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# American Journal of Preventive Cardiology

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## Do sex and gender aspects influence non-adherence to secondary prevention measures after myocardial infarction?

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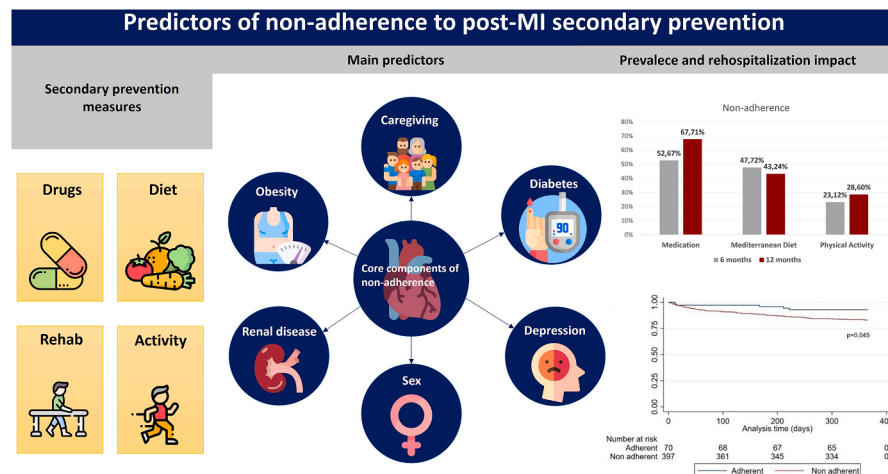
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### GRAPHICAL ABSTRACT

Visual summary: predictors of non-adherence to secondary prevention measures in patients with acute myocardial infarction. Summary of the main results. This figure shows the main predictors of non-adherence to secondary prevention: chronic kidney disease, female sex, high body mass index, symptoms of depression, family caregiver burden, and diabetes mellitus with organ damage. Adherence to all secondary prevention measures (Mediterranean diet, physical activity, and medication) was associated with a lower risk of hospitalization, as shown in the survival curve.



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<https://doi.org/10.1016/j.ajpc.2024.100713>

Received 9 March 2024; Received in revised form 24 July 2024; Accepted 28 July 2024

Available online 3 August 2024

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## ARTICLE INFO

## Keywords:

Secondary prevention  
Females  
Therapeutic Adherence  
Myocardial Infarction

## ABSTRACT

**Objective:** This study aimed to determine the prevalence of non-adherence to preventive interventions, its clinical consequences, and factors associated with non-adherence to secondary prevention measures, with a special emphasis on sex and gender.

**Methods:** Prospective observational study of patients hospitalized for acute myocardial infarction (AMI) in whom an evaluation of adherence to medication, Mediterranean diet, physical activity, and cardiac rehabilitation was performed after 6 and 12 months, with systematic assessment of predictors including patient-, disease-, psychological-, social-, and gender-related factors using self-administered questionnaires.

**Results:** Of 503 patients included, 101 (20,1%) were females. At one year, 85% of patients did not adhere to at least one of the recommendations with no differences between females and males. However, two factors more frequent in females, caregiver burden (adjusted OR, 1.45; 95%CI, 1.08-1.94) and depressive symptoms (adjusted OR, 1.40; 95%CI, 1.03-1.92) predicted non-adherence to all measures together. Chronic kidney disease (aOR, 3.24; 95%CI, 1.02-10.48) and being female (aOR, 2.21; 95%CI, 1.18-4.13) were associated with non-adherence to the Mediterranean diet; diabetes with organ damage (aOR, 12.06; 95%CI, 1.93-7.69) and older age (aOR, 0.96 per year; 95%CI, 0.93-0.99), among others, with physical activity; and higher body mass index with cardiac rehabilitation participation (aOR, 1.07; 95%CI, 1.002-1.14) and completion (aOR, 1.14; 95%CI, 1.03-1.26)

**Conclusion:** Adherence to all secondary prevention measures after AMI remains very low and is associated with several gender-related factors. Multidisciplinary intervention strategies targeting the most vulnerable patient groups, such as females or patients with diabetes, obesity, chronic kidney disease, or depression, are warranted.

## 1. Introduction

The death rate from acute myocardial infarction (AMI) has been declining in developed countries over the past few decades [1]. This decline has been attributed to the widespread adoption of effective therapeutic options, including percutaneous coronary intervention (PCI) and post-discharge pharmacological and non-pharmacological treatments (secondary prevention measures) [2]. Adherence to secondary prevention measures, both pharmacological and non-pharmacological, plays a key role in improving short- and long-term mortality and morbidity [3]. However, adherence to lifestyle recommendations and evidence-based cardiovascular medications after AMI is low [4].

Comorbidities, polypharmacy, and patients' limited understanding of the reasons for and benefits of prescribed medications are some of the barriers that hinder adherence. Psychosocial factors, including personality traits, coping styles, self-perception, illness beliefs, mental health disorders, and social factors such as family dynamics, and economic circumstances, can influence medication adherence [5].

