equivocal clinical and ECG findings, a baseline ECG might have been useful in avoiding an unnecessary hospitalization. They concluded that the baseline ECG has little value. Although a small study, it at least suggests that the commonly held usefulness of a baseline ECG might be more apparent than real.

In this article, we have reviewed the key epidemiologic studies to answer the question of whether the ECG should be used to screen large populations for cardiovascular disease. No study directly approached the question, so no direct answer is available. However, our findings lead us to suggest that high-risk asymptomatic people in middle age should undergo a screening ECG. At stake is the secondary prevention of silent MI, the aversion of the very poor prognosis of ST-depression-inclusive LVH, the marked reduction in risk from anticoagulation in AF, and the chance to alter risk factors in those found to have LBBB or ST depression. Increased awareness of the prognostic implications of ECG abnormalities should allow us to optimize one of our most useful tools in this new millennium.

### References

1. Yusuf S, Sleight P, Pogue J, et al: Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators *N Engl J Med* 342:145-153, 2000
2. Sox HC, Garber AM, Littenberg B: The resting electrocardiogram as a screening test. A clinical analyses. *Ann Intern Med* 111:48-50, 1989
3. Whincup PH, Wannamethee G, Macfarlane PW, et al: Resting electrocardiogram and risk of coronary heart disease in middle aged british men. *J Cardiovasc Risk* 2:533-543, 1995
4. Ashley EA, Raxwal VK, Froelicher VF: The prevalence and prognostic significance of electrocardiographic abnormalities. *Curr Probl Cardiol* 25:1-72, 2000
5. Sackett DL: Evidence-Based Medicine: How to Practice and Teach EBM. New York, NY, Churchill Livingstone, 1997
6. Averill K, Lamb L: Electrocardiographic findings in 67,375 asymptomatic subjects. *Am J Cardiol* 6:76-83, 1960
7. Hiss R, Lamb L: Electrocardiographic findings in 122,043 individuals. *Circulation* 25:947-961, 1962
8. Mathewson FA, Manfreda J, Tate RB, et al: The University of Manitoba Follow-up Study—an investigation of cardiovascular disease with 35 years of follow-up (1948–1983). *Can J Cardiol* 3:378-382, 1987
9. Strogatz DS, Tyroler HA, Watkins LO, et al: Electrocardiographic abnormalities and mortality among middle-aged black men and white men of Evans County, Georgia. *J Chronic Dis* 40:149-155, 1987
10. Sutherland SE, Gazes PC, Keil JE, et al: Electrocardiographic abnormalities and 30-year mortality among white and black men of the Charleston Heart Study. *Circulation* 88:2685-2692, 1993
11. Knutsen R, Knutsen SF, Curb JD, et al: The predictive value of resting electrocardiograms for 12-year incidence of coronary heart disease in the Honolulu Heart Program. *J Clin Epidemiol* 41:293-302, 1988
12. Ostor E, Schnohr P, Jensen G, et al: Electrocardiographic findings and their association with mortality in the Copenhagen City Heart Study. *Eur Heart J* 2:317-328, 1981
13. Miall WE, Del Campo E, Fodor J, et al: Longitudinal study of heart disease in a Jamaican rural population. 2. Factors influencing mortality. *Bull World Health Organ* 46:685-694, 1972
14. Whincup PH, Wannamethee G, Macfarlane PW, et al: Resting electrocardiogram and risk of coronary heart disease in middle-aged British men. *J Cardiovasc Risk* 2:533-543, 1995
15. De Bacquer D, De Backer G, Kornitzer M, et al: Prognostic value of ischemic electrocardiographic findings for cardiovascular mortality in men and women. *J Am Coll Cardiol* 32:680-685, 1988
16. Sigurdsson E, Sigfusson N, Sigvaldason H, et al: Silent ST-T changes in an epidemiologic cohort study—A marker of hypertension or coronary heart disease, or both: The Reykjavik study. *J Am Coll Cardiol* 27:1140-1147, 1996
