In-hospital myocardial infarction and adherence to evidence-based drug therapies: a real-world evaluation

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ABSTRACT

Objectives This study aimed to measure adherence to chronic polytherapy following an acute myocardial infarction (AMI) and to find out associations between adherence and the setting of AMI onset (in vs out of hospital) as well as other determinants.

Design Retrospective follow-up study.

Setting Population living in the Lazio Region, Italy.

Participants This study included 25 779 hospitalised patients with a first diagnosis of AMI in 2012–2016, after the exclusion of those with hospital admission for AMI or related causes in the previous 5 years.

Primary and secondary outcome measures Patients were classified as in-hospital AMI (IH-AMI) or out of hospital AMI (OH-AMI) according to present-on-admission codes. Adherence was measured based on prescription claims during a 6-month follow-up after hospital discharge, using medication possession ratio (MPR). Adherence to chronic polytherapy was defined as MPR ≥75% to at least 3 of the following medications: antithrombotics, beta-blockers, ACE inhibitors/angiotensin receptor blockers and statins.

Results Among the entire cohort, 1 044 (4%) patients suffered IH-AMI. Overall, 15 440 (60%) patients were deemed adherent to chronic polytherapy. Female gender, older age, mental disorders, renal disease, asthma and ongoing concomitant treatments were factors associated with poor adherence. By contrast, patients with more severe AMI and those already taking evidence-based (E-B) drugs were more likely to be adherent. A strong association between the setting of AMI onset and adherence was observed: IH-AMI patients were 46% less likely to be adherent to E-B medications during their 6-month follow-up as compared with OH-AMI patients (OR 0.54; 95% CI 0.47 to 0.62; p<0.001).

Conclusion Pharmacotherapy is not consistent with clinical guidelines, especially for IH-AMI patients. Our findings provide evidence on a previously unidentified groups of patients at risk for poor adherence, who might benefit from greater medical attention and dedicated healthcare interventions.

INTRODUCTION

Most studies investigating acute myocardial infarction (AMI) epidemiology have target patients with AMI admitted via the community emergency medical system or through the emergency department (out of hospital AMI (OH-AMI)). Findings from these observational studies have informed risk factors and optimal treatment of AMI, contributing to a progressive reduction in overall mortality and risk of recurrent AMI worldwide.1,2 It is increasingly recognised, however, that there are patients whose symptoms onset of AMI begin after being hospitalised for other medical conditions.3,4 Little is known, in literature, about patients experiencing in-hospital AMI (IH-AMI). One such recent study focused on the incidence, risk factors and mortality outcomes related to IH-AMI.5 Regardless of the setting of onset of AMI, evidence-based (E-B) secondary prevention strategies are based on changes in lifestyle and E-B drug therapy. With this regard, international guidelines recommend the combined use of drugs belonging to different anatomical therapeutic chemical (ATC) groups including antithrombotic agents, β-blockers,
ACE inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and statins.  

Poor medication adherence after AMI is a world-wide problem, which compromises patient outcomes and increases patient mortality. Post-AMI survival benefit deriving from long-term adherence to guidelines recommended polytherapy has been clearly shown in literature.  

However, observational studies highlighted suboptimal use and poor compliance in the general post-AMI population and in specific subset of affected individuals.

Moreover, the transition of care from hospital to the community-based setting might also represents an important aspect to be taken into account when assessing medication adherence: patients discharged from a specialised hospital ward (eg, cardiology, cardiac surgery, coronary care units) were found to be associated with higher adherence rates. Typically, the hospital takes care of patients in the ‘first phase’ of follow-up period. After this period, patients are definitively managed by cardiologists in the community-based setting. However, different hospitals have different follow-up protocols, according to the length of follow-up period and frequency of evaluation. These differences in healthcare delivery generate heterogeneity in the population and raise equity issues in terms of quality and effectiveness of the transition care from the acute setting to the outpatient setting. For these reasons, our research hypothesis is that the setting in which AMI develops may significantly impact on the probability of being discharge by specialised hospital wards and, consequently, on the recommended therapeutic strategies and adherence to them.