Secondary prevention measures remains suboptimal, particularly among females after AMI [4,6,7]. However, it is still unclear whether the lower adherence of females to secondary cardiovascular prevention is due to biological sex or other gender-related factors [7,8].

The objectives of this study were: 1) to determine the prevalence of non-adherence to preventive interventions, including prescribed medications and lifestyle recommendations (diet and physical activity), at 6 and 12 months, as well as cardiac rehabilitation and its clinical consequences (risk of rehospitalization); 2) to identify the factors associated with non-adherence to each specific recommendation, with particular attention to sex and gender-related aspects.

## 2. Methods

## 2.1. Design and participants

An observational study was conducted in a tertiary hospital in Madrid, Spain. The study population consisted of patients aged  $\geq 18$  years who were admitted for AMI with obstructive coronary artery disease (CAD) and treated with percutaneous coronary intervention (PCI). The recruitment period was May 2019 to June 2021. Only participants who agreed to participate in the study and met the inclusion criteria, such as having a satisfactory level of Spanish language comprehension and expression, and adequate cognitive function, were included. Individuals with cognitive impairments that would affect their ability to interact were excluded from the study. The patients were

followed-up prospectively at 6 and 12 months after AMI.

## 2.2. Variables and measures

All participants underwent a standardized assessment protocol during hospitalization that included a comprehensive set of validated questionnaires that were self-administered on paper during their stay in the cardiology ward, including sex, anthropometric data, psychosocial variables, biomedical variables, relevant cardiovascular risk factors, lifestyle factors, gender-related factors (such as domestic and family care workloads, by measuring the intensity, frequency, and duration of these types of care), comorbidities, and sociodemographic (see Supplementary Table 1). The variables were classified into five dimensions of risk adherence according to the World Health Organization (WHO) classification [9]: patient-related, disease-related, sociocultural and economic (including gender-related factors), therapy-related, and health-provider-related factors.

During hospitalization, patients were routinely provided with information about their medications, dietary recommendations, and physical and cardiac rehabilitation prior to discharge, in accordance with clinical guidelines, by the medical and nursing team [10]. Adherence to these three secondary prevention measures (medication, diet, and physical activity) was assessed via telephone interviews during follow-up using internationally validated questionnaires:

- Medication: Morisky-Green-Levine (MGL), which allows the classification of patients into adherent and non-adherent groups, with those scoring less than 4 being classified as non-adherent [11].
- Mediterranean Diet (MD): 14-point Mediterranean Diet Adherence Screener (MEDAS); patients with a score of less than 9 were classified as non-adherent [12].
- Physical Activity (PA): International Physical Activity Questionnaire (IPAQ). It allows individuals to be classified into three categories: physical activity intensity (low, moderate, or high). According to the questionnaire specifications, those in the low category were considered non-adherent [13].

Participation in and adherence to cardiac rehabilitation (CR) was assessed using direct questions in the interviews. Patients who started but did not complete CR were considered non-adherent, and patients who did not start CR were considered non-participants. A combined endpoint of three adherence measures, diet, physical activity, and medications was calculated. Patients who did not adhere to the entire treatment were identified based on data indicating non-adherence to at

least one of the three measures. To evaluate the impact of non-adherence, rehospitalization data were obtained from medical records. The data were collected only from patients who were alive at follow-up, as adherence was measured only during this period.

### 2.3. Statistical analysis

With an estimated medication compliance rate of 50% in patients with myocardial infarction and an estimated loss to follow-up rate of 20%. The alpha risk was set at 0.05, and a precision of 5% was assumed. Based on these parameters, a sample size of 481 participants was calculated.

Categorical variables were presented as frequencies and percentages, and continuous variables were presented as means and standard deviations. Normality of the distribution of continuous variables was analysed using the Shapiro-Wilk test. Univariate and multivariate logistic regression analyses were performed to determine the effects of patient-related factors, disease-related factors, sociocultural and economic factors, therapy-related factors, and health provider-related factors on the likelihood of non-adherence to secondary prevention measures (medication, Mediterranean diet, physical activity, and cardiac rehabilitation). The variable selection method for the multivariate analysis was based on a sequential inclusion and exclusion method, with a p-value of <0.05 for inclusion and >0.1 for exclusion, keeping age, sex, and type of myocardial infarction (STEMI vs NSTEMI) fixed in the models. The cardiac rehabilitation prediction models were constructed using multinomial logistic regression, with adjustments made for age, sex, marital status, employment status, and level of education. The same variable selection criteria were employed in all cases. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated.

A non-adjusted Cox regression model was used to assess the clinical impact of non-adherence to each secondary preventive measure and the combination of measures on the hospitalization hazard rate for any cause. Statistical significance was set at  $p < 0.05$ . All statistical analyses were performed using STATA software version 17 (StataCorp LLC).

