

# BMJ Open Long-term outcomes after acute myocardial infarction in countries with different socioeconomic environments: an international prospective cohort study

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## ABSTRACT

**Background** Hospital-based data on the impact of socioeconomic environment on long-term survival after myocardial infarction (MI) are lacking. We compared outcome and quality of secondary prevention in patients after MI living in three different socioeconomic environments including patients from three tertiary-care teaching hospitals with similar service population size in Switzerland, Poland and Ukraine.

**Methods** This is a prospective cohort study of patients with a first MI in three different tertiary-care teaching hospitals in Bern (Switzerland), Gdansk (Poland) and Luts'k (Ukraine) during the acute phase in the year 2010 and follow-up of these patients with a questionnaire and, if necessary, telephone interviews 3.5 years after the acute event. The study cohort comprises all consecutive patients hospitalised in every one of the three study centres during the year 2010 for a first MI in the age  $\leq 75$  years who survived  $\geq 30$  days.

**Results** The proportion of patients with ST-segment elevation myocardial infarction (STEMI) was high in Gdansk (Poland) (80%) and in Luts'k (Ukraine) (74%), while the ratio of STEMIs to non-STEMIs was nearly 50:50 in Bern (Switzerland) (50.6% STEMIs). Percutaneous coronary intervention (PCI) was the first choice therapy both in Bern (Switzerland) (100%) and in Gdansk (Poland) (92%), while it was not performed at all in Luts'k (Ukraine). We found substantial differences in treatment and also in secondary prevention interventions including cardiac rehabilitation. All-cause mortality at 3.5 year follow-up was 4.6% in Bern (Switzerland), 8.5% in Gdansk (Poland) and 14.6% in Luts'k (Ukraine).

**Conclusion** Substantial differences in treatment and secondary prevention measures according to low-income, middle-income and high-income socioeconomic situation are associated with a threefold difference in mortality 3.5 years after the acute event. Countries with low socioeconomic environment should increase efforts and be supported to improve care including secondary prevention in particular for MI patients. A greater number of PCIs per million inhabitants itself does not guarantee lower mortality scores.

## Strength and limitations of the study

- Substantial differences in treatment and secondary prevention measures according to low-income, middle-income and high-income socioeconomic situation were found in Bern (Switzerland), Gdansk (Poland) and Luts'k (Ukraine) and are associated with a threefold difference in mortality 3.5 years after the acute event.
- Key strengths of this study are its prospective design comparing original data from patients in three distinctly different socioeconomic environments, the fact that our results are based on a direct comparison between single hospitals with similar service population, and similar compliance to guideline-recommended therapies and comparable research activities, but acting under three different economic situations, whereas interventions and outcome after acute coronary syndrome are usually compared in the framework of registry studies including single or various hospitals within countries (without clear definition of the catchment area and no convincing indication that the selected hospital population would be representative for the whole country).
- Limitations of this study are the fact that extrapolation of such local results to a whole country has still to be performed with caution, that we used information about the socioeconomic situation only on a region/country level but not on an individual level, that secondary outcomes are only patient reported and not validated by other sources, and that the reliability of the data in regard to medication and cardiac rehabilitation is somewhat compromised by the fact that a limited number of patients did not answer the follow-up questionnaire and could not be reached by telephone for an interview.

## INTRODUCTION

Cardiovascular diseases, frequently elicited by acute coronary syndromes (ACS), are the

leading cause of death worldwide.<sup>1</sup> Over the past decades, numerous large-scale randomised clinical trials have demonstrated the benefits of timely interventions for patients with ACS, including antiplatelet therapy, thrombolysis and urgent cardiac catheterisation followed by revascularisation as appropriate.<sup>2</sup> The results of these trials have been incorporated in national and international guidelines providing treatment recommendations.<sup>3,4</sup> Following these guidelines, the use of prehospital thrombolysis and percutaneous coronary intervention (PCI), the appropriate prescription of adjunctive pharmacotherapy and referral to cardiac rehabilitation are now more widespread.<sup>5</sup> Recent evidence suggests that this remarkable progress was associated with a significant decline in mortality from cardiovascular diseases over the last years, more pronounced in high-income regions (especially Australasia, Western Europe and North America<sup>6</sup>). Despite these well-established guidelines for the management of ACS, there are still strong differences with regard to the epidemiology, diagnostics and treatment of patients with ACS, leading to diverging morbidity and mortality rates across the globe. Not all reasons for these differences are well understood. Outcome variations can be caused by differences in the disease itself, baseline characteristics of the population, treatment modalities, and in particular in the use of invasive cardiac procedures, or in any other unmeasured variable, such as socioeconomic characteristics of the population.<sup>7,8</sup> Interventions and outcomes after acute myocardial infarction (MI) in different areas and populations are usually compared in the framework of registries including various hospitals mostly within countries, whereas studies with direct comparison of treatment and outcome between single hospitals serving similar size populations in different socioeconomic environments are lacking.