Therefore, the main objectives of this study were: (1) to measure, in a real-world scenario, the adherence to chronic polytherapy following an AMI; (2) to identify determinants of adherence to E-B drugs specifically focusing on the potential association between setting of onset of AMI (ie, IH-AMI vs OH-AMI).

METHODS

Data sources

Our Department has access to health information systems of the Lazio region of Italy that contain mortality, hospital admission and drug claims data. We collected data from the Regional Hospital Information Systems (HIS), the Regional Admission and Discharge Information System (RAD), the Regional Healthcare Emergency Information System (HEIS), the Mortality Information System (MIS) and the Regional Drug Dispense Registry.

The HIS is an integrated information system designed to collect clinical and administrative information regarding hospital admissions for each patient discharged from public and private hospitals of the Lazio region. The HIS includes patients’ characteristics (single anonymous identifier, gender, date and place of birth, and place of residence); admission and discharge dates; discharge diagnoses (up to 6); procedure codes (up to 6) according to the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM); hospital admission and discharge ward and a regional code that corresponds to the admitting facility.

Since July 2008, tracking of additional information about hospital discharge record has been activated in the Lazio region thanks to RAD Information System (corporate decision nr. D4118). The ministerial directive of December 2010 establishes ‘the integration of the HIS with additional mandatory sections for the collection of additional information about hospital discharge data’. RAD collects additional information on comorbidities (eg, time to surgery, the presence of AMI diagnosis code at hospital admission time). This information is useful to characterise the severity of patient’s condition at the time of hospitalisation or surgery. These additional data are inserted into the RAD forms at the time of patient’s hospital discharge, when the diagnostic and therapeutic care pathways are clearly defined.

The HEIS includes all visits occurred in emergency departments of the Lazio region and collects patient demographic characteristics, admission information, visit and discharge dates and hours, ICD-9-CM diagnosis at discharge, reported symptoms on arrival, status at discharge (eg, dead, hospitalised or discharged at home) and triage score.

Information on drugs reimbursed by the national healthcare system and dispensed by public and private pharmacies or by hospital pharmacies at discharge is available from the Regional Drug Dispense Registry. The data available on each prescription include patient’s identification number, prescribing physician’s number, ATC code of the drug purchased, number of packs, number of units per pack, dosage, unit cost per pack and prescription date.

Any date of death was obtained from the MIS.

Data from different information systems have been integrated using a deterministic record linkage procedure based on unique and anonymous subject identifier. In this way, we created a chronological, demographical, residential, clinical and healthcare-related patient profile.

Setting and study cohort

The present observational study was based on the population living in the Lazio region, Italy. Using data from the regional HIS, the study included a cohort of all patients discharged from hospitals between 1 January 2012 and 31 December 2016 with a diagnosis of AMI. AMI was defined according to ICD-9-CM codes 410.xx (first or second diagnosis position). In case of multiple hospital admissions, the first admission during the study period was defined as the index admission. Subsequent hospitalisations for any reason were recorded, and repeated admissions within 2 days of discharge were regarded as one single ‘episode of care’.

Classification as to whether AMI occurred in-hospital was based on present-on-admission codes from RAD Information System, which provides information regarding
diagnostic codes (present, absent, presence cannot be deduced from clinical documentation, not applicable) at the time of hospital presentation. AMI patients with admission code diagnosis (present) were classified as OH-AMI, patients without admission code diagnosis (absent) were classified as IH-AMI. Admission code diagnosis (present or absent) was available in more than 98% of AMI patients. To improve identification of unambiguously IH-onset AMI, we excluded patients with unclear admission code diagnosis (‘presence cannot be deduced from clinical documentation’ or ‘not applicable’). In such manner, we should be able to reduce the possible misclassification of exposure due to critical situations, in which patients may have ambiguous diagnosis at the time of hospital admission.

Patients aged 18–100 years at discharge were screened for inclusion in the study. Only incident cases of AMI were included: patients with hospital admission for AMI or related causes (ie, percutaneous coronary intervention, bypass or surgery of the heart and great vessels) in the 5 years before index admission were excluded.

Patients who were not registered in the regional health assistance file at time of discharge from hospital were excluded (note that healthcare assistance in Italy is offered to all resident citizens without restrictions). Finally, patients who had an individual follow-up shorter than 30 days were excluded, to give all patients the chance to achieve clinical stability and to guarantee a minimum observation period of 1 month for consistently estimate adherence to polytherapy.