### 2.4. Ethics

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Hospital Universitario 12 de Octubre (internal code 19/047). Written informed consent was obtained from all the participants prior to their inclusion in the study.

## 3. Results

The study included 503 patients with AMI, of whom 402 (79.9%) were males and 101 (20.1%) were females, with a mean age of  $58.8 \pm 10.4$  years. ST-segment elevation myocardial infarction (STEMI) was present in 66.1% of patients. Most of the patients were Caucasian (all demographic and comorbidity profiles are shown in Table 1). At 6 months, 6.4% (n=32) were lost to follow-up (2.2%, n=11 deaths) and 10.1% (n=51) were lost to follow-up (3%, n=4 deaths) at 12 months.

### 3.1. Prevalence of non-adherence and clinical consequences

The rate of non-adherence to medications was 52.7% at 6 months and 67.7% at 12 months (Fig. 1). Among non-adherent patients, 15.1% had at least one hospitalization compared with 13.8% of adherent patients (HR, 1.09; 95%CI, 0.64-1.84) (Fig. 2D).

The rate of non-adherence to the Mediterranean diet was 47.7% at 6 months and 43.2% at 12 months (Fig. 1). Among non-adherent patients, 19.1% had at least one episode of hospitalization compared with 12.9% of adherent patients (HR, 1.52; 95%CI, 0.96-2.40) (Fig. 2C).

The rate of non-adherence to PA recommendations was 23.1% at 6 months and 28.6% at 12 months (Fig. 1). Among non-adherent patients, 19.9% had at least one episode of hospitalization compared with 13.9%

**Table 1**  
Sociodemographics, comorbidities and lifestyle risk factors.

	Male (N = 402) Mean (SD) / n (%)	Female (N = 101) Mean (SD) / n (%)	Total (N = 503) Mean (SD) / n (%)
Age	57.70 (9.50)	63.04 (12.32)	58.77 (10.34)
<b>Ethnicity</b>			
Caucasian	379 (94.28%)	94 (93.07%)	473 (94.04%)
Others	23 (5.72%)	7 (6.93%)	30 (5.96%)
<b>Nationality</b>			
Spanish	342 (85.07%)	89 (88.12%)	431 (85.69%)
Non-spanish	60 (14.93%)	12 (11.88%)	72 (14.31%)
<b>Marital status</b>			
Single	48 (11.94%)	13 (12.87%)	61 (12.13%)
Married	255 (63.43%)	53 (52.48%)	308 (61.23%)
Widowed	15 (3.73%)	24 (23.76%)	39 (7.75%)
Other	84 (20.90%)	11 (10.89%)	95 (18.88%)
<b>Employment status</b>			
Active employee	211 (55.24%)	26 (28.89%)	237 (50.21%)
Retired	114 (29.84%)	37 (41.11%)	151 (31.99%)
Unemployed	57 (14.92%)	27 (30.00%)	84 (17.80%)
<b>Level of education</b>			
Early childhood education	20 (5.21%)	9 (10.00%)	29 (6.12%)
Primary education	165 (42.97%)	48 (53.33%)	213 (44.94%)
Secondary education	152 (39.58%)	25 (27.78%)	177 (37.34%)
Bachelor or superior	47 (12.24%)	8 (8.89%)	55 (11.60%)
<b>Comorbidities</b>			
Heart failure	28 (6.97%)	10 (9.90%)	38 (7.55%)
Peripheral arterial disease	12 (2.99%)	3 (2.97%)	15 (2.98%)
Stroke	14 (3.48%)	7 (6.93%)	21 (4.17%)
Chronic renal disease	20 (4.98%)	3 (2.97%)	23 (4.57%)
Prior myocardial infarction	283 (70.40%)	61 (60.40%)	38 (7.55%)
Atrial fibrillation	4 (1.00%)	3 (2.97%)	7 (1.39%)
Diabetes mellitus	75 (18.66%)	29 (28.71%)	104 (20.68%)
Arterial hypertension	180 (44.78%)	59 (58.42%)	239 (47.51%)
Hyperlipidemia	217 (53.98%)	54 (53.47%)	271 (53.88%)
General anxiety disorder	42 (10.45%)	14 (13.86%)	56 (11.13%)
Major depressive disorder	28 (6.97%)	18 (17.82%)	46 (9.15%)
<b>Lifestyle risk factors</b>			
Current smoker	197 (49.00%)	48 (47.52%)	297 (59.05%)
Former smoker	150 (37.31%)	18 (17.82)	174 (34.59%)
Amount of tobacco consumed*	21.10 (13.38)	15.25 (8.89)	20.17 (12.93)
Histoy of enolism	50 (12.44%)	3 (2.97%)	53 (10.54%)

Note: SD: standard deviation.

\* Average number of cigarettes smoked.

of adherent patients (HR, 1.49; 95% CI 0.93-2.40) (Fig. 2B).

