OBJECTIVES: To explore the prognostic value of signs of prior myocardial infarction (MI) and atrial fibrillation (AF) on routine electrocardiograms (ECGs) at the age of 85 with respect to mortality and changes in functional status.

DESIGN: Observational, prospective cohort study with complete 6-year follow-up.

SETTING: General population.

PARTICIPANTS: A population-based sample of 566 85-year-old participants (377 women, 189 men), without exclusion criteria.

MEASUREMENTS: Annual ECG recording and evaluation using automated Minnesota Coding; annual assessment of functional status using validated questionnaires and tests; complete mortality data from civic and national registries.

RESULTS: Participants with prior MI at the age of 85 (prevalence 9%) showed greater all-cause mortality (relative risk (RR) = 1.7, 95% confidence interval (CI) = 1.2–2.2) and cardiovascular mortality (RR = 2.5, 95% CI = 1.6–3.8) but no accelerated decline in functional status during follow-up. Participants with AF at the age of 85 (prevalence 10%) showed greater all-cause (RR = 1.5, 95% CI = 1.2–2.0) and cardiovascular (RR = 2.0, 95% CI = 1.3–3.0) mortality, as well as an accelerated decline in functional status during follow-up.

CONCLUSION: Very elderly people with prior MI or AF on a routine ECG have markedly greater (cardiovascular) mortality risks. In addition, AF, but not prior MI, is associated with accelerated decline in functional status. These findings suggest that older patients with occasional findings of prior MI or AF on a routine ECG should receive optimal secondary preventive therapy. Furthermore, programmatic ECG recording could be of significant value for cardiovascular risk stratification in very elderly people and as targets for prevention of atherosclerotic disease. This is in spite of growing evidence that preventive actions in old age are effective.

The prevalence of cardiovascular disease (CVD), predominantly ischemic heart disease and stroke, increases exponentially with age, and CVD remains an important cause of mortality and morbidity up to the oldest age categories. In older people, treatment of CVD, as well as cardiovascular risk stratification, is generally managed by treating overt symptoms and controlling individual risk factors, which is the same approach used in middle age. Nevertheless, older patients are often undertreated, not only with respect to their risk factors, but also in the acute phase of cardiovascular events and secondary prevention thereafter. This is in spite of growing evidence that preventive actions in old age are effective.

Until now, “traditional” cardiovascular risk factors (e.g., high blood pressure, high total cholesterol levels) have been used as parameters for risk stratification in older people and as targets for prevention of atherosclerotic disease. However, these traditional risk factors, well established in the middle-aged, often become blurred in old age. It has recently been reported that, in very old people, it is not high blood pressure but low blood pressure that is associated with excess mortality and morbidity. Likewise, in people aged 85 and older, high total cholesterol concentrations are associated with longevity, not mortality. This implies that the effectiveness of prevention aimed at traditional risk factors in very elderly people is debatable. To improve cardiovascular risk stratification in old age, it is important to determine age-specific cardiovascular markers of mortality, morbidity, and functional decline.

To this end, it was thought possible that the recording of resting 12-lead electrocardiograms (ECGs) might be valuable. The ECG is a widely used diagnostic tool in clinical settings and could easily fit into any preventive strategy in old age. Furthermore, the ECG detects (at least) two of the most-relevant cardiac abnormalities in old age, namely...
prior myocardial infarction (MI) and atrial fibrillation (AF). Prior MI is known to have a high prevalence in the general older population, varying from 15% to 19% between studies, and is associated with high long-term mortality and morbidity. AF, which in old age is usually a sign of structural (atherosclerotic) cardiac disease and diminishing cardiac function, is the most common arrhythmia, with a prevalence that rises with age to approximately 10% in people aged 80 and older. It is related to mortality and morbidity, principally stroke.

To investigate the potential value of routine ECGs for cardiovascular risk stratification in elderly patients, the prognosis, including mortality risk and changes in functional status, of 85-year-olds with circumscribed ECG abnormalities (prior MI and AF) from the general population was studied.

METHODS

Study Population
The Leiden 85-Plus Study is an observational, prospective, population-based study of inhabitants of the city of Leiden, the Netherlands. Between September 1997 and September 1999, 705 persons of the 1912–14 birth cohort reached the age of 85 and were eligible to participate. There were no selection criteria regarding health or demographic characteristics. A total of 599 (87%) persons were enrolled (Figure 1). The medical ethical committee of the Leiden University Medical Center approved the study, and all participants gave informed consent. Subjects were visited annually at their homes, where face-to-face interviews, blood samples, and an ECG were obtained and various functional tests were completed.

