German nationwide data on current trends and management of acute myocardial infarction: discrepancies between trials and real-life

Eva Freisinger1*, Torsten Fuerstenberg2, Nasser M. Malyar1, Juergen Wellmann3, Ulrich Keil3, Guenter Breithardt1, and Holger Reinecke1,4

1Division of Vascular Medicine, Department of Cardiovascular Medicine, University Hospital Muenster, D-48149 Muenster, Germany; 2IGES Institute GmbH, Berlin, Germany; 3Institute of Epidemiology and Social Medicine, University of Muenster, Muenster, Germany; and 4DRG Research Group, Muenster, Germany

Received 4 July 2013; revised 4 November 2013; accepted 29 December 2013; online publish-ahead-of-print 20 February 2014

Aims
Recent guidelines on acute myocardial infarction (AMI) are based on randomized clinical trials (RCTs) and registries with selected patients, and may therefore not represent ‘real-life’. This analysis shows for the first time nationwide trends in AMI from Germany.

Methods and results
We were provided with data on all in-patient hospitalizations by the Federal Statistical Office. All hospitalized cases with AMI (onset of symptoms <28 days) from the years 2005, 2007, and 2009 were analysed regarding morbidity, in-hospital mortality, treatments, and costs. Analysis of a total of 16.1, 16.6, and 17.2 million hospitalizations showed the proportion of coded AMI to remain relatively constant (1276, 1272, and 1181 per 100 000 hospitalizations in 2005, 2007, and 2009). The proportion of ST-elevation AMI decreased over time (STEMI; 631, 546, and 454 per 100 000 hospitalizations), while non-ST-elevation AMI increased (NSTEMI; 645, 726, and 727 per 100 000 hospitalizations). The proportion of older patients (>75 years (+4.6%), of comorbidities such as hypertension (+5.8%), diabetes (+17.7%), left ventricular failure (+19.8%), peripheral artery disease (+13.3%), and chronic kidney disease (+165.4%) increased as well. In-hospital mortality remained relatively stable during this period in AMI cases overall (11.1, 10.7, 10.8%) but changed slightly in STEMI (11.2, 11.9, 12.2%) and NSTEMI (11.0, 9.9, 9.9%). Causing about 1.2% of hospitalizations, AMI accounted for 2.5% (1.2 billion €) of in-hospital health expenses.

Conclusion
This hospitalization-based analysis revealed a marked increase of NSTEMI among constant AMI frequency. Despite all current efforts, in-hospital mortality was stagnating on a high level compared with data of RCTs.

Keywords
Acute myocardial infarction • Cardiovascular disease • Mortality • Population-based study

Introduction
As a cause of death, cardiovascular disease ranks first in global mortality statistics during the past decades.1,2 Current guidelines and recommendations for the management of acute myocardial infarction (AMI)3 are based on data with limited comparability in terms of populations and data acquisition mode. Data on a large scale for Europe, or Germany in particular, are scarce, and yet populations differ markedly from the USA with respect to ethnic, geographic, or health economic characteristics. The often highly selected patients in randomized clinical trials (RCTs) lead to under-representation of certain population groups such as women, the elderly, or patients at high risk for complications or death.4,5 RCTs often include optimized diagnostic and therapeutic treatments which may not reflect real-life management. Accordingly, data from population-based surveys and registries revealed discrepancies drawn from RCTs have limited applicability to reality.6,7 Moreover, contemporary population-based epidemiological and socio-economic data on AMI have been extrapolated from small- to medium-sized regional cohorts to ascertain an estimate for a large-scale population. The acquisition of recent hospital data on unselected populations of an entire nation allows defining more reliable trends on AMI reflecting ‘real-life’.

*Corresponding author. Tel: +49 251 83 44933, Fax: +49 251 83 45101, Email: eva.freisinger@ukmuenster.de

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2014. For permissions please email: journals.permissions@oup.com

doi:10.1093/eurheartj/ehu043
In Germany, all hospitals are required by federal law to transfer data on all in-patient hospitalizations to the Institute for the Hospital Remuneration System (Institut für das Entgeltsystem im Krankenhaus, InEK; Siegburg, Germany; http://www.g-drg.de) since 2002. A large part of this data set was made available for scientific purposes by the Federal Statistical Office. Based on these nationwide data from the years 2005, 2007, and 2009, we analysed all hospitalizations with AMI with regard to morbidity, in-hospital mortality, treatments, and associated costs.

