A real-word analysis of the adherence, outcomes and healthcare costs in patients treated with

perindopril/bisoprolol as single-pill or free combination

Short title: The Single Pill Combination perindopril/bisoprolol in clinical practice

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SUPPLEMENTARY TABLES

Supplementary table 1. List of ICD-9-CN codes used to define diseases.

COMORBIDITY	IDENTIFICATION CODES
HYPERTENSIVE DISEASE	ICD-9-CM codes 401-405
ISCHEMIC HEART DISEASES	ICD-9-CM codes 410-414
HEART FAILURE	ICD-9-CM code 428
CEREBROVASCULAR DISEASES	ICD-9-CM codes 430-438
PERIPHERAL VASCULAR DISEASES	ICD-9-CM codes 440-442
DIABETES	ICD-9-CM code 250 or at least two prescriptions of anti-diabetic drugs (ATC code: A10)
CKD DISEASE:	ICD-9-CM codes 585.3-5
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD):	Identified by at least two prescriptions for ATC R03.
PSYCHIATRIC DISEASE:	ICD-9-CM codes 290-319

Supplementary table 2. List of ATC codes used to define the presence of concomitant prescriptions.

CO-TREATMENTS	ATC CODES
LIPID-LOWERING AGENTS:	at least two prescriptions for ATC C10 (statins were identified as ATC code C10AA)
ANTIHYPERTENSIVE TREATMENTS (EXCLUDED STUDY DRUGS):	at least two prescriptions for ATC C02, C03, C07, C08, C09, excluded ATC C09AA04, C07AB07, C09BX02.
ANTITHROMBOTIC AGENTS	at least two prescriptions for ATC B01AA, B01AE
ANTIARRHYTHMICS	at least two prescriptions for ATC C01B
ANTIINFLAMMATORY DRUGS:	identified by identified by at least two prescriptions for ATC M01;
ANTIDEPRESSANTS:	at least two prescriptions for ATC N06A.

Supplementary table 3. Clinical characteristics of the patients included in the study, stratified by SPC or FEC use before PSM.

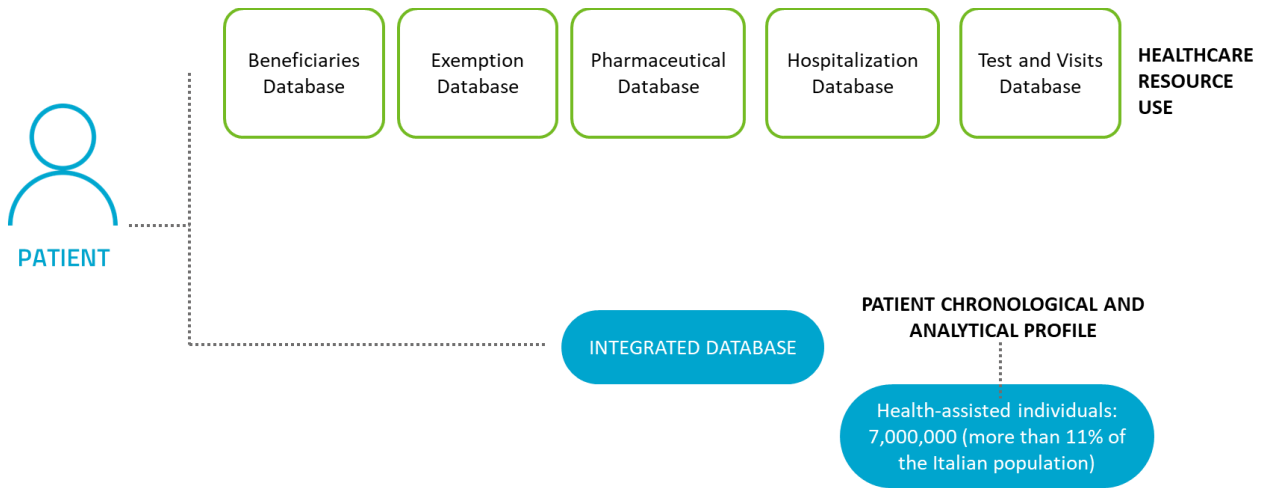|	Cohort FEC (N= 6,521)	Cohort SPC (N=11,440)	P-value
Age, mean (SD)	6,521	11,440	<0.001
Male, N (%)	72.9 (11.8)	63.3 (12.9)	<0.001
COPD, N (%)	3403 (52.2)	5131 (44.9)	0.500
Diabetes, N (%)	1975 (30.3)	3520 (30.8)	<0.001
Primary prevention, N (%)	1602 (24.6)	2146 (18.8)	<0.001
Secondary prevention, N (%)	4658 (71.4)	9721 (85.0)	
Ischemic heart disease, N (%)	1863 (28.6)	1719 (15.0)	<0.001
Heart failure, N (%)	1153 (17.7)	1157 (10.1)	<0.001
Cerebrovascular disease, N (%)	441 (6.8)	352 (3.1)	<0.001
Peripheral vascular disease, N (%)	677 (10.4)	517 (4.5)	<0.001
CKD disease, N (%)	230 (3.5)	228 (2.0)	<0.001
Psychiatric disease, N (%)	103 (1.6)	83 (0.7)	<0.001

Supplementary table 4. Drug prescription of the patients included in the study, stratified by SPC or FEC use before PSM.