17. Cullen K, Stenhouse NS, Wearne KL, et al: Electrocardiograms and 13 year cardiovascular mortality in Busselton study. *Br Heart J* 47:209-212, 1982
18. Casiglia E, Spolaore P, Mormino P, et al: The CASTEL project (CArdiovascular STudy in the Elderly): Protocol, study design, and preliminary results of the initial survey. *Cardiologia* 36:569-576, 1991
19. Rajala S, Haavisto M, Kattiala K, et al: ECG findings and survival in very old people. *Eur Heart J* 6:247-252, 1985
20. Furberg CD, Manolio TA, Psaty BM, et al: Major electrocardiographic abnormalities in persons aged 65 years and older (the Cardiovascular Health Study). Cardiovascular Health Study Collaborative Research Group. *Am J Cardiol* 69:1329-1335, 1992
21. Oopik AJ, Dorogy M, Devereux RB, et al: Major electrocardiographic abnormalities among American Indians aged 45 to 74 years (the Strong Heart Study). *Am J Cardiol* 78:1400-1405, 1996

22. Miall WE, Del Campo E, Fodor J, et al: Longitudinal study of heart disease in a Jamaican rural population. I. Prevalence, with special reference to ECG findings. *Bull World Health Organ* 46:429-441, 1972
23. Keys A: Coronary heart disease in seven countries. *Circulation* 41-42:11-1211, 1970
24. Rose G, Ahmeteli M, Checcacci L, et al: Ischaemic heart disease in middle aged men. *Bull World Health Organ* 38:885-895, 1968
25. Liao YL, Liu KA, Dyer A, et al: Major and minor electrocardiographic abnormalities and risk of death from coronary heart disease, cardiovascular diseases and all causes in men and women. *J Am Coll Cardiol* 12:1494-1500, 1988
26. Rose G, Baxter PJ, Reid DD, et al: Prevalence and prognosis of electrocardiographic findings in middle-aged men. *Br Heart J* 40:636-643, 1978
27. Curnow H, Cullen K, McCall M, et al: Health and disease in a rural community. *Aust J Science* 31: 281-285, 1969
28. Mathewson F, Varnam G: Abnormal electrocardiograms in apparently healthy people—long term follow up study. *Circulation* 21:196-203, 1960
29. Pooling Project Research Group: Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: Final report of the pooling project. The pooling project research group. *J Chronic Dis* 31:201-306, 1978
30. Rose G: Self administration of a questionnaire on chest pain and intermittent claudication. *British Journal of Preventive and Social Medicine* 31:42-53, 1977
31. Blackburn H, Keys A, Simonson E, et al: The electrocardiogram in population studies—a classification system. *Circulation* 21:1160-1175, 1960
32. Rose G, Blackburn H: *Cardiovascular Survey Methods*. Geneva, World Health Organization, 1968
33. Rautaharju PM: Use and abuse of electrocardiographic classification systems in epidemiologic studies. *Eur J Cardiol* 8:155-171, 1978
34. Savage D, Rautaharju P, Baile J, et al: The emerging prominence of computer electrocardiography in large population based surveys. *J Electrocardiol* 20: 48-52, 1987 (suppl)
35. Rautaharju P: *Electrocardiography in epidemiology and clinical trials*, in Macfarlane P, Veitch-Lawrie T (eds): *Comprehensive Electrocardiology* (ed 1). New York, NY, Pergamon Press, 1989, pp 1219-1266
36. Kors JA, van Herpen G, Wu J, et al: Validation of a new computer program for Minnesota coding. *J Electrocardiol* 29:83-88, 1996 (suppl)
37. de Bruyne MC, Kors JA, Hoes AW, et al: Diagnostic interpretation of electrocardiograms in population-based research: Computer program research physicians, or cardiologists? *J Clin Epidemiol* 50:947-952, 1997
38. Kornitzer M, Dramaix M: The Belgian Interuniversity Research on Nutrition and Health (B.I.R.N.H.): General introduction. For the B.I.R.N.H. Study Group. *Acta Cardiol* 44:89-99, 1989
39. Smith WC, Kenicer MB, Tunstall-Pedoe H, et al: Prevalence of coronary heart disease in Scotland: Scottish Heart Health Study. *Br Heart J* 64:295-298, 1990
