

# Age predicts initiation of and persistence with P2Y12 inhibitor treatment after acute coronary syndrome – results from a nationwide retrospective cohort in Finland

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## Background

Secondary preventive drug therapy following acute coronary syndrome (ACS) is recommended to reduce the risk of new cardiovascular events irrespective of age at initiation. However, only limited contemporary data are available on the association of age with the initiation of and persistence with secondary preventive drug therapy, especially regarding the use of oral antiplatelet treatment (OAP) with P2Y12 inhibitors in patients with ACS.

## Purpose

The aim of the present study was to describe ACS patients aged  $\leq 75$  and  $>75$  years, and to examine and identify eventual differences in initiation of and persistence with secondary preventive drugs in an outpatient setting in Finland.

## Methods

This observational cohort study linked patient-level data on diagnoses, interventions, and hospitalization periods from the Finnish Care Register for Health Care, and dispensed prescriptions and certain special reimbursement statuses from the Prescription Register. In order to interpret the gaps in drug exposure and persistence with treatment, data for institutionalization periods other than hospitalization (Care Register for Social Welfare), for living abroad (places of domicile), and for possible mortality (Statistics Finland) were also acquired from the authorities.

The included patients had to be hospitalized for unstable angina pectoris (UAP) (ICD-10 I20.0) or acute myocardial infarction (MI; ICD-10 I21) during the years 2009 to 2013. Index event was defined as first ACS event during the observation period. Patients were classified as either OAP-treated or non-OAP-treated based on their drug purchases within 7 days after discharge from the hospital. Patients were grouped based on age at index, and divided by  $\leq 75$  and  $>75$  years of age.

Baseline medication history data were searched for 120 days prior to index event hospitalization. Purchases of the secondary prevention drugs (other than OAPs) were searched for 30 days after the index date. Data on comorbidity status were retrieved for the 5 years prior to the index event.

Differences between the two age groups were tested with Pearson's chi-squared test. Sensitivity analyses were performed with logistic regression and Cox model. Furthermore, in persistence analysis patients were further stratified into 5-year intervals at age of 65–85 years.

## Results

Overall, 54,416 patients were included in the present study, of whom 29,372 (54%) were  $\leq 75$  years old and the remaining 25,044 (46%) patients were  $>75$  years old. Women were more frequently represented in the older population, with 55% versus 27% ( $p < 0.001$ ) among the younger age group.

The ACS event was more often ST-elevation MI (33% vs. 19%,  $p < 0.001$ ) and invasively treated in patients younger than or aged 75 years than in the older patient group, with PCI related to ACS being performed in 47% versus 20% of patients in those groups, respectively ( $p < 0.001$ ).

Comorbidity rates increased with age (Table 1), with hypertension and dyslipidaemia being the most common comorbidity.

The proportion of patients filling prescriptions for P2Y12 inhibitors was lower for the older patient group when compared with the patients aged 75 years or younger (34% versus 61%, respectively;  $p < 0.001$ ). Persistence with P2Y12 inhibitor therapy was high for patients  $\leq 75$  years old, with 70% completing 1 year of treatment (Figure 1). Persistence with P2Y12 inhibitor therapy decreased with advancing age, and  $< 50\%$  of patients older than 85 years completed 9 months of P2Y12 inhibitor treatment following their hospital discharge (Figure 2). Moreover, the proportion of patients receiving treatment with statins (77% vs. 52%), beta-blockers (77% vs. 63%), and angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) (61% vs. 47%) at discharge decreased with age above 75 years compared with patients aged 75 years or younger ( $p < 0.001$  for all).

## Conclusions

The proportion of ACS patients undergoing any invasive treatment and initiating treatment with P2Y12 inhibitors following their index event decreased to well below half of the population aged 75 years or younger. Patients over 75 years of age had a higher cardiovascular risk profile (history of MI and/or UAP, diabetes, heart failure, and atrial fibrillation) at baseline and lower persistence with P2Y12 inhibitors than younger patients. Age was independently associated with a lower initiation of and persistence with P2Y12 inhibitor use.

