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Rehospitalization due to Cardiovascular Events in Secondary Prevention Patients Treated with Lipid-Lowering Therapies in Italy

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INTRODUCTION

- Cardiovascular (CV) disease, primarily atherosclerotic CV disease (ASCVD), is responsible for approximately 207,000 deaths in Italy (35% of all deaths annually)[1]
- ASCVD is associated with an increased risk of experiencing CV events[2,3] that have a significant impact on morbidity, mortality, quality of life, and healthcare costs. Coronary heart disease (CHD) is estimated to be the leading cause of disability in Europe, accounting for 13% of total disability-adjusted life-years[4]
- Lipid-lowering therapy (LLT) plays a key role in secondary prevention in patients with ASCVD. Studies have demonstrated that low-density lipoprotein cholesterol (LDL-C) is causally associated with CHD risk, and that reductions in LDL-C are associated with a proportional reduction in the risk of CV events
- Evidence of the clinical and economic burden of atherosclerotic CV events in patients treated with LLT in Italy remains limited. This study aims to provide that evidence using real-world data, serving as an important basis for further health economic analyses in Italy

OBJECTIVES

- To describe the ASCVD secondary prevention population in Italy using Health Information Systems
- To describe treatment with LLT in the 6 months after the first CV hospitalization
- To estimate 1-year CV event rates
- To estimate the yearly cost of healthcare resource utilization (HRU) before, and in the year after, the index event

METHODS

- This was a retrospective observational study using a claims database from the Marche and Umbria Local Health Unit 2 (Umbria 2) regions (1.8 million inhabitants) of Italy
- Patients were aged 18–80 years with one or more hospitalizations for acute coronary syndrome (ACS), ischemic stroke/transient ischemic attack (IS), or peripheral artery disease (PAD), and were discharged between 2009 and 2012 (Marche) or between 2011 and 2014 (Umbria 2)
- Patients must have received at least two LLT prescriptions (statins and/or ezetimibe) in the 365 days before and/or in the 180 days after the first CV hospitalization (the index event)
- Pharmacologic treatment for each patient was identified based on the last LLT prescription registered within the 6 months after the index event. LLT was classified as follows[5]:
  - High-intensity LLT: atorvastatin (40–80 mg) and rosuvastatin (20–40 mg), with or without ezetimibe
  - Low- and moderate-intensity LLT: other statin regimens or ezetimibe monotherapy
  - Untreated: patients not receiving any LLT
- Patients were followed for 1 year and the occurrence of hospitalizations for subsequent CV events (ACS, IS, revascularization, and in-hospital mortality) was recorded. 1-year CV event rates were calculated
- HRU data were collected in the year prior to the event to calculate baseline cost for use as a reference
- HRU was estimated, including hospitalizations, outpatient care, and pharmaceutical prescriptions registered in the year before (baseline) and after the index event. Costs were calculated using Italian National Health Service reimbursement tariffs[6,7]
- Results were stratified by type of index event (i.e. ACS, IS, or PAD)
- For Umbria 2, the last LDL-C measurement available within 1 year after the index event was collected to determine whether patients' LDL-C levels were controlled according to clinical recommendations at that time (LDL-C <70 mg/dL)[8]

RESULTS

- Overall, 17,881 patients with a history of ACS (56.3%), IS (22.7%), or PAD (21.0%) were included
- In total, 44.3% of patients received high-intensity LLT, 49.6% received low- and moderate-intensity LLT, and 6.1% were untreated during the 6 months after the index event (**Table 1**)

Table 1. Use of LLT by Index Event

Index event N (%)	Untreated	LMS	HI	Total N
ACS	356 (3.5)	3,574 (35.5)	6,133 (60.9)	10,063
IS	395 (9.7)	2,989 (73.7)	669 (16.5)	4,053
PAD	345 (9.2)	2,300 (61.1%)	1,120 (29.7)	3,765
Total	**1,096 (6.1)**	**8,863 (49.6)**	**7,922 (44.3)**	**17,881**

ACS, acute coronary syndrome; HI, high-intensity LLT; IS, ischemic stroke/transient ischemic attack; LLT, lipid-lowering therapy; LMS, low- and moderate-intensity LLT; PAD, peripheral artery disease

- Overall, the first-year event rate was estimated at 17.6 per 100 patient-years (PY). The event rate was higher for patients with PAD (28.4 per 100 PY), followed by ACS (15.4 per 100 PY) and IS (13.9 per 100 PY) (**Table 2**)