The aim of this study was to compare interventions, secondary prevention and outcome in patients with acute MI between three different socioeconomic environments including patients from three tertiary-care teaching hospitals with comparable service populations in Switzerland (high income), Poland (middle income) and Ukraine (low income).

## METHODS

### Study design

This was a prospective cohort study with data analysis of patients with a first MI in three different tertiary-care teaching hospitals in Switzerland, Poland and Ukraine during the acute phase in the year 2010 and follow-up of these patients with a questionnaire and, if necessary, telephone interviews 3 to 4 years after the acute event.

### Study centres

The participating study centres were three tertiary-care teaching hospitals: Bern University Hospital (Switzerland), Gdansk University Hospital (Poland) and Lutsk City Hospital (Ukraine). The service population is approximately 1 million inhabitants in Switzerland and in Poland

and somewhat smaller in Ukraine. Population density in the service area is 171.4 persons/km<sup>2</sup> for Bern University Hospital, 124 persons/km<sup>2</sup> in the Pomeranian voivodship and 1805.5 persons/km<sup>2</sup> in Gdansk, Gdynia and Sopot (Tricity as one agglomeration) for the Gdansk University Hospital and 51.5 persons/km<sup>2</sup> in the Volyn region for the Lutsk City Hospital. All three centres have strict policies with regard to compliance with guideline-based therapies. All three centres are engaged in research and are participating in more than 10 clinical trials per year.

### Study population

This study included all consecutive patients hospitalised in one of the three study centres during the year 2010 for a first MI at the age  $\leq 75$  years who survived  $\geq 30$  days. The definition of MI was either ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI), both with elevated levels of troponin or creatine kinase-myocardial band (CK-MB) iso-enzyme.

### Patient and treatment characteristics

The study centres prospectively collected data about age, gender, cardiovascular risk factors (body mass index (BMI), diabetes mellitus, arterial hypertension, hypercholesterolaemia and smoking status) and significant comorbidities (chronic kidney disease, stroke, cancer, chronic lung disease). Data have been collected by dedicated researchers in each hospital by chart review. Obesity has been defined as BMI  $\geq 30$ , and smoker has been defined as former or current smoker.

Components of acute phase hospital treatment for MI were defined as fibrinolysis, PCI or drug treatment without intervention.

Furthermore, we obtained data about the medication at hospital discharge (antiplatelets, statins, ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), and  $\beta$ -blockers).

### Follow-up evaluation

The follow-up evaluation was carried out in the years 2013 and 2014 with a mean of 3.5 years after MI. All-cause mortality data were obtained from local or national registries. We sent questionnaires to all remaining patients with questions about rehospitalisation for any cardiovascular disease event, participation in a structured cardiac rehabilitation programme and about adherence to secondary preventive medication (antiplatelets, statins, ACEIs or ARBs, and  $\beta$ -blockers). If the questionnaire was not returned within 3 weeks, we pursued an interview by telephone.

### Clinical outcomes

The primary endpoint of this study was all-cause mortality at 3.5 years of follow-up. Deaths were ascertained from the national registries for death reports.

Secondary endpoints were participation in a structured cardiac rehabilitation programme (stationary or ambulatory) and adherence to secondary

**Table 1** Baseline characteristics of the study population in three different study centres in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine)

|               | <b>Bern<br/>(Switzerland)<br/>547 patients</b> | <b>Gdansk<br/>(Poland)<br/>375 patients</b> | <b>Lutsk<br/>(Ukraine)<br/>164 patients</b> | <b>p Value for all</b> | <b>Bern vs<br/>Gdansk</b> | <b>Bern vs<br/>Lutsk</b> | <b>Gdansk vs<br/>Lutsk</b> |
|---------------|--|---|---|------------------------|---------------------------|--------------------------|----------------------------|
| Age           | 58.4±10.4                                      | 58.9±9.9                                    | 60.0±10.2                                   | 0.21                   | 0.41                      | 0.08                     | 0.27                       |
| Women         | 26.5%<br>145/547                               | 26.9%<br>101/375                            | 33.5%<br>55/164                             | 0.19                   | 0.95                      | 0.1                      | 0.15                       |
| Smoking       | 49.4%<br>266/539                               | 56.0%<br>197/352                            | 35.6%<br>36/101                             | 0.001                  | 0.06                      | 0.02                     | <0.001                     |
| DM            | 12.9%<br>68/527                                | 22.3%<br>82/368                             | 15.9%<br>26/164                             | <0.001                 | <0.001                    | 0.41                     | 0.11                       |
| Obesity       | 20.1%<br>109/541                               | 33.0%<br>113/342                            | 28.7%<br>47/164                             | <0.001                 | <0.001                    | 0.03                     | 0.37                       |
| Renal disease | 5.1%<br>28/547                                 | 1.9%<br>7/375                               | 2.0%<br>2/101                               | 0.02                   | 0.02                      | 0.26                     | 1                          |
| Lung disease  | 3.7%<br>20/547                                 | 3.5%<br>13/375                              | 6.9%<br>7/101                               | 0.25                   | 1                         | 0.21                     | 0.21                       |
| Cancer        | 4.6%<br>25/547                                 | 1.3%<br>5/375                               | 1.0%<br>1/101                               | 0.009                  | 0.01                      | 0.16                     | 1                          |
| Stroke        | 1.1%<br>6/547                                  | 1.3%<br>5/375                               | 6.1%<br>10/164                              | <0.001                 | 0.99                      | <0.001                   | 0.005                      |
| STEMI         | 50.6%<br>277/547                               | 79.9%<br>271/339                            | 73.2%<br>120/164                            | <0.001                 | <0.001                    | <0.001                   | 0.11                       |

