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## Comparison of clinical profiles and care for patients with incident versus recurrent acute coronary syndromes in France: data from the MONICA registries

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1 **Comparison of clinical profiles and care for patients with incident versus recurrent acute**  
2 **coronary syndromes in France: data from the MONICA registries**

3

4 **Short title:** recurrent patients have more co-morbidities

5

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28

29 **Keywords:** acute coronary syndrome, mortality, morbidity, registry, STEMI, NSTEMI, incident  
30 event, recurrent event.

31

32 **Word count:** 3113 3 figures, 3 tables

33 **Abstract**

34 **Background**

35 Recurrence is common after an acute coronary syndrome (ACS). In order to better assess the  
36 prognosis for patients with ACS, we compared clinical profiles, treatments, and case fatality  
37 rates for incident vs. recurrent ACS.

38

39 **Methods**

40 We enrolled 1,459 men and women (age: 35-74) living in three geographical areas covered  
41 by French MONICA registries and who had been admitted to hospital for an ACS in  
42 2015/2016. We recorded and compared the clinical characteristics and medical care for  
43 patients with an incident vs. a recurrent ACS.

44

45 **Results**

46 Overall, 431 (30%) had a recurrent ACS. Relative to patients with an incident ACS, patients  
47 with recurrence were older ( $p<0.0001$ ), had a greater frequency of NSTEMI or UA  
48 ( $p<0.0001$ ), were less likely to show typical symptoms ( $p=0.045$ ), were more likely to have an  
49 altered LVEF ( $p<0.0001$ ) and co-morbidities. Angioplasty was less frequently performed  
50 among patients with recurrent than incident NSTEMI ( $p<0.05$ ). There were no intergroup  
51 differences in the prescription of the recommended secondary prevention measures upon  
52 hospital discharge, except for functional rehabilitation more frequently prescribed among  
53 incident patients ( $p<0.0001$ ). Although the crude 1-year mortality rate was higher for  
54 recurrent cases (14%) than for incident cases (8%) ( $p<0.05$ ), this difference was no longer  
55 significant after adjustment for age, sex, region, diagnosis category and LVEF.

56 **Conclusion**

57 Compared with incident patients, recurrent cases were more likely to have co-morbidities  
58 and to have suboptimal treatments prior to hospital stay, reinforcing the need for secondary  
59 prevention.

## 60 **Introduction**

61 Between 12% and 42% of patients hospitalized for an acute coronary syndrome (ACS) will  
62 have experienced a coronary event previously [1–6]. The few studies to have compared  
63 patients with incident vs. recurrent ACS evidenced marked differences in clinical profiles,  
64 management, and prognosis [3–10]. Compared with patients hospitalized for an incident  
65 event, patients hospitalized for a recurrent ACS generally have higher prevalences of  
66 diabetes, hyperlipidemia, hypertension and vascular disease and thus a worse prognosis [3–  
67 10].

68 Most published studies have compared incident and recurrent cases with regard to risk  
69 factors, acute-phase clinical care, and mortality rates [1–10]. However, very few studies have  
70 explored drug treatments before and after hospital admission and other types of medical  
71 care (revascularization, functional rehabilitation etc...) in this setting [2,5,8,10]. Furthermore,  
72 there were interstudy differences in the inclusion criteria (e.g. ST-segment elevation  
73 myocardial infarction (STEMI) only) and data sources (hospital databases, cohort studies,  
74 clinical trials, and population-based registries) [7–9,11].

75 The goal of the present study was to compare incident and recurrent cases of ACS with  
76 regard to clinical characteristics and care. More precisely, we compared (i) the distribution of  
77 the different types of ACS, (ii) the patients' cardiovascular risk factor profiles and their  
78 treatments before the acute event, (iii) the care received during the acute phase of the  
79 event and at discharge, and (iv) survival 28 days and 1 year after the event. To this end, we  
80 analyzed data from the French MONICA population-based registries.