Patient and public involvement
No patient involved.

Patient characteristics
Patients were characterised according to sociodemographic factors (age, gender), comorbidities that might contraindicate prescription of specific ATC group drugs, previous use of E-B drugs, previous use of other (non-E-B) medications, previous hospitalisation with a diagnosis of mental disorders (ICD-9-CM codes: 290–319), hospital discharge ward and ST-elevation myocardial infarction (STEMI) as indicator of severity of disease. STEMI patients were identified using ICD-9-CM diagnosis codes 410.xx, excluding 410.7x (non-ST-elevation AMI) and 410.9x (acute AMI, not otherwise specified) in any diagnostic position. The following diseases were assessed by health ticket exemption or during hospitalisation or emergency department visit for index admission as well as in the 2 years preceding the beginning of follow-up: asthma (ICD-9-CM diagnosis code 493), renal disease (ICD-9-CM diagnosis codes: 582–588, V.42.0, V.45.1, V.56, ICD-9-CM procedure codes: 38.95, 39.95, 54.98, 55.6), sinoatrial bradyheartia (ICD-9-CM diagnosis code 427.8). These clinical conditions might contraindicate drug prescription of specific ATC groups due to potential adverse effects (eg, β-blockers in patients suffering from asthma).

We used the number of distinct, non-E-B drugs, prescribed in the 6 months preceding the beginning of follow-up as a crude measure of ongoing concomitant treatments. Medications with the same first five digits of the ATC code were considered as a group.

Moreover, to better define patients’ clinical profile, during the 6 months preceding follow-up initiation, information was also collected on the use of all E-B drugs: antithrombotic agents, β-blockers, ACEIs, ARBs and statins.

Follow-up
We evaluated medication use ‘immediately’ after the acute event, by analysing prescription patterns during the 6 months following discharge from the index admission. Follow-up started the same date of hospital discharge of the index episode of AMI. The end of follow-up coincided either with the end of 6-month follow-up, the date of death or with the date of all-cause hospitalisation whichever came first. The last ‘censoring’ criterion allows one to measure the net impact of the hospital that has discharged the patient on medication adherence without the potential interference of subsequent hospitalisations.

Definition of exposure and outcome
AMI were classified as IH-AMI or OH-AMI according to ‘present-on-admission’ codes retrieved using the RAD Information System which provides information regarding diagnostic codes (present or absent) at the time of hospital presentation.

The main outcome of the study was adherence to chronic polytherapy at 6-month follow-up. All drugs in this study were included in the patients’ healthcare plans and were equally available to all residents, in accordance with the universal healthcare coverage provided to residents of Italy. Information about prescriptions of antithrombotics (ATC: B01AC06, B01AC04, B01AC05, B01AC22, B01AC24, B01AF01, B01AF02, B01AF03, B01AA03, B01AA07, B01AE07), β-blockers (ATC: C07), ACEI/ARBs (ATC: C09) and statins (ATC: C10AA) were retrieved for all patients. Adherence to medication was measured through the medication possession ratio (MPR), calculated as the number of days of medication supplied during the follow-up on the basis of defined daily doses (DDDs) divided by the number of calendar days in the follow-up. Adherence to individual medications was defined as an MPR ≥0.75. Adherence to chronic polytherapy was defined as a MPR ≥0.75 for at least three of the four E-B drugs.

Statistical analysis
Data are presented as frequencies and percentages for categorical variables and mean value ±SD for continuous variables. Considering the hierarchical data structure (patients are nested within hospitals), logistic multilevel models were performed to take into account potential intraclass correlation. The variance components were expressed in terms of median odds ratio (MOR), a measure that quantifies the variability between clusters, in this
case between different hospitals of discharge. The MOR quantifies the variation between clusters by comparing two persons from two randomly chosen different clusters. Consider two persons with the same covariates, chosen randomly from two different clusters. MOR is the median odds ratio between the person of higher propensity and the person of lower propensity. This measure is always greater than or equal to 1. MOR equal to 1 indicates no variability between clusters, as the variability between group increases MOR value increases. \(^{20}\) In a first step, MOR was estimated using an intercept-only model. In a second step, MOR was estimated controlling for patient characteristics, to ensure that of the heterogeneity of patients within groups (in terms of age, comorbidities or severity of AMI) did not influence the estimates of variance.

