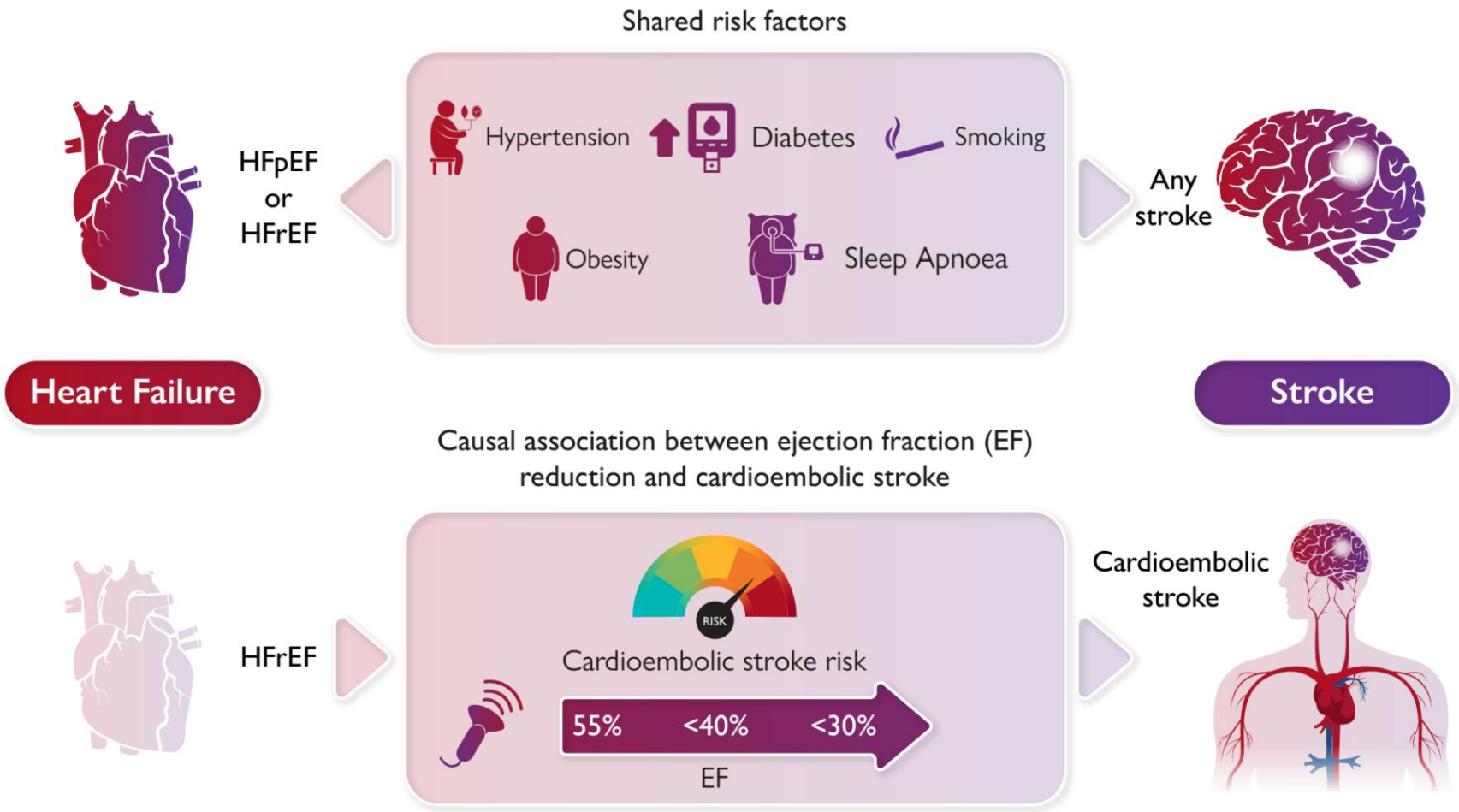
Ictus ischemico nei pazienti con scompenso cardiaco a frazione di eiezione ridotta o preservata