DM, diabetes mellitus; STEMI, ST-segment elevation myocardial infarction.

preventive medication (antiplatelets, statins, ACEIs or ARBs,  $\beta$ -blockers or diuretics).

The study had been approved by the regional ethical committees, and informed consent was obtained from the patients.

### Statistical analysis

Categorical variables were compared using the  $\chi^2$  test. Continuous variables were expressed as mean value±SD and compared using one-way analysis of variance. Multiple logistic regression was used to examine impact of risk factors, comorbidities and treatments to 3.5 year mortality after MI. ORs with their 95% CIs were obtained. Statistical analyses were performed with the use of R V.3.1.3 (R Foundation for Statistical Computing). All the statistical analyses were two-tailed. p values <0.05 were considered statistically significant, while Bonferroni corrections were applied for comparing each pair of groups.

## RESULTS

### Study population

The study population was drawn from three different tertiary-care hospitals in Switzerland, Poland and Ukraine, that is, 547 patients in Bern (Switzerland), 375 in Gdansk (Poland) and 164 in Lutsk (Ukraine) (table 1).

Table 1 shows the baseline characteristics of all included patients. The average age was comparable in all centres. The percentage of female patients was similar in all centres. The proportion of patients with STEMI was high

in Gdansk (Poland) and in Lutsk (Ukraine), whereas the ratio of STEMI to NSTEMI was nearly 50:50 in Bern (Switzerland). The distribution of all risk factors was lowest in Bern (Switzerland) except for the percentage of smokers, which was lowest in Ukraine due to a very low percentage of female smokers (7%) compared with male smokers (45%). Overall, the worst baseline risk profile was present in the patients from Gdansk (Poland). The higher stroke prevalence in Gdansk (Ukraine) compared with the other two study centres corresponds with the higher prevalence of stroke in the population.

In regard to comorbidities, the percentage of patients with renal disease was similar in Bern (Switzerland) and Lutsk (Ukraine) but was lower in Gdansk (Poland). Lung disease was most prevalent in Lutsk (Ukraine), while it was similar in Bern (Switzerland) and Gdansk (Poland). The incidence of cancer was low in all countries but highest in Bern (Switzerland), and the percentage of patients with previous stroke was highest in Lutsk (Ukraine), while it was similar in Bern (Switzerland) and Gdansk (Poland).

### Socioeconomic situation in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine)

The socioeconomic situation in the three participating countries is shown in table 2.

It is evident that the three participating countries represent three distinctly different levels of the socioeconomic situation. This is true for the per capita income, the unemployment rate and for insurance coverage.

**Table 2** Socioeconomic situation in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine) in 2010

| Socioeconomic environment 2010                       | Bern (Switzerland)  | Gdansk (Poland)   | Lutsk (Ukraine)   |
|--|---------------------|-------------------|-------------------|
| Per capita income                                    | €40 615/person/year | €9300/person/year | €1390/person/year |
| Unemployment rate                                    | 3.5%                | 5.5%              | 8.9%              |
| Percentage of patients with ACS covered by insurance | 100%                | 100%              | 5%                |

Data sources: Swiss Federal Statistical Office ([www.bfs.admin.ch](http://www.bfs.admin.ch)), Central Statistical Office of Poland ([www.stat.gov.pl](http://www.stat.gov.pl)) and Ukraine Government Website ([www.lutsk.ukrstat.gov.ua](http://www.lutsk.ukrstat.gov.ua)).

ACS, acute coronary syndrome.

Unemployment rate according to national registries may have been underestimated due to the fact that not all unemployed persons are registered. In Bern (Switzerland) and Gdansk (Poland), almost all patients with MI were covered by insurance, but in Lutsk (Ukraine) the great majority was not.

### Hospital characteristics and services

Hospital characteristics and services are shown in [table 3](#).