Logistic multilevel models were also applied to identify determinants of adherence to E-B drugs, considering the correlation within clusters. Determinants of adherence were selected based on a priori knowledge\(^{21-22}\): gender and age, discharge ward, ST-elevation AMI, use of E-B drugs (ie, antithrombotics, β-blockers, ACEI/ARBs, statins) during the 6 months prior to the index admission (defined as at least one prescription), ongoing concomitant treatments (ie, number of distinct non-E-B drugs) and relevant comorbidities retrieved from the hospital records for both the index admission and the two previous years.

Results were expressed as OR, 95% CI and p values. Statistical analyses were carried out using Stata software, V.15 (StataCorp.2015: Release 15).

**RESULTS**

**The study cohort**

The flow chart in figure 1 shows the selection process of the study cohort. Of the 34 854 patients discharged from hospital with a first diagnosis of AMI between 1 January 2012 and 31 December 2016, 25 779 (74%) met the inclusion criteria and were enrolled in the present study. Mean age was 68 years, 17 138 (66%) were male (table 1). Overall, 11 108 (43%) of patients suffered an AMI with ST segment elevation and the largest number of patients 20 207 (78%) was discharged from cardiology wards. More than 65% of patients had at least a prescription of E-B medications (β-blockers, antithrombotics, ACEI/ARBs or statins) during the 6 months prior to the index admission. Overall, more than two-thirds of patients were receiving concomitant treatments at the time of AMI and the prevalence of these treatments showed a parallel increase with age.

Among the entire cohort, 1 044 (4.0%) patients suffered an IH-AMI. They were older, had more comorbidities (eg, renal disease, asthma and mental disorders) and less frequently had a diagnosis of ST-elevation AMI (31% vs 44%) compared with patients experiencing an OH-AMI. In addition, the use of at least one E-B medication before hospitalisation was greater among patients suffering an IH-AMI compared with OH-AMI (78% vs 66%). Patients suffering IH-AMI also showed a higher prevalence of ongoing concomitant treatments (number of distinct non-E-B drugs prescribed in the 6 months preceding the beginning of follow-up) and less likely were discharged from cardiology wards (48% vs 80%).

**Post-AMI adherence to E-B medications**

The adherence to E-B medications by gender and age group is reported in table 2. Statins were characterised by the highest adherence (78%), followed by antithrombotics (69%), ACEI/ARBs (63%) and β-blockers (50%). Lower adherence was observed among women, most notably for statins and antithrombotics (14% and 12% points lower than men, respectively). This gender difference was attenuated as age increased. Older age groups showed lower adherence to all medications. The adherence to each of the recommended drugs decreased markedly, for both males and females, moving from the age group ‘75–84’ to the group ‘85+’ years.

Overall, 15 440 (60%) patients were adherent to chronic polytherapy (as per protocol definition) following an AMI. However, only 6 463 (25%) patients were adherent to the full combination of E-B treatments considered in this study. Women were less likely to be treated with a combination of E-B drugs compared with males (51% vs 64%). This gender difference was less pronounced as age increased (table 3).

A strong variability in adherence to chronic polytherapy between different hospitals of discharge was observed, even after controlling for patients’ characteristics. As reported in tables 4 and 5 and a higher and statistically significant (p=0.0042) variability among discharge hospitals was observed for patients suffering IH-AMI (MOR 1.57; 95% CI 1.33 to 2.06; p=0.019) as compared with OH-AMI (MOR 1.46; 95% CI 1.33 to 1.64; p<0.001).

