Decline in Out-of-Hospital Coronary Heart Disease Deaths Has Contributed the Main Part to the Overall Decline in Coronary Heart Disease Mortality Rates Among Persons 35 to 64 Years of Age in Finland

The FINAMI Study

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Background—Out-of-hospital deaths constitute the majority of all coronary heart disease (CHD) deaths and are therefore of considerable public health significance.1–3 During the past 25 years, the CHD mortality rate has declined substantially in many Western countries, including Finland, due to the successful prevention efforts and improved treatment of both chronic CHD and acute coronary syndromes.4 Epidemiological studies and clinical trials have shown that the 28-day case-fatality rate of myocardial infarction (MI) among patients reaching the hospital alive has declined to ≈10% or even lower.5,6 It has become apparent, however, that the population view of the case-fatality rate of MI events is very different from the view of clinical trials and other hospital-based studies.7,8

Only few longitudinal studies have analyzed trends in sudden or out-of-hospital cardiac deaths.2,3,9 Most of these have been based on vital statistics, not on standardized data collection procedures, and deal with all sudden cardiac deaths instead of focusing specifically on sudden deaths caused by CHD. Accordingly, relatively little is known about time trends in sudden out-of-hospital CHD deaths during the recent steep decline in CHD mortality rate.

In the current study, we have analyzed trends in out-of-hospital CHD deaths in 4 geographical areas in Finland.
during the 15-year period 1983 to 1997. To consider the effects of primary and secondary prevention, we broke these trends further down to out-of-hospital deaths in persons with and those without a history of MI. We also calculated the contribution of the decline in out-of-hospital CHD deaths to the overall decline in CHD mortality rate. The main analyses focused on persons 35 to 64 years of age, but for the last 5-year period, 1992 to 1997, we included data on persons older than 64 years.

Methods
FINAMI is a population-based MI register aiming to record every CHD event in the populations of monitored areas.10 It continues the work of the FINMONICA MI register,11 with comparable data collection procedures. The geographical areas covered by the register are the towns of Turku in southwestern Finland, the town of Kuopio in eastern Finland, the town of Joensuu, and some surrounding rural areas in North Karelia, eastern Finland. Also included is the town of Oulu in northwestern Finland. Oulu joined in the project at a later stage, but was monitored for the years 1993 and 1997, and the other areas have data for the whole 15-year period of 1983 to 1997. In 1995, there were 104 014 men and 127 683 women ≥35 years of age living in these areas.

Data for the first 10 years of this report originate from the FINMONICA MI register and for the last 5 years from the FINAMI register. The main difference is that during the FINMONICA project, the upper age limit of registration was 64 years, which was removed in 1993. Sources of case finding were the hospital admission and discharge diagnoses and death certificates of each area.10 Trained nurses collected the information from hospital documents, death certificates, and autopsy reports. The local registration teams periodically sent their data to the coordinating center at the National Public Health Institute. The data were annually cross-checked with the national Causes-Of-Death Register and the national Hospital Discharge Register for completeness. These registers cover all deaths of Finnish residents and every hospitalization in Finland. Interna- tional Classification of Diseases (ICD) 9 codes 410–414 and 798, and ICD-10 codes I20–I25, R96, R98, I46.1, and I46.9 were used for cross-checking with the national Causes-Of-Death register. ICD-9 was used in Finland until the end of 1995 and ICD-10 thereafter.

The suspected CHD events were classified into 5 diagnostic categories, which have been described.10,11 Four of these categories were relevant for fatal events. For these, the classification criteria were the same as in the WHO MONICA Project:12 (1) definite MI, appearance of fresh MI by visual inspection and/or recent coronary occlusion found at necropsy; (2) possible acute MI or coronary death: fatal cases, in which there is no good evidence for another cause of death, (a) with symptoms typical or atypical or inadequately described, (b) without symptoms but with evidence of chronic coronary occlusion or stenosis or old myocardial scarring at necropsy, or (c) with a good history of chronic ischemic heart disease in the absence of significant valvular disease or cardiomyopathy; (3) no acute MI: fatal cases in which another diagnosis has been made; (4) fatal unclassifiable events: cases with no autopsy, no history of symptoms, no previous history of chronic ischemic heart disease, and no other diagnosis. There were very few fatal unclassifiable events (n = 42, which is 0.5% of all CHD events registered during the 15-year period).