ECG Recording
ECGs were recorded on a Siemens Sicard 440 (Erlangen, Germany) and transmitted to the ECG Core Laboratory in Glasgow Royal Infirmary for automated Minnesota Coding. All ECGs were reviewed to exclude coding errors due to technical causes. A prior MI was defined as the presence of Minnesota Code 1-1 or 1-2 (excluding 1-2-8), and AF as the presence of Minnesota Code 8-3-1. During follow-up, an incident MI was defined as the first appearance of Minnesota Codes 1-1 or 1-2 or the first appearance of Minnesota Code 1–3 in combination with the first appearance of Minnesota Code 5-x in the same myocardial area. One of the authors (PWM) visually confirmed all incident MIs. Incident AF during follow-up was defined as the appearance of Minnesota Code 8-3-1. Clinical MIs or AFs were not included unless they were found at the next ECG recording. The maximum number of successive ECGs was six. Treating physicians were not informed about ECG results unless abnormalities were observed with therapeutic consequences according to existing guidelines.

Functional Status
Functional status, including cognitive function, depressive symptoms, and disability, was assessed annually using validated questionnaires and tests. Cognitive function was assessed using the Mini-Mental State Examination (MMSE), with scores ranging from 0 to 30 (optimal).

Depressive symptoms were measured in those with MMSE scores greater than 18 using the 15-item Geriatric Depression Scale, with scores ranging from 0 (optimal) to 15. Disability was assessed using the Groningen Activity Restriction Scale, which is a combination of nine activities of daily living and nine instrumental activities of daily living, with scores ranging from 18 (optimal) to 72.

Clinical Cardiovascular Characteristics
In the Netherlands, the general practitioner or nursing home physician maintains the medical history of the patient, including diagnostic results and specialist letters. For all participants, the general practitioner or nursing home physician was interviewed about the medical history using standardized questionnaires, including questions on present and past cardiovascular pathologies.

Cardiovascular Medication
Pharmacists provided detailed information on all medication used by participants. All relevant medications prescribed for prior MI or AF were listed. These included anticoagulants, platelet inhibitors, beta-blockers, statins, and angiotensin-converting enzyme inhibitors.
Mortality
All participants were followed for mortality until age 91. Dates of death were obtained from the municipality. Specific data on causes of death were obtained from Statistics Netherlands, where all national death certificates were coded according to the International Classification of Diseases and Related Disorders, 10th revision (ICD-10). Causes of death were divided into cardiovascular causes (ICD-10 codes I00-I99) and noncardiovascular causes (all other ICD-10 codes). The assignment of causes of death was done independently of ECG results.

Data Analysis
Mortality risks and corresponding 95% confidence intervals (CIs) were calculated in a Cox proportional hazards model with incident events (MI or AF) as time-dependent covariates and adjusted for sex and income. The associations between ECG abnormalities and changes in functional status over time were analyzed using linear mixed models. Mixed models use all available data during follow-up, properly account for correlation between repeated measurements, and appropriately handle missing data. Differences in changes in cognitive function, depressive symptoms, and disability from age 85 to 90 were estimated using linear mixed models adjusted for sex and income and presented as (predicted) means with standard errors. Data analysis was performed using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL).

RESULTS
Of the 599 participants in the Leiden 85-Plus Study who gave their informed consent, 33 died before or refused the baseline routine ECG recording, resulting in a total of 566 evaluated routine ECGs. Mainly because of mortality, the annual number of ECGs diminished gradually to 276 at age 90 (Figure 1).

At age 85, two-thirds of the study population was female, and more than 80% were noninstitutionalized. Median MMSE was 26 points, with 91 (16%) participants scoring 5 or greater. The median disability score was 28 points (Table 1).

According to the treating physician, 50% of the subjects had one or more cardiovascular pathologies. Prior MI and arrhythmias were noted in 57 (10%) and 115 (20%) of the population at baseline, respectively (Table 2).

