# Impact of medication adherence on mortality and cardiovascular morbidity: a population-based cohort study. IMPACT study

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1. Background
2. Justification & Hypothesis
3. Objectives
4. Methods
5. Results
6. Conclusions
7. References

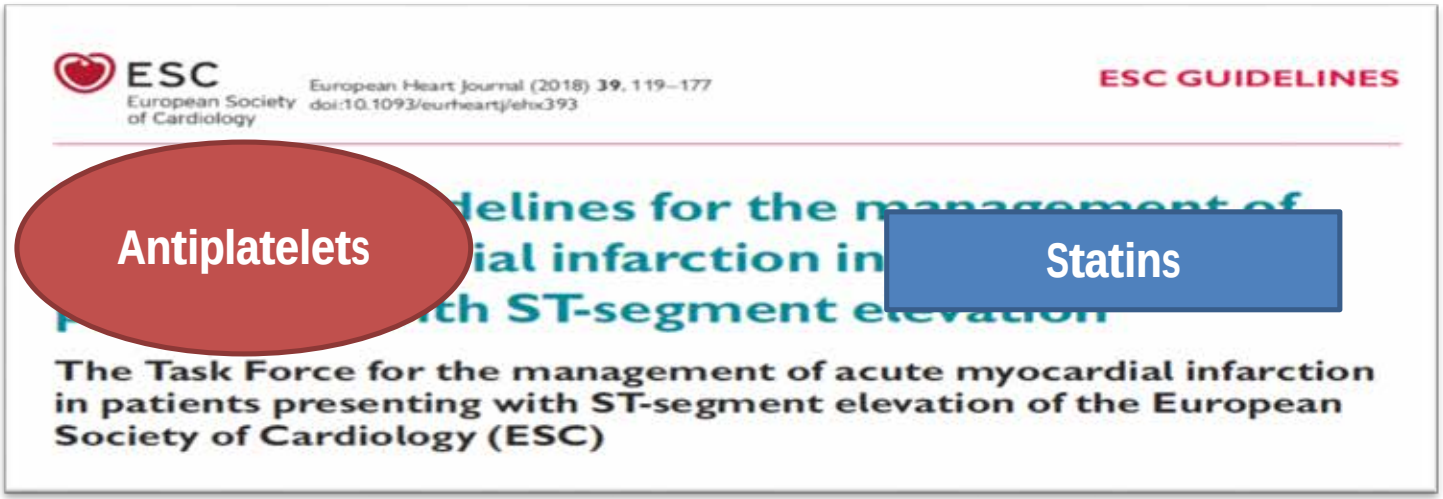
# 1. Background (1)

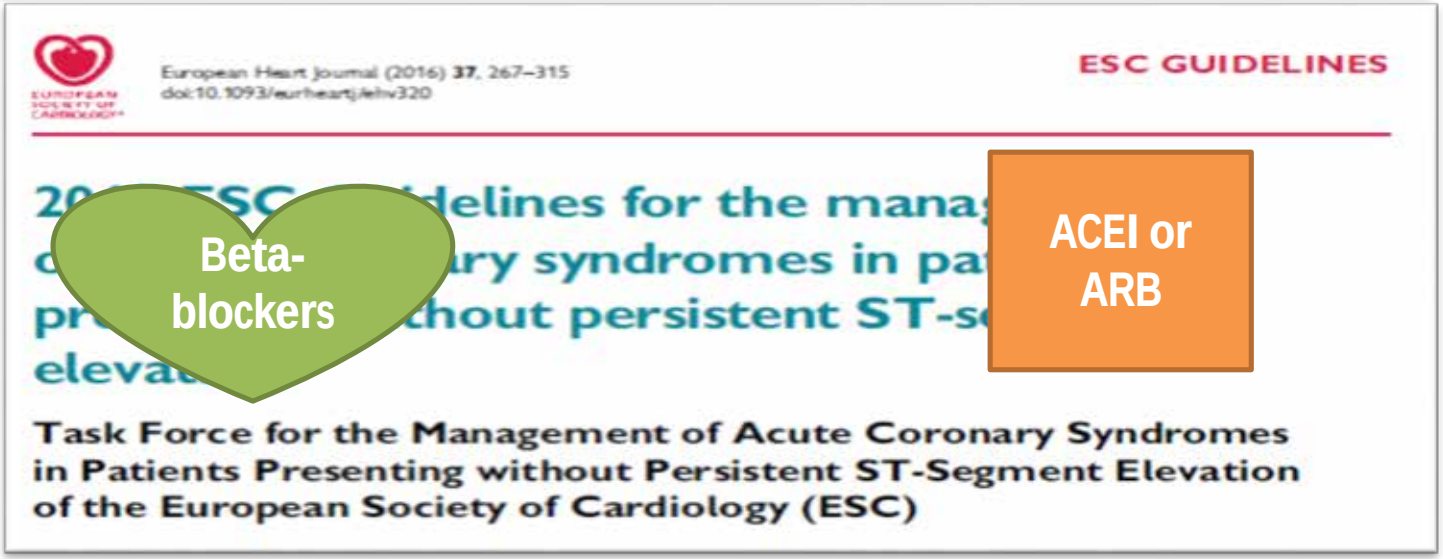
The incidence of cardiovascular disease has decreased over the last four decades:

- population-level **lifestyle changes**.
- development of **effective interventions** to treat individuals.