We defined out-of-hospital CHD deaths as cases of death that had occurred out-of-hospital or in the emergency room or within 1 hour after the onset of symptoms and had been classified into the diagnostic category definite MI, possible MI, coronary death, or fatal unclassifiable event. The frequency of autopsies among these cases was high: 70% among men and 76% among women. According to the practice of the WHO MONICA Project,12 the time frame for one event was 28 days. Thus, we did not include in out-of-hospital CHD deaths those deaths that occurred after hospitalization but within 28 days since the beginning of symptoms. During 1988 to 1997 there were 31 cases among men and 12 cases among women who died after discharge from a hospital but within 28 days since the beginning of the event. The event was considered to be incident (first for a particular person) if there was no indication of a previous, clinically recognized MI in the patient’s history; otherwise the event was considered as recurrent. History of CHD was considered positive if the review of medical records revealed evidence for (a) previous clinically recognized MI, or (b) clinically symptomatic coronary insufficiency or angina pectoris in the absence of a firm diagnosis of valvular heart disease or cardiomyopathy.

Statistical Methods
Out-of-hospital, in-hospital, and total CHD mortality rates were expressed per 100 000 persons and age-standardized according to the direct method using 5-year age groups and the European standard population.13 The annual population counts for the denominators were obtained from the National Population Register, which is updated continuously. For the calculation of out-of-hospital CHD death rates among persons with and without prior MI, the denominators were derived by using data from the FINAMI areas every 5 years. Surveys for the years 1982, 1987, 1992, and 1997 were used in the analyses, and the years between these surveys were estimated by means of regression analysis. We took the proportions of persons who reported having had an MI for each 5-year age group beginning from age 45 years and then applied these proportions to the population counts of the FINAMI areas to establish the proportions of population with and without a history of prior MI. The age group 35 to 44 years was excluded from this analysis because of small numbers. Also, these rates were age-standardized to the European Standard Population. The 95% CIs were calculated assuming Poisson distribution for the annual numbers of deaths.

The proportion of out-of-hospital CHD deaths and the 28-day case-fatality rate were age-standardized by using weights derived from the combined age distribution of patients with MI and stroke in the WHO MONICA Project.15 The trends in event rates and case-fatality rates were determined by means of log-linear Poisson regression models, with the year as the independent variable.16 Trends were estimated for the age group 35 to 64 years, because that was the common age group for the whole 15-year period. Oulu was excluded from the trend analyses because it had data only for the years 1993 and 1997. Data for the other areas were pooled because the results for each area were similar.

The proportion of CHD mortality rate decline due to the decline in out-of-hospital CHD deaths was estimated using the formula 100×(dMs/dMt), where dMs = out-of-hospital CHD mortality rate in 1983 minus out-of-hospital CHD mortality rate in 1997, and dMt = total CHD mortality rate in 1983 minus total CHD mortality rate in 1997. Smoothed mortality rates taken from the log-linear models were used for these calculations. For the age group–specific analyses, we included all age groups ≥35 years and all FINAMI areas, but only the last 5-year period 1993 to 1997 for which we had data on persons older than 64 years.

Results
During the 15-year period, 1622 out-of-hospital CHD deaths occurred in the FINAMI areas among men and 242 among women 35 to 64 years of age. Another 853 out-of-hospital CHD deaths were observed during the period 1993 to 1997 among men and 777 among women ≥65 years of age. The average age-standardized proportion of out-of-hospital CHD deaths of all CHD deaths in the age group of 35 to 64 years was 73% among men and 60% among women. These proportions did not change during the study period (trend, 0.3% per year (95% CI, -0.8, 1.5%) among men and -0.4% per year (-3.5, 2.7%) among women).

The out-of-hospital CHD death rate declined on average by 6.1% per year (-7.3, -5.0%) among men and by 7.0% per year (-10.0, -4.0%) among women (Table 1). Rates and
trends in in-hospital CHD mortality rate and in total CHD deaths are also shown for comparison. The declining trends did not differ much, but the rates in in-hospital CHD deaths were much lower than those in out-of-hospital CHD deaths.

The out-of-hospital CHD death rate was further broken down to deaths among persons with and without a history of prior MI (Figure 1). Significant declines were observed in both, but the rates were much higher in persons with prior MI. Among the victims of out-of-hospital death from a recurrent CHD event, the time interval to the previous MI showed an increasing trend: Among men who died during the 5-year period 1983 to 1987, 1988 to 1992, and 1993 to 1997, the time intervals to the previous MI event were 4.7, 5.6, and 7.1 years, respectively. Among women, the corresponding time intervals were 3.1, 4.8, and 5.2 years.