## 81 **Methods**

### 82 *Population*

83 The study population comprised all men and women aged 35-74 and who had been  
84 hospitalized for an ACS between October 1<sup>st</sup>, 2015, and March 31<sup>st</sup>, 2016. All the included  
85 patients resided in one of the three distinct geographical areas covered by the MONICA  
86 registries, each of which covers a population of about one million inhabitants: the Lille urban  
87 area in northern France, the Bas-Rhin county in eastern France, and the Haute-Garonne  
88 county in south-western France [12]. The registries are part of a national network of  
89 registries depending of *Santé Publique France*, the national agency of epidemiological  
90 surveillance. The methodology is validated and approved by Santé Publique France and used  
91 for national statistics.

92 The MONICA registries cover all public and private hospitals (including emergency  
93 departments) and all hospitalized patients - regardless of the admission department.  
94 Multiple sources were cross-checked to ensure exhaustive data collection: discharge letters,  
95 computerized lists containing the diagnosis stated upon hospital discharge, emergency  
96 department computer lists, death certificates, etc... The documentation of ACS was based on  
97 the patient's clinical history and hospital records. Clinical diagnoses were obtained from  
98 medical records. To be included in the study, patients had to have been hospitalized with  
99 one of the following clinical diagnoses: acute myocardial infarction (AMI), acute coronary  
100 syndrome (ACS) or unstable angina (UA). Coronary deaths were also included. Sudden  
101 deaths were excluded because clinical, laboratory and electrocardiographic data were often  
102 missing. Other nonfatal coronary episodes (such as decompensations of pre-existing  
103 coronary heart diseases) and ACS in already hospitalized patients (for another disease than

104 ACS) were also excluded, in order to reduce heterogeneity. Multiple events within a 28-day  
105 period were treated as a single event [13]. An incident case was defined as an ACS occurring  
106 in a patient with no history of acute or chronic coronary heart disease. A recurrent case was  
107 defined as an ACS occurring in a patient with a history of coronary heart disease, at least 28  
108 days after their incident event [14].

#### 109 *Ethical approval*

110 The study was approved by the Advisory Committee on Data Processing in Health Research  
111 (*Comité Consultatif sur le Traitement de L'information en Matière de Recherche dans le*  
112 *domaine de la Santé*; reference: 97002.A), the French National Data Protection Commission  
113 (*Commission Nationale de l'Informatique et des Libertés*; reference: 986001v3) and the  
114 French National Registry Committee (reference: 2016/11/9). The need for individual consent  
115 was waived by the ethics committee, only a general information notice in hospital structures  
116 is displayed. All data were fully anonymized before analyses.

#### 117 *Data collection*

118 For each case, the registry investigators collected every week data on clinical, laboratory,  
119 electrocardiographic variables, risk factors (hypertension, dyslipidemia, diabetes, and  
120 smoking status) and cardiovascular or non-cardiovascular comorbidities from the patient's  
121 medical records.

122 Electrocardiograms (ECGs) were coded as (i) 'ST+' for the occurrence of a new Q-wave  
123 and/or occurrence of a new left bundle-branch block (LBBB) or the occurrence or presence  
124 of ST elevation; (ii) 'non-ST+' for other repolarization abnormalities (such as a negative T  
125 wave) and normal ECGs; (iii) 'not classifiable' for patients with a pacemaker, interventricular  
126 block, complete atrioventricular block, Wolf-Parkinson-White syndrome, ventricular



127 fibrillation, ventricular rhythm, pre-existing LBBB, or right bundle-branch block, or (iv)  
128 'missing' when the data were missing.

129 The left ventricular ejection fraction (LVEF) was classified (regardless of the measurement  
130 method) as 'normal' if it was above 50%, 'moderately altered' if it was between 35% and  
131 50%, and 'altered' if it was below 35%. If several LVEF measurements were available, only  
132 the value recorded nearest to the time of hospital discharge was kept.