**Adherence to prescribed medication is poor for long-term drug treatment.**

# 1. Background (2)




- *2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2018. doi:10.1093/eurheartj/ehx393*
- *2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2016;37(3):267-315. doi:10.1093/eurheartj/ehv320*

# 1. Background (3)

NICE National Institute for Health and Care Excellence

NICE guideline

American Heart Association®

Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease

Clinical guideline
Published: 13 November 2013
nice.org.uk/guidance/cg172

## 1.3 *Drug therapy*

1.3.1 Offer all people who have had an acute MI treatment with the following drugs:

- ACE (angiotensin-converting enzyme) inhibitor
- dual antiplatelet therapy (aspirin plus a second antiplatelet agent)
- beta-blocker
- statin. [2007, amended 2013]

*National Institute for Health and Care Excellence. Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease. London: NICE; 2013.*

# 2. Justification & Hypothesis (1)

## Justification

- Due to the **improvement of morbidity and mortality found with the quadruple drug therapy** (antiplatelet, beta-blocker, ACEI or ARB and statin) in patients with established CVD.

- It is necessary **to assess the long-term adherence** to these drugs in **our population** and its **relationship with cardiovascular events and mortality.**

Giner-Soriano M, Sotorra Figuerola G, Cortés J, Pera Pujadas H, Garcia-Sangenis A, Morros R, *et al*. Impact of Medication Adherence on Mortality and Cardiovascular Morbidity: Protocol for a Population-Based Cohort Study. *JMIR Res Protoc* 2018;**7**(3):e73

# 2. Justification & Hypothesis (2)

## Hypothesis

The patients with established CHD **who adhere to drug therapy** with the four recommended pharmacological groups have **a lower risk of major adverse cardiac events and all-cause mortality compared with patients who do not adhere to drug therapy**.

# 3. Objectives (1)

## Main Objective

To assess the relationship between **adherences to the four pharmacological groups** recommended for secondary prevention and **the clinical outcomes of cardiovascular morbidity and mortality** in patients with established CHD.

The outcomes which are included as components of the **composite endpoint** are: **all-cause mortality, ACS, and ischaemic stroke.**

# 3. Objectives (2)

## Secondary Objectives

1) To assess the incidence of the **composite endpoint** in patients who are adherent to treatment with **all four drugs compared** with patients who are adherent to **any combination of three, two or one drug, or no drug.**
2) To assess the relationship between baseline **socio-demographic and clinical characteristics** and **adherence** to drug therapy.
3) To compare the number of **days on sickness leave** due to any cause according to **adherence** to drug therapy.
4) To estimate **prevalence of use** of the four drug treatments.
5) To describe the **posology prescribed** for the four drugs.

# 4. Methods (1)

## Design, period, population and data sources

**Design:** Population-based cohort study.

**Period**: 2009-2016.

**Population:** Individuals ≥ 18 years with an incident diagnosis of Acute Coronary Syndrome (AMI or unstable angina) admitted in hospital of Catalan Health Institute.

**Data sources**: SIDIAP

*SIDIAP: contains anonymized clinical information of all 279 PHC centres managed by the ICS, covering about 80% of the population in Catalonia (5.8 million patients) The information is registered by professional heaths in ECAP (electronic health records): comprehensive socio-demographic information, health conditions registered as ICD10 codes, clinical parameters, toxic habits, laboratory test results, GPs prescriptions and their corresponding pharmacy invoice data registered.*

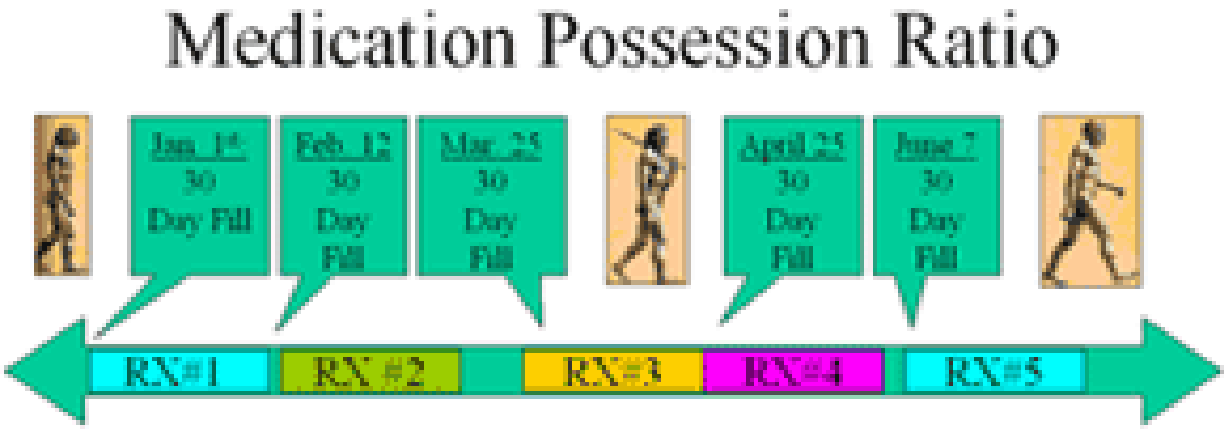
# 4. Methods (2)

