

# **First one-year care pathway after Myocardial Infarction in 2018: prescription, medical care and medication adherence using a French health insurance reimbursement database**

Parcours de soins post infarctus du myocarde aigu en 2018 : suivi médical, prescription et adhésion médicamenteuse à partir de la base de données de remboursement de l'assurance maladie française d'Aquitaine

Short running title: one-year patient care pathway after acute myocardial infarction

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## Summary

**Background:** Myocardial infarction remained a major cause of morbidity and mortality. Guidelines have been published to optimize medical care and the latter involves the optimization of the care pathway and the hospital-city coordination

**Aims:** To describe the MI care pathway during the year following hospital discharge and the use and adherence to secondary prevention drugs.

**Methods:** A cohort study was conducted using data from the main French health insurance reimbursement database of the ex-Aquitaine region. The medical and pharmaceutical cares of hospitalized patients in 2018 were collected for 12 months. Medication adherence was assessed by using the proportion of days covered by the treatment and the persistence.

**Results:** 3,015 patients were included, and the mean age was 66. Almost 76% of the patients had a reimbursement for a BAS, BASI or AS treatment. The medication adherence is around 83% for aspirin and 75% for lipid-lowering drugs for the one-year persistence. During the same time, the proportion of days covered was sub-optimal. Almost 4% of the patients died after leaving hospital. 45% went to a cardiac rehabilitation center and 23% had at least one hospital readmission whatever the reason. The patients had a mean number of 11 general practitioner consultations during the year. Almost 41% of the patients did not have a consultation with a cardiologist and 38.4% had at least two consultations. Rehabilitation and general practitioner consultations were associated with adherence.

**Conclusions:** The new results provide clear information on the medical care environment of patients and help us improve care transition. A close collaboration between healthcare practitioners is very important in the early stages of outpatient follow up.

**Keywords:** myocardial infarction/Medication adherence/ Databases, Factual/ Insurance, Health, Reimbursement/health care/France, Care pathway

## Résumé

**Contexte :** L'infarctus du myocarde (IDM) reste une cause majeure de morbi/mortalité.

**Objectifs :** Décrire le parcours de soins de l'IDM en 2018 pendant l'année suivant la sortie de l'hôpital et l'utilisation et l'adhésion des médicaments de prévention secondaire.

**Méthodes :** Les patients hospitalisés pour un IDM en 2018 ont été identifiés. Leurs soins médicaux et leurs médicaments au cours des 12 mois suivants ont été analysés à partir de la base de données de remboursement de l'assurance maladie française de la région ex-Aquitaine. L'adhésion au traitement a été évaluée en utilisant la proportion de jours couverts par le traitement et la persistance.

**Résultats :** 3015 patients ont été inclus avec un âge moyen de 66 ans. Près de 76% des patients ont eu un remboursement pour un traitement BAS, BASI ou AS. La persistance à un an était de 83 % pour l'aspirine et 75 % pour les hypolipémiants, mais la proportion de jours couverts était sous-optimale. Près de 45 % des patients sont allés en centre de réadaptation et 23 % a eu au moins une réhospitalisation. 4% des patients sont décédés après retour à domicile. Les patients ont consulté en moyenne 11 fois un médecin généraliste dans l'année. Près de 41 % des patients n'ont pas eu de remboursement de consultation chez le cardiologue de ville et 38,5 % ont eu au moins deux consultations. La réadaptation et les consultations de médecine générale sont associés à l'adhésion médicamenteuse.

**Conclusions :** Ces nouveaux résultats pourraient nous aider à améliorer la transition des soins, et la collaboration entre les professionnels de santé impliqués dans un suivi ambulatoire.

**Mots clés :** infarctus du myocarde/ Adhésion médicamenteuse/ Bases de données/ Assurance maladie/ France, Parcours de soins.

## Background

Prognosis for patients with myocardial Infarction (MI) has improved over the past decade due to the use of guideline-recommended therapies, such as early revascularization, antithrombotic therapies and other secondary prevention measures [1–3]. However, few but regular studies convincingly and repeatedly showed the low short-and long-term adherence to treatment in the post-MI setting [4–7].

Non-adherence medication is a complex and multidimensional phenomenon precluding the achievement of therapeutic targets [8]. The discontinuation of the recommended post-MI therapy predisposes patients to serious thrombotic events, particularly myocardial infarction, and disease progression and destabilization [9–12].