40. De Bacquer D, De Backer G, Kornitzer M, et al: Prognostic value of ECG findings for total, cardiovascular disease, and coronary heart disease death in men and women. *Heart* 80:570-577, 1998
41. Menotti A, Seccareccia F: Electrocardiographic Minnesota Code findings predicting short-term mortality in asymptomatic subjects. The Italian RIFLE Pooling Project (Risk Factors and Life Expectancy). *G Ital Cardiol* 27:40-49, 1997
42. Pedoe HD: Predictability of sudden death from resting electrocardiogram. Effect of previous manifestations of coronary heart disease. *Br Heart J* 40:630-635, 1978
43. Kannel WB: Prevalence and natural history of electrocardiographic left ventricular hypertrophy. *Am J Med* 75:4-11, 1983
44. Kannel WB, Gordon T, Offutt D: Left ventricular hypertrophy by electrocardiogram. Prevalence, incidence, and mortality in the Framingham study. *Ann Intern Med* 71:89-105, 1969
45. Douglas PS, Katz SE, Weinberg EO, et al: Hypertrophic remodeling: Gender differences in the early response to left ventricular pressure overload. *J Am Coll Cardiol* 32:1118-1125, 1998
46. Weinberg EO, Thienelt CD, Katz SE, et al: Gender differences in molecular remodeling in pressure overload hypertrophy. *J Am Coll Cardiol* 34:264-273, 1999
47. Kuch B, Muscholl M, Luchner A, et al: Gender specific differences in left ventricular adaptation to obesity and hypertension. *J Hum Hypertens* 12:685-691, 1998
48. Liao Y, Cooper RS, Mensah GA, et al: Left ventricular hypertrophy has a greater impact on survival in women than in men. *Circulation* 92:805-810, 1995
49. Dimitrow PP, Czarnicka D, Jaszcz KK, et al: Comparison of left ventricular hypertrophy expression in patients with hypertrophic cardiomyopathy on the basis of sex. *J Cardiovasc Risk* 5:85-87, 1998
50. Kannel WB, Cobb J: Left ventricular hypertrophy and mortality—Results from the Framingham Study. *Cardiology* 81:291-298, 1992
51. Kannel WB: Cardioprotection and antihypertensive therapy: The key importance of addressing the associated coronary risk factors (the Framingham experience). *Am J Cardiol* 77:6B-11B, 1996
52. Kannel WB: Left ventricular hypertrophy as a risk factor: The Framingham experience. *J Hypertens Suppl* 9:S3-8; discussion S8-9, 1991
53. Froelicher VF, Thompson AJ, Wolthuis R, et al: Angiographic findings in asymptomatic aircrewmembers with electrocardiographic abnormalities. *Am J Cardiol* 39:32-38, 1977

54. Schlaich MP, Schmieder RE: Left ventricular hypertrophy and its regression: Pathophysiology and therapeutic approach: Focus on treatment by antihypertensive agents. *Am J Hypertens* 11:1394-1404, 1998
55. Jennings G, Wong J: Regression of left ventricular hypertrophy in hypertension: Changing patterns with successive meta-analyses. *J Hypertens Suppl* 16:S29-34, 1998
56. Mosterd A, D'Agostino RB, Silbershatz H, et al: Trends in the prevalence of hypertension, antihypertensive therapy, and left ventricular hypertrophy from 1950 to 1989. *N Engl J Med* 340:1221-1227, 1999
57. Levy D, Salomon M, D'Agostino RB, et al: Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. *Circulation* 90:1786-1793, 1994
58. Jousilahti P, Vartiainen E, Korhonen HJ, et al: Is the effect of smoking on the risk for coronary heart disease even stronger than was previously thought? *J Cardiovasc Risk* 6:293-298, 1999
59. Roseman M: Painless myocardial infarction: A review of the literature and analysis of 220 cases. *Ann Intern Med* 41:1-8, 1954
60. Nadelmann J, Frishman WH, Ooi WL, et al: Prevalence, incidence and prognosis of recognized and unrecognized myocardial infarction in persons aged 75 years or older: The Bronx Aging Study. *Am J Cardiol* 66:533-537, 1990
61. Kannel WB, Abbott RD: Incidence and prognosis of unrecognized myocardial infarction. An update on the Framingham study. *N Engl J Med* 311:1144-1147, 1984
62. Medalie JH, Kahn HA, Neufeld HN, et al: Myocardial infarction over a five-year period. I. Prevalence, incidence and mortality experience. *J Chronic Dis* 26:63-84, 1973
