

# Do Triple Single-Pill Combinations Make a Difference in Treatment Adherence, Outcomes and Healthcare Resource Utilization in Hypertension? A Real-World Analysis of Patients on Perindopril/Indapamide/Amlodipine in Italy

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## BACKGROUND AND OBJECTIVES

Sub-optimal adherence to antihypertensive treatment is an important cause of poor blood pressure control, and is associated with increased risk of CV events, comorbidities, mortality and healthcare costs [1]. It has been reported that increasing the number of antihypertensive medications is associated with a higher rate of nonadherence [1].

**KEY OBJECTIVE.** The objective of this **real-world analysis** was to compare adherence, outcomes and healthcare costs in hypertensive patients prescribed perindopril/indapamide/amlodipine (PER/IND/AML) as single-pill vs free combination, in Italy.

[1] Borghi C, Desideri G, Tocci G, Trimarco B, Nati G. Aderenza alla terapia delle malattie cardiovascolari croniche: nuove soluzioni. *G Ital Cardiol* 2021;22(5 Suppl 1):e86-e91

## METHODOLOGY

**DATA SOURCE:** This retrospective analysis used administrative databases of a sample of Local Health Units covering approximately 7 million health-assisted individuals.

**POPULATION:** Adult patients treated with PER/IND/AML during 2010-2020 were categorized into **2 cohorts**: those taking **single-pill or free** (defined as 2 or 3 pills) **combination**.

The **index date** corresponded to the first prescription of a single-pill combination (single-pill cohort) or the first prescription of the 3 drugs simultaneously (within 30 days) (free cohort).

**PROPENSITY SCORE MATCHING (PSM):** was applied to minimize selection bias and reduce potential imbalances between the two cohorts [the following variables were considered for PSM matching: age, sex, comorbidities (hypertensive disease, ischemic heart diseases, heart failure, cerebrovascular diseases, peripheral vascular diseases, diabetes, CKD disease: chronic obstructive pulmonary disease, psychiatric disease, co-treatments as ACE inhibitors, angiotensin II receptor blockers, beta blocking agents, calcium channel blockers, antithrombotic agents, antiarrhythmics, diuretics, lipid lowering drugs, digoxin, ivabradine, antiinflammatory drugs, antidepressants)].

## IN PSM-MATCHED COHORTS

**ADHERENCE:** was calculated as the proportion of days covered (PDC) during 12 months of follow-up; patients with PDC $\geq$ 80% were considered adherent.

**OUTCOMES: Incidence of mortality and CV events** (ischemic heart disease, heart failure, cerebrovascular disease, peripheral vascular disease) was analyzed after the first year of follow-up and reported as event rate per 1,000-person/year.

**HEALTHCARE COSTS: Total healthcare direct costs** (sum of costs for all-drugs, hospitalizations, outpatient services) covered by the Italian National Health System were reported in Euros (€).