**Methods**

The introduction of a diagnosis and procedure-related remuneration system (German Diagnosis Related Groups, G-DRG) system for all somatic in-patient services in Germany in 2003 has led to a precise and comprehensive acquisition of defined cases of illness. Detailed mandatory coding guidelines were implemented to ensure uniform documentation and billing. Thereby, all hospitals are required to transfer patient data on diagnoses, co-morbidities, medical services, or procedures and procedure-related complications to the Institute for the Hospital Remuneration System (InEK).

**Data source**

We obtained and analysed data from the Research Data Centers of the Federal Statistical Office and the Statistical Offices of the Laender (Statistisches Bundesamt, DESTATIS; https://www.destatis.de) for the years 2005, 2007, and 2009 with respect to in-hospital outcomes and time trends related to AMI. The database comprises all in-patient treatments in German hospitals aggregated on a case base, except for treatments in psychiatric or psychosomatic units. We excluded medical care provided by office-based specialists with special admitting rights (1% of AMI in-patient treatments). Due to data privacy protection, all sub-groups less than six cases were excluded from the analysis. Access to the data was by remote execution directly on the anonymized original data. A statistical analysis program written in SAS (SAS 9.3; SAS Institute Inc., Cary, NC, USA) was executed by the Research Data Center.

**Diagnoses and procedure codes**

The German remuneration system requires the coding of a principal diagnosis for all in-patient cases reflecting the underlying cause for hospital admission. Furthermore, an infinite number of additional diagnoses can be coded to document coexisting morbidities and complications. Each diagnosis must be coded according to the German Modification of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10-GM). Annual adaptation is made by the German Institute for Medical Documentation and Information (Deutsches Institut fuer Medizinische Dokumentation und Information, DIMDI; Cologne, Germany; http://www.dimdi.de) but did not affect the established diagnoses during the analysed time period.

All hospitalized patients with an AMI (meaning within 28 days of onset of symptoms, diagnosis code: I21-I22) as their principal diagnosis were included in the analysis (see Supplementary material online, Figure S1).

**Results**

In the years 2005, 2007, and 2009, there were a total of 619 289 hospitalizations coded as AMI in Germany, corresponding to an average 1.3% of all in-patient admissions. The frequency of hospitalized AMI cases remained relatively constant at 249 per 100 000 population in 2005, 257 in 2007, and 248 in 2009, respectively (Figure 1). In 2005, the ratio between ST-elevation AMI (STEMI; 101 423 cases; 49.47%) and non-ST-elevation AMI (NSTEMI; 103 598 cases; 50.53%) was almost balanced. Whereas the STEMI cases further decreased to 90 585 in 2007 and 78 113 in 2009, the case number of NSTEMI increased (120 574 and 124 996, respectively), and therefore the ratio of STEMI to NSTEMI continuously decreased (Table 1).

Key characteristics of patients are displayed in Table 1. With regard to age, 154 838 of 203 109 cases coded with AMI (76%) were 60 years and beyond in 2009. That year, the age group of 60–74 years old accounted for more than one-third (35.7%) of all myocardial infarctions in Germany. Whereas the mean age among STEMI cases was 66.4 years, the average NSTEMI patient was 5.3 years older over the time period 2005–2009 (Supplementary material online, Figure S2). The above-mentioned increase of NSTEMI cases resulted basically in an increase in the age group 65–89 years, and to a smaller extent in the age group 45–59 years. However, the ratio of NSTEMI in each individual age group remained relatively stable (Supplementary material online, Figure S3). In STEMI, a trend towards younger age groups could be observed. The proportion of STEMI patients ≥60 years continuously decreased from 70.6% (2005) to 67.9% (2007), and 66.6% (2009). Regarding patients ≥75 years, a slight increase of 1.5 percentage points in 2009 compared with the 2005 data occurred in STEMI (NSTEMI +1.1 percentage points).

With regard to gender, the frequency of AMI was about 1.7 times higher in men compared with women. The proportion of comorbidities increased with regard to hypertension (+5.8%), diabetes type 2...
In-hospital management

In AMI, the number of coronary angiographies (CA) increased from 108,423 in 2005 to 120,387 in 2007 and 125,884 procedures in 2009 (Table 2). Thus, 52.9, 57.0, and 62.0% of all AMI patients underwent CA during these three 1-year periods. In 2009, 73.1% of STEMI and 55% of NSTEMI patients underwent CA. The proportion of CA in NSTEMI to STEMI cases remained constant at 1 to 1.3. However, from 2005 to 2009, a steady increase of CAs per hospitalized AMI case could be observed in both types of AMI.