The care capacity of the cardiology department in Bern (Switzerland) was almost twice as large as the one in Lutsk (Ukraine). In the year 2010 in Lutsk City Hospital, facilities for coronary angiography and PCI were not available, whereas in Gdansk (Poland) most patients and in Bern (Switzerland) all patients fulfilling the inclusion criteria receive coronary angiography and, if considered to be appropriate, one or more stent implantations. The average duration of hospitalisation in ACS patients was inversely related to the socioeconomic situation.

### Treatment

Treatment modalities and medication at discharge in the three study centres are summarised in [table 4](#).

Coronary angiography was performed in the acute phase in all patients fulfilling the inclusion criteria for this study in the study centre in Bern (Switzerland) and in

almost all patients in Gdansk (Poland). PCI was the first choice therapy if indicated both in Bern (Switzerland) and in Gdansk (Poland), while it was not performed at all at the study centre in Lutsk (Ukraine) where some patients received fibrinolysis therapy. The remaining patients did not receive any reperfusion therapy at all in this Ukrainian centre.

At discharge, most patients were treated with antiplatelets, statins, ACEIs or ARBs, and  $\beta$ -blockers in all three study centres. The prescription of ACEIs or ARBs at discharge was somewhat lower in Lutsk (Ukraine), whereas the prescription of  $\beta$ -blockers was considerably higher in Bern (Switzerland) and Lutsk (Ukraine) compared with Gdansk (Poland).

### Follow-up

Medication, cardiac rehabilitation attendance and all-cause mortality at follow-up are summarised in [table 5](#).

The response rate was 84.3% in Switzerland and 61.6% in Poland, whereas in Gdansk (Poland) only 205/375 patients (54%) agreed and took part at follow-up evaluation sharing with us their data. In Bern (Switzerland), the use of antiplatelets, statins, ACEIs or ARBs, and  $\beta$ -blockers remained relatively high at follow-up. In Gdansk, there was a slight but significant decrease in the

**Table 3** Hospital characteristics and services of three different study centres in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine)

| Hospital/cardiology department structure 2010           | Bern (Switzerland)             | Gdansk (Poland)                 | Lutsk (Ukraine)              |
|---|--------------------------------|---------------------------------|------------------------------|
| Carrying capacity                                       | 931 beds                       | 950 beds                        | 700 beds                     |
| Carrying capacity of the cardiology department          | 110 beds                       | 83 beds                         | 60 beds                      |
| Intensive care unit for patients with ACS               | Yes                            | Yes                             | Yes                          |
| Total no of MI patients                                 | 679                            | 914                             | 259                          |
| Total no of PCI   | 2273                           | 2718                            | 0                            |
| Total no of angiographies                               | 4859                           | 3910                            | 0                            |
| Average duration of hospitalisation in patients with MI | 3.3 days                       | 7.8 days                        | 14.1 days                    |
| Population density of catchment area                    | 169.25 persons/km <sup>2</sup> | 1757.35 persons/km <sup>2</sup> | 5196 persons/km <sup>2</sup> |

ACS, acute coronary syndrome; MI, myocardial infarction; PCI, percutaneous coronary intervention.

**Table 4** Acute treatment and medication at discharge in three different study centres in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine) (denominators in percentage)

| Treatment                 | Bern (Switzerland) | Gdansk (Poland) | Lutsk (Ukraine) | p Value for all | Bern vs Gdansk | Bern vs Lutsk | Gdansk vs Lutsk |
|---------------------------|--------------------|-----------------|-----------------|-----------------|----------------|---------------|-----------------|
| Fibrinolysis              | 0% (547)           | 0% (375)        | 30.8% (164)     | <0.001          |                | <0.001        | <0.001          |
| PCI                       | 98% (547)          | 92.3% (375)     | 0% (164)        | <0.001          | <0.001         | <0.001        | <0.001          |
| Antiplatelet at discharge | 100% (547)         | 100% (375)      | 97.2% (147)     | <0.001          |                | 0.002         | 0.006           |
| Statin at discharge       | 97.6% (547)        | 97% (375)       | 94.6% (147)     | 0.153           | 0.602          | 0.054         | 0.169           |
| ACEIs or ARB at discharge | 89% (547)          | 88% (375)       | 81.6% (147)     | 0.052           | 0.628          | 0.016         | 0.058           |
| β-Blocker at discharge    | 87.9% (547)        | 77.1% (375)     | 92.5% (147)     | <0.001          | <0.001         | 0.116         | <0.001          |

Comparisons between the three study centres with regard to fibrinolysis, PCI and medication.

ACEIs, ACE inhibitors; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention.

use of antiplatelets, statins, ACEIs or ARBs ( $p<0.001$  for decrease in antiplatelets and statins,  $p=0.022$  for ACEIs or ARB), whereas the use of β-blockers increased slightly over time ( $p=0.217$ ). In Lutsk (Ukraine), drug use decreased drastically ( $p<0.001$  for decrease in the use of all drugs) and was significantly lower than in both other hospital populations.