Often, the studies on medication adherence only described a single aspect of this phenomenon, providing analyses of either its prevalence or consequences or its determinants and not the full aspect that is needed to have a more complete vision. Moreover, most of these studies have used data from 10 to 15 years ago [7,13,14] and there is a need to update it especially since the management of MI has constantly evolved and these previous studies do not reflect current practices.

The French health and reimbursement organizations recommend that strategy in preventing cardiovascular recurrence after hospitalization for myocardial infarction should be based on an optimal cardiovascular prescription at discharge, a cardiac rehabilitation in the weeks after hospital discharge, a regular follow-up every three months with the general practitioner and at least one consultation per year with a cardiologist [15, 16].

Cardiac rehabilitation (CR) program was associated with improved patient survival and a better long-term adherence. As the latest studies published data between seven to fifteen years ago showed that approximately 25% to 40% of the patients went to CR [17-19], it is also interesting to update the data and to see if the access to cardiac rehabilitation is better and definitely improve cardiovascular disorders.

During the first year after discharge, cardiovascular evolution and treatment are often reassessed and therapeutical education program may be proposed to patients. Thus, one may consider that patients are thoroughly followed during the first year after the cardiovascular event, a great part in hospital.

Few authors have reported on global care trajectory outhospital including adherence focus for the first year [4,7,20–22]. The aim of this study was to describe the whole and the most recent

available patient' acute myocardial infarction care pathway during the one year after hospital discharge and to describe their use and adherence to secondary prevention drugs.

## **Methods**

### *Study design and source of data*

A historical cohort study was conducted using data from the main French health insurance reimbursement database of the ex-Aquitaine region (southwest France) [23] in 2018. In this region, which includes approximately 5 % of the French population, 2.5 million patients are covered by this insurance.

### *Inclusion criteria*

Patients hospitalized for MI between January 1<sup>st</sup> and December 31<sup>st</sup> 2018, and followed-up after hospital discharge were selected whatever their medical becoming for one year, therefore until December 31<sup>st</sup>, 2019 maximum.

### *Assessment of medical conditions and drug reimbursed*

Identification of MI in the database was based on ICD-10 which allowed selection of patients hospitalized for MI and vascular endoprosthesis. These codes are identical in all French hospitals and are disease specific. The ICD-10 codes considered was I21: acute myocardial infarction [24,25].

Records for all patients included were reviewed for the 12 months- period following their event/hospitalization. Sociodemographic characteristics including age and gender were retrieved.

We also retrieved data to assess patients care pathway across the year: length of hospital stay, medication at discharge, medical care and medical events after discharge for a year and medication adherence during the study period for lipid lowering agents and aspirin.

The medical care for a year after discharge included: rehabilitation center stay, onset' delay for the first medical consultation in primary care, the number of medical consultations for general practitioners (Gps) and cardiologists, the number of reimbursement of drug prescription and onset' delay for the first reimbursement (in France the date of reimbursement is similar to the date of purchase).

The medical events for a year after discharge included hospitalization whatever the reason and/or death after hospital discharge regardless of the cause.

We described in Figure 1 the optimal care pathway after MI as published by the French health and reimbursement organizations as a common thread to present the results.

Drugs of interest were identified in the database according to their “Club Inter Pharmaceutique” (CIP) code which is a unique product identifier [26].

Classes were beta-blockers (Anatomical Therapeutic Chemical classification code: C07), antiplatelet agents (B01AC), lipid lowering agents (statins and ezetimibe or anti-PCSK9) (C10), angiotensin-converting-enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) with the ATC code C09.

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### *Statistical analysis*

We described the care pathway including all the variables presented above. Continuous variables were described with mean and 95% confidence intervals or median if the latter was different from the mean. Discontinuous variables were described with percentage.

The medication adherence was assessed for lipid-lowering agents and aspirin. Those are the two pharmacological classes of drugs that are most expected to be stable for one year regardless of the medical diagnosis. Indeed, the other classes of drugs included in the BASI treatment may vary according to diagnosis, prognosis, or tolerance thus medication adherence may be more difficult to interpret.

For lipid-lowering agents, we analyzed statins and/or ezetimibe adherence to consider the medical desire to treat hypercholesterolemia independently of statin tolerance.