Percutaneous coronary interventions (PCI) were performed in 86.7, 89.9, and 91.1% of patients undergoing CA in STEMI, and 63.9, 66.5, and 66.5% in NSTEMI patients in 2005, 2007, and 2009, respectively. Although the proportion of CA decreased with increasing age ≥80 years, the ratio of PCI among those who received CA remained stable in STEMI (88.4% in ≥80 years) and further increased in higher age groups with NSTEMI (Figure 2). Stenting was applied to 93,211 patients, corresponding to 95% of PCIs performed in AMI patients in 2009 (96% STEMI, 95% NSTEMI). Among those, the majority of patients received bare-metal stents (65.6%) compared with 29.8% of implanted drug-eluting stents. Drug-eluting stents were used markedly more often in NSTEMI (55.8% of total stenting) than in STEMI (37.4% of total stenting).

Thrombolytic therapy was applied to a minority of AMI patients (2.0% in STEMI and 0.5% in NSTEMI) in 2009. Antiplatelet agents such as glycoprotein IIb/IIIa inhibitors were applied to 14.3% of patients in 2009. The direct thrombin inhibiting drug bivalirudin played a minor role.

Coronary artery bypass surgery (CABG) was performed in an increasing number of AMI patients (2005: 9,402, 2007: 10,296, 2009: 10,501). In STEMI, the rate of bypass surgery was 4.3% in 2009, and in NSTEMI 5.7%.

Trends in in-hospital mortality

In-hospital mortality data for 2005 showed similar rates for STEMI (11.2%) and NSTEMI (11.0%, Table 3). Examining the course over the evaluated time, rates for STEMI increased (11.9% in 2007 and 12.2% in 2009). In contrast, NSTEMI mortality decreased to 9.9% in 2007 and remained stable at this level in 2009. In-hospital mortality was higher in STEMI compared with NSTEMI among all age groups (except for cases 35–39 years) and steeply rising with age in both STEMI and NSTEMI (Figure 3). As stated above, cases with NSTEMI
Table 1  Characteristics of acute myocardial infarction cases from 2005 to 2009

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
</tr>
<tr>
<td>Number of cases, n (% of all in the respective year)</td>
<td>101 423 (49.5)</td>
<td>205 021</td>
<td>306 444</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>66 477 (65.5)</td>
<td>128 060 (62.5)</td>
<td>294 537</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>66.6</td>
<td>66.3</td>
<td>66.2</td>
</tr>
<tr>
<td>Age ≥ 60, n (%)</td>
<td>71 577 (70.6)</td>
<td>157 872 (77.0)</td>
<td>229 449</td>
</tr>
<tr>
<td>Age ≥ 75, n (%)</td>
<td>31 974 (31.5)</td>
<td>79 461 (38.8)</td>
<td>111 435</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>60 769 (59.9)</td>
<td>128 198 (62.5)</td>
<td>188 967</td>
</tr>
<tr>
<td>DM type 2, n (%)</td>
<td>23 502 (23.2)</td>
<td>54 594 (26.6)</td>
<td>78 096</td>
</tr>
<tr>
<td>LVF, n (%)</td>
<td>24 835 (24.5)</td>
<td>52 860 (25.8)</td>
<td>77 715</td>
</tr>
<tr>
<td>PAD, n (%)</td>
<td>3597 (3.5)</td>
<td>9247 (4.5)</td>
<td>12 844</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>3828 (3.8)</td>
<td>10 694 (5.2)</td>
<td>14 522</td>
</tr>
</tbody>
</table>

P-values were calculated for trend over time for STEMI and NSTEMI (P < 0.01 was considered significant).