The participation in any cardiac rehabilitation programme was highest in Bern (Switzerland) and lowest in Lutsk (Ukraine). In Bern (Switzerland), most patients have easy access to outpatient cardiac rehabilitation programmes and are referred to inpatient rehabilitation on request or if they are at increased risk or in need of intense surveillance and treatment. In Gdansk (Poland), only half of the patients have access to cardiac rehabilitation programmes mostly due to lack of insurance coverage. In Ukraine, the cardiac rehabilitation system is in a transitional state. Although the old Soviet system with cardiac rehabilitation resorts (sanatoria) has neither shown to be effective in economical nor medical aspects, this system still exists. Lutsk City Hospital has a

rehabilitation department with 20 beds for early rehabilitation after MI and stroke. Ten patients attended this inpatient rehabilitation programme, six patients were in sanatoria and eight patients attended an outpatient rehabilitation programme. Theoretically, all patients receive recommendations for self-rehabilitation and are regularly controlled by a cardiologist in an outpatient department in Lutsk (Ukraine).

All-cause mortality at 3.5 year follow-up was 4.6% in Bern (Switzerland), 8.5% in Gdansk (Poland) and 14.6% in Lutsk (Ukraine).

To find independent predictors of 3.5 year mortality, multivariate logistic regression analysis was performed. Lung disease (12.03 (2.16 to 67.11),  $p=0.005$ ), renal disease (6.31 (1.63 to 24.5),  $p=0.008$ ) and diabetes (7.6 (2.58 to 22.38),  $p=0$ ) were found to be mortality predictors in Bern (Switzerland), whereas age (1.09 (1.02 to 1.17),  $p=0.015$ ) was found to be a mortality predictor in Gdansk (Poland). No single baseline parameter was found to predict mortality in Lutsk (Ukraine). Although the relation of STEMI versus non-STEMI varies significantly

**Table 5** Medication, cardiac rehabilitation attendance and mortality at 3.5 year follow-up in in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine) (denominators in percentage)

| Follow-up                               | Bern (Switzerland) | Gdansk (Poland) | Lutsk (Ukraine) | p Value for all | Bern vs Gdansk | Bern vs Lutsk | Gdansk vs Lutsk |
|---|--------------------|-----------------|-----------------|-----------------|----------------|---------------|-----------------|
| Antiplatelet at follow-up               | 98.3% (461)        | 83.9% (205)     | 78.2% (101)     | <0.001          | <0.001         | <0.001        | 0.223           |
| Statin at follow-up                     | 90.9% (461)        | 78.5% (205)     | 31.7% (101)     | <0.001          | <0.001         | <0.001        | <0.001          |
| ACEIs or ARB at follow-up               | 73.3% (461)        | 81% (205)       | 34.7% (101)     | <0.001          | 0.034          | <0.001        | <0.001          |
| β-Blocker at follow-up                  | 74.4% (461)        | 81.5% (205)     | 52.5% (101)     | <0.001          | 0.047          | <0.001        | <0.001          |
| Participation in cardiac rehabilitation | 69.4% (343)        | 51.4% (204)     | 26% (92)        | <0.001          | <0.001         | <0.001        | <0.001          |
| 3.5 year mortality                      | 4.6% (547)         | 8.5% (375)      | 14.6% (164)     | <0.001          | 0.014          | <0.001        | 0.033           |

Comparison between the three study centres in regard to follow-up medication, rehabilitation attendance and mortality.

ACEIs, ACE inhibitors; ARB, angiotensin receptor blocker.

between countries, this relation was not found to predict mortality in the three study centres ( $p=0.626$  for Bern (Switzerland),  $p=0.379$  for Gdansk (Poland) and  $p=0.802$  for Lutsk (Ukraine)).

## DISCUSSION

This prospective cohort study delivers important information in regard to characteristics, management and outcomes of patients admitted for ACS (STEMI or NSTEMI) in three different socioeconomic environments in teaching hospitals in Bern (Switzerland) (high income), Gdansk (Poland) (middle income) and Lutsk (Ukraine) (low income) during the year 2010. The three participating hospitals are comparable in regard to their service population, to their compliance to follow guidelines (as demonstrated by the prescription of guideline-based drugs at discharge) and by their research and teaching activities. The main finding is a striking disparity of mortality at the 3.5 year follow-up: in Bern (Switzerland), mortality was 4.6%, while in Gdansk (Poland) it was nearly twofold with 8.5% and in Lutsk (Ukraine) almost threefold with 14.6%. Total mortality is inversely related to the socioeconomic status of the participating countries.