## RESULTS

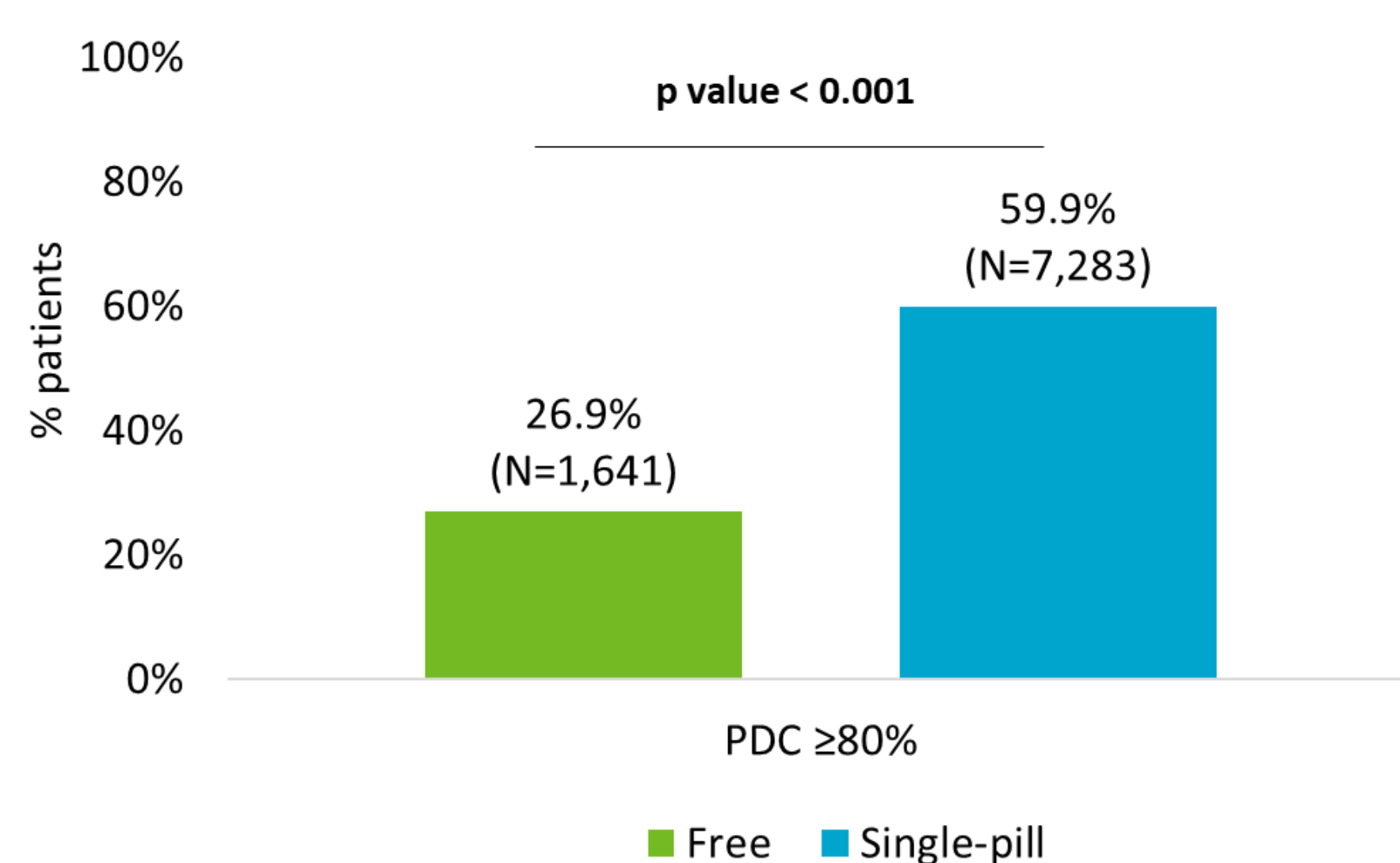
### DESCRIPTION OF STUDY POPULATION

✓ The analysis included 37,365 patients (54.3% male, mean age 66.0 $\pm$ 12.3 years) in the **single-pill cohort** and 6,105 (50.8% male, 68.2 $\pm$ 11.9) in the free cohort. **Post-PSM**, cohorts were balanced for their characteristics and comprised: **12,150** patients among **single-pill-cohort** and **6,105** patients among **free-cohort**.

### PATIENT ADHERENCE TO INDEX TREATMENT IN PSM-MATCHED COHORTS

✓ In the **single-pill-cohort**, a significantly **higher percentage** of patients were adherent versus the free-cohort (59.9% vs 26.9%, p<0.001) (**Figure 1**).