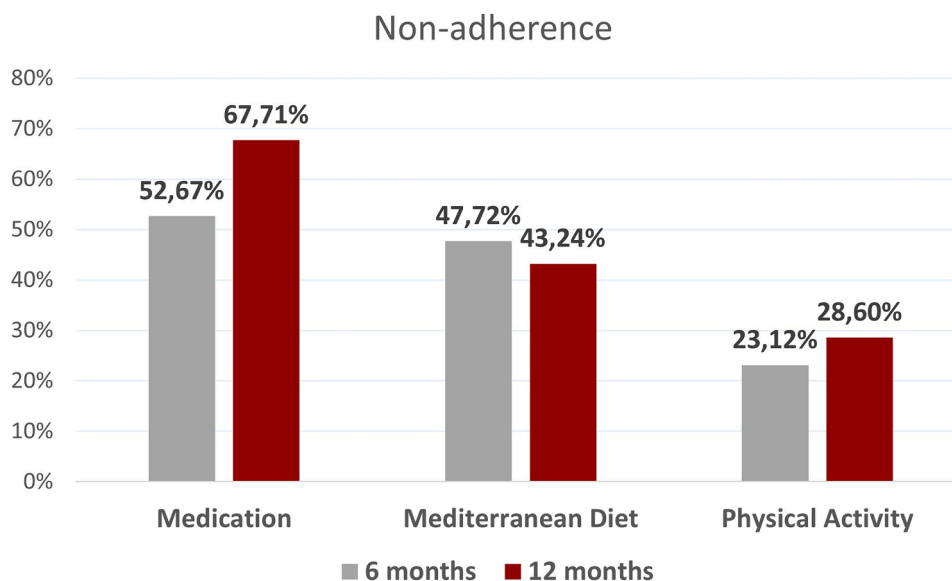
Of the patients referred to cardiac rehabilitation programs, 45.0% started and 33.7% completed the program. Among patients who started but did not complete the program, 17.7% had at least one hospitalization, compared with 10.5% of adherents (HR, 1.72; 95%CI, 0.76-3.91) and 16.5% of those who did not start a cardiac rehabilitation program (HR, 1.63; 95%CI, 0.92-2.92) (Fig. 2E).

Most patients (84.6%) were non-adherent to at least one of the three secondary prevention measures (medication, Mediterranean diet, or physical activity) at 12 months. Among patients who did not adhere to the combined measures, 17.1% had at least one episode of hospitalization, compared with 7.1% among patients who adhered to all recommendations (HR, 2.53; 95%CI, 1.02-6.28) (Fig. 2A). However, no significant differences were found between adherent and non-adherent patients for hospitalization due to cardiovascular causes (HR, 2.23; 95%CI, 0.80-6.18).

### 3.2. Factors associated with non-adherence

#### 3.2.1. Non-adherence to medication

Predictors of non-adherence adjusted for age, sex, and type of AMI



**Fig. 1.** Prevalence of the secondary prevention measures 6- and 12-months after AMI. Non-adherence to medication and physical activity increased over time, whereas non-adherence to the Mediterranean diet remained stable.

included being treated by a cardiologist rather than a primary care physician (OR, 2.03; 95%CI, 1.07-3.88), having a history of previous myocardial infarction (OR, 3.23; 95%CI, 1.85-5.63) and a history of prior difficulties with medication (OR, 2.26; 95%CI, 1.15-4.43). Nevertheless, adherence to the Mediterranean diet was associated with a lower risk of non-adherence to medication (OR, 0.85; 95%CI, 0.73–0.99) (Fig. 3D and Supplementary Table 2).

### 3.2.2. Non-adherence to Mediterranean diet

Independent predictors of non-adherence were the presence of chronic kidney disease (OR, 3.27; 95%CI, 1.02-10.48) and being female (OR, 2.21; 95%CI, 1.18-4.13). Previous good Mediterranean lifestyle (OR, 0.85; 95%CI, 0.79-0.92), previous good physical quality of life (OR, 0.98; 95%CI, 0.95-0.99), and family support for treatment monitoring (OR, 0.55; CI95% 0.32-0.96) were associated with lower risks of non-adherence to the Mediterranean diet (Fig. 3C and Supplementary Table 3).

### 3.2.3. Non-adherence to physical activity

Independent predictors of PA non-adherence were the number of cigarettes smoked (OR, 1.03; 95%CI, 1.01-1.05) and diabetes mellitus with organ involvement (OR, 12.06; 95%CI, 1.93-7.69). Low-density lipoprotein (LDL) levels (OR, 0.99; 95%CI, 0.98-0.99), good physical quality of life (OR, 0.97; 95%CI, 0.94-0.99), adherence to the Mediterranean diet (OR, 0.75; 95%CI, 0.64-0.88), and older age (OR, 0.96 per year; 95%CI, 0.93-0.99) were associated with lower risks of non-adherence to physical activity (Fig. 3B and Supplementary Table 4).