The two most important differences between the three hospital populations leading to these striking differences in total mortality are most probably the number of patients treated with PCI in the acute phase and the lack of insurance coverage during follow-up (figure 1). Besides lack of insurance, impaired socioeconomic situations with considerably lower budgets for health-care services and lower income per capita are other important determinants for access to PCI and for long-term compliance with medical therapies. However, an important finding is the fact that although acute PCI was only slightly less frequently applied in Gdansk (Poland), long-term mortality was still twofold in Gdansk (Poland) compared with Bern (Switzerland). Indeed, similar levels of access to PCI correspond to different medium-term to

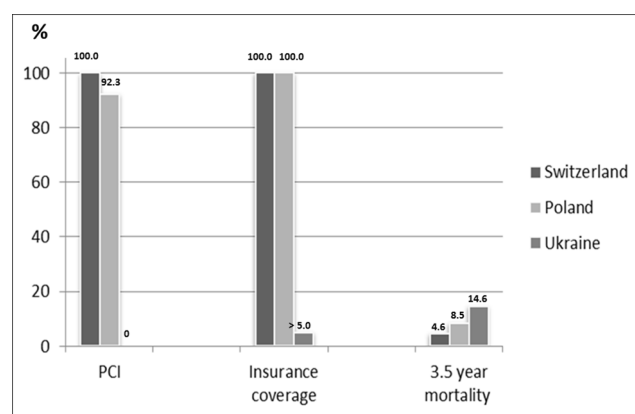
long-term mortality. This indicates that a greater number of PCI per million inhabitants do not guarantee lower mortality scores. Although we cannot exclude differences in acute intervention times and also in procedural success rates between the two countries as a contributing factor (because this has not been evaluated in this study population), this finding underlines the importance of secondary prevention interventions through comprehensive cardiac rehabilitation.

It is apparent that the lower adherence to guidelines recommending early reperfusion therapy for patients with acute MI in Ukraine is not due to ignorance but rather the consequence of a difficult socioeconomic situation. In regard to medication prescription at discharge, the results from Ukraine indicate good adherence to actual guidelines.

Our study reflects the situation in the three countries in general. The number of PCI per 1 million inhabitants in 2010 and 2011 was 506 in Switzerland, 735 in Poland and only 25 in Ukraine. The lower number of PCIs in Switzerland compared with Poland is due to a significant drop in the number of acute MIs in the country during the past few years, whereas the higher rate of NSTEMI compared with STEMI in Switzerland may indicate a greater number of heart attacks 'only' troponin positive. At the time of the study, there was no centre with capabilities for acute PCI in Lutsk, Ukraine; a first such centre was created in 2013 and a second in 2015.

Another explanation for the significantly higher mortality in Gdansk (Poland) and Lutsk (Ukraine) compared with Bern (Switzerland) could be a worse baseline risk profile or a higher incidence of comorbidities in patients of those two countries. Based on our multivariate regression analysis, it is unlikely that such differences contribute to a great extent to the striking differences in 3.5 year mortality between the three study populations. Whereas lung disease, renal disease and diabetes were found to be mortality predictors in Bern (Switzerland) and age in Gdansk (Poland), neither baseline risk factors nor comorbidities were found to be predictors for 3.5 year mortality in Lutsk (Ukraine). However, it cannot be excluded that this is due to the smaller sample size in Lutsk.

Orlandini *et al*<sup>7</sup> found that several higher risk characteristics were more common in lower-income countries and less common in higher-income countries. Jakobsen *et al*<sup>8</sup> found that patients with low socioeconomic status were older and had a worse baseline risk profile than high SES and therefore argued that the poor outcome related to low socioeconomic status was primarily explained by differences in baseline characteristics, including higher comorbidity. Although we found some differences in baseline characteristics, they fail to fully explain the striking gap in mortality between our three study areas. In particular, the average age and the percentage of females were nearly the same in all countries and the percentage of smokers was even lowest in Lutsk (Ukraine) (due to very low smoking rates in women). However, lung disease and



**Figure 1** Use of percutaneous coronary intervention (PCI), insurance coverage and 3.5 year mortality of patients with acute coronary syndromes in three study cities regions in Bern (Switzerland), Gdansk (Poland) and Lutsk (Ukraine).



previous strokes were most prevalent in Lutsk (Ukraine) and obesity and diabetes were significantly more common in Gdansk (Poland) and Lutsk (Ukraine) compared with Bern (Switzerland). This explains mortality differences between our study populations only to a small extent.

The finding that mortality is inversely related to the socioeconomic status of each country is in line with some previous studies, such as Orlandini *et al*<sup>7</sup> who found a large difference in the mortality rates, namely 12.1% in low-income countries and 4.9% in high-income countries. Furthermore, Rosvall *et al*<sup>8</sup> obtained detailed information from patients after their first MI during the period 1993 to 1996 on the use of revascularisation, cumulative household income and 5 year survival after the MI. They found that patients with the highest cumulative income underwent a revascularisation procedure within 1 month after their first MI two to three times as often as patients with the lowest cumulative income and had half the risk of death within 5 years. Patients who underwent revascularisation showed a similarly lowered mortality risk in the different income groups, while there were strong socioeconomic differences in long-term mortality among patients who did not undergo revascularisation.<sup>10 11</sup> Rosevall suggested that low socioeconomic position is associated with increased delays in seeking treatment and is an early determinant of major cardiovascular risk factors. Furthermore, it could be that those having a revascularisation are more likely to be followed up by a cardiologist and more likely to receive specific secondary prevention advice and a prescription for acetylsalicylic acid,  $\beta$ -blockers, ACEIs or statins.