Medication adherence was assessed by using two parameters: medication availability and persistence.

The medication availability is defined as the proportion of days covered during the period in which patients could have been on therapy. The medication availability (also termed proportion of days covered) was estimated using the “Continuous Multiple-interval measures of medication Availability” (CMA) definition [27–32]. The CMA is defined as the sum of the days of medication supplied divided by the number of days between the first fill and the last refill and assesses the number of days covered by treatment due to the purchase of medications. The theoretical days’ supply is calculated by dividing the number of units dispensed by the daily dose for the drug considered. The daily dose is the recommended dose per day for its main indication in adults. The CMA was assessed using a consensual cut-off at

80 %, *i.e.* 80% of the time covered by the medication-intake. A CMA lower than 80% was considered as unsatisfactory in several previous studies for treatment of cardiovascular diseases).

Persistence was measured as the duration of uninterrupted therapy on the patient's index product using the anniversary Model. The patient is deemed persistent for 1 year if she/he refills a prescription within a specific interval surrounding the anniversary of her/his first prescription [31,32].

The analysis of both persistence and medication availability allows to assess if patients continue their treatment for a long period (persistence) and to assess if the gap is not big enough to induce recurrences or worsening (medication availability) whatever the duration of the treatment.

Analysis was performed using SAS software version 9.1 for PC; the Student t and Chi tests were used.

At last, we assessed factors associated with medication adherence (CMA upper than 80%) (independent variable) and each explicative factor was firstly measured by an odds ratio (OR) using conditional univariate logistic regression. The level of statistical significance was set at 0.05 and the statistical uncertainty of the estimates was assessed by 95% confidence intervals (95% CI). Then variables with a level of statistical significance  $<0.05$  or  $p < 0.20$  and those clinically relevant were included in a matched multivariate logistic regression model. The final model was determined using a backward stepwise procedure, with 0.1 as the threshold for eviction from the model.

The one-year indicators were given excluding patients who died during the year.

### *Ethical considerations*

We performed an observational study on anonymous data. Thus, based on the French legislation, it did not need to be approved by an ethic committee, although this study did conform to the principles of the Helsinki Declaration.

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## Results

### *Baseline characteristics of the study population*

The study included 3,015 patients hospitalized between January 1<sup>st</sup> and December 31<sup>st</sup> 2018, in the Aquitaine region, with the diagnosis of myocardial infarction (MI) (ICD-10). The sex ratio was 2.1 with 32% of female and a mean age of 66 (median: 66, CI95% [65.4;66.4]). 37.6% (n=834) of the population was over 75 years old (Table 1).

We detailed the results below, following the patient care pathway described in the Figure 1 as a common thread.

### *Time course of Myocardial infarction care pathway*

#### *Hospitalization*

The mean duration of hospitalization was 6 days (median: 6, CI95% [6.0;6.3]) (Table 1).

#### *Medication at Discharge*

At discharge, 53.7% of the patients asked for a reimbursement (ask the pharmacist) of a combined prescription including betablockers, antiaggregant, lipid-lowering agents and ACE inhibitors (name as BASI treatment).

The Figure 2 details the percentage of prescription of the different pharmacological classes and the main combination found. Almost 78% had a betablocker prescription, 83.7% had a lipid-lowering agent prescription and 69% had an ACEi prescription. Almost all the patients had at least one antiaggregant or anticoagulant therapy (Table 2).

The median delay between discharge and drugs delivery was 0 day (Table 1) with 62% of the patients who buy their medication the day of hospital discharge and 83% in the week after hospital discharge.

#### *Medical care after discharge*

During the study period, 45.2% of the patients went to a cardiac rehabilitation center of whom 98.2% during the first three months. As compared to patients not referred to rehabilitation, patients that went to a cardiac rehabilitation were statistically younger (mean=63 vs. 66,  $p < 10^{-6}$ ), and the percentage of male patients was higher (71% vs. 65.5%,  $p = 10^{-3}$ ).

For a one-year period, the mean number of general physician consultation was 11, *i.e.* one a month and only 4% had less than 3 general physician consultations during the year.

The median delay between discharge and the first outhospital GP medical consultation was 6 days, (mean=26, CI95% [24.8-28.4]). Most of the patients had a GP consultation in the first week after discharge and another group of patients had a GP consultation about a month (see Supplementary files).