### 3.2.4. Participation in and non-adherence to cardiac rehabilitation

Higher body mass index (BMI) was identified as an independent predictor of non-participation in cardiac rehabilitation (OR, 1.07; 95% CI, 1.01-1.14). On the contrary, openness to experience personality trait was associated with a lower risk of non-participation in CR (OR, 0.95; 95%CI, 0.91-0.99). The only independent predictor of non-adherence to cardiac rehabilitation was higher BMI (OR, 1.14; 95%CI, 1.04-1.24) (Supplementary Table 5).

### 3.2.5. Non-adherence to all measures together

Independent predictors of non-adherence to the combination of medication, Mediterranean diet and physical activity were the presence of depressive symptoms (OR, 1.40; 95%CI, 1.03-1.92) and the burden of

family caregiving (days spent caring for family or other people) (OR, 1.45; 95%CI, 1.08-1.94) (Fig. 3A and Table 2).

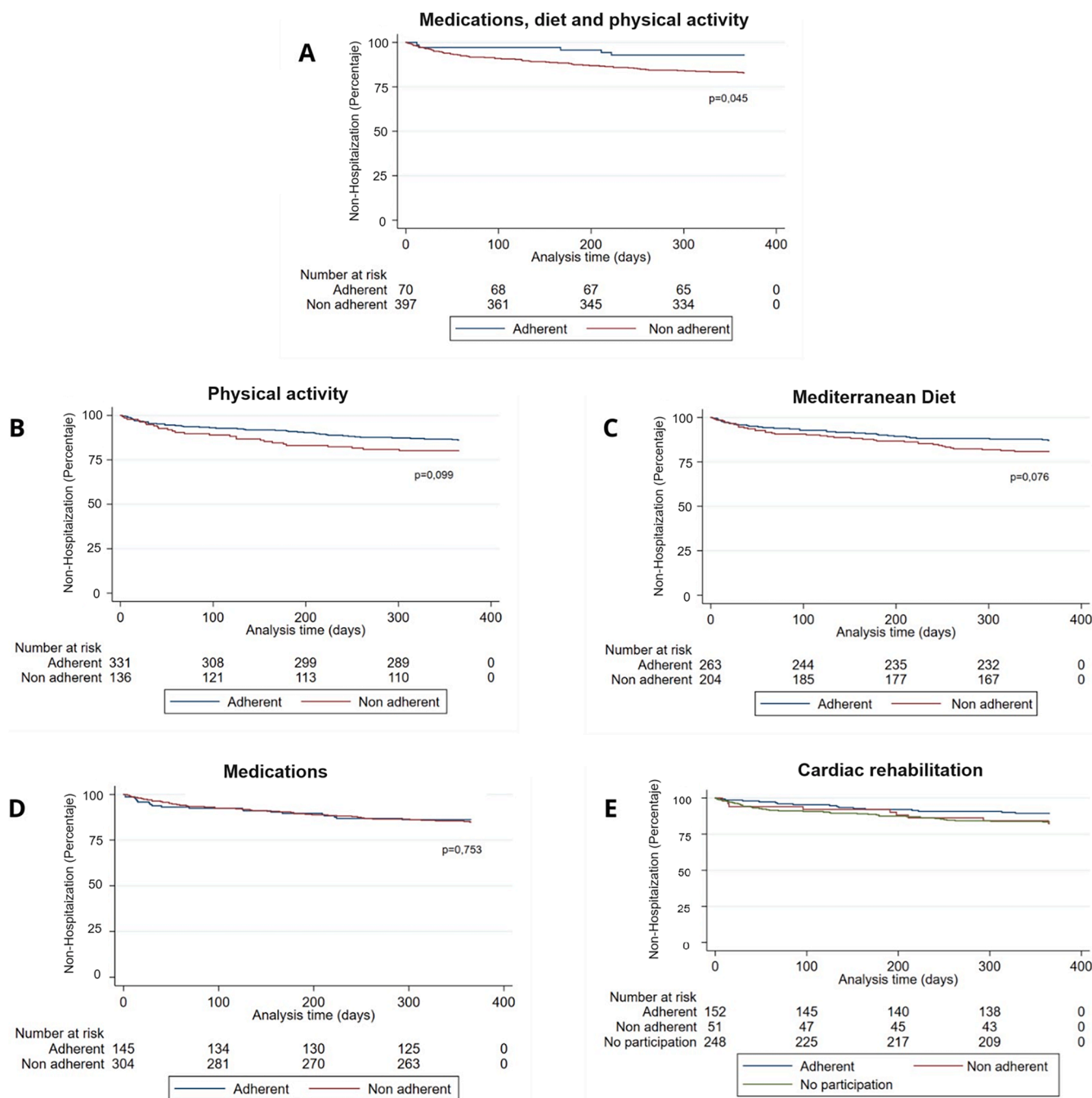
## 4. Discussion

Our prospective study confirms previous studies reporting low adherence to secondary prevention measures and expands information on non-adherence to diet and physical activity at one year, not evaluated previously in a systematic manner as in our study. This is also the first study to assess non-adherence to the combined preventive measures: medication, diet, physical activity, and cardiac rehabilitation, showing a striking 85% of patients who did not adhere to at least one of these recommendations in the first year of follow-up. Moreover, it shows the clinical impact of non-adherence in such a short time as one year after hospital discharge after an AMI. Finally, our systematic evaluation of non-adherence predictors, including patient-, disease-, psychological-, social-, and gender-related factors, showed new results that may help in designing interventions to improve adherence in specific subgroups of more vulnerable patients.