An important question arises if the three hospital-based cohorts are representative for the populations of their respective countries. This is true for Bern/Switzerland (with a service area comprising one large and some smaller cities, villages of different sizes, rural areas and mountain regions, a representative mix in regard to demographic characteristics and socioeconomic situation, very similar medical services and identical insurance situation) and most likely true also for Gdansk/Poland (representative demographic and socioeconomic situation of the service population, one national insurance payer covering costs of all MIs in public and private hospitals with identical sets of procedures and requirements and similar results of recent outcome analyses performed in the years 2009–2014 by the National Institute of Public Health with small differences in 1 and 3 year mortality between the reference university hospitals). However, for Lutsk, the comparison is more complicated for Ukraine, being a country in transition typically with greater fragmentation within the country. In 2010, however, when patients entered this study, Ukraine had only 25 PCI/1 million inhabitants in comparison to 506 (Switzerland) and 735 (Poland)/1 million inhabitants; as the number for PCIs in Ukraine has been very small overall, it seems unlikely that this has led to important differences in ACS mortality between different regions of Ukraine, perhaps with the exception of somewhat lower mortality in the

capital city Kiev. Nevertheless, after 2010, the number of PCIs increased steadily and substantially, which can be seen in the context of the ‘Stent for Life’ initiative.

Widimsky *et al*<sup>12</sup> first suspected that medical and non-medical staff are the main barriers for wider primary PCI implementation: low staffing levels are often related to conservative attitudes of physicians and to insufficient motivation of medical staff to run demanding non-stop PCI services for ACS. However, such an argument was not pertinent to Lutsk City Hospital, Ukraine, where no catheter laboratory was available at the time. In a follow-up study of the former survey of Widimsky *et al*, Kirstensen *et al*<sup>13</sup> assumed that one possible explanation for the observed variations could be the countries’ disparate reimbursement schemes. This is in line with our survey that showed big differences in the reimbursement schemes. In Switzerland and Poland, almost all patients with ACS are covered by insurance, but in Ukraine, more than 95% are not. There is no obligatory medical insurance in Ukraine. A voluntary medical insurance (VMI) system is only developing in this country. Experts consider that not more than 5% of Ukrainians are covered by this kind of insurance<sup>14</sup> and expenses related to VMI represent less than 1% among sources of revenue of total expenditure on healthcare in Ukraine.<sup>15</sup> Kirstensen *et al*<sup>13</sup> found that the scant evidence within the field indicates that the barriers for PCI implementation are a complex mix of medical, organisational, patient-related, regulatory and economic factors. Furthermore, they suggested that major efforts are highly necessary to increase public knowledge on the symptoms of ACS and of the awareness for immediate contact to the emergency medical system in order to shorten patient delay. Nevertheless, prehospital delays (229 min in Poland and 240 min in Switzerland) and door-to-needle time in patients undergoing invasive treatment (around 25 min over the study period in both countries) cannot explain the difference in mortality between the two countries.

Differences in hospital characteristics and services are also important. In the year 2010, at the index hospital in Ukraine, angiographies or PCIs were not performed in acute MI, while in Poland the index hospital performed 3910 and in Switzerland even 4859 angiographies. The average duration of hospitalisation was shortest in Bern (Switzerland) with 3.3 days and longest in Lutsk (Ukraine) with 14.1 days, which indicates that the treatment duration within the hospital does not improve the prognosis under these circumstances.

In addition, Laut *et al* found a correlation between the availability of physicians and increase in PCI utilisation. Countries with both low and high population density per square kilometre had a slower increase in PCI utilisation for ACS compared with countries with a medium population density. They assumed that differences in utilisation rates of PCI for ACS could partly be explained by the countries’ supply factors such as the number of physicians and number of acute care beds, rather than financial factors.<sup>16 17</sup>

Furthermore, Puymirat *et al*<sup>18</sup> suggested that one of the key determinants of improved outcomes is the implementation of regional networks, which is now strongly advocated in the most recent European Society of Cardiology guidelines.