Background

- Stroke is an important problem in patients with heart failure, but the intersection between the two conditions is poorly studied across the range of ejection fraction, even though each is common and results in considerable morbidity and premature loss of life.
- Patients with heart failure, including those in sinus rhythm, are at increased risk of stroke, probably because of underlying atherosclerosis and a heightened risk of thromboembolism. In patients with reduced ejection fraction, the left ventricular endocardium may be abnormal and blood stasis may occur, along with activation of blood coagulation; in this context, atrial myopathy, without atrial fibrillation, may also be relevant. Other factors such as hypotension and abnormal autoregulation of the cerebral circulation may also be important
- Very little is known in either heart failure phenotype about the characteristics and outcomes of patients with prevalent stroke, despite a history of stroke being reported in up to 15% of ambulatory patients with heart failure, compared with 1%-3% of the general population.

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Hypothetical relationship between heart failure and ischemic stroke



Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Stroke in patients with heart failure and reduced or preserved ejection fraction

Mingming Yang[1,2], Toru Kondo[1,3], Jawad H. Butt [1,4], William T. Abraham [5], Inder S. Anand [6,7], Akshay S. Desai [8], Lars Køber[4], Milton Packer [9], Marc A. Pfeffer[8], Jean L. Rouleau[10], Marc S. Sabatine[11], Scott D. Solomon [8], Karl Swedberg[12,13], Michael R. Zile[14], Pardeep S. Jhund [1], and John J.V. McMurray [1]*

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Methods and aims

- Because the overlap between heart failure and prevalent stroke has not been studied in detail, the authors examined the clinical characteristics of patients with HFrEF and HFpEF with prior stroke, compared with those without a history of stroke, and the clinical outcomes in patients with prior stroke compared with those without.
- The aims included
  - Description of the potential impact of stroke on quality of life and non-atherothrombotic outcomes in patients with heart failure, across the spectrum of ejection fraction
  - Description of the use of therapies to improve atherothrombotic as well as heart failure outcomes as this may identify gaps in care and the opportunity to improve outcomes.
- Using patient-level data from three recent HFrEF trials (ATMOSPHERE, PARADIGM-HF, and DAPA-HF) and four HFpEF trials (CHARM-Preserved, I-Preserve, TOPCAT, and PARAGON-HF).

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Baseline characteristics

- Patients with a history of stroke were slightly older and more likely to come from North America but did not differ by sex.