133 Treatments administered before and during the hospital stay and upon discharge (including  
134 revascularization therapies like angioplasty, fibrinolysis, and coronary bypass) were also  
135 documented.

136 With regard to the patient's symptoms, 'typical symptoms' were defined as chest pain  
137 lasting more than 20 minutes or crescendo angina, and 'major symptoms' were defined as  
138 resuscitated cardiac arrest, acute pulmonary oedema, or cardiogenic shock.

139 Troponin values are looked for in the medical records of the patients. If a rise and/or a  
140 decrease in troponin values is described, only the highest troponin value of the peak is  
141 recorded and the value is coded as positive (defined as a serum troponin level greater than  
142 or equal to twice the laboratory's normal upper limit), negative, or equivocal.

143 The types of ACS were defined as follows [14]: STEMI corresponded to an ST+ ECG and a  
144 positive troponin assay; NSTEMI corresponded to a non-ST+ ECG and a positive troponin  
145 assay; UA corresponded to a non-ST+ ECG and a negative troponin assay; "other" events  
146 corresponded to patients who had an acute coronary syndrome with an ST+ ECG but with  
147 equivocal or normal troponins (11%) or patients for whom the ECG data was unclassifiable or

148 was missing (36%), or the troponin assay was missing (44%) or both ECG and troponines  
149 were missing (9%).

#### 150 *Survival status*

151 Survival 28 days and 1 year after the event was documented whenever possible. Vital status  
152 and causes of death were checked (i) in the hospital's medical records, (ii) with the patient's  
153 general practitioner, (iii) in the city registry office and (iv) in the MONICA registry database.

#### 154 *Statistical analyses*

155 After having validated the year 2017 in the registry, the statistical analyses were performed.  
156 All the study variables were categorical and are presented as the frequency (percentage).  
157 Groups were compared using a chi-squared test or (for small sample sizes) Fisher's exact  
158 test. All analyses were adjusted for age and sex using a generalized linear model, a  
159 cumulative link model or multinomial logistic regression, as appropriate. Survival was  
160 analyzed using the Kaplan-Meier method and (when valid) the log-rank test. Adjusted Cox  
161 models were performed to assess mortality. All tests were two-sided, and the threshold for  
162 statistical significance was set to  $p < 0.05$ . Analyses were performed using RStudio (version  
163 1.2.1335).

164

#### 165 **Results**

166 The characteristics of hospitalized patients are summarized in Table 1. When considering the  
167 1,459 patients hospitalized for an ACS, there were 1,028 (70%) incident cases and 431 (30%)  
168 recurrent cases. There was no significant difference in sex ratio between incident and  
169 recurrent cases ( $p=0.15$ ). Compared with patients with an incident ACS, patients with a

170 recurrent ACS were older, more likely to present with UA (6% vs. 18%, respectively) or  
171 NSTEMI (38% vs. 44%, respectively) and less likely to present with STEMI (48% vs. 23%,  
172 respectively). Patients with a recurrent ACS were less likely to show typical symptoms (63%)  
173 than incident cases (72%); however, there was no significant intergroup difference in the  
174 frequency of major symptoms. The proportion of patients with an altered LVEF was higher  
175 for recurrent ACS.

#### 176 *Risk factors and comorbidities*

177 Concerning smoking status, recurrent cases were more likely to be former smokers than  
178 incident cases (39% vs. 23%, respectively) and less likely to be current smokers (33% vs. 49%,  
179 respectively) (Table 2). The prevalence of hypertension, dyslipidemia, obesity, and especially  
180 that of diabetes mellitus and complicated diabetes was higher among recurrent cases than  
181 among incident cases. Comorbidities such as a history of stroke ( $p=0.0002$ ), peripheral artery  
182 occlusive disease ( $p<0.0001$ ), aortic aneurysm ( $p=0.038$ ), and renal failure ( $p<0.0001$ ) were  
183 also significantly more common among recurrent cases.