Of all men 35 to 64 years of age who died of CHD out-of-hospital during the 15-year period, 37.1% (35.9% to 38.3%) had a history of MI. Another 20.8% (18.8% to 22.8%) had a history of symptomatic CHD without MI. Among women of similar age, 29.0% (26.8% to 31.2%) had a history of MI, and another 22.6% (17.4% to 27.8%) had a history of CHD without MI. Thus, for approximately half of the cases, out-of-hospital death was the first clinical manifestation of CHD.

The case-fatality rate due to out-of-hospital CHD death increased with age, in particular among women (Table 2). However, the proportion of out-of-hospital deaths of all CHD deaths declined with age. Among persons younger than 75 years, out-of-hospital CHD deaths constituted the majority of all CHD deaths, but not among persons ≥75 years of age. Likewise, the proportion of out-of-hospital deaths of all CHD deaths was smaller for recurrent than for first events (66.2% for recurrent and 77.7% for first events among men and 46.8% and 65.3% among women 35 to 64 years of age).

Figure 2 depicts changes in total CHD mortality rate partitioned to out-of-hospital and in-hospital CHD deaths among men and women 35 to 64 years of age. Rates shown in the figure are smoothed by use of the log-linear model. The decline in out-of-hospital CHD death rate contributed among men 70% and among women 58% to the overall decline in CHD mortality rate.

### Discussion

Consistent with other epidemiological studies,1–3 our study confirmed that the majority of CHD deaths take place out-of-hospital. The out-of-hospital CHD death rate in FINAMI areas declined significantly during the 15-year period. A similar development has recently been reported on the basis of routine mortality statistics from the United States2 and from Scotland.3 In our study, the proportion of out-of-hospital deaths of all CHD deaths did not change over time, whereas in the United States, the proportion of sudden cardiac deaths of all cardiac deaths increased by 12.4% during the period 1989 to 1998.2 Both in Finland and in the United States, the proportion of out-of-hospital deaths decreased with increasing age. In the Scottish study, however, the proportion of patients with MI who survived to hospital decreased with age.3 These different findings may reflect technical differences between the studies but may also reflect real differences in the behavior of patients and health care systems.

The decline in CHD mortality rate has been a universal finding in all Western countries.15 To our knowledge, however, no earlier study has partitioned the mortality rate decline to the contributions of out-of-hospital and in-hospital CHD deaths. Our calculations showed that more than two thirds of the mortality rate decline in men and more than half in women were due to the decline in out-of-hospital CHD deaths. In the United States, the Minnesota Heart Survey has reported a faster decline in in-hospital than in out-of-hospital mortality rates.16 In our study, the declining trends in out-of-hospital and in-hospital deaths did not differ substantially, but
the much larger amount of out-of-hospital CHD deaths made their contribution to the decline in total CHD mortality rate greater. This supports the importance of the roles that primary prevention and treatment of chronic CHD have played in the decline in CHD mortality rate in Finland.

The FINAMI register data allowed us to analyze the history of prior MI or CHD among the persons who had out-of-hospital CHD death. We found that for less than half of these cases, out-of-hospital death was the first manifestation of CHD, whereas more than half were receiving treatment for CHD or previous MI at the time of their fatal event. The history of clinically manifest CHD among persons who had out-of-hospital death appears to be of the same order of magnitude in Finland as in Olmsted County, Minnesota, since a recent study reported that the proportion of “unexpected” sudden cardiac deaths of all sudden cardiac deaths was 49% in the Olmsted county.9 Our results clearly show that for a substantial proportion of cases, out-of-hospital death does not come out of the blue, and thus there are possibilities for prevention with appropriate treatment of chronic CHD.

The declining trends in out-of-hospital CHD deaths tended to be steeper among persons with a history of MI than among those without such history, but the 95% CIs were overlapping. A special feature of these analyses was that by using data from the FINRISK population surveys,14 we were able to calculate the annual numbers of persons in the population who had and who had not had a prior MI. Thus, we could use correct denominators for persons at risk of out-of-hospital death from first or recurrent MI. Our results also showed that the time interval between the out-of-hospital death from a recurrent CHD event and the previous MI event was increasing over time. Furthermore, the proportion of out-of-hospital deaths was smaller for recurrent than for the first-MI events. Taken together, these findings suggest that primary prevention and secondary prevention and the treatment of chronic CHD have all contributed to the reduction of out-of-hospital CHD deaths. The slightly faster decline in persons with prior MI than in those without prior MI is consistent with recent findings from the Olmsted County, Minnesota,9 and emphasizes the need for effective primary prevention measures.
A strength of our study is the long period of data collection, according to a standardized protocol. Completeness of case finding could be ascertained by using national registers, causes-of-death register, and the hospital discharge register. Furthermore, the frequency of autopsies among cases of out-of-hospital death was high, 70% among men and 76% among women. Two features of the study limited the representativeness of the results. First, the FINAMI register covered 4 mainly urban areas, which may not be representative of the country as a whole. Since the out-of-hospital death rate is higher in rural than in urban areas, our study may give a slightly too optimistic view on out-of-hospital deaths in rural areas.