The median number of cardiologist consultation per patient was 2 per year. However, almost 41% % had no cardiological consultation in clinical setting during the year and 38.4% had two or more consultations (Table 1).

#### *Medical events after discharge*

During the study period, 22.7% of the patients were admitted to hospital whatever the reason with a median delay of 100 days (approximately three months). The percentage of death during the year after the initial hospital discharged for MI was 3.7% (mean and median delay = 4.6 months, CI95% [4-5]).

#### *Assessment of medication adherence*

For the study period, patients also went to the pharmacy once a month to buy their medications.

At the end of the year, 83.1% of patients still use low dosage of aspirin (rate of persistence= duration of uninterrupted therapy) and for the remaining 16.9%, the treatment's purchase was not found in the database. During the same period 64.2% of the patients have taken at least 80% of their dose of aspirin (proportion of days covered  $\geq 80\%$ ) with a mean delay between two refills of 37 days although size of medication's packagings is scheduled to last 28 to 30 days.

At the end of the year, 75% of patients still used lipid-lowering agents (statin or ezetimibe) and for the remained 25%, the treatment' purchase was not found in the database. During the same period 69.4% of the patients have taken at least 80% of their dose of medication (proportion of days covered  $\geq 80\%$ ) with a mean delay between two refills of 48 days but this data is not interpretable due to the existence of both boxes of 30 and 90 units of this class of drugs.

There was a statistically positive association between non-adherence to lipid-lowering drugs and non-adherence to aspirin with correlation for 67% of the patient ( $p < 10^{-6}$ ).

During the year, almost 14.5% (n=438) of the patients had a reimbursed prescription for oral anticoagulant and 92.2% of the 14.5% had a refill. In this population, 63.4% (CI95% [58.6-68.1]) still used oral anticoagulant at the end of the study period.

*Factors of medication adherence for aspirin and statins*

In univariate analysis, 86% of the adherent patients to low-dosage aspirin (LDA) had at least 6 GPs consultations that year vs 69.4% for non-adherent LDA patients ( $p < 10^{-5}$ ) and 48% went to cardiac rehabilitation center vs 38% for non-adherent LDA patient ( $p < 10^{-6}$ ).

Considering adherence to lipid-lowering agents, in univariate analysis, 87% of the adherent patients had at least 6 GPs consultations that year vs 75.5% for non-adherent patients ( $p < 10^{-14}$ ) and 50% went to cardiac rehabilitation center vs 38% for non-adherent patient ( $p < 10^{-8}$ ).

Seven variables were included in the multivariate logistic regression model as the result of univariate analysis: age, gender, rehabilitation center, number of general practitioner consultation during the year, number of cardiologist consultation during the year, delay of first medication delivery and delay of first medical consultation.

In multivariate analysis, a rehabilitation program, a low delay of first consultation and the mean number of medical consultations per year were associated with aspirin adherence. For statin adherence the delay of first medication's delivery was also associated (Tables 3 and 4).

## Discussion

The originality of this study was to describe the recent (2018) patient's care pathway in primary care after discharge from hospital for myocardial infarction. We described the recent patient' MI medical and pharmaceutical care pathway for a year and described their use and persistence of secondary prevention drugs. To our knowledge, no study has recently investigated such a global outcome.

There are 6 important findings:

- i. Most patients purchased cardiovascular therapy with 75.8% of the patients with a reimbursement for a BAS, a BASI or a AS treatment. However, 16.3% have not purchased a lipid-lowering agents. Almost all the patients had at least one antiaggregant or anticoagulant therapy
- ii. Most of the patients collect their medication immediately after discharge.
- iii. 45.2% of the patients went to a rehabilitation center.
- iv. Patients consult their GP early and extensively as soon as they leave hospital (mean of one per month), almost 41% of the patients did not have a consultation with a cardiologist during the year and 38.4% had at least two consultation per year.
- v. The medication adherence is suboptimal during the first year, with 17% of the days where the aspirin treatment is not taken and 25% of the days without taking lipid-lowering drugs.
- vi. Optimal medication adherence was statistically associated with a stay in a rehabilitation center and well associated with the number of medical consultations. Depending on the drug, the delay between the 1<sup>st</sup> GP consultation and the hospital discharge can be positively or negatively associated and is well associated with delay of first medication delivery. There were no association with age and gender.