One of the most important findings from this study is that the two independent predictors of global non-adherence, that is, measuring all recommendations together, are gender-related: caregiving burden and depression symptoms, both more prevalent among females [14,15]. This finding is particularly relevant because the female sex itself was not a predictor of non-adherence for most interventions, suggesting that there is no biological reason to think that females should be less adherent to preventive recommendations, but rather aspects related to gender inequities could influence adherence, and these could specifically penalize females. Marked differences in caregiving burden between females and males have been reported worldwide, with a much heavier burden falling systematically in females [16,17]. It is known that caregivers usually look after themselves much less than after the patients they take care of, so it is not surprising that caregiving burden influences adherence to preventive therapies [18]. However, this aspect is seldom assessed in routine clinical practice; therefore, it may be unnoticed when planning secondary prevention interventions, particularly cardiac rehabilitation and physical activity, which is the most demanding timewise. A systematic assessment of caregiving burden should be considered in all patients discharged from cardiology units, particularly in females, when planning secondary prevention strategies.

## Kaplan-Meier survival estimates

### Hospitalization for any cause



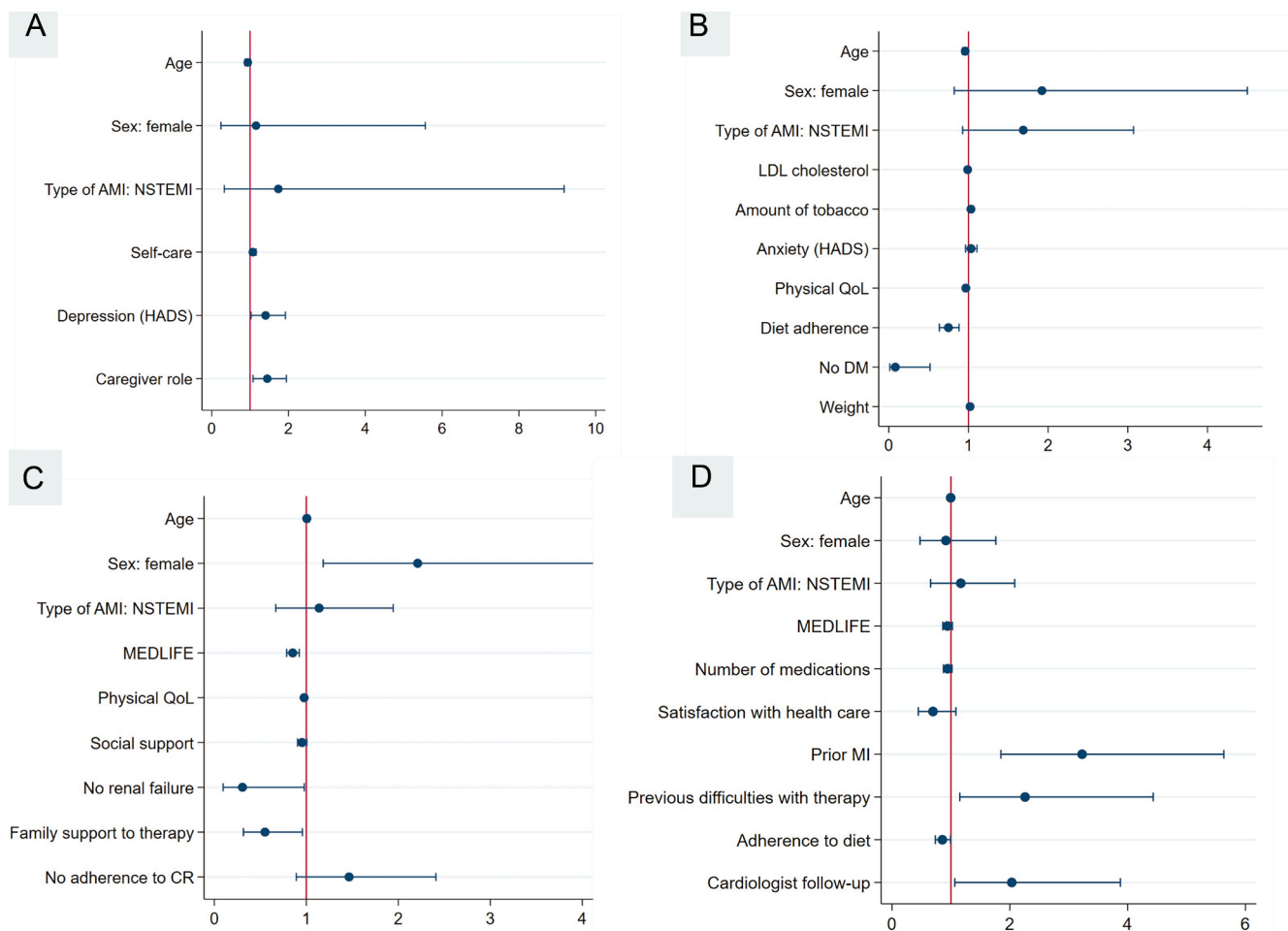
**Fig. 2.** Survival curves free of rehospitalization according to the adherence or not to: A) Medications, diet and physical activity combined; B) Physical activity; C) Mediterranean Diet; D) Medications; E) Cardiac rehabilitation. There were no differences in hospitalization for any cause between adherence and non-adherence to each prevention measure. However, there are differences in hospitalization between those who adhere to all preventive measures and those who do not.