DM, diabetes mellitus; LVF, left ventricular failure; PAD, peripheral artery disease; CKD, chronic kidney disease.
<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th></th>
<th></th>
<th>2007</th>
<th></th>
<th></th>
<th>2009</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Number of cases,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (% of all in</td>
<td>101 423 (49.5)</td>
<td>103 598 (50.5)</td>
<td>205 021</td>
<td>90 585 (42.9)</td>
<td>120 574 (57.1)</td>
<td>211 159</td>
<td>78 113 (38.5)</td>
<td>124 996 (61.5)</td>
<td>203 109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>the respective</td>
<td>year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLoS (days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.09</td>
<td>9.37</td>
<td>9.23</td>
<td>8.68</td>
<td>9.01</td>
<td>8.87</td>
<td>8.49</td>
<td>8.76</td>
<td>8.66</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLoS in CA</td>
<td>8.88</td>
<td>8.67</td>
<td>8.79</td>
<td>8.72</td>
<td>8.56</td>
<td>8.64</td>
<td>8.61</td>
<td>8.43</td>
<td>8.51</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>HLoS in PCI</td>
<td>8.53</td>
<td>7.69</td>
<td>8.23</td>
<td>8.52</td>
<td>7.78</td>
<td>8.20</td>
<td>8.49</td>
<td>7.78</td>
<td>8.16</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Total costs, €</td>
<td>No data available</td>
<td></td>
<td></td>
<td>535 078</td>
<td>162 643</td>
<td>303 1 178</td>
<td>114 465</td>
<td>230 272</td>
<td>702 217</td>
<td>1 203 447</td>
<td></td>
</tr>
<tr>
<td>CA, n (%)</td>
<td>61 088 (60.2)</td>
<td>47 335 (45.7)</td>
<td>108 423 (52.9)</td>
<td>59 882 (66.1)</td>
<td>60 505 (50.2)</td>
<td>120 387 (57.0)</td>
<td>57 086 (73.1)</td>
<td>68 798 (55.0)</td>
<td>125 884 (62.0)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>52 979 (52.2)</td>
<td>30 296 (29.2)</td>
<td>83 275 (40.6)</td>
<td>53 828 (59.4)</td>
<td>40 329 (33.4)</td>
<td>94 157 (44.6)</td>
<td>51 998 (66.6)</td>
<td>45 700 (36.6)</td>
<td>97 698 (48.1)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>PCI (% of CA)</td>
<td>(86.7)</td>
<td>(64.0)</td>
<td>(76.8)</td>
<td>(89.9)</td>
<td>(66.7)</td>
<td>(78.2)</td>
<td>(91.1)</td>
<td>(66.4)</td>
<td>(77.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM stent, n (%</td>
<td>42 244 (79.7)</td>
<td>22 125 (73.0)</td>
<td>64 369 (77.3)</td>
<td>42 322 (78.6)</td>
<td>28 559 (70.8)</td>
<td>70 881 (75.3)</td>
<td>36 317 (69.8)</td>
<td>27 803 (60.8)</td>
<td>64 120 (65.6)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>of PCI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DE stent, n (%</td>
<td>7923 (15.0)</td>
<td>6161 (20.3)</td>
<td>14 084 (16.9)</td>
<td>9111 (16.9)</td>
<td>9628 (23.9)</td>
<td>18 739 (19.9)</td>
<td>13 589 (26.1)</td>
<td>15 502 (33.9)</td>
<td>29 091 (29.8)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>of PCI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis, n</td>
<td>3959 (3.9)</td>
<td>597 (0.6)</td>
<td>4556 (2.2)</td>
<td>2497 (2.8)</td>
<td>666 (0.6)</td>
<td>3163 (1.5)</td>
<td>1550 (2.0)</td>
<td>659 (0.5)</td>
<td>2209 (1.1)</td>
<td>STEMI &lt;0.0001; NSTEMI 0.2865</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GpIb/lla, n (%)</td>
<td>No data available</td>
<td></td>
<td></td>
<td>No data available</td>
<td></td>
<td></td>
<td>No data available</td>
<td></td>
<td>No data available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bivalirudin, n %</td>
<td>4531 (4.5)</td>
<td>4871 (4.7)</td>
<td>9402 (4.6)</td>
<td>3955 (4.4)</td>
<td>6301 (5.2)</td>
<td>10 296 (4.9)</td>
<td>3327 (4.3)</td>
<td>7174 (5.7)</td>
<td>10 501 (5.2)</td>
<td>STEMI 0.0944; NSTEMI &lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Quantity numbers, hospital length of stay, and costing data are displayed annually for STEMI, NSTEMI, and total AMI. Sub-groups are given as total number of cases and percentages related to the respective type of AMI and year. \( P \)-values were calculated for trend over time for STEMI and NSTEMI \( P < 0.01 \) was considered significant.