Using logistic multilevel model, determinants of adherence to chronic polytherapy were determined (table 6). A lower probability of adherence was observed.
This page contains statistical data and discussion on adherence to chronic polytherapy in women and elderly patients, as well as the impact of other factors such as age group, gender, renal disease, sinoatrial bradycardia, asthma, mental disorders, ongoing concomitant treatments, and E-B drugs use on adherence. The study cohort includes patients experiencing AMI in Lazio region between 1 January 2012 and 31 December 2016. The table highlights the adherence rates for IH-AMI and OH-AMI patients, showing significant differences. The discussion section explores the implications of these findings, suggesting potential strategies for improving adherence among hospitalised patients.
cohort selection in figure 1), the proportion of patients with IH-AMI of all patients with AMI was 4.0%. Our study has several key findings. First, compared with OH-AMI patients, those suffering IH-AMI were more often female, older, and less likely to be discharged from cardiology wards, possibly reflecting a higher burden of comorbidities. Indeed, IH-AMI patients had more often a history of renal disease, asthma, mental disorders and more frequently were treated with beta-blockers, antithrombotic agents, ACE-Is/ARBs or statins in the 6 months prior the index event. Interestingly, IH-AMI patients less frequently suffered from ST-elevation AMI. Much of these findings are concordant with the observations from a previous study by Zahn et al. In addition, Maynard et al. reported that patients who had AMI while hospitalised for other medical conditions were older, more likely to have atypical symptoms, and had higher rates of renal disease, cerebrovascular disease, congestive heart failure, diabetes mellitus, chronic obstructive pulmonary disease, dementia and cancer than patients who presented as OH-AMI to the Department of Veterans Affairs Health System.

Second, and possibly even more important, we observed that patients experiencing IH-AMI were less likely to be adherent to E-B medications for secondary prevention of AMI during 6-month follow-up. Moreover IH-AMI patients were more likely to be discharged from non-cardiological wards and this may have negatively impacted on the quality of care after the acute event.

Adherence to chronic polytherapy
Concerning the whole study period, we found that after a hospital discharge for AMI, only 60% of patients were deemed adherent to polytherapy in the following 6 months. Treatments with proven benefit in secondary prevention following AMI were underused in this study. This result is alarming if we consider that our definition of adherence was not very restrictive (ie, adherence defined as MPR ≥ 75% for at least three of the four predefined E-B drugs) and that adherence was evaluated only for the first 6 months after AMI (adherence should be greater in the initial stages of care and may decrease over time). Our findings are consistent with the results of other investigations, which reported unsatisfactory prescribing rates of E-B therapies after AMI during different time frames and in different countries. To the best of our knowledge, our study was the first to assess, whether adherence differed between patients who had IH-AMI as compared with those who experienced OH-AMI. Interestingly, the setting of AMI onset had a significant impact on polytherapy adherence. In fact, patients who had AMI during their hospital stay were less likely to be adherent to chronic polytherapy compared with patients who had AMI outside of the hospital. In

| Age group (years) | β-blockers (%) | ACEI/ARBs (%) | Antithrombotics (%) | Statins (%) |
|------------------|---------------|--------------|---------------------|------------|
| Males 18–54      | 55.20         | 62.50        | 77.18               | 87.74      |
| 55–64            | 54.41         | 68.83        | 78.00               | 88.37      |
| 65–74            | 51.44         | 68.64        | 74.20               | 83.74      |
| 75–84            | 45.18         | 61.81        | 65.80               | 73.83      |
| 85+              | 37.44         | 50.25        | 54.99               | 58.93      |
| Total            | 51.10         | 64.94        | 73.20               | 82.59      |
| Females 18–54    | 48.95         | 49.20        | 66.83               | 76.33      |
| 55–64            | 51.67         | 61.61        | 68.83               | 78.97      |
| 65–74            | 52.00         | 65.37        | 65.27               | 76.24      |
| 75–84            | 48.92         | 61.77        | 58.74               | 67.44      |
| 85+              | 40.21         | 53.99        | 51.69               | 51.15      |
| Total            | 48.34         | 59.90        | 61.03               | 68.81      |
| Whole cohort 18–54 | 54.13     | 60.21        | 75.39               | 85.77      |
| 55–64            | 53.84         | 67.33        | 75.99               | 86.41      |
| 65–74            | 51.62         | 67.59        | 71.33               | 81.34      |
| 75–84            | 46.93         | 61.79        | 62.50               | 70.84      |
| 85+              | 39.19         | 52.61        | 52.91               | 54.03      |
| Total            | 50.18         | 63.25        | 69.12               | 77.97      |