The association of depression or depressive symptoms, both more prevalent among females [14] — with lower therapeutic adherence after AMI is well known [19,20]. Specific planning for patients with depressive symptoms involving psychologists and specific psychological interventions during and beyond are warranted [21].

Follow-up by primary care physicians seems to improve medication adherence, which decreases when patients are treated by cardiologists. In our study, the frequency of patient visits was higher for primary care. As regular contact with clinicians has been shown to have a positive

effect on medication adherence, this factor may be influential [22].

Other findings from our study offer opportunities for post-myocardial infarction secondary improvement in specific patient subgroups, mostly through collaborative work and multidisciplinary approaches. To the best of our knowledge, this study is the first to evaluate adherence to a Mediterranean diet 12 months after AMI. The difficulty of patients with chronic kidney disease to adhere to this diet is probably conditioned by their specific dietary requirements; therefore, targeted dietary planning for patients with renal and vascular diseases should be



**Fig. 3.** Predictors of non-adherence to secondary prevention measures. A) Predictors of the combination of medication, diet and physical activity; B) Predictors of physical activity; C) Predictors of Mediterranean Diet; D) Predictors of medication. AMI: acute myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; HADS: Hospital Anxiety and Depression Scale; LDL: low-density lipoprotein; QoL: Quality of Life; DM: diabetes mellitus; MEDLIFE: MEDiterranean LIFestyle index;; CR: Cardiac rehabilitation; MI: myocardial infarction.

**Table 2**

Odds ratio of the univariate and independent predictors of non-adherence to the combination of secondary prevention measures (medication, diet and physical activity) at 12 months.

	Univariate analysis				Multivariate analysis			
	OR	p value	95% CI		OR	p value	95% CI	
Mediterranean lifestyle (MEDLIFE)	0.89	<b>0.016</b>	0.82	0.97	-	-	-	-
Stress (PSS)	1.03	<b>0.014</b>	1.007	1.06	-	-	-	-
Friends Social Support (MPSS)	0.96	0.081	0.92	1.004	-	-	-	-
Family Social Support (MPSS)	0.92	<b>0.021</b>	0.86	0.98	-	-	-	-
Social Support: Others (MPSS)	0.93	<b>0.044</b>	0.87	0.99	-	-	-	-
Baseline physical quality of life (SF-12)	0.97	<b>0.047</b>	0.94	0.99	-	-	-	-
Baseline mental quality of life (SF-12)	0.98	0.181	0.95	1.007	-	-	-	-
Physical quality of life at 12 months (SF-12)	0.96	<b>0.011</b>	0.93	0.99	-	-	-	-
Mental quality of life at 12 months (SF-12)	0.97	<b>0.048</b>	0.95	0.99	-	-	-	-
Self-care (ASA)	0.97	<b>0.039</b>	0.94	0.99	1.07	0.065	0.99	1.15
Age	0.97	<b>0.046</b>	0.95	0.99	0.94	0.096	0.87	1.01
Anxiety (HADS)	1.01	0.568	0.95	1.08	-	-	-	-
Depression (HADS)	<b>1.11</b>	<b>0.011</b>	<b>1.02</b>	<b>1.21</b>	<b>1.40</b>	<b>0.034</b>	<b>1.03</b>	<b>1.92</b>
Illness disease perception (BIPQ)	1.008	0.481	0.98	1.03	-	-	-	-
Caregiver role (CUIDAR-SE)	<b>1.42</b>	<b>0.004</b>	<b>1.12</b>	<b>1.81</b>	<b>1.45</b>	<b>0.014</b>	<b>1.08</b>	<b>1.94</b>
History of medication management difficulties	3.83	<b>0.006</b>	1.48	9.95	-	-	-	-
Smoking during follow-up	0.295	<b>0.011</b>	0.11	0.75	-	-	-	-
Female sex	-	-	-	-	1.15	0.857	0.24	5.56
AMI type (NSTEMI)	-	-	-	-	1.73	0.517	0.33	9.18