#### 184 *Medical treatments before the hospital stay and upon discharge*

185 On admission to hospital, platelet aggregation inhibitors, beta-blockers, ACE inhibitors and  
186 statins were administered to respectively 86%, 72%, 46% and 74% of the recurrent cases,  
187 whereas, as expected, they were dispensed to less than 20% of the incident cases (Figure 1).  
188 These proportions were higher upon discharge for recurrent cases: 98%, 87%, 59%, and 91%  
189 for platelet aggregation inhibitors, beta-blockers, ACE inhibitors, and statins, respectively. At  
190 discharge, there were no significant differences in the recommended treatments for  
191 secondary prevention (i.e. beta-blockers/platelet aggregation inhibitors/statins/ACE  
192 inhibitors) between incident and recurrent cases (Figure 2).

193 Other treatments (such as insulin, orally administered antidiabetics and diuretic drugs) were  
194 more frequently prescribed in recurrent than in incident cases before the hospital stay  
195 (Figure 1). This is consistent with a higher prevalence of diabetes, hypertension, and renal  
196 failure in patients with a recurrent ACS (Table 2). Similar differences persisted between the  
197 two patient groups at discharge (Figure 2). Of note, recurrent patients with diabetes were  
198 treated with insulin at least twice as often as incident patients with diabetes, both before  
199 the hospital stay and at discharge. Last, upon discharge and after adjustment for sex and  
200 age, functional rehabilitation was more frequently prescribed for incident cases than for  
201 recurrent cases (44% vs. 17%, respectively) (Figure 2).

#### 202 *Revascularization therapy*

203 When considering STEMI/UA, there was no significant difference between incident and  
204 recurrent cases with regard to the incidence of revascularization therapy during the hospital  
205 stay and at discharge (Table 3). In contrast, in NSTEMI, angioplasty was significantly less  
206 frequent in recurrent cases than in incident cases during the hospital stay (63% vs 74%,  
207 respectively,  $p=0.015$ ) and upon discharge (7% vs 14%, respectively,  $p=0.038$ ).

#### 208 *Survival outcome*

209 The 28-day and 1-year survival rates were both lower ( $p=0.0073$  and  $p=0.00037$ ,  
210 respectively) in recurrent than in incident patients (Figure 3). The mortality rates were 9% vs  
211 5% at 28 days and 14% vs 8% at 1 year, in recurrent and in incident patients, respectively  
212 (Table 1). However, the adjusted hazard ratios [95% CI] for the 28-day and 1-year mortality  
213 were no longer different (after adjustment for age, sex, region, diagnosis category and LVEF)  
214 between the two groups (0.71 [0.45-1.12] and 0.87 [0.59-1.28], respectively).

## 215 **Discussion**

216 In this ancillary study of the French MONICA CHD registries all consecutive patients who had  
217 been hospitalized for an ACS were investigated for symptoms, biology, risk factors, acute-  
218 phase clinical care procedures and treatments. STEMI were more common than any other  
219 ACS subtypes among incident patients, whereas NSTEMI and UA predominated among  
220 recurrent cases. Patients with a recurrent ACS were more likely to have comorbidities, risk  
221 factors and CHD treatments prior to admission than incident ACS. The proportion of  
222 revascularization therapy was similar between STEMI and UA incident and recurrent patients  
223 but was lower in recurrent than incident NSTEMI patients. Finally, the incident and recurrent  
224 cases did not differ with regard to secondary prevention treatments at discharge.

### 225 *Categories of ACS*

226 During the observation period, the prevalence of incident and recurrent ACS was 70% and  
227 30%, respectively. When considering only incident events, the prevalence of STEMI, NSTEMI  
228 and UA were respectively 48%, 38% and 6%; these proportions differed for recurrent  
229 patients reaching 23%, 44% and 18%, respectively. These values are in line with literature  
230 reports of a higher prevalence of NSTEMI among recurrent patients than among incident  
231 patients [2,3,5]. This observation might be due to greater awareness of the symptoms and  
232 risks of ACS among patients who have already experienced an ACS event; these patients  
233 might reach the hospital sooner (i.e. before they develop a STEMI) than incident patients do.  
234 In agreement with this hypothesis, other studies have reported shorter time intervals  
235 between symptom onset and hospital admission in patients with recurrent as compared  
236 with incident events [6,15]. Furthermore, secondary prevention with drugs might attenuate  
237 the severity of ACS, resulting in recurrent NSTEMI and UA rather than a STEMI. Plaque