## Variables

- **Exposure definition:**
  - **Patients exposed:** if they are prescribed any of study drug after the episode ACS (up to two months after the event).
- **Primary outcome variable:**
  - Incidence of **major adverse cardiac events**
- **Adherence definitive:**
  - **PDC** (proportion of days covered) **= MPR** (medication possession ratio).

# 4. Methods (3)

## MPR (medication possession ratio):




$$MPR = \frac{\text{30 Day refills * 5 times = 150 Days of Medication}}{\text{January 1 through May 19(+30days}^{1}\text{)= 187 Days}} = 80\%$$

[1] Days supply of the last refill is added to estimate expiration of supply.

**Adherent Patient> if MPR ≥ 80% o ≥ 75%**

https://rxoutcomesadviser.files.wordpress.com/2011/03/mpr-example.gif

# 4. Methods (4)

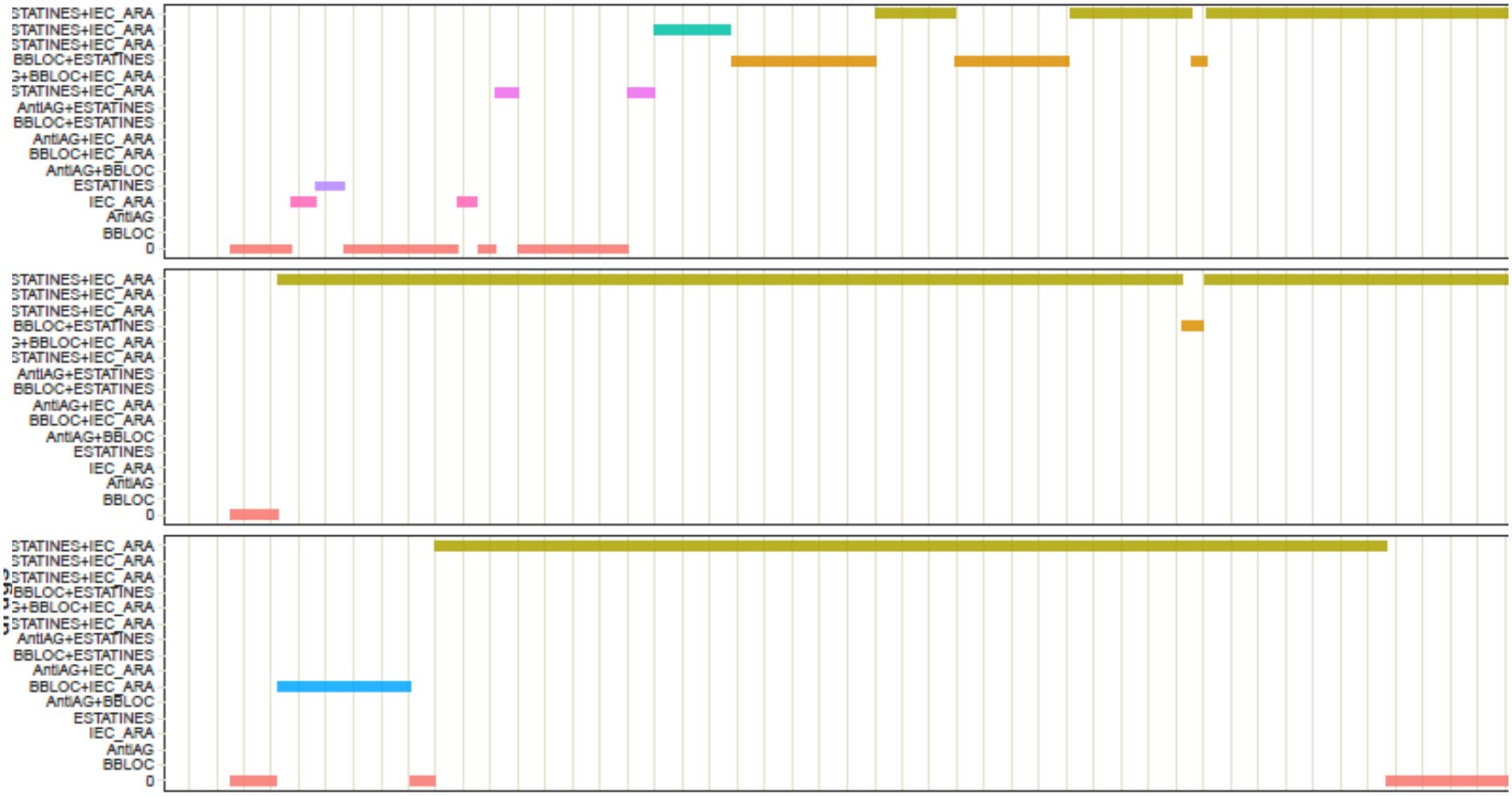
## Statistical analysis

- Demographic and baseline characteristics:
  - § Categorical variables: **frequencies and percentages.**
  - § Continuous variables: **mean** (standard deviation) or **median** (interquartile range).

- **Adherence: HRs** – using **Cox proportional Hazard regression models.**

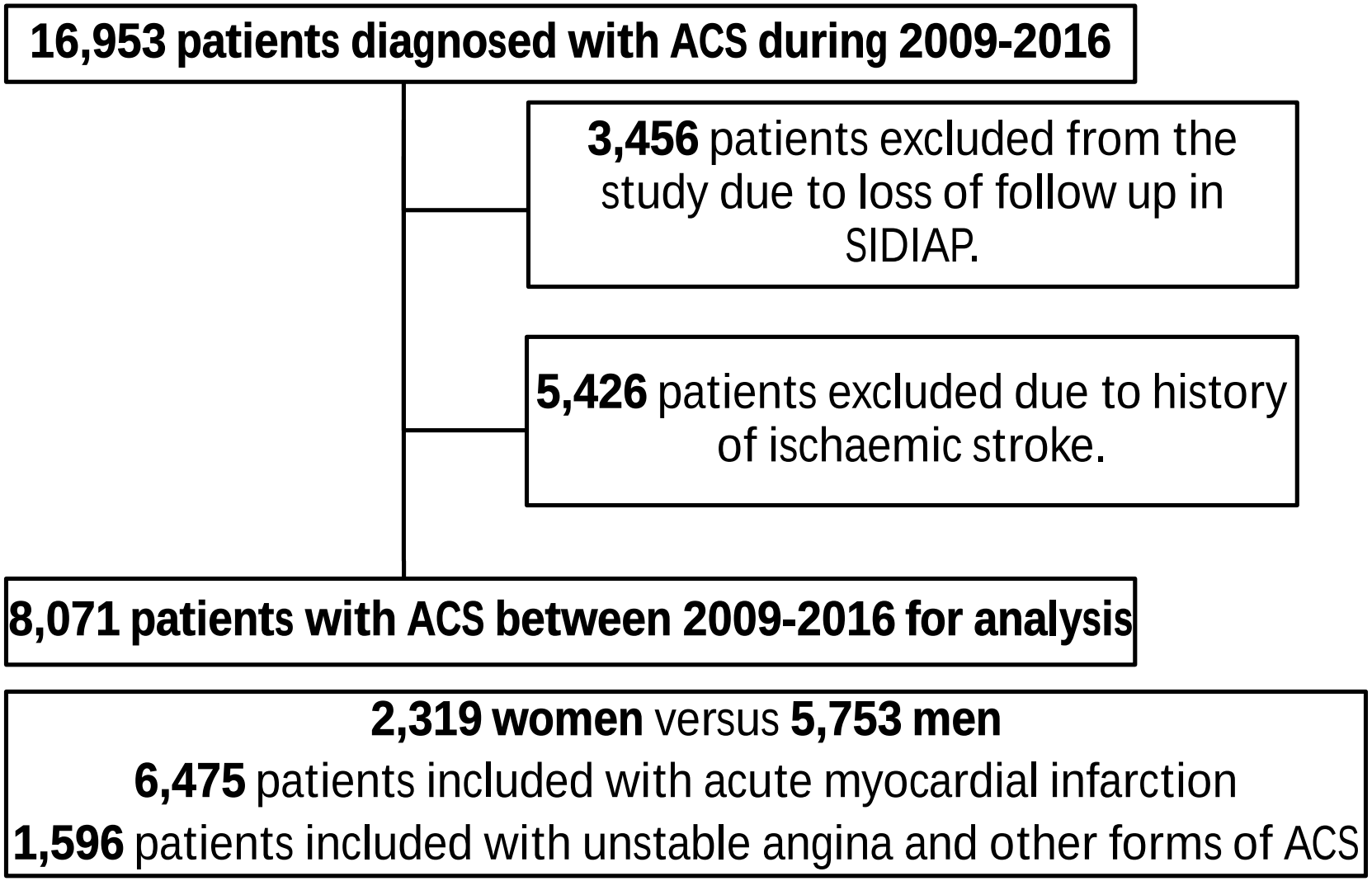
# 4. Methods (5)