ACEI/ARBs, ACE inhibitors/angiotensin receptor blockers.
to multiple secondary prevention therapies for IH-AMI patients. This finding might reflect the lack of standardised and homogeneous clinical care pathways within hospitals of discharge for patients who have suffered AMI during hospitalisation for other medical conditions. Of note, estimates were adjusted for all variables identified as determinants of adherence to chronic polytherapy as such as age, gender, renal disease, sinoatrial bradycardia, asthma, mental disorders, ST-elevation AMI, ongoing concomitant treatments and E-B drugs use during the 6 months prior to hospitalisation. Although being discharge from a specialised hospital ward (eg, cardiology, cardiac surgery, coronary care units) was found to be associated with higher adherence rates, we decided not to adjust for discharge ward because we felt it could be a proxy for setting of AMI onset. IH-AMI patients were less likely discharged from cardiology wards (48% vs 80%) and this reflects a different care pathway for those compared with patients who had OH-AMI. In this situation, an adjustment for discharge ward, could have introduced (rather than eliminated) a bias (overadjustment).26

We also found that female gender, older age, mental disorders, renal disease, asthma and ongoing concomitant treatments were significantly associated with non-adherence to chronic polytherapy. Conversely, adherence was positively and significantly associated with patients who had a severe form of disease (ST-elevation AMI) and patients who have already begun E-B drugs in the 6 months before index admission.

Our findings are consistent with the results of other investigations. It is notable that the current study demonstrates that women are receiving less optimal medical therapy in all age groups and all drug categories. The clinical relevance of gender differences varies by age and type of medication. For example, small differences are observed in the use of beta-blockers, larger differences are observed in the use of statins. Smolina et al27 confirmed these gender differences and showed that treatment was less often initiated in women. Older age was also found to be associated with lower adherence in several previous studies.15 17 18 A higher prevalence of cognitive disorders, memory impairment and limited ability to absorb new information in the elderly population have been associated with lower adherence.28 Tuppin et al18 reported that adherence to E-B treatment was decreased significantly by an age greater than 74 years, confirming our findings. The prescription of complex regimens including multiple drugs has been widely acknowledged as a barrier to patient adherence29: the longer the list of drugs prescribed, the lower the adherence of patients. Chronic conditions like asthma, sinoatrial bradycardia and renal disease reduce drug prescription of specific ATC groups due to adverse effects and contraindications increasing the probability of poor adherence to chronic polytherapy. A previous hospitalisation with a diagnosis of mental disorders decreased the odds of adherence: the mechanisms by which mental disorders can affect adherence may include poor motivation, pessimism about treatment

| Table 3 | Adherence to chronic polytherapy by gender and age group |
|---|---|
| **Age group (years)** | **Males** | **Females** | **Whole cohort** |
| | **Adherence (%) (MPR ≥75% at least 3 of 4 E-B drugs)** | **Adherence (%) (MPR ≥75% for all 4 E-B drugs)** | **Adherence (%) (MPR ≥75% at least 3 of 4 E-B drugs)** |
| 18–54 | 67.95 | 32.20 | 64.13 |
| 55–64 | 70.53 | 32.47 | 64.71 |
| 65–74 | 67.12 | 27.72 | 64.10 |
| 75–84 | 54.05 | 20.12 | 51.49 |
| 85+ | 39.15 | 11.81 | 25.07 |
| **Total** | **64.13** | **27.66** | **51.49** |
| 18–54 | 65.19 | 30.71 | 59.89 |
| 55–64 | 68.47 | 31.06 | 59.89 |
| 65–74 | 64.47 | 26.71 | 59.89 |
| 75–84 | 52.66 | 19.16 | 59.89 |
| 85+ | 37.40 | 11.63 | 25.07 |
| **Total** | **59.89** | **25.07** | **59.89** |

E-B, evidence based; MPR, medication possession ratio.