Fifty-two subjects (9%) had a prior MI according to their routine ECG, 56 (10%) had AF, and six (1%) had both. Thirty-six of the 52 prior MIs (69%) were clinically unrecognized, as were 23 of the 56 cases of AF (41%). Of the 57 participants with clinical history of MI, 33 used anticoagulants or platelet inhibitors, compared with eight of the 36 participants with unrecognized prior MI on their routine ECG (58% vs 22%, P = .001). For beta-blockers, these rates were 17 (30%) and five (14%) (P = .08). Use of angiotensin-converting enzyme inhibitors was roughly similar in both groups (23% vs 19%, P = .70), and use of statins was nearly absent in both groups (0% vs 2%, P = .42). Of the 115 participants with a clinically known history of arrhythmia, 45 (39%) used anticoagulants or platelet inhibitors, whereas seven (30%) of the 23 subjects with AF on their routine ECG received one of these drugs (chi-square P = .43). During follow-up, the incidence of nonfatal MI was 29 cases per 2,140 person years (1.4% per year, 95% CI = 0.9–1.9), whereas for AF it was 55 cases per 2,066 person years (2.7% per year, 95% CI = 2.0–3.4).

During follow-up, 305 (54%) of the 566 participants died (mortality rate 12.3% per year, 95% CI = 10.9–13.7). Participants with prior MI at age 85 had a 1.7 times (95% CI = 1.2–2.2) greater risk of mortality than those without prior MI. Participants with AF had a 1.5 times (95% CI = 1.2–2.0) greater risk of mortality than those without AF. Of the 305 deaths that occurred during follow-up, 120 (39%) were from CVD. Participants with prior MI at age 85 had a 2.5 times (95% CI = 1.6–3.8) and those with AF a 2.0 times (95% CI = 1.3–3.0) greater cardiovascular mortality risk. ECG abnormalities were not associated with noncardiovascular mortality (Table 3). Relative risks remained roughly similar after additional adjustments for known history of MI or history of arrhythmia.

At age 85, there were no differences in functional status between participants with prior MI or AF and those with-
predictors up to the highest age categories. and AF on routine ECGs are (cardiovascular) mortality for this observation.\textsuperscript{25,26} CVD has previously been revealed by brain MRI, are an apparent explanation. (Silent) strokes, for function, additional increase in depressive symptoms, and disability that was observed during follow-up. Subjects with prior MI at age 85 did not suffer a greater decline in any of the three aspects of functional status. In contrast, participants with AF at age 85 had a significantly steeper decline in all three aspects of functional status.

### DISCUSSION

In the general population of the oldest old, prior MI and AF are highly prevalent on a routine ECG. The consequences for prognosis are considerable, because cardiovascular mortality risk is approximately double for subjects with prior MI or AF on a routine ECG, independent of a clinical history of MI or history of arrhythmia, respectively. Moreover, AF on routine ECGs is associated with accelerated decline in functional status over time. Only some of these ECG abnormalities were clinically recognized and adequately treated according to current guidelines.

These data on the prevalence and incidence of MI and AF are consistent with other studies in elderly populations.\textsuperscript{11,12,14} Also, similar increases in all-cause and cardiovascular mortality have been observed in earlier studies in populations of younger elderly with prior MI.\textsuperscript{11,12} Regarding AF, in the Framingham cohort, a comparable increase in all-cause mortality risk was observed in those who developed AF (mean age 74–76).\textsuperscript{15,17} Thus, prior MI and AF on routine ECGs are (cardiovascular) mortality predictors up to the highest age categories.

In addition to these earlier reports, the current study showed that AF on routine ECGs was associated not only with mortality but also with additional decline in cognitive function, additional increase in depressive symptoms, and additional increase in disability score. (Silent) strokes, for instance revealed by brain MRI, are an apparent explanation for this observation.\textsuperscript{25,26} CVD has previously been related to accelerated functional decline.\textsuperscript{27} It was not possible to show an association between signs of prior MI on the ECG and decline in functional status. One might argue that the group of old infarctions was heterogeneous; some infarctions had occurred decades before, and some were more recent. This could in part explain why the overall influence on changes in functional status was absent. Preferential mortality in subjects with prior MI or AF may have led to an underestimation of functional decline. These findings present further arguments for identification of prior MI and AF in old age and optimal intervention.

This study confirmed earlier observations that preventive medication is underused in older people, especially in those with previously unrecognized CVD.\textsuperscript{2,3,28} In old age, the primary care physician is usually responsible for continuation of medication, even if a specialist initially prescribed this medication. Guidelines of the Dutch College of General Practitioners on preventive post-MI medication and anticoagulant medication in patients with AF were not available until 2005 and 2003, respectively. Prescription routines in patients with recognized CVD may therefore have improved over time.