238 instability and inflammation status can also play a role. Lastly, the presence of coronary  
239 lesions in patient with history of coronary heart disease can lead to angina pectoris, changes  
240 on the ECG, troponin elevation resulting in a more frequent diagnosis of NSTEMI or UA for  
241 recurrent ACS. This hypothesis is supported by the observation that recurrent cases were  
242 less likely to present typical symptoms than incident cases. The practical implications of this  
243 observation is that after a first ACS, patients should be informed that the clinical  
244 presentation of recurrent infarction might differ from the initial infarction [16].

#### 245 *Mortality at 1 year*

246 Our results showed that the mortality rate at 1 year was higher among recurrent cases than  
247 among incident cases (14% vs. 8%, respectively), independently of age and sex. The same  
248 trend was found for mortality at 28 days (9% vs. 5%, respectively), indicating that the  
249 difference in prognosis between recurrent and incident events arises soon after the acute  
250 event. Similar results have been reported in other studies [3–5]. However, the rates in these  
251 studies were not always adjusted for confounding variables such as age, sex, comorbidities,  
252 and other relevant variables. In the Cox multivariate analysis, the difference in 1-year  
253 mortality between recurrent and incident patients was no longer statistically significant  
254 (after adjustment for age, sex, region, diagnosis category and LVEF) suggesting that a poorer  
255 risk factors profile, including older age and altered cardiac function, explain the worse  
256 prognosis in recurrent patients [17].

#### 257 *Risk factors and comorbidities*

258 The prevalence of risk factors and comorbidities was substantially higher in recurrent  
259 patients than in incident patients which might have contributed to the recurrence [18]. In  
260 addition, the recurrent patients are more likely to have undergone screening for

261 cardiovascular risk factors resulting in higher prevalence of these risk factors. With regard to  
262 smoking, and although the prevalence of current smoking was lower among recurrent  
263 patients than among incident patients in our study, an unhealthily high proportion (33%) of  
264 recurrent patients were still smoking. Given that smoking cessation in patients with CHD is  
265 associated with a lower mortality rate [19], intense efforts must be undertaken to achieve  
266 smoking cessation.

267 Among patients with ACS, those with diabetes mellitus are at particularly high risk of  
268 recurrent cardiovascular events and premature death. In pooled 10 European registries,  
269 diabetes mellitus was associated with higher all-cause death, higher cardiovascular death  
270 and major bleeding [20]. In an Italian registry with around 2500 patients, it was shown that  
271 hyperglycemic patients with obstructive acute MI had higher inflammatory markers and  
272 larger infarct sizes compared to normoglycemic ones [21]. In addition, admission stress-  
273 hyperglycemia predicted higher in-hospital and long-term (3 year) mortality, regardless of  
274 diabetes, in both patients with obstructive or non-obstructive coronary arteries [22].

275 Altogether, these data suggest that secondary prevention is suboptimal, as it has been  
276 shown in several EUROASPIRE studies over the last 20 years in Europe [23,24].