	HFrEF (*N* = 20 159)		SMD[a] 95% (CI)	HFpEF (*N* = 13252)		SMD[a] 95% CI
	No prior stroke (*n* = 18 476)	Prior stroke (*n* = 1683)		No prior stroke (*n* = 11 965)	Prior stroke (*n* = 1287)	
Baseline characteristics						
Age, years	64.0 ± 11.6	66.8 ± 10.0	0.262 (0.212–0.312)	71.0 ± 9.1	72.2 ± 8.4	0.140 (0.082–0.198)
Age groups, years			0.276 (0.226–0.326)			0.141 (0.083–0.198)
≤40	642 (3.5)	18 (1.1)		33 (0.3)	0 (0.0)	
41–55	3413 (18.5)	190 (11.3)		588 (4.9)	42 (3.3)	
56–70	8653 (46.8)	837 (49.7)		4826 (40.3)	477 (37.1)	
>70	5768 (31.2)	638 (37.9)		6518 (54.5)	768 (59.7)	
Sex			0.049 (−0.001 to 0.099)			0.042 (−0.016 to 0.099)
Female	4124 (22.3)	342 (20.3)		6284 (52.5)	649 (50.4)	
Male	14 352 (77.7)	1341 (79.7)		5681 (47.5)	638 (49.6)	
Region			0.206 (0.156–0.256)			0.153 (0.096–0.211)
North America	1304 (7.1)	152 (9.0)		2999 (25.1)	368 (28.6)	
Latin America[b]	3118 (16.9)	251 (14.9)		1281 (10.7)	95 (7.4)	
Western Europe	4068 (22.0)	384 (22.8)		3640 (30.4)	381 (29.6)	
Eastern Europe[c]	5749 (31.1)	625 (37.1)		3149 (26.3)	319 (24.8)	
Asia/Pacific and other	4237 (22.9)	271 (16.1)		896 (7.5)	124 (9.6)	
Race			0.167 (0.117–0.217)			0.116 (0.058–0.173)
White	12 244 (66.3)	1225 (72.8)		10 385 (86.8)	1109 (86.2)	
Black	690 (3.7)	73 (4.3)		526 (4.4)	67 (5.2)	
Asian	4116 (22.3)	273 (16.2)		636 (5.3)	86 (6.7)	
Others	1426 (7.7)	112 (6.7)		418 (3.5)	25 (1.9)	
SBP, mmHg	122.2 ± 16.6	123.1 ± 16.6	0.056 (0.006–0.106)	133.1 ± 16.4	133.5 ± 16.8	0.027 (−0.031 to 0.084)
SBP category			0.075 (0.025–0.125)			0.045 (−0.012 to 0.103)
<110	4059 (22.0)	359 (21.3)		676 (5.7)	83 (6.4)	
110–119	3936 (21.3)	314 (18.7)		1526 (12.8)	151 (11.7)	
120–129	4232 (22.9)	410 (24.4)		2361 (19.7)	249 (19.3)	
130–129	3263 (17.7)	308 (18.3)		2834 (23.7)	310 (24.1)	

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Baseline characteristics

- Blood pressure, pulse pressure, heart rate, BMI, did not differ meaningfully between patients with and without a history of stroke.
- A history of AF and AF of the baseline ECG, diabetes, hypertension, CAD, and PAD was more frequent in patients with a history of stroke. Mean eGFR was lower in patients with a history of stroke, as was the proportion of patients with CKD