63. Yano K, MacLean CJ: The incidence and prognosis of unrecognized myocardial infarction in the Honolulu, Hawaii, Heart Program. *Arch Intern Med* 149:1528-1532, 1989
64. Sigurdsson E, Thorgeirsson G, Sigvaldason H, et al: Unrecognized myocardial infarction: Epidemiology, clinical characteristics, and the prognostic role of angina pectoris. The Reykjavik Study. *Ann Intern Med* 122:96-102, 1995
65. Medalie JH, Snyder M, Groen JJ, et al: Angina pectoris among 10,000 men. 5 year incidence and univariate analysis. *Am J Med* 55:583-594, 1973
66. Kannel WB, Anderson K, McGee DL, et al: Nonspecific electrocardiographic abnormality as a predictor of coronary heart disease: The Framingham Study. *Am Heart J* 113:370-376, 1987
67. Rabkin SW, Mathewson FL, Tate RB: The electrocardiogram in apparently healthy men and the risk of sudden death. *Br Heart J* 47:546-552, 1982
68. Ostrander LD Jr: The relation of "silent" T wave inversion to cardiovascular disease in an epidemiologic study. *Am J Cardiol* 25:325-328, 1970
69. Joy M, Trump DW: Significance of minor ST segment and T wave changes in the resting electrocardiogram of asymptomatic subjects. *Br Heart J* 45:48-55, 1981
70. Clark LT: Primary prevention of cardiovascular disease in high-risk patients: Physiologic and demographic risk factor differences between African American and white American populations. *Am J Med* 107:225-245, 1999
71. Tervahauta M, Pekkanen J, Punsar S, et al: Resting electrocardiographic abnormalities as predictors of coronary events and total mortality among elderly men. *Am J Med* 100:641-645, 1996
72. Reunanen A, Aromaa A, Pyorala K, et al: The Social Insurance Institution's Coronary Heart Disease Study. *Acta Medica Scandinavica* 673:1-120, 1983 (suppl)
73. Rabkin SW, Mathewson FA, Tate RB: Natural history of left bundle-branch block. *Br Heart J* 43:164-169, 1980
74. Schneider JF, Thomas HE, Kreger BE, et al: Newly acquired right bundle-branch block: The Framingham Study. *Ann Intern Med* 92:37-44, 1980
75. Kitchin AH, Milne JS: Longitudinal survey of ischaemic heart disease in randomly selected sample of older population. *Br Heart J* 39:889-893, 1977
76. Caird FI, Campbell A, Jackson TF: Significance of abnormalities of electrocardiogram in old people. *Br Heart J* 36:1012-1018, 1974
77. Rajala S, Kaltiala K, Haavisto M, et al: Prevalence of ECG findings in very old people. *Eur Heart J* 5:168-174, 1984
78. Golden GS, Golden LH: The "Nona" electrocardiogram: findings in 100 patients of the 90 plus age group. *J Am Geriatr Soc* 22:329-332, 1974
79. Bensaid J, Barrillon A, Moreau P, et al: Etude de l'ectrocardiogramme de 110 sujets ages de plus 90 ans. *Arch Mal Coeur Vaiss* 67:133-145, 1974
80. Bonard E, Sears V: L'ectrocardiogramme des octogenaires. *Rev Med Suisse Romande* 79:683-694, 1959
81. Luderitz B: Atrial fibrillation and atrial flutter: Pathophysiology and pathogenesis. *Z Kardiol* 83:1-7, 1994 (suppl 5)
82. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators: The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 323:1505-1511, 1990
83. Rubenstein LZ, Greenfield S: The baseline ECG in the evaluation of acute cardiac complaints. *JAMA* 244:2536-2539, 1980
84. Hoffman JR, Igarashi E: Influence of electrocardiographic findings on admission decisions in patients with acute chest pain. *Am J Med* 79:699-707, 1985
85. Kreger BE, Kannel WB, Cupples LA: Electrocardiographic precursors of sudden unexpected death:

- the Framingham study. *Circulation* 75:1122-1124, 1987
86. Kreger BE, Cupples LA, Kannel WB: The electrocardiogram in prediction of sudden death: Framingham Study experience. *Am Heart J* 113:377-382, 1987
  87. Kannel WB, McNamara PM, Feinleib M, et al: The unrecognized myocardial infarction. Fourteen-year follow-up experience in the Framingham study. *Geriatrics* 25:75-87, 1970