### 277 *Treatments*

278 On admission to hospital, the proportions of patients taking various cardiovascular  
279 medications (platelet aggregation inhibitors, beta-blockers, ACE inhibitors, and statins) were  
280 higher among recurrent cases than among incident patients - although the overall values  
281 appeared to be suboptimal. Similar observations for recurrent cases have been reported in  
282 other settings [2,5]. Many factors may contribute to the failure of suboptimal medical  
283 treatment after a first ACS, including adverse drug reactions, poor treatment adherence, and

284 poor coordination between specialists and family physicians. The fact that incident and  
285 recurrent patients had similar and apparently optimal treatment profiles at discharge from  
286 hospital shows that the level of secondary prevention is not influenced by MI history and  
287 that it is possible to achieve the required level of treatment among recurrent patients.  
288 Finally, the proportion of patients who were prescribed functional rehabilitation was more  
289 than twice as high among incident cases than among recurrent cases (44% vs. 17%,  
290 respectively). This difference might be explained by the fact that some of the recurrent  
291 patients had already undergone functional rehabilitation after their first ACS. Yet as  
292 recurrent patients have more co-morbidities they might benefit from further rehabilitation  
293 program after their recurrent event.

#### 294 *Revascularization therapy*

295 The prevalence of revascularization therapy during the hospital stay and at discharge was  
296 similar for incident and recurrent STEMI and UA patients - suggesting that revascularization  
297 is not influenced by previous status among these ACS subtypes. In contrast, angioplasty  
298 among patients with NSTEMI was less frequent among recurrent cases than among incident  
299 cases (63% vs. 74% during the hospital stay, and 7% vs. 14% at discharge, respectively).  
300 These observations are consistent with a study in which prior MI did not influence the  
301 revascularization approach for STEMI patients but was associated with less frequent use of  
302 angiography and revascularization for NSTEMI patients [2]. This difference might be due to a  
303 greater prevalence of complex coronary lesions in recurrent NSTEMI patients.

#### 304 *Limitations and strengths*

305 Our study had some limitations. First, although data were collected in 2015-2016 and  
306 survival monitoring extended until 2017, these are the most-updated direct comparisons of



307 incident and recurrent ACS to date, especially with regard to the lethality which has  
308 decreased over the past decade. Second, with regard to the lower proportion of recurrent  
309 patients prescribed functional rehabilitation, we could not determine whether or not they  
310 had already participated in this activity after their incident event. Third, given the relatively  
311 low number of recurrent cases recorded (n=431), some of our analyses might have lacked  
312 statistical power. Fourth, it would have been interesting to analyse the impact of the site of  
313 myocardial infarction on mortality but this variable was not collected in the registry. Lastly,  
314 as the age limit for inclusion in the registry was 74, our results cannot be extrapolated to  
315 older age groups. The present study had several methodological strengths. It included  
316 exhaustive 6-month data from three French morbidity registries. Data were recorded in  
317 accordance with the MONICA registry's methodology by trained investigators able to  
318 adjudicate all coronary events. The MONICA registries cover all public and private hospitals  
319 and all hospitalized patients - regardless of the admission pathway. The registries are  
320 reliable, and the coverage in each region is close to 100%.

### 321 *Conclusion*

322 Our results show that in the areas of France covered by our registries, around 30% of  
323 patients hospitalized for an ACS had experienced a recurrent event. The higher 1-year  
324 mortality rate observed among recurrent cases (relative to incident cases) was explained by  
325 older age, comorbidities and worse cardiac function - emphasizing the need to reinforce  
326 secondary prevention after an ACS and thus act on persistent risk factors.

327

328

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330 We would like to thank the Investigators of the three French centers for their valuable  
331 contribution to the careful collection and validation of the data, the physicians and the  
332 cardiologists who helped in this process.

333

334 **Data Availability statement**

335 Data cannot be made publicly available due to restrictions concerning participant  
336 confidentiality, imposed by the CNIL (Commission Nationale de l'Informatique et des Libertés  
337 (<https://www.cnil.fr/>). Proposals to access data from this study can be submitted to the  
338 corresponding author or to [Registre.cardiopathies@pasteur-lille.fr](mailto:Registre.cardiopathies@pasteur-lille.fr) and the data may thus be  
339 made available upon reasonable request.

340

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415 **Figure legends**

416 **Figure 1.** Drug treatments before hospital admission in patients with an incident or recurrent  
417 acute coronary syndrome.

418 \* $p < 0.0001$ , after adjustment for sex and age.