	HFrEF ($N = 20\,159$)		SMD[a] 95% (CI)	HFpEF ($N = 13252$)		SMD[a] 95% CI
	No prior stroke ($n = 18\,476$)	Prior stroke ($n = 1683$)		No prior stroke ($n = 11\,965$)	Prior stroke ($n = 1287$)	
≥140	2984 (16.2)	292 (17.3)		4565 (38.2)	494 (38.4)	
DBP, mmHg	74.0 ± 10.6	74.1 ± 10.4	0.010 (−0.040 to 0.060)	76.0 ± 10.6	75.5 ± 10.8	0.053 (−0.004 to 0.111)
PP, mmHg	48.2 ± 13.0	49.0 ± 13.0	0.063 (0.013–0.113)	57.1 ± 14.4	58.1 ± 15.0	0.069 (0.012–0.127)
MAP, mmHg	90.1 ± 11.4	90.4 ± 11.3	0.033 (−0.017 to 0.083)	95.0 ± 10.9	94.8 ± 11.1	0.021 (−0.036 to 0.079)
HR, bpm	72.0 ± 12.1	71.2 ± 12.0	0.064 (0.014–0.114)	70.7 ± 11.7	71.4 ± 12.1	0.064 (0.006–0.122)
BMI, kg/m^2	27.1 (24.0–31.0)	27.1 (24.2–31.0)	0.029 (−0.021 to 0.079)	29.4 (26.2–33.7)	29.4 (26.2–33.6)	0.007 (−0.051 to 0.064)
Weight category			0.069 (0.019–0.119)			0.045 (−0.013 to 0.102)
< 18.5	372 (2.0)	22 (1.3)		60 (0.5)	3 (0.2)	
18.5–25.0	5363 (29.1)	463 (27.6)		1964 (16.5)	215 (16.7)	
25.0–30	6929 (37.6)	663 (39.5)		4346 (36.4)	469 (36.5)	
≥ 30.0	5784 (31.4)	532 (31.7)		5559 (46.6)	599 (46.6)	
CHA_2DS_2-VASc[d]	3.0 (2.0–4.0)	6.0 (5.0–7.0)	1.784 (1.731–1.837)	4.0 (4.0–5.0)	7.0 (6.0–7.0)	1.947 (1.872–2.022)
Comorbidities and personal habits						
Atrial fibrillation (history)	6501 (35.2)	798 (47.4)	0.250 (0.200–0.300)	4657 (38.9)	620 (48.2)	0.188 (0.130–0.246)
Hypertension	12 448 (67.4)	1347 (80.0)	0.291 (0.241–0.341)	10 345 (86.5)	1160 (90.1)	0.114 (0.057–0.172)
CHD[e]	11 507 (62.3)	1239 (73.6)	0.245 (0.195–0.295)	6340 (53.0)	760 (59.1)	0.122 (0.065–0.180)
Angina pectoris[f]	4608 (24.9)	527 (31.3)	0.142 (0.092–0.192)	3902 (32.6)	449 (34.9)	0.048 (−0.009 to 0.106)
MI	7717 (41.8)	856 (50.9)	0.183 (0.133–0.233)	3052 (25.5)	411 (31.9)	0.142 (0.085–0.200)
Prior PCI/CABG	6092 (33.0)	633 (37.6)	0.097 (0.047–0.147)	2900 (24.2)	362 (28.1)	0.089 (0.031–0.146)
PCI	4378 (23.7)	426 (25.3)	0.038 (−0.012 to 0.087)	1574 (19.1)	187 (21.1)	0.049 (−0.021 to 0.118)
CABG	2752 (14.9)	328 (19.5)	0.122 (0.072–0.172)	1272 (15.4)	169 (19.0)	0.095 (0.026–0.164)
Cerebral vascular disease						
Subtypes of stroke						
Ischaemic[g]		1130 (94.9)			402 (79.1)	
Haemorrhagic[g]		56 (4.7)			25 (4.9)	
Other/unknown[g]		-			81 (15.9)	
Prior TIA	494 (2.7)	125 (7.4)	0.218 (0.168–0.268)	172 (4.0)	54 (10.7)	0.256 (0.164–0.349)
Carotid artery disease[h]	641 (3.5)	190 (11.3)	0.303 (0.253–0.353)	238 (5.6)	55 (10.9)	0.193 (0.101–0.285)

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Baseline characteristics

- History of carotid artery disease (including carotid endarterectomy) and TIA were more frequent in patients with a history of stroke.
- Patients with a history of stroke were more likely to have an ischaemic aetiology and longer-standing heart failure.
- They were also more likely to have worse NYHA functional class and patient-reported health-related quality of life.