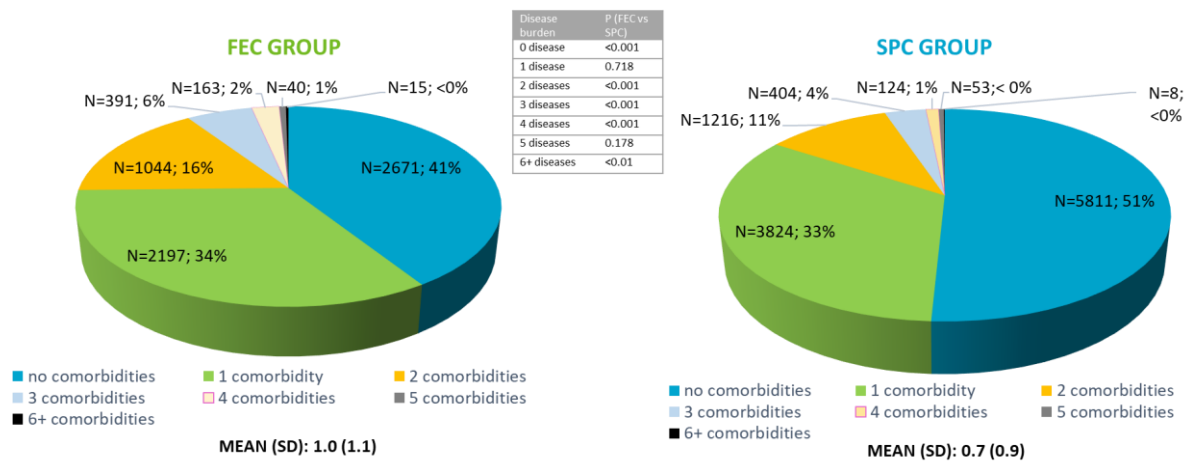| *Previous treatment*	Cohort FEC (N= 6,521)	Cohort SPC (N=11,440)	P-value
Other antihypertensive treatment, N (%)	4889 (75.0)	9051 (79.1)	<0.001
Lipid-lowering treatment, N (%)	3717 (57.0)	4484 (39.2)	<0.001
Statins, N (%)	3416 (52.4)	4100 (35.8)	<0.001
ACE inhibitors*, N (%)	2469 (37.9)	5081 (44.4)	<0.001
Angiotensin II Receptor Blockers , N (%)	1307 (20.0)	3641 (31.8)	<0.001
Beta Blocking Agents, N (%)	1265 (19.4)	4256 (37.2)	<0.001
Calcium Channel Blockers, N (%)	2061 (31.6)	2564 (22.4)	<0.001
Diuretics**, N (%)	2143 (32.9)	1959 (17.1)	<0.001
Antithrombotic Agents, N (%)	805 (12.3)	515 (4.5)	<0.001
Antiarrhythmics, N (%)	654 (10.0)	560 (4.9)	<0.001
Digoxin, N (%)	340 (5.2)	191 (1.7)	<0.001
Ivrabadina, N (%)	134 (2.1)	200 (1.7)	0.143
Antiinflammatory treatment, N (%)	3641 (55.8)	6927 (60.6)	<0.001
Antidepressants, N (%)	1194 (18.3)	1853 (16.2)	<0.001

Note. * excluded those used for inclusion. **Diuretics analyzed comprised: thizides, high-ceiling diuretics, spironolactone.

SUPPLEMENTARY FIGURES

Supplementary Figure 1.

Supplementary Figure 2.
Disease burden in the subjects taking SPC or FEC included in the study those in the FEC group.

Supplementary Figure 3. Pill burden in the subjects taking SPC or FEC included in the study those in the FEC group.

FEC GROUP

N=211; 3%
N=91; 1%
N=62; 1%
N=478; 7%
N=1023; 16%
N=2770; 43%
N=1886; 29%

pill burden	P (FEC vs SPC)
No extra pills	<0.001
1 extra pills	<0.01
2 extra pills	<0.05
3 extra pills	<0.01
4 extra pills	<0.01
5 extra pills	=0.05
6+ extra pills	0.057

■ no extra pills ■ 1 extra pill ■ 2 extra pills ■ 3 extra pills
□ 4 extra pills ▨ 5 extra pills ■ 6+ extra pills

MEAN (SD): 1.5 (1.4)

SPC GROUP

N=702; 6%
N=293; 3%
N=122; 1%
N=79; 1%
N=1647; 14%
N=5503; 48%
N=3094; 27%

■ no extra pills ■ 1 extra pill ■ 2 extra pills ■ 3 extra pills
□ 4 extra pills ▨ 5 extra pills ■ 6+ extra pills

MEAN (SD): 1.3 (1.3)