## Statistical analysis: algorithm and smooth methods



# 5. Results (1)

## Study Flow chart




*ACS, Acute Coronary Syndrome; SIDIAP, System for the Improvement of Research in Primary Care*

# 5. Results (2)

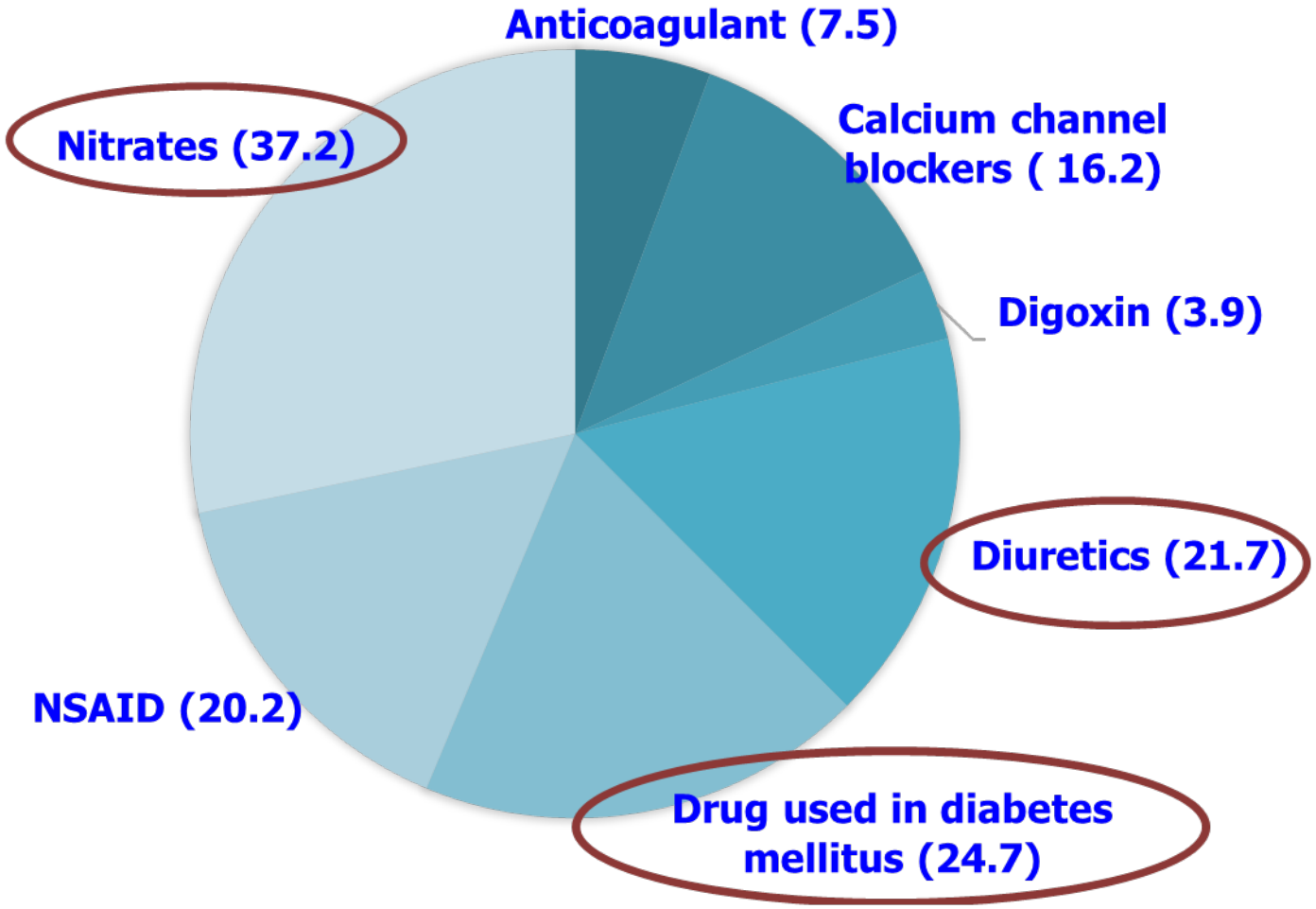
## Baseline characteristics, laboratory data and comorbidities

| Total | 8071 |
|---|---|
| Acute myocardial infarction (n, %) | 6475 (80.2) |
| Unstable angina and other forms of ACS (n, %) | 1596 (19.8) |
| Sex; Female (n, %) | 2318 (28.7) |
| Age (years; mean, SD) | 65.33 (13.61) |
| ≥ 65 years (n, %) | 4323 (53.5) |
| Smoking status (n, %); Smokers (n, %) | 2320 (31.1) |
| Alcohol intake (n, %); High risk (n, %) | 5 (0.1) |
| BMI (kg/m2; mean, SD) | 29.03 (4.71) |
| BMI ≥ 30: obesity (%) | 2387 (37.4) |
| Cholesterol Total mg/dL (mean, (SD)) | 208.93 (43.30) |
| Cholesterol LDL mg/dL (mean, (SD)) | 129.43 (36.57) |
| Cholesterol HDL mg/dL (mean, (SD)) | 49.03 (13.38) |
| Triglycerides mg/dL (mean, (SD)) | 154.74 (104.22) |
| Diabetes mellitus (n, %) | 2170 (26.9) |
| Dyslipidaemia (n, %) | 3451 (42.8) |
| Heart failure (n, %) | 297 (3.7) |
| Hypertension (n, %) | 4298 (53.3) |
| Peripheral artery disease (n, %) | 385 (4.8) |
| Renal impairment (%) GFR < 45 ml/min/1.73m2 | 528 (7.6) |