	HFrEF ($N = 20\,159$)		SMD[a] 95% (CI)	HFpEF ($N = 13252$)		SMD[a] 95% CI
	No prior stroke ($n = 18\,476$)	Prior stroke ($n = 1683$)		No prior stroke ($n = 11\,965$)	Prior stroke ($n = 1287$)	
Carotid artery stenosis	579 (3.1)	184 (10.9)	0.309 (0.259–0.359)	191 (4.5)	42 (8.3)	0.156 (0.064–0.249)
Carotid artery revascularization	183 (1.0)	52 (3.1)	0.149 (0.099–0.199)	30 (0.7)	8 (1.6)	0.083 (–0.009 to 0.175)
Carotid artery endarterectomy	-	-		41 (1.0)	19 (3.7)	0.184 (0.092–0.276)
PAD[i]	1053 (5.7)	171 (10.2)	0.166 (0.116–0.216)	393 (6.7)	72 (10.8)	0.147 (0.066–0.227)
Lower limb stenosis	341 (2.4)	53 (4.4)	0.108 (0.050–0.167)	90 (2.1)	16 (3.2)	0.065 (–0.027 to 0.157)
Lower limb revascularization	350 (1.9)	44 (2.6)	0.049 (–0.001 to 0.098)	102 (2.4)	13 (2.6)	0.011 (–0.081 to 0.103)
Intermittent claudication	587 (4.1)	87 (7.1)	0.131 (0.072–0.189)	131 (3.1)	29 (5.7)	0.129 (0.037–0.221)
PAOD	273 (6.4)	51 (10.9)	0.163 (0.067–0.258)	-	-	
Renal artery stenosis	55 (0.3)	14 (0.8)	0.071 (0.021–0.121)	22 (0.5)	10 (2.0)	0.132 (0.040–0.224)
Abdominal aortic aneurism	242 (1.3)	43 (2.6)	0.091 (0.041–0.140)	54 (1.3)	9 (1.8)	0.042 (–0.050 to 0.134)
Non-cardiovascular systems						
COPD/asthma	2686 (14.5)	269 (16.0)	0.040 (–0.010 to 0.090)	1513 (15.7)	213 (20.0)	0.112 (0.048–0.175)
Diabetes Mellitus	6173 (33.4)	661 (39.3)	0.122 (0.072–0.172)	4170 (34.9)	541 (42.0)	0.148 (0.091–0.206)
Anaemia[j]	4245 (23.4)	367 (22.2)	0.028 (–0.023 to 0.078)	2296 (22.3)	286 (25.2)	0.068 (0.007–0.129)
Current smoker	2559 (13.9)	243 (14.4)	0.017 (–0.033 to 0.067)	1371 (11.5)	155 (12.1)	0.018 (–0.040 to 0.075)
HF characteristics and investigations						
Ischaemic aetiology[k]	10 498 (56.8)	1142 (67.9)	0.229 (0.179–0.279)	4417 (36.9)	539 (41.9)	0.102 (0.044–0.159)
Time since HF diagnosis			0.277 (0.227–0.327)			0.101 (0.040–0.163)
≤1 year	5647 (30.6)	335 (19.9)		4610 .6)	448 (39.8)	
>1–5 years	6978 (37.8)	638 (37.9)		3712 (35.9)	431 (38.2)	
>5 years	5847 (31.7)	710 (42.2)		2011 (19.5)	248 (22.0)	
Previous hospitalization for HF	10720 (58.0)	993 (59.0)	0.020 (–0.030 to 0.070)	6223 (52.0)	679 (52.8)	0.015 (–0.043 to 0.072)
NYHA class III/IV	5574 (30.2)	623 (37.0)	0.145 (0.095–0.195)	5188 (43.4)	619 (48.1)	0.095 (0.038–0.153)
Quality of life scores						
KCCQ clinical summary score	74.7 ± 19.7	70.5 ± 20.9	0.205 (0.152–0.257)	69.1 ± 20.9	65.9 ± 20.9	0.154 (0.073–0.235)
MLWHF	-	-		42.0 (26.0–58.0)	44.0 (28.0–61.0)	0.101 (–0.005 to 0.206)
Signs of congestion						
Dyspnoea on effort	12 110 (85.4)	1057 (86.9)	0.041 (–0.017 to 0.100)	7812 (94.9)	836 (94.1)	0.035 (–0.035 to 0.104)

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Baseline characteristics

- History of stroke was associated with a higher frequency of fatigue, oedema, and a higher NT-proBNP concentration, even in patients without AF.
- Mean LVEF did not differ between patients with and without a history of stroke.

