Direct healthcare costs and resource consumption after acute coronary syndrome: a real-life analysis of an Italian subpopulation

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Abstract

Background: Acute coronary syndrome (ACS) is the most common cause of morbidity and mortality in Italy and worldwide. Aim of this study was to evaluate the average annual direct healthcare costs for the treatment of patients with a recent hospitalization for ACS.

Design and methods: The direct medical costs of patients with a first ACS hospitalization (index event) in the period from 1 January 2008 to 31 December 2008 were estimated for a 1-year follow-up period. The resource consumption was measured in terms of: reimbursed drugs, diagnostic procedures, outpatient visits, and hospitalizations. The analysis was performed from the Italian National Health Service perspective.

Results: A total of 2,758,872 subjects were observed, 7082 (35.8% women) of whom being hospitalized for ACS during the accrual period (2.6%). Among patients with ACS, 60% were medically treated, 33.1% were treated with percutaneous coronary intervention (PCI), and 6.9% died during the index hospitalization. Dual antiplatelet treatment (ASA plus clopidogrel) was prescribed in 25.9% of the medically treated ACS patients and in 70.1% of the ACS patients treated with PCI. The average yearly cost per patient for the total ACS population was 11,464€/year (drugs 1304€; hospitalizations 9655€; diagnostic and outpatient visits 505€). The average annual cost was 10,862€ for medically treated patients and 14,111€ for patients treated with PCI. Patients who died of cardiovascular events during follow up had an average cost of 16,231€/patient.

Conclusions: Patients with ACS had higher direct healthcare costs, their management and rehospitalizations being the main cost drivers.

Keywords
Acute coronary syndrome, cost of illness, direct healthcare costs, healthcare resource use

Introduction

Acute coronary syndrome (ACS) represents the most common cause of morbidity and mortality worldwide. In Italy, mortality due to ischemic heart disease accounts for 12% of all deaths and myocardial infarction accounts for 8% in the population aged between 35 and 74 years.1,2 The economic burden of ACS in Europe3 and in Italy4,5 is extremely high and is mainly related to hospitalizations, pharmaceutical costs, diagnostic procedures, and visits.

In 2010, cardiovascular (CV) drugs represented the most widely prescribed drug class in Italy with an expenditure of over €5 billion, more than 93% of

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which covered by the Italian National Health Service (INHS). The prescription of these drugs increased with age for both men and women (more than 90% of the population over 75 years old used these medicines), with more prescriptions in men than in women.

The use of antiplatelet agents was also significant: 63 defined daily doses (DDD)/1000 inhabitants, corresponding to an expenditure of 2.4€ per capita at territorial level. Acetylsalicylic acid (ASA) (43.3 DDD/1000 inhabitants) and lysine acetylsalicylate (7.8 DDD/1000 inhabitants) were among the 30 most frequently prescribed active principles. In 2010, the use of clopidogrel declined at territorial level by 6.4% and increased in public structures by 30.4%; related expenditure dramatically decreased (−38.8%) mostly due to the market launch of generic drugs and to the increase, at regional level, in direct distribution and in the so-called ‘distribution on behalf’ of the local (national) health authority (the direct distribution programme enables the distribution of drugs directly to patients either via hospitals and local healthcare units or through retail pharmacists; the ‘distribution on behalf’ brings about important savings for the INHS due to the reduction in the pharmacy and wholesaler margins).

The Italian Ministry of Health estimated for 20107 a health-related expenditure of more than €5 billion for CV hospitalizations, around €700 million of which related to ACS. Although several studies have been carried out to evaluate the cost of ACS management in clinical trials,6–8 real world data extracted from regional databases are only available for other EU Countries.3,9 The aim of this study was to evaluate healthcare resource consumption and average annual direct healthcare costs for the INHS for the treatment of patients with a recent hospital admission for ACS.

**Design and methods**

**Data sources**

The data-warehouse contained data on 2,758,872 subjects (5% of the total Italian population) and was gathered from the administrative databases of seven local healthcare units located in four different regions (Veneto, Toscana, Abruzzo and Puglia). Information was included on demographic characteristics, prescriptions of drugs reimbursed by the INHS, hospital discharge records, outpatient visits and diagnostic-therapeutic procedures. The age distribution of patients is similar to that of the whole regional and Italian population.

**Study design and data analysis**

In this retrospective observational study, the population of patients with a first hospitalization for ACS (defined as index event) during the period from 1 January 2008 to 31 December 2008 was selected and analysed for a 1-year follow-up period. Patients were divided in two groups by type of therapy received at index event, i.e. medical treatment or percutaneous coronary intervention (PCI).