Our results for medication at discharge are similar to previous published studies even if the temporality of the studies carried out and methods to analyze medication adherence are not fully comparable. Their percentages of betablockers and statins prescription were around 82 to 85% [12,22] except for Blin *et al* [13] with 92% and almost 99% with one or two antiaggregant or anticoagulants. In their recent article, Dibao-Dina *et al* [33] found that the reason for non-prescription of betablockers is due to medical contraindications (bradycardia, COPD...). For statins, the reason is well known, patients are afraid of side effects and

perceived side effects, and sometimes, do not purchase it even if it has been prescribed [34]. Non-prescription may also result from a concerted choice between doctor and patient. Considering medication adherence, our results with 81% of aspirin persistence and 75% of statin persistence are slightly higher than previous studies assessing persistence where results varied from 45 to 65%. The proportion of days covered  $\geq 80\%$  ranged around 65% is similar to previous studies that went from 56% to 72% depending on the duration of the study [5,7,9]. However, it is difficult to compare as methods used to define persistence or study periods are different. One may conclude that medication adherence remains suboptimal across time.

The delay between MI hospital discharge and purchase of medication was very optimal. We did not find previous published studies to compare this parameter.

The percentage of cardiac rehabilitation program (CR) of 45% in our study is known to have a beneficial effect on patient survival [17] and is similar to other recent studies with a percentage of 41% who attended at least half of the sessions in the EUROASPIRE IV survey [35,36], and almost 37% for Gabet *et al* [19] 44% for Dibao-Dina *et al* [33] and Puymirat E *et al* [37]. This percentage was higher than most older studies such as FAST-MI 2005 and the French nationwide PREVENIR in 1998 with 22 % to 24 % [17,18] suggesting an improved access to cardiac rehabilitation for the last ten years. Our recent results confirm the impact of CR on medication adherence.

There is a high number of general practitioners (GPs) medical consultations over the first year after MI with a mean of one a month. There are several possible explanations. The social health insurance system allows patients to regularly visit their GPs without most of the time paying and advancing the costs of the consultation and French people are used to seeing their GPs regularly. Moreover GPs may want to be able to follow their patients frequently during their first year after MI. However as cardiovascular risks have been assessed and treated in hospital after their MI and that mostly half of the patients went to rehabilitation center in the first three months, one may consider that there is no need for GPs' consultation in the first three months. Moreover, our results showed that the impact of medical consultation on medication adherence is extremely low while this induces reimbursement costs for health insurance. The patients return every month to the pharmacy for the medication which may be due in part to every month GPs consultation and the prescription of a month period treatment. However, the packaging is changing and last up to three months in France and we may hope that the number of medical consultations will be reduced.

In our study, mortality after discharge is comparable with previous studies that published a six-month mortality of approximately 5% [7,33]. It remains lower than another study with 10% for a year for Blin *et al* [13]. It may be explained by different inclusion criteria.

### Strengths and limitations

Due to the use of a reimbursement database, this historical study has the advantage of not altering the behavior of either prescribers or patients. As adherence is a multifaceted question, two standardized parameters were used. These have been extensively discussed in the literature [38]. One factor that may be debated is the use of 80% treatment coverage as the cut-off for assessing adherence. This is commonly used in literature, yet it may not be appropriate for all types of drugs [39]. However, this cut-off of 80% is commonly used for cardiovascular studies. We can easily consider that below this threshold, there is a problem with pill taking and medication efficacy.

A study conducted using a reimbursement database suffers from some limitations. The results presented are likely to be an overestimation of adherence since some patients who buy their treatment, may not take it. Patients may have been classified as having discontinued if they moved outside the administrative region (Aquitaine) but this can be considered as only marginal as the population over 50 years old is geographically quite stable. Discontinuation for financial reasons is also improbable owing to the extent of the national health insurance system, which offers full coverage for underprivileged and unemployed people. Conversely, the cost of cardiovascular drugs is high enough to practically preclude claims for reimbursement not to be made and the electronic system used in France for reimbursement (SESAM-ViTALE) [23] guarantees the exhaustive capture of deliveries in the database in real-time. Moreover, MI belongs to the French list of chronic diseases ("Affections de longue durée" or ALD) for which the national health insurance funds reimbursement at 100% of expenses. Patients may ask to be registered as a patient with MI on this list in order to not pay [40].