Note: OR: Odds ratio; CI: Confidence interval; MEDLIFE: MEDiterranean LIFestyle index; PSS: Perceived Stress Scale; MPSS: The Multidimensional Scale of Perceived Social Support; SF-12: 12-Item Short-Form Health Survey; ASA: Self-care Agency Scale; HADS: Hospital Anxiety and Depression Scale; BIPQ: Brief Illness Perception Questionnaire; AMI: Acute Myocardial Infarction; NSTEMI: non-ST-elevation myocardial infarction.

developed with nephrologists and nutritionists [23]. More intriguing is our finding that females are less likely to adhere to a Mediterranean diet in a Mediterranean country. The reasons for this may require further research, but are more likely related to gender issues, as discussed for global adherence, than to biological causes [24]. The fact that diabetes mellitus is the strongest predictor of non-adherence to physical activity recommendations may be explained by disease-related complications that may impair their mobility [25] but given the extreme importance of physical activity in secondary cardiovascular prevention as well as for the optimal care of diabetes, specific interventions to overcome this difficulty are warranted. Finally, the finding that higher BMI is an independent predictor of lower participation and adherence to cardiac rehabilitation suggests that specific activities for obese patients may be needed in cardiac rehabilitation programs to stimulate and improve their participation.

The clinical consequences of non-adherence are well known [26]. The finding of an increased risk of readmission in such a short time as 12 months after discharge (considering that the mortality risk could be assessed as adherence questionnaires are missing among patients who died during follow-up) emphasizes the importance of setting strategies for improving adherence to all components of secondary prevention specifically directed to the most vulnerable groups, with special attention to gender issues in females.

#### 4.1. Study limitations

The discovery of gender factors associated with females in a predominantly male sample reinforces the concept of gender inequality. These findings are robust and will be confirmed in larger samples. The COVID-19 pandemic and the use of online rehabilitation programs may have influenced adherence rates. However, our centre implemented an online rehabilitation program to ensure patients' continuity in the program and the impact of the programs affected only 11% of patients of the study. COVID-19 did not affect the estimate of adherence to the Mediterranean diet and medication. Patients lost to follow-up and patients who died were not included in the analysis because it was not possible to obtain data on their adherence. However, the rates of death and loss to follow-up in our study were low. We lack alternative measures of medication non-adherence, and the questionnaire used in this study does not allow for distinguishing between different medications. Our study did not include other secondary prevention measures such as smoking cessation, weight control, or blood pressure and the determinants of these adherence habits, which should be addressed in future studies. Future research should aim to include more diverse populations, both geographically and culturally, ideally using objective measures (or other adherence measurement methods) and considering local external factors.

## 5. Conclusions

Adherence to all secondary prevention measures after AMI remains very low, with several factors playing an important role specifically for different preventive measures, among which gender issues, such as caregiving burden and depressive symptoms are particularly relevant. Given the clinical consequences of non-adherence and the variety of factors involved, multidisciplinary intervention strategies targeting the most vulnerable patient groups, such as females or patients with diabetes, obesity, chronic kidney disease, or depression, should be developed during and after hospitalization for AMI.

#### Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

#### Author declaration

We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author.

#### CRediT authorship contribution statement

**Guillermo Moreno:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation, Conceptualization. **Lourdes Vicent:** Writing – review & editing. **Nicolás Rosillo:** Writing – review & editing. **Juan Delgado:** Writing – review & editing. **Enrique Pacheco Del Cerro:** Writing – review & editing. **Héctor Bueno:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Hector Bueno reports financial support was provided by Spanish Society of Cardiology. Hector Bueno reports a relationship with AstraZeneca Pharmaceuticals LP that includes: consulting or advisory and funding grants. Hector Bueno reports a relationship with Janssen Pharmaceuticals Inc that includes: consulting or advisory and funding grants. Hector Bueno reports a relationship with Novartis Pharmaceuticals Corporation that includes: consulting or advisory and funding grants. Hector Bueno reports a relationship with Bayer Pharma AG that includes: consulting or advisory. Lourdes Vicent reports a relationship with Carlos III Health Institute that includes: funding grants. Nicolas Rosillo reports a relationship with Carlos III Health Institute that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Funding

This research was funded through a grant from the Spanish Society of Cardiology (SEC Project for Clinical Research in Cardiology 2019 to the work “Predictors of non-compliance with secondary prevention measures in myocardial infarction”).

### Acknowledgments

Our gratefulness to the patients of the University Hospital 12 de Octubre and the Spanish Society of Cardiology (SEC) for their support.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ajpc.2024.100713](https://doi.org/10.1016/j.ajpc.2024.100713).

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