419 PAI: Platelet aggregation inhibitor; BB: Beta-blocker; ACEI: Angiotensin-converting-enzyme  
420 inhibitor; ARBs: Angiotensin receptor blockers; S: Statin.

421

422 **Figure 2.** Drug treatments upon hospital discharge in patients with an incident or recurrent  
423 acute coronary syndrome.

424 \* $p < 0.05$ , \*\* $p < 0.0001$ , after adjustment for sex and age.

425 PAI: Platelet aggregation inhibitor; BB: Beta-blocker; ACEI: Angiotensin-converting-enzyme  
426 inhibitor; ARBs: Angiotensin receptor blockers; S: Statin.

427

428 **Figure 3.** 28-day and 1-year survival curves

429 A. 28-day survival curves

430 B. 1-year survival curves

431 **Table 1.** Main characteristics of patients admitted to hospital for an incident or recurrent  
 432 acute coronary syndrome.

	N (%)	Incident cases	Recurrent cases	p	p*
	1,459	1,028 (70%)	431 (30%)		
Men	1,129 (77%)	787 (77%)	342 (79%)	0.24	0.15
35-44 years of age	92 (6%)	82 (8%)	10 (2%)		
45-54 years of age	319 (22%)	252 (25%)	67 (16%)		
55-64 years of age	475 (33%)	359 (35%)	116 (27%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
65-74 years of age	573 (39%)	335 (33%)	238 (55%)		
STEMI	589 (40%)	492 (48%)	97 (23%)		
NSTEMI	576 (39%)	388 (38%)	188 (44%)		
Unstable angina	143 (10%)	64 (6%)	79 (18%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Other events	151 (10%)	84 (8%)	67 (16%)		
Typical symptoms	1,006 (69%)	734 (72%)	272 (63%)	<b>0.005</b>	<b>0.045</b>
Major symptoms :	188 (13%)	128 (12%)	60 (14%)	0.46	0.89
- resuscitated cardiac arrest	103 (7%)	78 (8%)	25 (6%)	0.22	0.3
- acute pulmonary edema	67 (5%)	36 (4%)	31 (7%)	<b>0.002</b>	0.051
- cardiogenic shock	87 (6%)	63 (6%)	24 (6%)	0.68	0.38
Normal LVEF	970 (66%)	737 (72%)	233 (54%)		
Moderately altered LVEF	266 (18%)	180 (18%)	86 (20%)		
Altered LVEF	83 (6%)	46 (4%)	37 (9%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Missing LVEF	140 (10%)	65 (6%)	75 (17%)		
Deceased at 28 days	96 (7%)	56 (5%)	40 (9%)	<b>0.007</b>	0.1
Deceased at 1 year	131 (9%)	75 (8%)	56 (14%)	<b>0.0004</b>	<b>0.023</b>

434 STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation  
 435 myocardial infarction; LVEF: left ventricular ejection fraction.

436 \*Adjusted for age and sex.

437 Significant p values are indicated in bold type.

438 **Table 2.** Risk factors and comorbidities in patients admitted to hospital for an incident or  
 439 recurrent acute coronary syndrome

	N=1459	Incident cases 1028 (70%)	Recurrent cases 431 (30%)	p	p*
Never smoker	373 (28%)	266 (28%)	107 (28%)		
Current smoker	595 (44%)	467 (49%)	128 (33%)	<b>&lt;0.0001</b>	<b>0.0005</b>
Former smoker	373 (28%)	222 (23%)	151 (39%)		
Hypertension	735 (51%)	448 (44%)	287 (67%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Dyslipidemia	742 (51%)	422 (41%)	320 (75%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Diabetes mellitus	401 (28%)	202 (20%)	199 (46%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Complicated diabetes	86 (6%)	35 (3%)	51 (12%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Obesity	390 (28%)	250 (25%)	140 (34%)	<b>0.001</b>	<b>0.0004</b>
Previous transient ischemic attack	22 (2%)	11 (1%)	11 (3%)	<b>0.03</b>	0.15
Previous stroke	66 (5%)	29 (3%)	37 (9%)	<b>&lt;0.0001</b>	<b>0.0002</b>
Peripheral artery occlusive disease	132 (9%)	43 (4%)	89 (21%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>
Aortic aneurysm	22 (2%)	9 (1%)	13 (3%)	<b>0.002</b>	<b>0.038</b>
Chronic obstructive pulmonary disease	82 (6%)	47 (5%)	35 (8%)	<b>0.007</b>	0.076
440 Renal failure	102 (7%)	40 (4%)	62 (14%)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>