A crude logistic multilevel model, IH-AMI patients were 53% less likely to be adherent as compared with OH-AMI patients (OR 0.47; 95% CI 0.41 to 0.54; p<0.001). After adjustment for potential confounders, this relationship was only slightly attenuated but remained strongly significant (OR 0.54; 95% CI 0.41 to 0.62; p<0.001). Moreover, we observed a greater variability in terms of adherence to multiple recommended secondary prevention therapies for IH-AMI patients. This finding might reflect the lack of standardised and homogeneous clinical care pathways within hospitals of discharge for patients who have suffered AMI during hospitalisation for other medical conditions. Of note, estimates were adjusted for all variables identified as determinants of adherence to polytherapy such as age, gender, renal disease, sinoatrial bradycardia, asthma, mental disorders, ST-elevation AMI,

| Table 4 | Variation between clusters for OH-AMI patients: the MORs |
|---|---|
| **Multilevel model** | **Level of analysis** | **Explanatory variables** | **MOR (95% CI)** | **P value** |
| Two-level regression | (Patients)—HoD | Intercept only | 1.71 (1.50 to 2.02) | <0.001 |
| Two-level regression | (Patients)—HoD | Patient’s characteristics | 1.46 (1.33 to 1.64) | <0.001 |

HoD, hospital of discharge; MOR, median OR; OH-AMI, out of hospital acute myocardial infarction.
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effectiveness, diminished attention, memory and cognition, decreased self-care and even intentional self-harm.\(^\text{30}\) Moreover, patients suffering from ST-elevation AMI or those who had already begun E-B drugs before index AMI were more likely to be adherent to chronic polytherapy. The former have had a more severe form of the disease and were probably more carefully monitored and made aware of the long-term benefits generated by a continuous and persistent drug treatment. The latter were already used to the chronic and continuous intake of those drugs that are recommended for the secondary prevention of AMI, as a sort of ‘inertial effect’.

### Table 5 Variation between clusters for IH-AMI patients: the MORs

| Multilevel model          | Level of analysis | Explanatory variables | MOR (95% CI)       | P value |
|---------------------------|-------------------|-----------------------|--------------------|---------|
| Two-level regression      | (Patients)—HoD    | Intercept only        | 1.69 (1.43 to 2.16) | 0.005   |
| Two-level regression      | (Patients)—HoD    | Patient’s characteristics | 1.57 (1.33 to 2.06) | 0.019   |

AMI, acute myocardial infarction; HoD, hospital of discharge; IH-AMI, in-hospital acute myocardial infarction; MOR, median OR.

### Table 6 Association between adherence to chronic polytherapy and symptom onset (IH-AMI vs OH-AMI), sociodemographics and clinical characteristics

| Category                        | Subcategory | OR   | 95% CI          | P value |
|---------------------------------|-------------|------|------------------|---------|
| Symptom onset of AMI            | OH-AMI      | 1.00 | –                | –       |
|                                 | IH-AMI      | 0.54 | 0.47 to 0.62     | <0.001  |
| Gender of patient               | Male        | 1.00 | –                | –       |
|                                 | Female      | 0.75 | 0.71 to 0.79     | <0.001  |
| Age group (years)               | (18–54)     | 1.00 | –                | –       |
|                                 | (55–64)     | 1.12 | 1.03 to 1.22     | 0.007   |
|                                 | (65–74)     | 0.98 | 0.90 to 1.07     | 0.618   |
|                                 | (75–84)     | 0.67 | 0.61 to 0.73     | <0.001  |
|                                 | (85+)       | 0.40 | 0.35 to 0.44     | <0.001  |
| Renal disease                   | No          | 1.00 | –                | –       |
|                                 | Yes         | 0.58 | 0.53 to 0.64     | <0.001  |
| Sinoatrial bradycardia          | No          | 1.00 | –                | –       |
|                                 | Yes         | 0.83 | 0.64 to 1.08     | 0.171   |
| Asthma                          | No          | 1.00 | –                | –       |
|                                 | Yes         | 0.51 | 0.37 to 0.69     | <0.001  |
| ST-elevation AMI                | No          | 1.00 | –                | –       |
|                                 | Yes         | 1.48 | 1.40 to 1.56     | <0.001  |
| Ongoing concomitant treatments  | (0–1)       | 1.00 | –                | –       |
|                                 | (2–4)       | 1.05 | 0.98 to 1.13     | 0.147   |
|                                 | (5–7)       | 0.92 | 0.84 to 1.00     | 0.055   |
|                                 | (8–10)      | 0.90 | 0.81 to 0.99     | 0.046   |
|                                 | (10+)       | 0.73 | 0.64 to 0.82     | <0.001  |
| E-B drugs use in the 6 months   | No          | 1.00 | –                | –       |
| before index admission (at least one prescription) | Yes         | 1.57 | 1.47 to 1.67     | <0.001  |
| Mental disorders                | No          | 1.00 | –                | –       |
|                                 | Yes         | 0.72 | 0.63 to 0.82     | <0.001  |