### TABLE 2. Age Group–Specific Case-Fatality Rate (%, 95% CI) due to Out-of-Hospital CHD Death and Proportion of Out-of-Hospital Deaths (%, 95% CI) of All CHD Deaths Within 28 Days Since Beginning of Symptoms During 1993 to 1997

<table>
<thead>
<tr>
<th>Age Group</th>
<th>n*</th>
<th>Case Fatality Rate due to Out-of-Hospital Death, %</th>
<th>Proportion of Out-of-Hospital Deaths of All CHD Deaths, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–54</td>
<td>205</td>
<td>22(19–25)</td>
<td>75(69–82)</td>
</tr>
<tr>
<td>55–64</td>
<td>397</td>
<td>26(24–29)</td>
<td>73(69–78)</td>
</tr>
<tr>
<td>65–74</td>
<td>801</td>
<td>25(23–27)</td>
<td>59(55–62)</td>
</tr>
<tr>
<td>75–84</td>
<td>580</td>
<td>24(22–27)</td>
<td>44(40–48)</td>
</tr>
<tr>
<td>85+</td>
<td>291</td>
<td>30(25–34)</td>
<td>41(36–47)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–54</td>
<td>16</td>
<td>10(4–16)</td>
<td>65(43–86)</td>
</tr>
<tr>
<td>55–64</td>
<td>78</td>
<td>12(8–15)</td>
<td>52(41–64)</td>
</tr>
<tr>
<td>65–74</td>
<td>429</td>
<td>17(15–19)</td>
<td>52(47–57)</td>
</tr>
<tr>
<td>75–84</td>
<td>786</td>
<td>17(15–19)</td>
<td>38(34–41)</td>
</tr>
<tr>
<td>85+</td>
<td>768</td>
<td>24(22–27)</td>
<td>35(31–38)</td>
</tr>
</tbody>
</table>

*n indicates No. of persons who died during the 28-day period after the beginning of symptoms.

**Figure 2.** Declines in overall CHD mortality rates (per 100 000 persons) partitioned to out-of-hospital (black area) and in-hospital (gray area) CHD deaths among men and women 35 to 64 years of age in the FINAMI areas during 1983 to 1997. Event rates are age-standardized to the European standard population and smoothed with the use of a log-linear model.
Finland. Second, the first 10 years of our study included only persons younger than 65 years. We were therefore not able to calculate 15-year trends in out-of-hospital CHD deaths for persons $\geq$65 years of age, even though the majority of CHD events occurs in this age group. We have, however, included all age groups in the FINAMI register since 1993. In the current study, we show results for the last 5-year period of 1993 to 1997, including also elderly individuals to improve the coverage of this important segment of patients with CHD. The third limitation was the composite definition of out-of-hospital CHD deaths used in our study. Clinical studies often define sudden, out-of-hospital deaths as deaths within 1 hour after the onset of symptoms. It is, however, the inherent nature of out-of-hospital deaths that exact information about the time between the onset of symptoms and the death is often not available. We agree with the conclusion presented by Zheng and coworkers\(^2\) that this makes the 1-hour definition impractical for public health surveillance. Therefore, the wider definition is often the only feasible solution.

In conclusion, out-of-hospital CHD death rates have been declining in the FINAMI areas, and their decline explains the main part of the overall decline in CHD mortality rate. Despite this favorable development, out-of-hospital CHD deaths continue to constitute the majority of all CHD deaths in persons younger than 75 years. In almost half of the cases, out-of-hospital death is the first clinical manifestation of CHD. The main way to reduce these deaths further is the primary prevention of CHD at the population level. The other half of out-of-hospital CHD deaths occurs among persons who are receiving treatment for symptomatic CHD. For them, carefully tailored treatment and secondary prevention provides a possibility to reduce the risk of out-of-hospital death.

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References
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