The subpopulation treated with dual antiplatelet therapy (aspirin plus clopidogrel, the only antiplatelet available at the time of the analysis) was analysed separately because, according to recent guidelines, dual antiplatelet therapy should always be prescribed after an ACS episode.10–12

The following resource consumptions were evaluated: reimbursed drugs (source: public price reimbursed by the INHS for drugs distributed by pharmacies and real price to be paid by the INHS for drugs distributed via direct distribution or ‘distribution on behalf’; reference years 2008–2009), diagnostic-therapeutic procedures and outpatients visits (source: national and regional tariffs), and hospitalizations and 1-day hospital stays (source: Regional Health Service (RHS) tariffs for the supply of hospital care for the years 2008 and 200913).

The analysis was performed from the perspective of the INHS.

**Statistical analysis**

A nonparametric statistical hypothesis test (Wilcoxon–Mann–Whitney) was used to compare the average annual medical costs between women and men, whereas a nonparametric test (Kruskal–Wallis) was used to compare the average annual medical costs among age classes, rehospitalized versus not rehospitalized patients, and patients alive versus patients who died of an in-hospital CV event. The latter test was also applied to compare treatment methods at index event in the total population and in patients treated with aspirin plus clopidogrel.

**Results**

Within the total population of 2,758,872 subjects, 7082 (2.6‰ of the observed population) were hospitalized for ACS during the 1-year accrual period, 35.8% of whom were females. Age (mean ± SD) was 72 years (69 ± 12 years for men and 77 ± 12 years for women) and over 60% of the population was ≥70 years old. Age was a major discriminating factor between genders: about 50% of male patients were ≥70 years old, while the same age class included 75% of women.

Among patients with an index event of ACS, 60% (n = 4250) were medically treated, 33.1% (n = 2342) were treated with PCI, and 6.9% (n = 490) died during the first hospitalization. Patient gender is also
relevant in these populations. Women accounted for 40% of the medically treated patients, 25% of the PCI patients, and 51% of the patients who died at the index event. Accordingly, ages were different in the three groups (73 ± 12 years for medically treated, 67 ± 12 years for PCI patients, and 81 ± 11 years for patients who died during the index event).

Antiplatelet therapy was prescribed in 79% of patients; 26.8% of the total population was prescribed ASA alone. Dual antiplatelet therapy was prescribed in 41.6% of patients (25.9%, \( n = 1099 \), with medically treated ACS, and 70.1%, \( n = 1641 \), with PCI-treated ACS).

All-cause mortality after discharge from the index event until the end of the 1-year follow up was 12.2%, 66% of which due to CV reasons. During the follow-up rehospitalizations, death from all causes occurred in 9.7% of cases (CV death accounted for 52.3% of cases).

Kaplan–Meier survival curves by age class highlight that survival probability decreased with increasing age (Figure 1).

At least one rehospitalization occurred in 58.6% of cases (18.4% due to recurrent ACS episodes, 24.8% for other CV reasons, and 15.4% for non CV reasons).

**Resource utilization and costs**

The most frequently prescribed drugs at territorial level (excluding antiplatelet agents, drugs administered during index event hospitalizations, and drugs provided to patients upon discharge) were lansoprazole (53.4% of patients), ramipril (42%), atorvastatin (39.2%), furosemide (34.8%), bisoprolol (26.4%), and nitrates (25.8%).

For the total ACS population, the average annual direct healthcare costs per patient amounted to 11,464€/year; men were associated with a significantly higher mean annual cost than women (12,112€ vs. 10,307€, \( p < 0.001 \)). Hospitalizations were the major cost driver (more than 80% of total costs for both men and women) and resource consumption was proportionally similar between genders (Figure 2). Index event costs (almost entirely due to hospitalization) accounted for about 48% of total costs both in men and women.

The average annual costs by age groups were not significantly different except for patients older than 80 years (30% of the total population). This group had a 23% lower annual average cost than the weighted average cost of the previous age classes (9541€ vs. 12,347€, respectively; \( p < 0.001 \)) with a significant decrease in all cost items and in index event costs (Figure 3).

The average annual costs for patients treated with PCI at index event were significantly higher (30%) than the average costs of medically treated patients both in the total population (14,111€ vs. 10,862€, \( p < 0.001 \)) and in the population treated with dual antiplatelet therapy (13,776€ vs. 11,043€, respectively; \( p < 0.001 \)). Moreover, in the total ACS population, the costs of

![Figure 1. Kaplan–Meier survival curves by age class.](image)
**Figure 2.** Average annual cost per ACS patient by gender.

**Figure 3.** Average annual cost per ACS patients by age class.
index event in medically treated patients accounted for about 37% (4065€) of the total annual costs, while in patients treated with PCI at index event accounted for 60% (8405€) of total costs. During follow up, rehospitalization costs in patients treated with PCI at index event were 27% lower than in patients treated medically.

Patients treated with clopidogrel plus aspirin with a medically treated relapse of myocardial infarction had an average annual cost per patient of 14,651€ while those with a PCI-treated relapse of myocardial infarction had an average annual cost of 12,537€.