AMI, acute myocardial infarction; E-B, evidence based; IH-AMI, in-hospital acute myocardial infarction; OH-AMI, out of hospital acute myocardial infarction.
Using DDDs to calculate drug coverage, we run
ence to drug treatment was estimated on the basis of the
information on the prescribed daily doses and adher-
Moreover, our pharmaceutical database does not contain
information on the prescribed daily doses and adher-
drug treatment was estimated on the basis of the
DDD.32 Using DDDs to calculate drug coverage, we run
the risk of not accounting for the real-life dosing of a
drug when it is used for other than its principal indica-
Therefore, misclassification of drug utilisation may
have occurred because the dosage instructions were not
known, and the DDDs were used as the dosage assum-
However, in our study, we tried to overcome this
limitation by considering DDDs of beta-blockers reviewed
by a panel of physicians, seeing that in secondary preven-
tion post AMI, DDDs are prescribed at lower dosages than
the main therapeutic indication.
In addition, MPR method does not depend on whether
patients take their medication as prescribed but depends
on the prescription given by physicians. Although we
cannot be sure that patients actually took the drug,
collecting their medications from the pharmacy is a
reasonable indication of an intention to continue with
therapy; nevertheless, the results of adherence based on
claims data may be overestimated.
Finally, although all available potential confounders
were included in the models to adjust for differences in
patients’ characteristics, we cannot exclude that the lack
of more detailed clinical data might have caused unmea-
sured confounding. We tried to counteract this limit
by applying several restrictions to obtain a cohort with
patients that were as homogeneous as possible.

**CONCLUSIONS**
The availability of information systems offers the oppor-
tunity to monitor the quality of care and identify weak-
nesses in public healthcare systems. Although most
attention has been paid to patients with AMI admitted
via the community emergency medical system or through
the emergency department, AMI occurring during hospital-
isation for other medical problems is an important
clinical problem.
The results of our study show that, in clinical practice,
pharmaco therapy for secondary prevention of AMI is
not fully consistent with recommended clinical guide-
lines, especially for IH-AMI patients. Moreover, a strong
association between the setting of AMI onset and adher-
ence to multiple E-B drugs was observed. Our findings
provide evidence on a previously unidentified groups of
patients at risk for poor adherence, who might benefit
from greater medical attention and dedicated healthcare
interventions. The data strongly support the need for
continued efforts to improve adherence to chronic poly-
therapy post AMI. These findings could also stimulate
efforts to implement hospital strategies to give the same
‘attention’ to IH-AMI patients as OH-AMI patients. In
light of the impressive and highly significant impact of
the type of discharge ward on the adherence to chronic poly-
therapy, it is feasible that much of the ‘disadvantage’ of
IH-AMI patients is attributable to the discharge processes,
in particular through how far they support effective transi-
tions in and continuity of care. A range of policy tools
could be appropriate to reduce this gap, for example, by
planning differentiated healthcare transition interven-
tions according to the setting of AMI onset. However,
further studies are needed to confirm this association.

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the statistical methodology required for the analytic modelling, the interpretation
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the statistical methodology required for the analytic modelling, the interpretation
of results, and the writing of the article. DC contributed to the clinical interpretation
of results, and the writing of the article. MD and DF contributed to the design of
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| Symptom onset of AMI | β-blockers (%) | ACEI/ARBs (%) | Antithrombotics (%) | Statins (%) |
|----------------------|---------------|--------------|---------------------|------------|
| OH-AMI               | 50.24         | 63.85        | 69.88               | 78.78      |
| IH-AMI               | 48.66         | 48.95        | 51.15               | 58.72      |
| Whole cohort         | **50.18**     | **63.25**    | **69.12**           | **77.97**  |

ACEI/ARBs, ACE inhibitors/angiotensin receptor blockers; IH-AMI, in-hospital acute myocardial infarction; OH-AMI, out of hospital acute myocardial infarction.
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