The use of guideline-recommended medications at discharge was relatively high in all three countries, but still there were some differences. Nearly all patients received antiplatelets and statins at discharge, while ACEIs or ARBs and  $\beta$ -blockers were prescribed to 80%–90% of all patients in all three hospitals. However, an important difference between patients from these three countries is the adherence to guideline-recommended medications during follow-up. After 3.5 years of follow-up, in Lutsk (Ukraine) only 78.2% of patients were on antiplatelets and only 31.7% on statins. This circumstance may play a significant role for mortality differences. Low compliance to medical treatment after MI is a complex issue and financial problems may play a key role. The striking difference in income per capita, reimbursement and insurance coverage in Ukraine compared with Switzerland and Poland engenders a big financial burden to Ukrainian patients who have to pay for each drug themselves.

The participation in a cardiac rehabilitation programme was highest in Bern (Switzerland) with 69% and lowest in Lutsk (Ukraine) with 26%. Despite the fact that secondary prevention through cardiac rehabilitation is a guideline-recommended treatment modality that improves morbidity and mortality in patients after acute MI,<sup>19–21</sup> there are obviously still large differences among the three countries mainly because participation in cardiac rehabilitation is recommended, but availability is limited in Poland and Ukraine. In Poland, there is restricted access for most patients to such programmes. The only public and obligatory health insurer, that is, the National Health Fund, covers all costs of modern in-hospital acute MI therapy, but has limited resources for post-MI cardiac rehabilitation. In 2009, only 22% of all patients with post-MI in Poland underwent modern comprehensive cardiac rehabilitation.<sup>22</sup> This indicates that secondary prevention is underestimated and underfinanced by decision makers. Whereas statin usage increased largely during the last decade in Poland, no significant changes in dietary habits were observed during this period.<sup>23</sup> In Lutsk (Ukraine), theoretically all patients receive recommendation for self-rehabilitation with periodical controls by a cardiologist in the outpatient department, and there are some limited opportunities to attend outpatient or inpatient rehabilitation programmes. However, access to comprehensive ambulatory cardiac rehabilitation is highly restricted due to socioeconomic factors.

While making cross-country comparisons is challenging, the results of this study nevertheless are instructive in presenting a picture of the striking variation of the invasive and medical management of patients with ACS in three European countries. The main obstacle limiting analyses of healthcare utilisation and outcomes is the lack of a sound scientific European database on PCI and ACS.

Good-quality data are a necessity for identifying barriers and an instrument to target goals, as well as for monitoring and evaluating treatment use, quality of care and effects. In an attempt to reduce differences in a number of European countries, the Stent for Life initiative, supporting the implementation of timely PCI, was established in 2008.<sup>24 25</sup> The participating countries reported significant rises in PCI utilisation, reduction in mortality and an overall more effective management of the STEMI treatment system. This strongly calls for a continuation of a strategy of implementation and for support of countries with yet low activities, such as Ukraine.<sup>26 27</sup>

A major strength of this study is its prospective design comparing original data from patients in three distinctly different socioeconomic environments and the fact that our results are based on a direct comparison between single hospitals with similar service population, similar compliance to guideline-recommended therapies and comparable research activities, but acting under three different economic situations. In contrast, international comparison studies are usually performed in the framework of registry studies including single or various hospitals within countries but without clear definition of the catchment area and no convincing indication that the selected hospital population would be representative for the whole country.

### Limitations

Extrapolation of such local results to a whole country has to be performed with caution. Whereas there is little variation in treatment modalities of patients with MI in Switzerland and only slightly more variation in Poland, there was a great heterogeneity in Ukraine in the year 2010. Furthermore, PCI for ACS has also been fostered in Ukraine during the past few years and therefore mortality from acute MI may have decreased since. Information about the socioeconomic situation was used only on a regional/country level but not on an individual level. Secondary outcomes are only patient reported and not validated by other sources. In regard to follow-up data, the reliability of the data in regard to medication and cardiac rehabilitation is somewhat compromised by the fact that a limited number of patients did not answer the follow-up questionnaire and could not be reached by telephone for an interview.

### CONCLUSIONS

In conclusion, we found striking disparities in mortality in patients during a follow-up of 3.5 years between the three study populations. Mortality was almost twofold higher in Gdansk (Poland) and threefold higher in Lutsk (Ukraine) compared with Bern (Switzerland). These differences could not be explained by worse baseline risk profile or higher incidence of comorbidities and therefore is probably mainly due to socioeconomic differences between the three countries. In addition, a greater



number of PCIs per million inhabitants itself does not guarantee lower mortality scores.

**Contributors** JK, AY, TZ, HS: conception/study design. JK, AY, TZ, HS, SW, BM, LR, MP, IS, PK, MGr, MG: data acquisition, analysis and/or interpretation. JK, AY, TZ, HS, SW, BM, LR, MP, IS, PK, MGr, MG: manuscript draft/revision. JK, AY, TZ, HS, SW, BM, LR, MP, IS, PK, MGr, MG: final approval. JK, AY, TZ, HS, SW, BM, LR, MP, IS, PK, MGr, MG: accountability agreement.

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# Long-term outcomes after acute myocardial infarction in countries with different socioeconomic environments: an international prospective cohort study

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