*ACS, acute coronary syndrome, BMI, body mass index; LDL-C, Low density lipoprotein-cholesterol; HLD-C, high density lipoprotein- cholesterol. GFR, glomerular filtration rate*

# 5. Results (3)

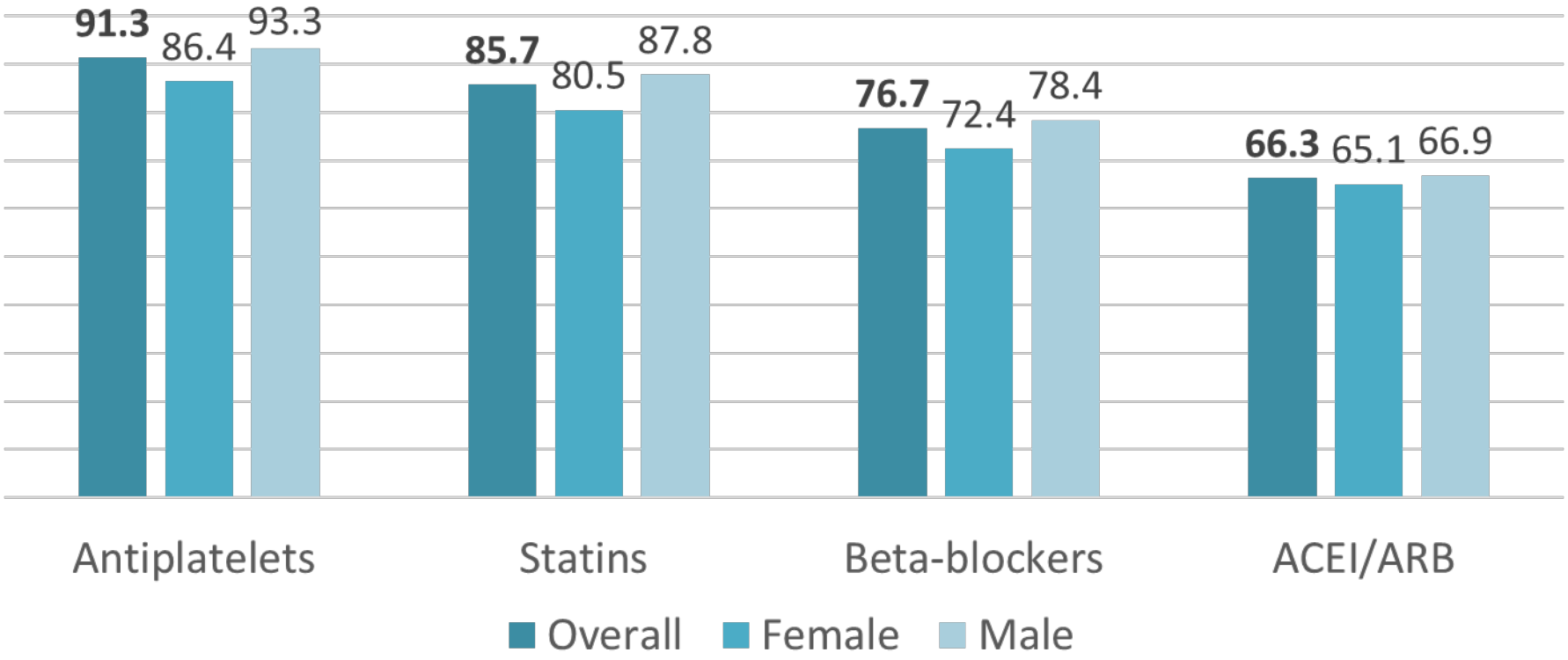
## Co-medication in use at baseline (% of patients)