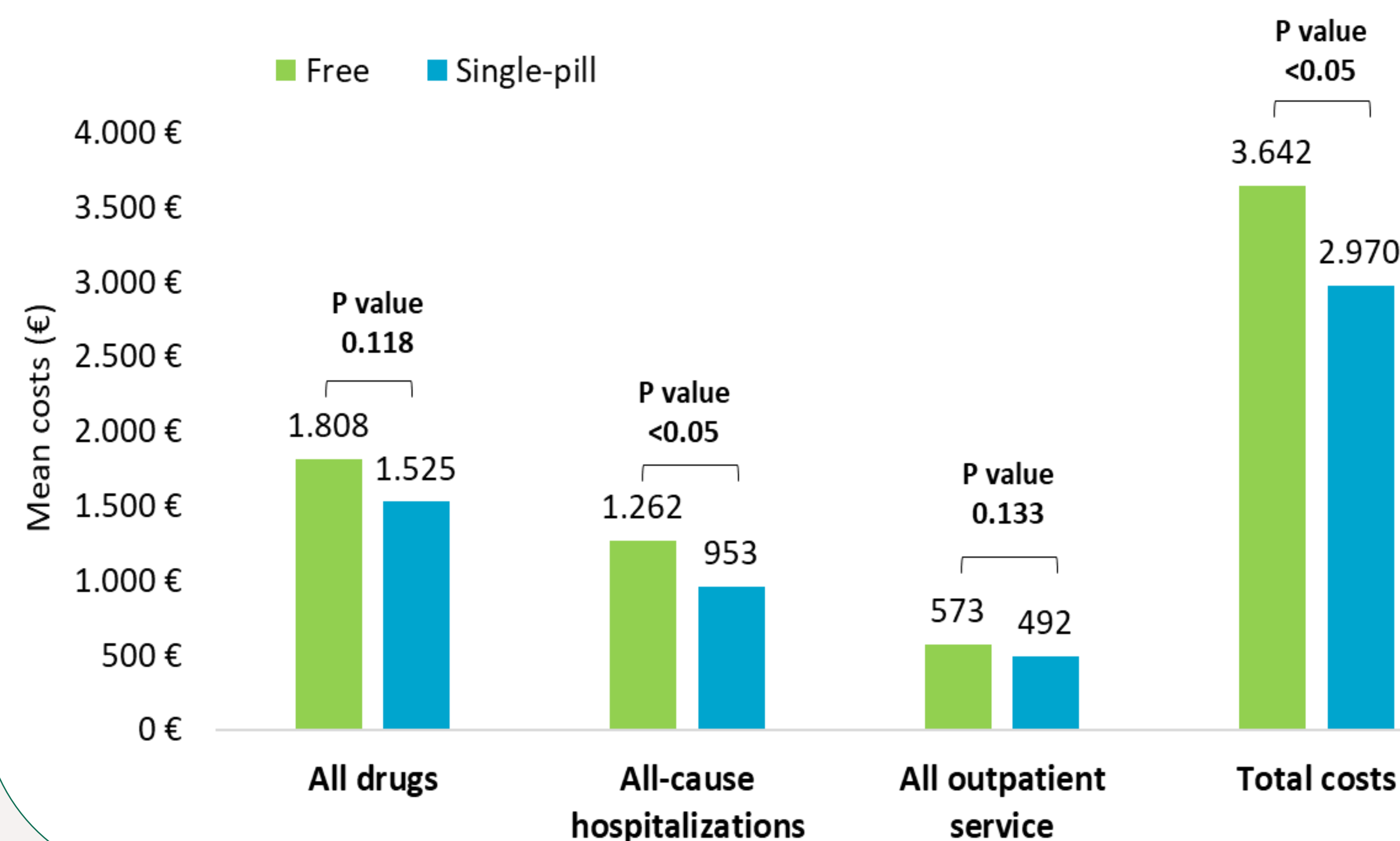
Figure 1. Adherence to treatment among the two PSM-matched cohorts, during one-year follow-up



### AVERAGE ANNUAL DIRECT HEALTHCARE COSTS IN PSM-MATCHED COHORTS

✓ In **free-combination versus single-pill cohort**, total healthcare direct costs/patient were higher (**€3,642 vs €2,970**, p<0.05). Among major cost drivers, drug-related costs did not decrease significantly (€1,808 vs €1,525, p=0.118), while hospitalizations decreased significantly (€1,262 vs €953, p<0.05) (**Figure 3**).