Finally, the average cost of patients who died of a CV event during hospitalizations in the follow-up period (median survival 180 days) and receiving at least one prescription of antiplatelet drugs during follow up was significantly higher than the average cost of patients who survive one year from the index event, both in the population as a whole (16,231€ vs. 12,287€, respectively; \( p < 0.001 \)) and in the population treated with ASA and clopidogrel (19,198€ vs. 12,673€, respectively; \( p < 0.001 \)).

A multivariate analysis performed on the total ACS population showed that variables explaining a higher expenditure were gender (male), PCI at index event, prescription of at least one antiplatelet agent, time of observation, and number of all-cause hospitalizations after index event (Table 1). However, a bivariate analysis of patients older vs. younger than 80 showed a highly significant cost reduction in the elderly (\( p < 0.001 \)), even though the other variables considered were more powerful in explaining an increase in expenditure.

### Discussion

In this study, the average age of the ACS population is slightly higher than the corresponding value reported in national \(^{14-16} \) and international studies; \(^{17,18} \) the increased percentage of women in the elderly population is supported by international evidence (CRUSADE registry \(^{18} \)).

The percentage of patients treated with PCI is lower in females (25% of women vs. 40% of men), which is in line with international evidence (CURE study \(^{19,20} \)); the limited use of revascularization procedures in females is also reported by a statement from the American Heart Association which found that, in the USA, out of a total of 1.2 million PCIs performed, only 33% involved women. \(^{21-25} \)

Considering patients discharged alive from the index event, 64% were medically treated and 36% were treated with PCI; if we consider the population \( \geq 70 \), the proportion of patients undergoing PCI was only 27% and this percentage decreased to 21% in the population \( \geq 80 \) years old. This finding is in line with a paper by Savinotto et al., \(^{26} \) which pointed out that, compared to younger patients, the elderly received less effective treatments and, in particular, fewer coronary reperfusion procedures despite their higher risk characteristics. Similar results were also found in the CRUSADE registry, \(^{18} \) which reported that PCI within 48 hours from the event was performed in 38.7% of patients \(< 65 \), 29.6% of patients 65–74 years old, 21% of patients 75–84 years old, and only 10.1% of patients \( \geq 85 \). Similar findings came from the BLITZ-2 study, where only 23% of elderly patients vs. 44% of younger patients were treated with PCI. \(^{27} \)

The average annual costs found in our study are generally lower than in US studies \(^{28-30} \) but comparable with other European data. \(^{3,9} \) In a Swiss study, the average cost per patient in the first year after an ACS event was 26,563 CHF \(^{3} \) (21,964€, exchange rate 0.8269 as of 2 December 2012) in 2008, whereas a Spanish study reported an average annual cost per patient ranging from 12,380€ to 22,750€ (including indirect costs); \(^{9} \) these studies also support the cost-driver role of hospitalizations found in our study. The differences versus US data were possibly due to the different healthcare settings (type of healthcare coverage), value of reimbursement for hospitalizations, drug prices, and analysis perspective.

The major limitations of this study are mostly related to the database structure; although a wide population was included, the database cannot be considered as fully representative of the whole Italian population. Furthermore, data regarding the drugs administered during hospitalizations were not available. However, administrative databases are a reliable tool for analysing the frequencies of prescription and costs to be paid by the healthcare services, despite the fact that they do not contain information on disease severity and appropriateness of treatment.

### Table 1. Multivariate analysis

<table>
<thead>
<tr>
<th>Total expenditure (hospitalizations, drugs, procedures, and visits)</th>
<th>Regression coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>(-0.06 (-0.09 to -0.03))</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age ( \geq 80 ) years</td>
<td>(-0.02 (-0.05 to 0.02))</td>
<td>0.40</td>
</tr>
<tr>
<td>Mortality</td>
<td>(-0.12 (-0.28 to 0.05))</td>
<td>0.17</td>
</tr>
<tr>
<td>PCI at index event</td>
<td>0.41 (0.37 to 0.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of hospitalizations</td>
<td>0.04 (0.04 to 0.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of the observation</td>
<td>0.003 (0.002 to 0.004)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription of at least one antiplatelet therapy</td>
<td>0.04 (0.003 to 0.07)</td>
<td>0.03</td>
</tr>
<tr>
<td>Constant</td>
<td>7.62 (7.24 to 8.00)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% CI.; PCI, percutaneous coronary intervention.
Considering that data recorded in administrative databases are limited to expenditure to be paid by the INHS, out-of-pocket expenditure and indirect costs were not included, which can justify an average cost per patient lower than in other recent studies.

In conclusion, this analysis showed that ACS patients had major direct healthcare costs and that hospitalizations were the most important cost driver. Significant differences were found in costs between men and women and between elderly and young patients. Considering that the population ≥80 years of age accounted for 30% of the ACS population and that the age of the general population is increasing, ACS-related expenditure is likely to grow in the next years despite the lower expenditure associated with the elderly.

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ARNO Cardiovascular Observatory


Conflict of interest

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References