441 \*Adjusted for age and sex. Significant p values are indicated in bold type.



442 **Table 3.** Reperfusion therapy during the hospital stay and at discharge in patients admitted to hospital for an incident or recurrent acute  
 443 coronary syndrome, according to the type of event (STEMI, NSTEMI, UA, and other events)

		STEMI					NSTEMI				
		N = 589	Incident cases	Recurrent cases	p	p**	N = 576	Incident cases	Recurrent cases	p	p**
			492 (84%)	97 (16%)			388 (67%)	188 (33%)			
<u>During the hospital stay</u>	Angioplasty	533 (90%)	445 (90%)	88 (91%)	0.9	1	404 (70%)	286 (74%)	118 (63%)	<b>0.007</b>	<b>0.015</b>
	Fibrinolysis	13 (2%)	12 (2%)	1 (1%)	0.7	0.5	3 (1%)	2 (1%)	1 (1%)	1	0.81
	Coronary bypass	9 (2%)	8 (2%)	1 (1%)	1	0.8	29 (5%)	21 (5%)	8 (4%)	0.69	0.14
	All revascularizations	542 (92%)	453 (92%)	89 (92%)	0.9	0.9	431 (75%)	305 (79%)	126 (67%)	<b>0.002</b>	<b>0.001</b>
<u>Upon discharge*</u>	Angioplasty	62 (11%)	49 (10%)	13 (13%)	0.4	0.6	65 (12%)	52 (14%)	13 (7%)	<b>0.029</b>	<b>0.038</b>
	Coronary bypass	8 (1%)	7 (1%)	1 (1%)	1	0.8	18 (3%)	10 (3%)	8 (4%)	0.3	0.47
		Unstable Angina					Other				
		N = 143	Incident cases	Recurrent cases	p	p**	N = 151	Incident cases	Recurrent cases	p	p**
			64 (45%)	79 (55%)			84 (56%)	67 (44%)			
<u>During the hospital stay</u>	Angioplasty	99 (69%)	45 (70%)	54 (68%)	0.8	0.7	95 (63%)	60 (71%)	35 (52%)	<b>0.015</b>	<b>0.018</b>
	Fibrinolysis	-	-	-	-	-	2 (1%)	1 (1%)	1 (2%)	1	0.78
	Coronary bypass	5 (3%)	3 (5%)	2 (3%)	0.7	0.4	4 (3%)	3 (4%)	1 (1%)	0.63	0.31
	All revascularizations	102 (71%)	47 (73%)	55 (70%)	0.6	0.5	100 (67%)	63 (75%)	37 (56%)	<b>0.015</b>	<b>0.013</b>
<u>Upon discharge*</u>	Angioplasty	11 (8%)	7 (11%)	4 (5%)	0.2	0.2	19 (15%)	10 (14%)	9 (17%)	0.62	0.59
	Coronary bypass	5 (4%)	2 (3%)	3 (4%)	1	0.8	6 (5%)	4 (5%)	2 (4%)	1	0.92

444

445 The “all reperfusion therapies” group included fibrinolysis, angioplasty and coronary bypass surgery. STEMI: ST-segment elevation myocardial  
446 infarction; NSTEMI: non-ST-segment elevation myocardial infarction.

447 \*As a percentage of patients who survived the acute event. \*\*Adjusted for age and sex. Significant p values are indicated in bold type.