### Conclusions

The new results provide clear information on the medical care environment of patients and help us improve care transition. A close collaboration between healthcare practitioners is very important in the early stages of outpatient follow up. Moreover these results concerning adherence and higher medical care plead for the development of therapeutic patient

education in order to optimize the patients' implication in their chronic disease. This will help limit medical costs, which aren't always completely effective.

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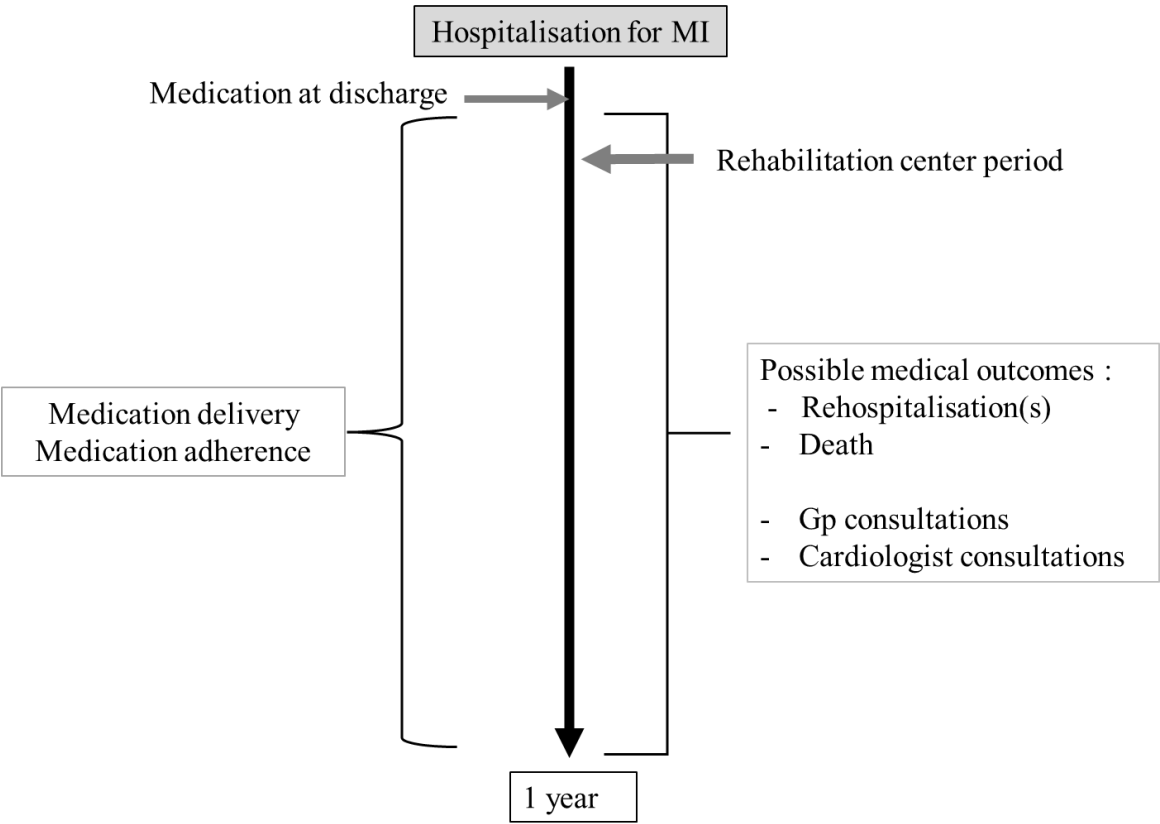
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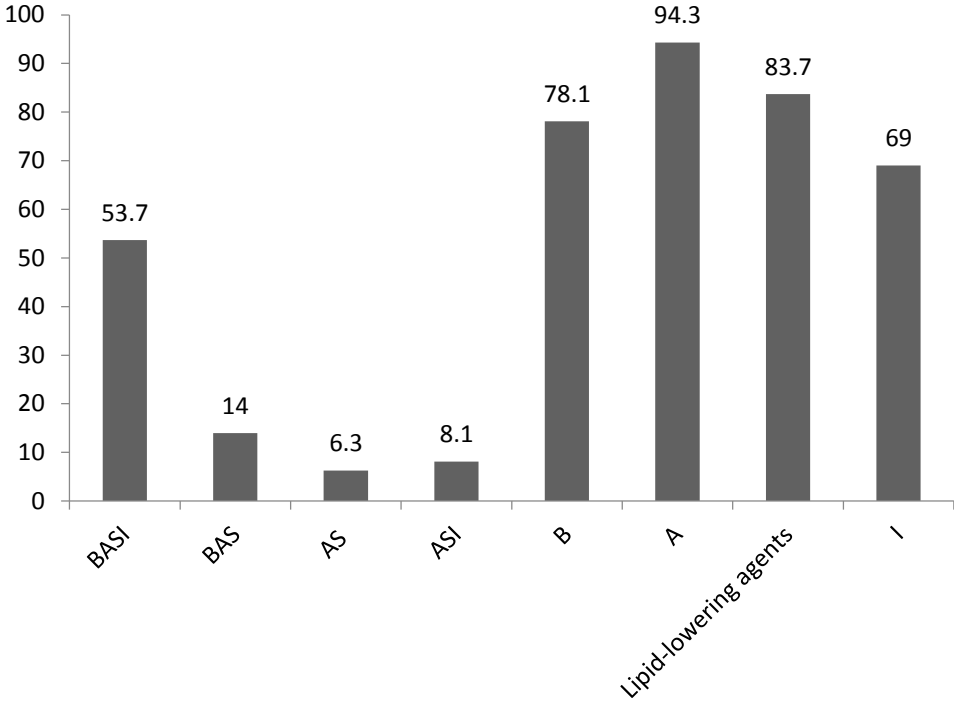
**Figure 1: Care pathway after MI according to the French health and reimbursement organizations and possible medical outcome**