HLoS, hospital length of stay; CA, coronary angiography; PCI, percutaneous coronary intervention; BM-stent, bare-metal stent; DE-stent, drug-eluting stent; GpIb/lla, glycoprotein IIb/lla inhibitors; CABG, coronary artery bypass graft.
were older and more often multimorbid than the average STEMI case. However, in-hospital mortality among the elderly (aged 75 years and beyond) with NSTEMI declined from 16.8% in 2005 to 14.9% in 2009 (STEMI 21.2–22.9%, respectively).

Among all age groups and independent of the type of AMI, women were at higher risk of death compared with men (mortality in women 13.3% and men 9.2%). Although women represented only 37% of all cases, 47.1% of AMI cases with fatal outcome were female. However, the ratio of women among the dead decreased in STEMI (47.9% in 2005, 46% in 2007, and 44.6% in 2009) as well as in NSTEMI (49, 48.2, and 46%, respectively).

Despite the higher proportion of concomitant diseases in NSTEMI, mortality was markedly lower compared with STEMI. In 2009, 16.8% of STEMI and 13.8% of NSTEMI patients died of their myocardial infarction when diagnosed LVF. Further, 13.8% of diabetic STEMI patients died compared with 9.8% diabetics in NSTEMI in 2009. Thus, more than one in four dead suffered diabetes (31.4% NSTEMI, 26.4% STEMI). Mortality of AMI cases with hypertensive disease, which was among the most common comorbidities of AMI (66.1% in 2009), slightly increased from 6.6% in 2005 to 6.8% in 2009. Moreover, CKD stages 3–5 involved elevated risk of death in STEMI (20.5%) and NSTEMI (13.3%). Further, recent mortality within the group of PAD patients was increased compared with the overall rate in STEMI (17.7 vs. 12.2%) and NSTEMI (12.0 vs. 9.9%).

Regarding the applied medical procedures, there was a slight increase of mortality in cases with PCI in both STEMI (6.3, 7.2, and 8.1% in 2005, 2007, and 2009) and NSTEMI (3.2, 3.2, and 3.8%, respectively, Figure 4). Thereof, implantation of drug-eluting stents was associated with significantly lower mortality compared with bare-metal stents (mortality 3.8% DE stent, 6.3% BM stent in 2009). When thrombolytic agents were applied, in-hospital mortality was highly elevated in 2005 (mortality in STEMI 14.3, and 33.3% in NSTEMI). Rates further increased, and in 2009 almost every third STEMI (29%) and 40.1% of NSTEMI died upon thrombolysis. In-hospital mortality of patients treated with antiplatelet agents such as glycoprotein IIb/IIIa inhibitors was much lower compared with thrombolytic therapy: among treated patients, death occurred in 7.4% of STEMI and 5% of NSTEMI in 2009. Analyses of in-hospital mortality of CABG revealed a higher percentage in STEMI (11.6%) in 2009 compared with NSTEMI (7.5%).

**Costs and length of hospital stay**

For 2005, no costing data were transferred and therefore could not be analysed. In 2007, the annual costs of the management of hospitalized AMI patients amounted to 1.18 billion € corresponding to 2.49% of total health expenses of all hospitalizations. The average cost per STEMI case was 5907 € (1.13% of total expenses) and 5333 € per NSTEMI case (1.36%, respectively, Table 2). In the time course, the costs of AMI in 2009 remained stable in comparison with 2007 with 1.2 billion €, corresponding to 2.28% of total expenses. Thereof 6417 € applied per STEMI case (0.95% of total expenses) and 5618 € per NSTEMI case (1.33%). The length of hospital stay (HLoS) for AMI slightly decreased from 9.2 days in 2005 to 8.9 days in 2007, and to 8.7 days in 2009. Throughout these three 1-year periods, HLoS was lower in STEMI than in NSTEMI patients (e.g. in 2009, 8.5 vs. 8.8 days), but trend reversed in case of invasive procedure (CA or PCI). Coronary angiographies led to a prolonged HLoS in STEMI (8.61 vs. 8.49 at average) but reduced HLoS in NSTEMI (8.43 vs. 8.76). The length of hospital stay was further shortened in cases with PCI (STEMI 8.49, NSTEMI 7.78).