This was an observational, prospective study in the general population of oldest old with a recruitment algorithm of approximately 90% and almost complete follow-up, which was achieved by making annual home visits, thus minimizing dropout rate. Instead of being an exceptional cohort, the population of oldest old that was studied in the Leiden 85-Plus Study was a segment of the general population with the fastest growth in industrialized societies. In the Netherlands, from the birth cohort 1912–14, one in three women and one in 10 men has reached the age of 85, and the overwhelming majority are noninstitutionalized and functioning independently, with good quality of life.\textsuperscript{29}

ECGs were evaluated using a validated computerized method based on the Minnesota Code, which has been used frequently in large epidemiological studies worldwide. Nevertheless, the prevalence and incidence of MI could be underestimated because of occasional disappearance of abnormal Q-waves after the initial signs of Q-wave MI, the occurrence of non-Q-wave infarctions, and the study ECG interval itself.\textsuperscript{30} This interval also accounts for the possible missing of paroxysmal AF, again leading to underestimation of true prevalence and incidence. These factors may have led to an underestimation of the relative risks, which further reinforces the results.

What are the clinical implications of these findings? Recording of a routine ECG in old age is an effective method of identifying people at risk of (cardiovascular) death and accelerated functional decline. In daily clinical practice, findings of prior MI or AF on a routine ECG in individual older patients should be an incentive for full cardiovascular preventive therapy. Moreover, routine ECGs could possibly be used in programmatic prevention strategies in old age, although before programmatic ECG screening for cardiovascular risk stratification in old age can be considered, all principles of screening need to be fulfilled.\textsuperscript{31} Taking into consideration the observed undertreatment in old age, these results lead to the question of what the effect would be of comprehensive secondary prevention in accordance with current guidelines. Ample studies have indicated significant beneficial effects of individual secondary preventive drugs in old age,\textsuperscript{4–7} although a recent Finnish trial of comprehensive secondary preventive treatment in a population of community-dwelling, randomly selected older people with a con-

### Table 3. All-Cause and Cause-Specific Mortality Risks According to Electrocardiogram (ECG) Abnormalities at Age 85 (N = 566)

<table>
<thead>
<tr>
<th>ECG Abnormalities at Age 85</th>
<th>Mortality</th>
<th>Relative Risk (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All-cause</td>
<td>Cause-specific</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiovascular*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Noncardiovascular†</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>1.7 (1.2–2.2)</td>
<td>2.5 (1.6–3.8)</td>
</tr>
<tr>
<td>(n = 52)</td>
<td></td>
<td>2.0 (1.3–3.0)</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.5 (1.2–2.0)</td>
<td>1.2 (0.8–1.9)</td>
</tr>
<tr>
<td>(n = 56)</td>
<td></td>
<td>1.3 (0.9–1.9)</td>
</tr>
</tbody>
</table>

Note: Cox proportional-hazard model with incident events as time-dependent covariate, adjusted for sex and income.

* International Classification of Diseases, 10th Revision (ICD-10) codes 100–199.
† All other ICD-10 codes.
firmed history of CVD could not demonstrate a significant reduction in cardiovascular events or total mortality. Further studies are necessary to assess the meaning of this single negative observation so far.32

In conclusion, prior MI and AF as identified on a routine ECG at age 85 are predictors of mortality risk up to the highest age groups. In addition, AF, but not prior MI, is associated with accelerated decline in functional status. These findings suggest that older patients with occasional findings of prior MI or AF on a routine ECG should receive optimal secondary preventive therapy. When the observed incomplete clinical recognition of these ECG abnormalities is also taken into consideration, programmatic ECG recording could be of significant value for cardiovascular risk stratification in old age and needs further exploration.

ACKNOWLEDGMENTS

Financial Disclosure: The Leiden 85-Plus Study was partly supported by an unrestricted grant from the Dutch Ministry of Health, Welfare and Sports.

Author Contributions: Westendorp and Gussekloo were responsible for study concept and design, as well as acquisition of subjects and data. All authors participated in analysis and interpretation of data and preparation of the manuscript.

Sponsor’s Role: The sponsor had no role in the design, methods, subject recruitment, data collection, analysis, or preparation of the manuscript.

REFERENCES