**Table 1: Characteristics of patients hospitalized for myocardial infarction and included in the study and main medical follow-up outcome results**

	<b>Total n=3,015</b>	<b>CI<sub>95%</sub></b>
<b>Demographic characteristics</b>		
Mean age	65.9	65.4 - 66.4
Sex ratio <sub>M/F</sub>	2.1	-
<b>Main medical follow-up outcome results</b>		
Mean duration of hospitalization in days	6	6.0 - 6.3
Rehabilitation center (%)	45.2	43.5 - 47.0
Rehospitalization in the year (%)	22.7	21.2 - 24.3
Death (%)	3.7	3.1 - 4.5
Mean delay (in months)	4.6	4 - 5
Mean number of General Practitioner consultations in the year		
Median	11	-
Mean	10.7	10.6 - 10.9
Mean number of cardiologist consultations in the year		
Median	2	-
Mean	3.3	3.2 - 3.4
Percentage of cardiologist consultation in the year		
0	40.9	-
1	20.7	
2	10.2	
3	8.6	
More than 4	19.6	
Median delay between discharge and drugs delivery (in days)		
	0	-
Delay between discharge and the first outhospital GP medical consultation (in days)		
Mean	26	24.8 - 28.4
Median	6	-

**Figure 2: Percentage of prescription reimbursed at discharge**



**Table 2: Antiagregants and anticoagulants treatments characteristics at discharge**

	<b>n</b>	<b>%</b>
Aspirin alone	255	8.5
Others antiagregants (AAG) than aspirin	173	5.7
Anticoagulant (OAC) alone	44	1.5
At least one AAG or OAC	2,886	98.6
At least one antiagregant (AAG)	2,842	95.7
Biantiagregant therapy	2,214	73.4
Single antiagregant+OAC	62	2.1
Biantiagregant+OAC	137	4.5

**Table 3: Multivariate regression analysis for aspirin adherence**

<b>Attribute</b>	<b>OR</b>	<b>Low</b>	<b>High</b>	<b>p</b>
Medical readaptation	1.30	1.07	1.59	0.008
Number of general practitioner consultation	1.17	1.14	1.18	$< 10^{-6}$
Delay for first consultation	1.004	1.002	1.006	$10^{-4}$



**Table 4: Multivariate regression analysis for lipid-lowering drug adherence**

<b>Attribute</b>	<b>OR</b>	<b>Low</b>	<b>High</b>	<b>p</b>
Medical readaptation	1.53	1.27	1.84	$10^{-5}$
Number of general practitioner consultation	1.16	1.13	1.19	$10^{-6}$
Delay of first medical consultation	0.97	0.96	0.98	$< 10^{-6}$
Delay of first medication delivery	1.04	1.03	1.05	$< 10^{-6}$