**Discussion**

Current guidelines for the management of AMI are predominantly based on RCTs that often include optimized diagnostic and therapeutic procedures which may not reflect real-life management. But also major European studies such as the questionnaire-based ENACT or the European Heart Survey on ACS (ACS-I and ACS-II) derived their data from selected medical centres with comparatively high rate of on-site catheterization facilities. The EUROASPIRE survey or the MONICA/ KORA registry excluded old patients (>70 years and > 74 years, respectively) and therefore lead—to the often highly selected populations of RCTs—to under-representation of population groups at high risk for complications or death. Other contemporary population-based
### Table 3  In-hospital mortality

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th></th>
<th>2007</th>
<th></th>
<th>2009</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
<td>STEMI</td>
<td>NSTEMI</td>
<td>Total</td>
</tr>
<tr>
<td>Number of cases, n</td>
<td>101 423</td>
<td>103 598</td>
<td>205 021</td>
<td>90 585</td>
<td>120 574</td>
<td>211 159</td>
<td>78 113</td>
<td>124 996</td>
<td>203 109</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>11 396 (11.2)</td>
<td>11 378 (11.0)</td>
<td>22 774 (11.1)</td>
<td>10 744 (11.9)</td>
<td>11 935 (9.9)</td>
<td>22 679 (10.7)</td>
<td>9498 (12.2)</td>
<td>12 362 (9.9)</td>
<td>21 860 (10.8)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>5934 (8.9)</td>
<td>5796 (9.4)</td>
<td>11 730 (9.2)</td>
<td>5801 (9.6)</td>
<td>6179 (8.5)</td>
<td>11 980 (9.0)</td>
<td>5259 (9.9)</td>
<td>6671 (8.7)</td>
<td>11 930 (9.2)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>5462 (15.6)</td>
<td>5582 (13.3)</td>
<td>11 044 (14.4)</td>
<td>4943 (16.5)</td>
<td>5.755 (12.0)</td>
<td>10 698 (13.8)</td>
<td>4239 (16.9)</td>
<td>5691 (11.7)</td>
<td>9930 (13.5)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>6767 (21.2)</td>
<td>7964 (16.8)</td>
<td>14 731 (18.5)</td>
<td>6312 (22.5)</td>
<td>8399 (15.0)</td>
<td>14 711 (17.5)</td>
<td>5451 (22.9)</td>
<td>8711 (14.9)</td>
<td>14 162 (17.2)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>4266 (7.0)</td>
<td>4242 (6.3)</td>
<td>8508 (6.6)</td>
<td>4088 (7.5)</td>
<td>4819 (6.0)</td>
<td>8907 (6.6)</td>
<td>3627 (7.5)</td>
<td>5546 (6.4)</td>
<td>9173 (6.8)</td>
<td>&lt;0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM type 2, n (%)</td>
<td>3189 (13.6)</td>
<td>3264 (10.5)</td>
<td>6453 (11.8)</td>
<td>2996 (14.3)</td>
<td>3649 (9.8)</td>
<td>6645 (11.4)</td>
<td>2463 (13.8)</td>
<td>3836 (9.8)</td>
<td>6299 (11.1)</td>
<td>STEMI 0.1086; NSTEMI &lt;0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVF, n (%)</td>
<td>4131 (16.6)</td>
<td>4138 (14.8)</td>
<td>8269 (15.6)</td>
<td>4074 (16.9)</td>
<td>5095 (14.0)</td>
<td>9169 (15.2)</td>
<td>3702 (16.8)</td>
<td>5623 (13.8)</td>
<td>9325 (14.9)</td>
<td>STEMI 0.7596; NSTEMI &lt;0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>957 (25.0)</td>
<td>1162 (16.9)</td>
<td>2119 (19.8)</td>
<td>1086 (22.7)</td>
<td>1780 (14.2)</td>
<td>2866 (16.6)</td>
<td>1476 (20.5)</td>
<td>2772 (13.3)</td>
<td>4248 (15.1)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CA, n (%)</td>
<td>3967 (6.5)</td>
<td>1674 (3.5)</td>
<td>5641 (5.2)</td>
<td>4420 (7.4)</td>
<td>2113 (3.5)</td>
<td>6533 (5.4)</td>
<td>4819 (8.4)</td>
<td>2774 (4.0)</td>
<td>7593 (6.0)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>3323 (6.3)</td>
<td>982 (3.2)</td>
<td>4305 (5.2)</td>
<td>3873 (7.2)</td>
<td>1297 (3.2)</td>
<td>5170 (5.5)</td>
<td>4236 (8.1)</td>
<td>1752 (3.8)</td>
<td>5988 (6.1)</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>492 (10.9)</td>
<td>387 (7.9)</td>
<td>879 (9.4)</td>
<td>460 (11.5)</td>
<td>452 (7.2)</td>
<td>912 (8.9)</td>
<td>387 (11.6)</td>
<td>541 (7.5)</td>
<td>928 (8.8)</td>
<td>STEMI 0.4892; NSTEMI 0.3073</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In-hospital mortality is displayed as total number of deaths and percentages related to the respective type of AMI and year. In-hospital mortality among sub-groups is annually displayed as absolute number of deaths and deaths per registered cases of the respective sub-group. P-values were calculated for trend over time for STEMI and NSTEMI (P < 0.01 was considered significant).