*NSAID, non-steroidal anti-inflammatory drugs*

# 5. Results (4)

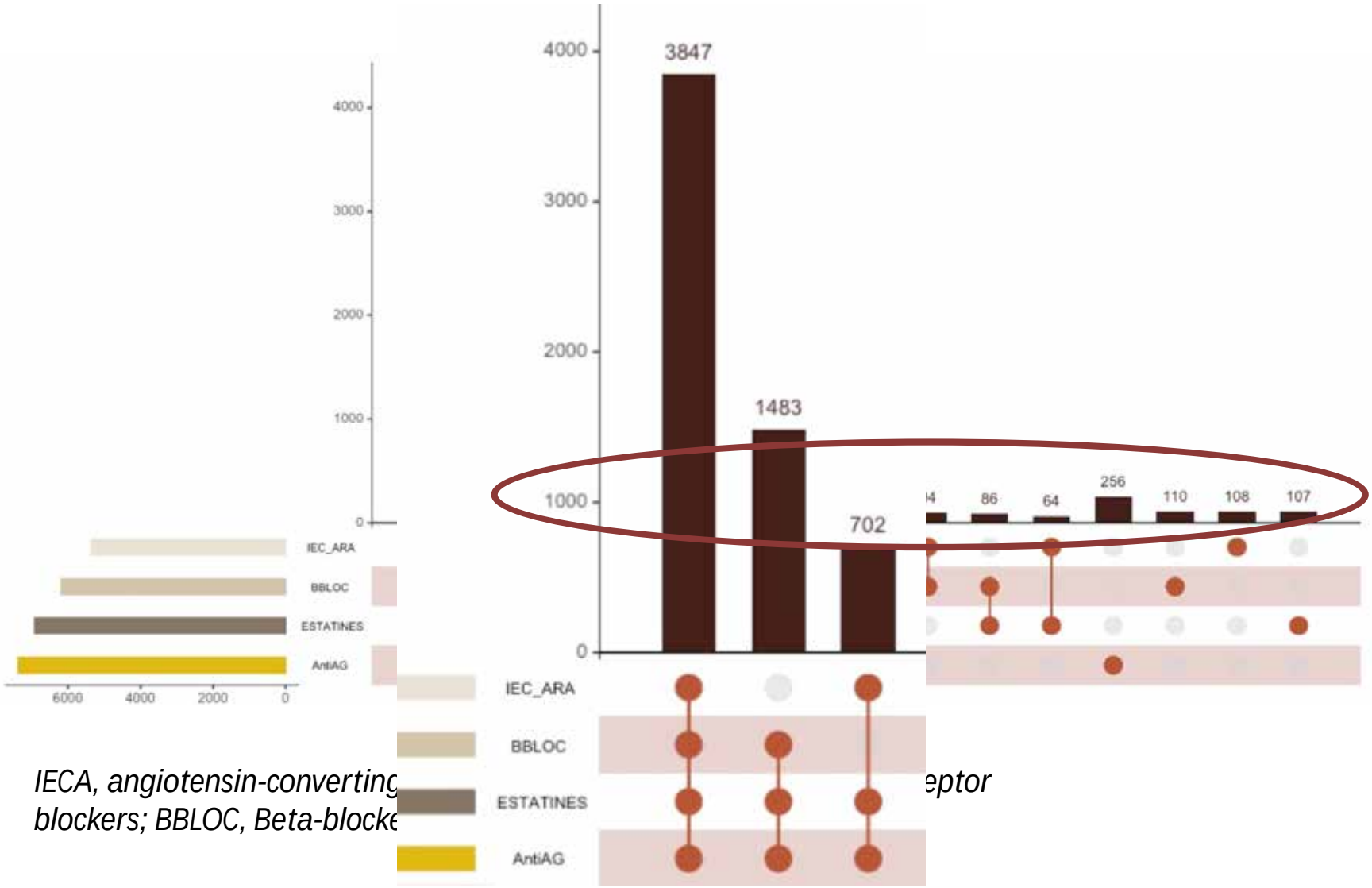
## Population that initiate treatment for secondary prevention (overall and stratified by sex) (%)




*ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers*

# 5. Results (5)

## Study drug combinations for secondary prevention (n)



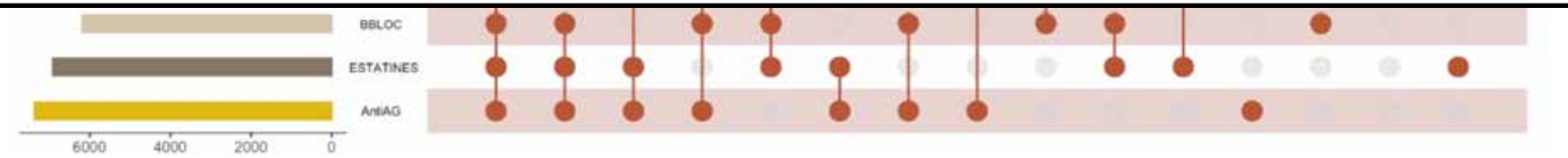

*IECA, angiotensin-converting* *eptor blockers; BBLOC, Beta-blocke*

# 5. Results (5)

## Study drug combinations for secondary prevention (n)


| | Female | Male | p value |
|---|---|---|---|
| **Antiplatelets + Statins + Beta-blockers** | 368 (15.9) | 1115 (19.4) | <0.001 |
| **Antiplatelets + Statins + Beta-blockers + ACEI/ARB** | 968 (41.8) | 2879 (50.0) | <0.001 |
| **Antiplatelets + Statins + ACEI/ARB** | 210 (9.1) | 492 (8.6) | 0.491 |