  88. Kannel WB, McGee DL, Schatzkin A: An epidemiological perspective of sudden death. 26-year follow-up in the Framingham study. *Drugs* 28:1-16, 1984 (suppl 1)
  89. Framingham Research Group: The Framingham Heart Study: Design, Rationale, and Objectives. Available at [www.Framingham.org](http://www.Framingham.org). Accessed 2000
  90. Schneider JF, Thomas HE Jr, Kreger BE, et al: Newly acquired left bundle-branch block: The Framingham study. *Ann Intern Med* 90:303-310, 1979
  91. Wolf PA, Abbott RD, Kannel WB: Atrial fibrillation as an independent risk factor for stroke: The Framingham study. *Stroke* 22:983-988, 1991
  92. Benjamin EJ, Wolf PA, D'Agostino RB, et al: Impact of atrial fibrillation on the risk of death: The Framingham Heart study. *Circulation* 98:946-952, 1998
  93. Krahn AD, Manfreda J, Tate RB, et al: The natural history of atrial fibrillation: Incidence, risk factors, and prognosis in the Manitoba Follow-Up study. *Am J Med* 98:476-484, 1995
  94. Cullen K, Wearne KL, Stenhouse NS, et al: Q waves and ventricular extrasystoles in resting electrocardiograms. A 16 year follow up in Busselton study. *Br Heart J* 50:465-468, 1983
  95. Cullen KJ, Murphy BP, Cumpston GN: Electrocardiograms in the Busselton population. *Aust N Z J Med* 4:325-330, 1974
  96. Daviglus ML, Liao Y, Greenland P, et al: Association of nonspecific minor ST-T abnormalities with cardiovascular mortality: The Chicago Western Electric Study. *JAMA* 281:530-536, 1999
  97. Truelsen T, Prescott E, Gronbaek M, et al: Trends in stroke incidence. The Copenhagen City Heart Study. *Stroke* 28:1903-1907, 1997
  98. Ostrander L, Brandt R, Kjelsberg M, et al: Electrocardiographic findings among the adult population of a total natural community, Tecumseh, Michigan. *Circulation* 31:888-898, 1965
  99. Epstein F, Ostrander L, Johnson B, et al: Epidemiological studies of cardiovascular disease in a total community—Tecumseh, Michigan. *Annals of Internal Medicine* 62:1170-1185, 1965
  100. Chiang B, Perlman L, Fulton M, et al: Predisposing factors in sudden cardiac death in Tecumseh, Michigan. A prospective study. *Circulation* 41:31-37, 1970
  101. De Bacquer D, Martins Pereira LS, De Backer G, et al: The predictive value of electrocardiographic abnormalities for total and cardiovascular disease mortality in men and women. *Eur Heart J* 15:1604-1610, 1994
  102. Rautaharju PM, Neaton JD: Electrocardiographic abnormalities and coronary heart disease mortality among hypertensive men in the Multiple Risk Factor Intervention Trial. *Clin Invest Med* 10:606-615, 1987
  103. Crow RS, Prineas RJ, Hannan PJ, et al: Prognostic associations of Minnesota Code serial electrocardiographic change classification with coronary heart disease mortality in the Multiple Risk Factor Intervention Trial. *Am J Cardiol* 80:138-144, 1997
  104. The Multiple Risk Factor Intervention Trial Group: Statistical design considerations in the NHLI multiple risk factor intervention trial (MRFIT). *J Chronic Dis* 30:261-275, 1977
  105. Knutsen R, Knutsen SF, Curb JD, et al: Predictive value of resting electrocardiograms for 12-year incidence of stroke in the Honolulu Heart Program. *Stroke* 19:555-559, 1988
  106. Tyroler HA, Knowles MG, Wing SB, et al: Ischemic heart disease risk factors and twenty-year mortality in middle-age Evans County black males. *Am Heart J* 108:738-746, 1984
  107. Hames CG, Rose K, Knowles M, et al: Black-white comparisons of 20-year coronary heart disease mortality in the Evans County Heart Study. *Cardiology* 82:122-136, 1993
  108. Arnett DK, Rautaharju P, Sutherland S, et al: Validity of electrocardiographic estimates of left ventricular hypertrophy and mass in African Americans (The Charleston Heart Study). *Am J Cardiol* 79:1289-1292, 1997