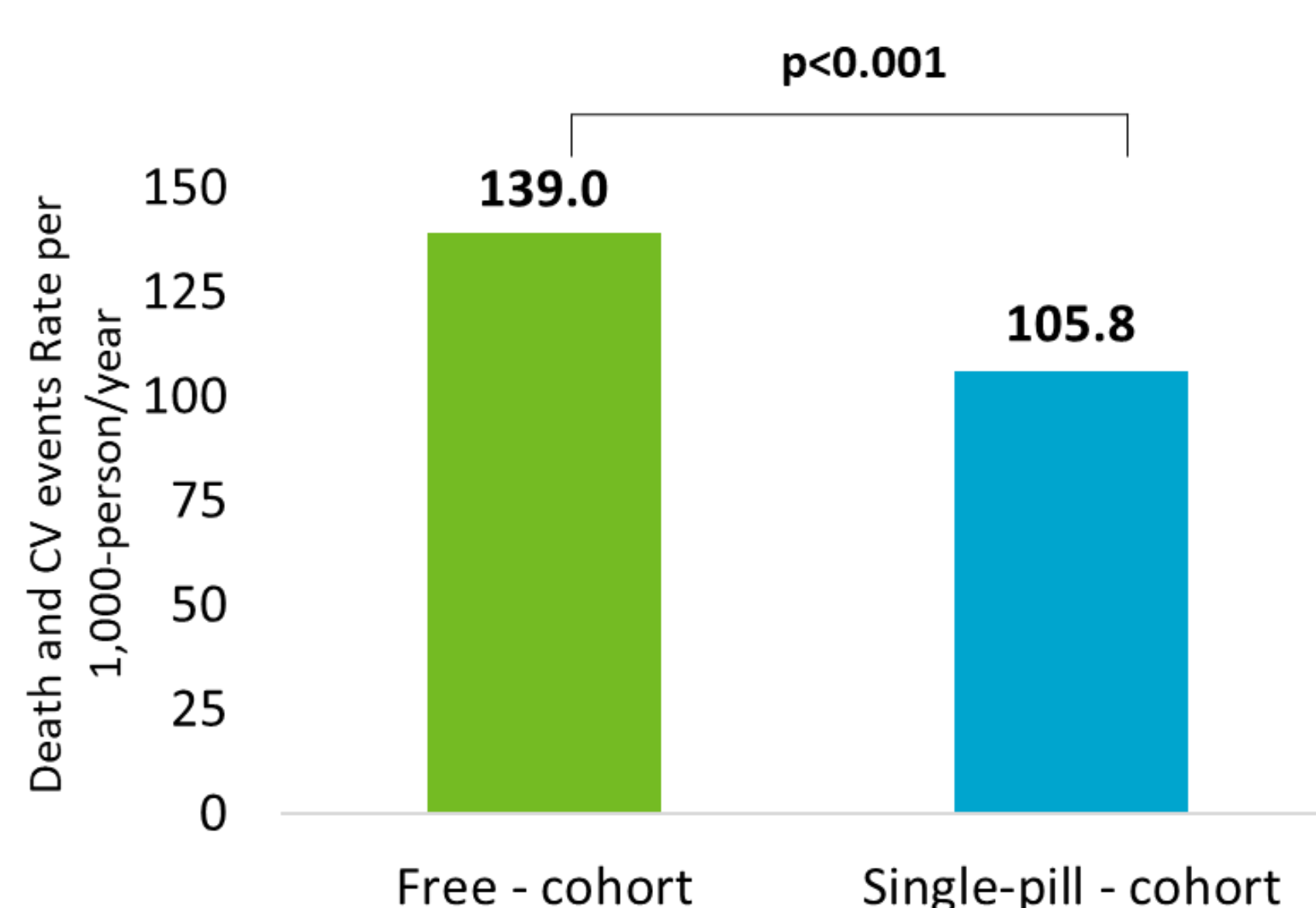
Figure 3. Mean annual healthcare direct costs evaluated during follow-up period



### INCIDENCE OF MORTALITY AND CV EVENTS IN PSM-MATCHED COHORTS

✓ The incidence of **death and CV events** (composite endpoint) was **significantly lower** in **single-pill-cohort** compared to free-cohort (105.8 vs 139.0 per 1,000-person/year, p<0.001) (**Figure 2**).

Figure 2. The death and CV events rate as a composite endpoint in free vs single-pill cohorts.



## CONCLUSIONS

This real-world analysis carried out in Italian clinical practice setting demonstrates that PER/IND/AML as single-pill, compared with a free combination, improved adherence and clinical outcomes and provided cost savings to the Italian National Healthcare System (funder).

**COI DISCLOSURES:** C.B. has received consultation fees and lecture honoraria from Servier, Novartis, Menarini Corporate, Novo Nordisk, Alfasigma, Sanofi; L.A.B. is a member of advisory board for Servier, Medtronic and Merck; J.R.S. is involved in data analyses and advisory services for Servier; P.B.J., A.K., L.D.E., V.P. declare no conflict of interest.