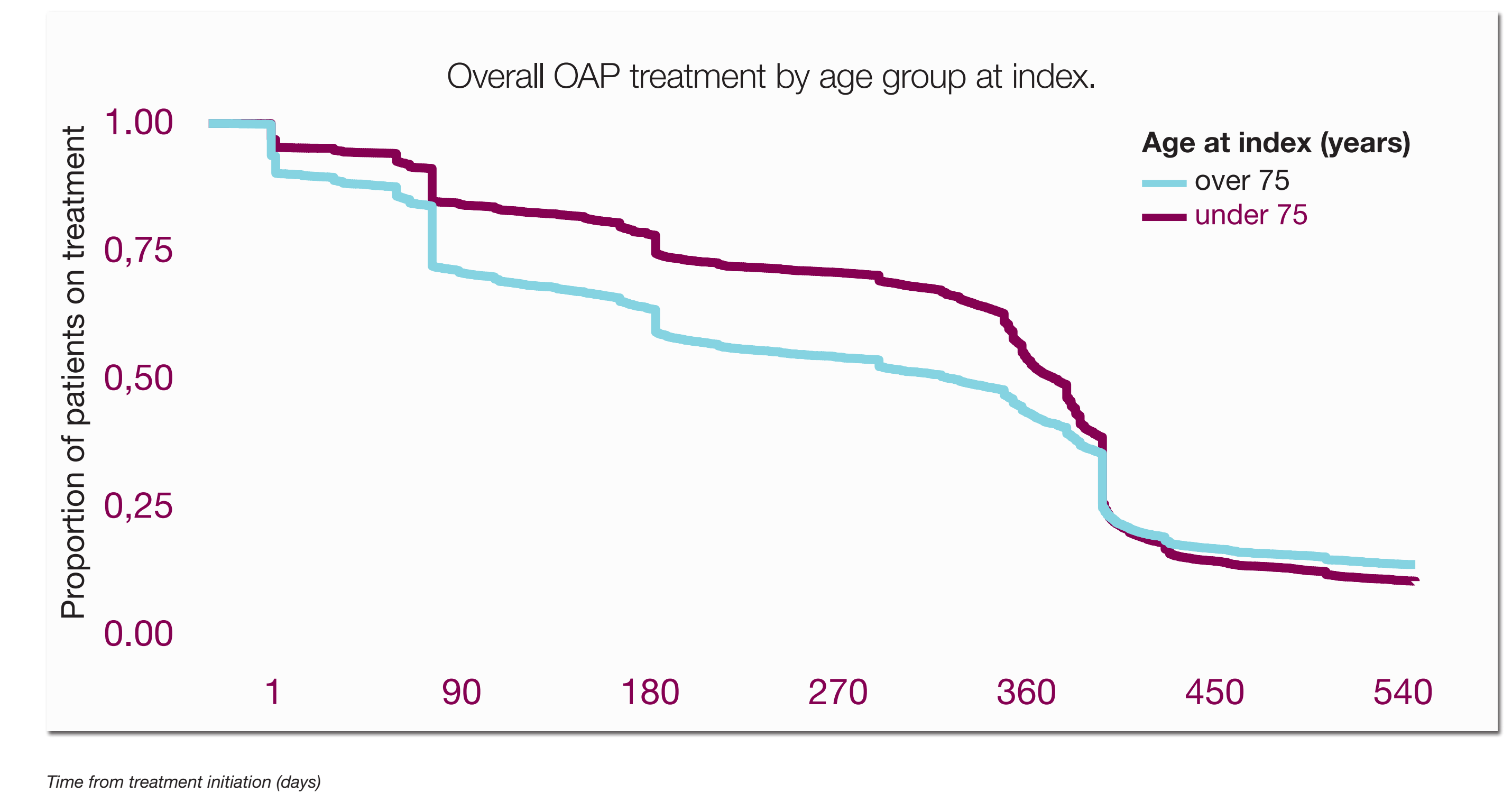
**Table 1.** Baseline patient characteristics.

	Age $\leq 75$ years, (n=29,372)	Age $>75$ years, (n=25,044)
Age, years, mean (SD)	62.5 (8.8)	83.4 (5.3)
Female gender	7804 (26.6)	13,840 (55.3)
NSTEMI	13,242 (45.1)	15,779 (63.0)
STEMI	9736 (33.1)	4771 (19.1)
Unstable angina pectoris	6394 (21.8)	4494 (17.9)
Angiography	17,788 (60.6)	7131 (28.5)
PCI	13,844 (47.1)	5032 (20.1)
<b>Comorbidity</b>		
Previous MI	1154 (3.9)	1955 (7.8)
Previous unstable angina pectoris	567 (1.9)	753 (3.0)
Heart failure	1132 (3.9)	3932 (15.7)
Stroke (total)	1240 (4.2)	2507 (10.0)
Hypertension	19241 (65.5)	22257 (88.9)
Dyslipidaemia	13922 (47.4)	13416 (53.6)
Diabetes mellitus	6607 (22.5)	6837 (27.3)
Dementia/Alzheimer's disease	133 (0.5)	1731 (6.9)
Cancer	1212 (4.1)	2078 (8.3)
<b>Drugs at discharge</b>		
P2Y12 inhibitors, all	18,027 (61.4)	8472 (33.8)
Clopidogrel	15,893 (54.1)	8084 (32.3)
Prasugrel	833 (2.8)	84 (0.3)
Ticagrelor	1301 (4.4)	304 (1.2)
Statins	25459 (86.7)	16051 (64.1)
Beta-blockers	25325 (86.2)	19326 (77.2)
ACE inhibitor or ARB	17989 (61.2)	11800 (47.1)

RSD, Relative Standard Deviation

ACE=angiotensin-converting enzyme; ARB=angiotensin receptor blocker; MI=myocardial infarction; NSTEMI=non-ST-elevation myocardial infarction; PCI=percutaneous coronary intervention; SD=standard deviation; STEMI=ST-elevation myocardial infarction

**Figure 1.** Overall P2Y12 persistence by age group at index.



**Figure 2.** P2Y12 persistence by age categories.