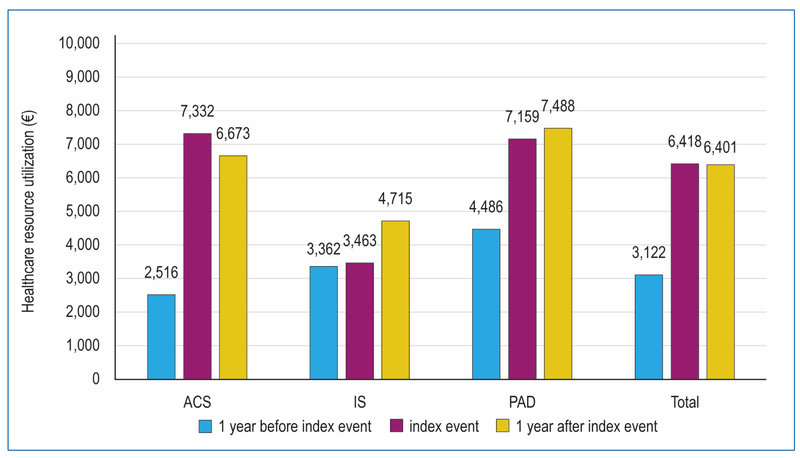
Table 2. One-year CV Event Rate

Index event N	Patients	Patient-years	Events	Event rate[a] (%)
ACS	10,063	8,898	1,374	15.4
IS	4,053	3,664	508	13.9
PAD	3,765	3,082	876	28.4
Total	**17,881**	**15,644**	**2,758**	**17.6**

[a]Event rate per 100 patient-years
ACS, acute coronary syndrome; CV, cardiovascular; IS, ischemic stroke/transient ischemic attack; PAD, peripheral artery disease

- HRU cost was estimated at €229.3 million: €114.8 million related to the index event and €114.5 million related to subsequent hospitalizations, drugs, and specialist visits during the following year
- Cost per patient was €12,819, comprising €6,418 (50.1%) corresponding to index event hospitalization and €6,401 (49.9%) incurred in the year after the index event (**Figure 1**)
- Baseline annual cost per patient was €3,122
- The economic impact due to the event could be estimated at €9,697 per patient in the first year after the index event

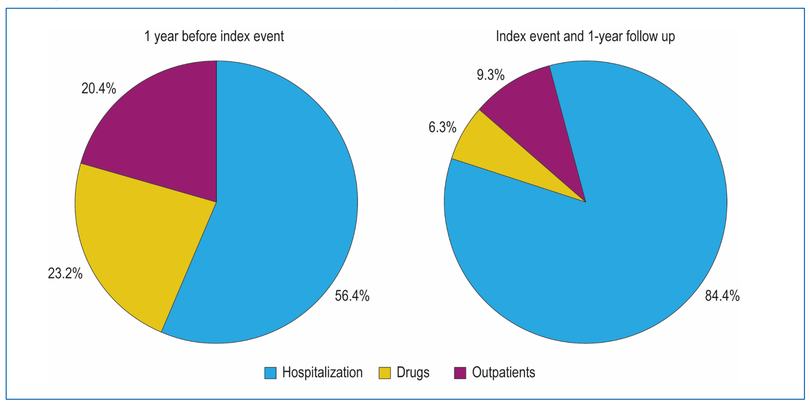
Figure 1. Costs in the 1 Year Before and After the Index Event



ACS, acute coronary syndrome; IS, ischemic stroke/transient ischemic attack; PAD, peripheral artery disease

- Higher costs (related to the index event and follow-up) were observed for the PAD and ACS cohorts (€14,647 and €14,005, respectively); the costs for patients with IS were significantly lower (€8,178)
- Most of the cost was related to hospitalizations, followed by pharmaceutical prescriptions and outpatient care
- The percentage of cost related to hospitalizations increased from 56.4% at baseline to 84.4% in the first year after the index event (**Figure 2**); this was due to the cost of hospitalization for the index event and the high number of rehospitalizations within 1 year

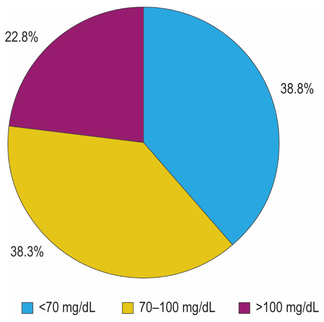
Figure 2. Distribution of Cost by HRU



HRU, healthcare resource utilization

- A preliminary analysis of achieved LDL-C levels in a subset of patients (n=788 [4.4%]) showed that only 38.8% achieved LDL-C <70 mg/dL, which was the recommended target level at the time (**Figure 3**)
- Using the current threshold of 55 mg/dL, the proportion of patients achieving target LDL-C levels would drop to 15.7%

Figure 3. Distribution of LDL-C Levels[a]



[a]This analysis included 788 patients only
LDL-C, low-density lipoprotein cholesterol

CONCLUSIONS

- A high proportion of patients are not adequately treated after a CV event and do not reach target LDL-C levels
- The rate of rehospitalization during the first year after the index CV event remains very high
- Costs related to HRU in the year after a CV event are four-times higher than costs in the previous year. Most of the HRU and costs in the year after the event are related to hospitalizations
- The high proportion of rehospitalizations and the high HRU and costs in these patients, despite LLT, highlights the need for improved patient care in this population with a substantial unmet need

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DISCLOSURES

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