DM, diabetes mellitus; LVF, left ventricular failure; CKD, chronic kidney disease; CA, coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.
epidemiological and socio-economic data on AMI have been extrapolated from small- to medium-sized regional cohorts to ascertain an estimate for a large-scale population.

This is the first time that comprehensive data from the unselected, complete hospital population of an industrialized nation have been analysed. These ‘real-life’ data are unique since they are based on obligatory electronic documentation of all patients hospitalized in Germany and, as part of the legally enforced DRG system being indispensable for reimbursement.

Frequency and hospitalization rate

In summary, with a frequency of 248 per 100 000 inhabitants and 1182 per 100 000 in-hospital treatments in 2009, the total AMI rate in Germany remained on a comparatively high level. In contrast, the frequency of STEMI decreased markedly (−23%) in the German population from 2005 to 2009. This downward trend may be attributed to multiple factors, such as improvements in primary and secondary prevention, as well as in diagnostic and therapeutic procedures. In particular, there has been evidence for favourable changes in smoking behaviour or cholesterol levels in the recent past. On the contrary, an upward trend in the frequency of NSTEMI cases could be seen which is consistent with most reports from other industrial nations. Possible explanations for the increased frequency of NSTEMI include the use of high-sensitive troponin leading to elevated rates of diagnosed AMI. However, the use of high-sensitive troponin and change of AMI definition were already implemented in the European Society of Cardiology/American College of Cardiology guidelines since 2000, and therefore well before the evaluated years in our analysis (2005, 2007, and 2009). Additionally, NSTEMI patients had higher proportions of co-morbidities such as diabetes, hypertension, LVF, chronic kidney failure, and peripheral arterial disease in comparison with those with STEMI and therefore are at greater risk to suffer an acute cardiac event. Our data revealed consistently with others that NSTEMI patients were older than the averaged STEMI patient, suggesting that the progressive ageing of the population may additionally support the upward trend in NSTEMI frequency. Indeed, the absolute increase of NSTEMI with respect to age is mainly due to an increase of patients aged 65–89 years old, but relative data indicated that the risk of NSTEMI in each individual age group remained about stable over the evaluated period of time. In how far and to which magnitude the in-patient coding was driven by the reimbursement policy, thereby leading to misclassification has to
be evaluated in coding quality control studies. However, it should be noted that over the entire time period both, the DRGs and the reimbursement for patients with STEMI and NSTEMI were identical. Therefore, there was no financial incentive to change the coding of STEMI or NSTEMI.

With regard to gender, almost two-thirds of all reported STEMI and about 60% of all NSTEMI occurred in men with a further reduction of the female proportion in both AMI types from 2005 to 2009. Therefore, an increasing number of AMI in women as has been reported previously could not be ascertained, but female gender was associated with higher in-hospital mortality.

**Management and in-hospital mortality**

Our data showed an increase of CA and PCI in both STEMI and NSTEMI. Coronary angiography and PCI ratios are comparable with values reported in other recent population-based studies. It could be shown that old patients receive less CA in STEMI and NSTEMI. However, those who got invasively diagnosed had the same chance for coronary intervention compared with younger age groups.