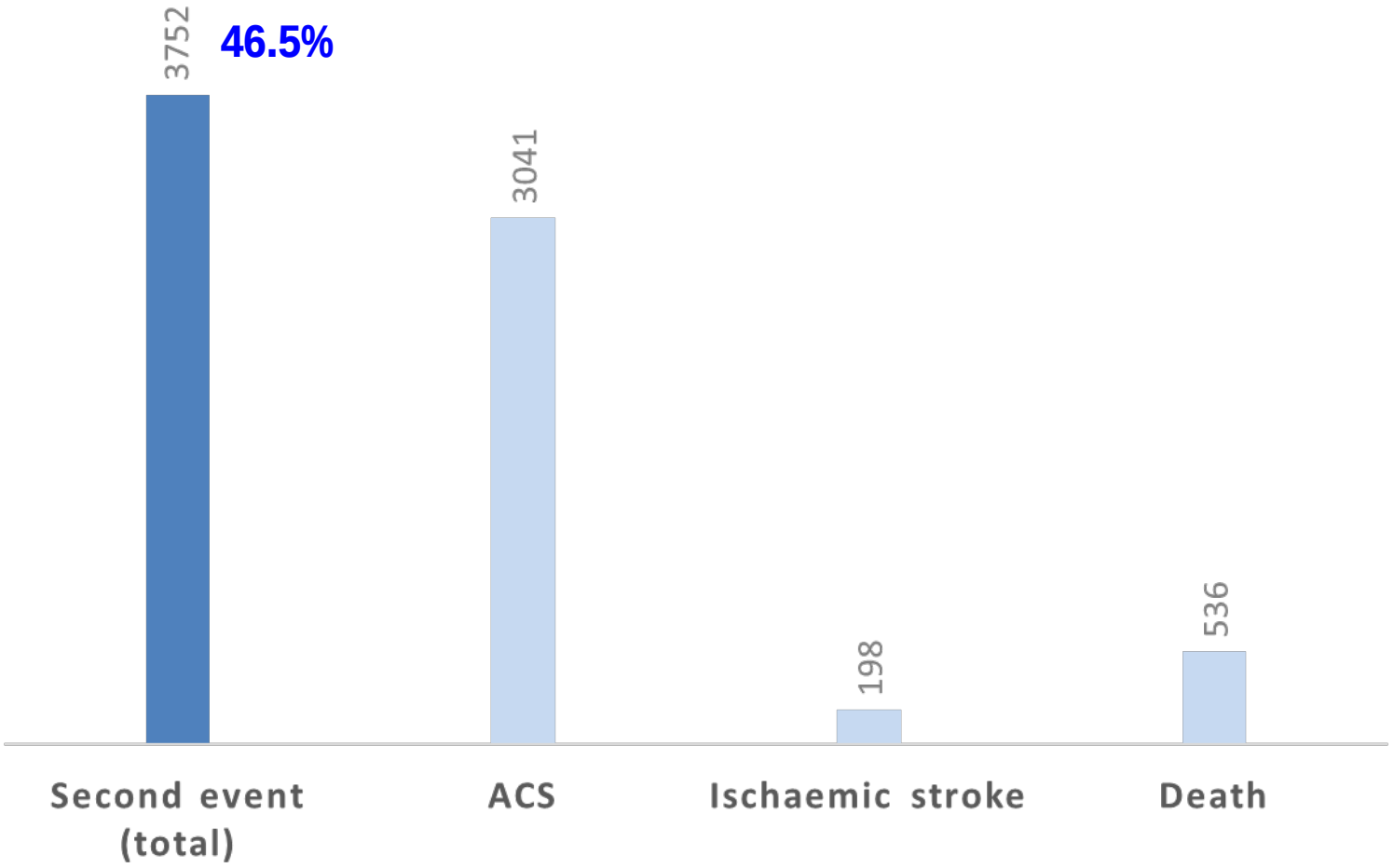
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers




*IECA, angiotensin-converting enzyme inhibitors; ARA, angiotensin-receptor blockers; BBLOC, Beta-blockers; AntiAG, Antiplatelets*

# 5. Results (6)

## Patients who experience a second event after index date (n)




*ACS, Acute Coronary Syndrome*

# 8. Conclusions

- We describe a large set of ACS patients that initiate treatment with the 4 pharmacological groups recommended for secondary prevention.

- Most of the patients are men (71.3%) of ≥ 65 years-old (53.5%) that have had an AMI (80.2%).

- Most of them (91.3%) initiate treatment with antiplatelets. The other pharmacological groups are prescribed with less frequency. There are always more men than women treated.

- Almost half (48%) of patients initiate treatment with a combination of 4 drugs, the difference between men (50%) and women (41.8%) is significative.

# 9. References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# Moltes gràcies per la seva atenció.