In-hospital mortality was relatively stable at about 11% in AMI during 2005 to 2009. With a current mortality of 12.2% in STEMI and 9.9% in NSTEMI, rates are highly elevated compared with findings in recent RCTs (TRITON-TIMI 38 trial: STEMI 2.6% CF at 30 days; PLATO trial: NSTEMI 5% CF at 1 year). These differences may plausibly be explained by both, inherent selection processes and optimized treatments in RCTs. Compared with the German data from the MONICA/KORA registry from 2004 to 2010, the nationwide in-hospital mortality presented here was even higher than the 28-day case fatality (CF) of this regional registry (MONICA/KORA: STEMI 8.4%; NSTEMI 7.2%). However, MONICA/KORA did not include patients older than 74 years who were consistently with others shown firstly, to represent the majority of deceased patients (64.8% of all dead in 2009), and secondly, to have a noticeably higher CF than the average AMI patient. Furthermore, the separate consideration of the highly fatal left bundle branch block led to lower mortality rates in the STEMI group of the MONICA/KORA registry. Data on all cardiac units from the German ALK registry showed a decreasing mortality in favour of early coronary revascularization.

Because of such differences in AMI definitions, sub-group characteristics, and context, there is limited comparability with recent cohort data from other European nations and the USA. Thus, the enrolment of younger patients with better risk profiles and a higher rate of invasive therapy accounted for the extremely low in-hospital mortality rate of 3.4% of AMI in the French registry FAST-MI. This applies analogously for data presenting a 28-day CF of 4.7% on Q-wave AMI in Spain. The inclusion of patients aged ≥75 years as performed in the Swedish SWEDHEART registry, the British MINAP registry, the Italian BLITZ-Survey, and the Polish PL-ACS registry resulted in significantly higher in-hospital mortality rates (SWEDHEART: STEMI 4.9% in male and 10.4% in female; MINAP: STEMI 5.8% in male and 12.5% in female; BLITZ: STEMI 7.5%; PL-ACS: STEMI 9.3%). These are within the range of American data based on the National Registry of Myocardial Infarction, the National Hospital Discharge Service, or the Olmsted County Area showing a short-term mortality for AMI between 6.3 and 9.4%. Moreover, recent registries on large and rather unselected populations from the Netherlands, Denmark, and the UK showed a similarly high in-hospital mortality as here it was shown for Germany. However, short-term mortality of AMI was reported to significantly decrease in industrialized nations during the past decades. This trend is commonly attributed to better risk factor stratification as well as to improved medical treatment according to evidence-based medicine. Moreover, reduction of major complications and severity of AMI were shown to entail higher survival of AMI. Despite a reduced ratio of women and the elderly, who represent populations at high risk of death and despite the more frequent use of invasive therapy, STEMI mortality in Germany further increased against general trends. It can be assumed that the increased proportions of CKD and LVF were likely to redound to the rising mortality of STEMI patients. In-hospital mortality of NSTEMI patients slightly decreased despite even higher risk profiles and less aggressive therapeutic management. This presumably was owed to the detection of less severe cases by the use of high-sensitive biomarkers. Further, there is evidence that NSTEMI and STEMI frequencies are converging with regard to the long-term mortality.

**Strengths and limitations**

The strengths of the presented data include its basis on the large-sized unselected population of a whole nation. Taking account of the diverse characteristics of patients, the observed trends are of high applicability to daily practice. The findings of the analysis must be considered within the context of the limitations. First, the ICD classification did not allow to distinguish between first and subsequent event of myocardial infarction. Thus, a declining frequency of first AMI and an improved survival of events may mislead to the interpretation of stagnating hospitalizations. Second, in certain cases, hospital transfer was arranged in order to perform therapies with limited availability, such as catheterization or bypass surgery. Combined with the fact that the diagnosis of AMI included events within 28 days of onset of symptoms, this may have added to an underestimated ratio of interventional therapies (PCI, CABG). However, possible downward deviation of these ratios is unlikely to affect trends over time since methodology did not change. Importantly, data acquisition was case- but not patient-based and therefore implicated a certain number of double-counts of patients, e.g. by hospital transfer. Finally, this would lead to further underestimation of the presented mortality data.

**Author’s contributions**

T.F. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. H.R., E.F., and T.F. were responsible for design, data processing, and analysis. E.F., N.M., U.K., G.B., and H.R. wrote this article; U.K. and J.W. provided particularly epidemiological and statistical review and interpretation.

**Supplementary Material**

Supplementary material is available at European Heart Journal online.
Acknowledgements

The authors like to thank the personnel of the Research Data Centres of the Federal Statistical Office and the Statistical Offices of the Laender for providing the data and technical support during the analysis. Further, the authors like to express their gratitude to Mrs Susanne Schueler for her excellent assistance and contribution to this work.

Conflict of interest: none declared.

References