	HFrEF ($N = 20\,159$)		SMD[a] 95% (CI)	HFpEF ($N = 13252$)		SMD[a] 95% CI
	No prior stroke ($n = 18\,476$)	Prior stroke ($n = 1683$)		No prior stroke ($n = 11\,965$)	Prior stroke ($n = 1287$)	
Baseline characteristics						
Age, years	64.0 ± 11.6	66.8 ± 10.0	0.262 (0.212–0.312)	71.0 ± 9.1	72.2 ± 8.4	0.140 (0.082–0.198)
Age groups, years			0.276 (0.226–0.326)			0.141 (0.083–0.198)
≤40	642 (3.5)	18 (1.1)		33 (0.3)	0 (0.0)	
41–55	3413 (18.5)	190 (11.3)		588 (4.9)	42 (3.3)	
56–70	8653 (46.8)	837 (49.7)		4826 (40.3)	477 (37.1)	
>70	5768 (31.2)	638 (37.9)		6518 (54.5)	768 (59.7)	
Sex			0.049 (−0.001 to 0.099)			0.042 (−0.016 to 0.099)
Female	4124 (22.3)	342 (20.3)		6284 (52.5)	649 (50.4)	
Male	14 352 (77.7)	1341 (79.7)		5681 (47.5)	638 (49.6)	
Region			0.206 (0.156–0.256)			0.153 (0.096–0.211)
North America	1304 (7.1)	152 (9.0)		2999 (25.1)	368 (28.6)	
Latin America[b]	3118 (16.9)	251 (14.9)		1281 (10.7)	95 (7.4)	
Western Europe	4068 (22.0)	384 (22.8)		3640 (30.4)	381 (29.6)	
Eastern Europe[c]	5749 (31.1)	625 (37.1)		3149 (26.3)	319 (24.8)	
Asia/Pacific and other	4237 (22.9)	271 (16.1)		896 (7.5)	124 (9.6)	
Race			0.167 (0.117–0.217)			0.116 (0.058–0.173)
White	12 244 (66.3)	1225 (72.8)		10 385 (86.8)	1109 (86.2)	
Black	690 (3.7)	73 (4.3)		526 (4.4)	67 (5.2)	
Asian	4116 (22.3)	273 (16.2)		636 (5.3)	86 (6.7)	
Others	1426 (7.7)	112 (6.7)		418 (3.5)	25 (1.9)	
SBP, mmHg	122.2 ± 16.6	123.1 ± 16.6	0.056 (0.006–0.106)	133.1 ± 16.4	133.5 ± 16.8	0.027 (−0.031 to 0.084)
SBP category			0.075 (0.025–0.125)			0.045 (−0.012 to 0.103)
<110	4059 (22.0)	359 (21.3)		676 (5.7)	83 (6.4)	
110–119	3936 (21.3)	314 (18.7)		1526 (12.8)	151 (11.7)	
120–129	4232 (22.9)	410 (24.4)		2361 (19.7)	249 (19.3)	
130–129	3263 (17.7)	308 (18.3)		2834 (23.7)	310 (24.1)	

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Baseline characteristics

- Patients with a history of stroke were more likely to be treated with a calcium channel blocker, statin, and anticoagulant.
- The use of statins was relatively low in patients with arterial disease (74% in HFrEF and 66% in HFpEF), as was the use of anticoagulants in those with AF (76% in HFrEF and 62% in H pEF).
- Patients with prior stroke were also more likely to have a pacemaker

	HFrEF ($N = 20\,159$)		SMD[a] 95% (CI)	HFpEF ($N = 13252$)		SMD[a] 95% CI
	No prior stroke ($n = 18\,476$)	Prior stroke ($n = 1683$)		No prior stroke ($n = 11\,965$)	Prior stroke ($n = 1287$)	
BUN, mmol/L	7.0 (5.5–8.9)	7.5 (6.1–9.7)	0.233 (0.183–0.283)	7.1 (5.7–9.3)	7.5 (6.0–10.0)	0.110 (0.048–0.171)
Creatinine, μmol/L	93.0 (79.0–111.0)	99.9 (83.3–121.0)	0.261 (0.211–0.311)	88.4 (71.0–108.7)	95.0 (79.0–118.0)	0.194 (0.133–0.255)
eGFR, mL/min/1.73 m^2	68.0 (55.0–82.0)	63.0 (50.0–76.0)	0.279 (0.23–0.329)	65.2 (51.7–80.0)	61.1 (47.7–76.5)	0.191 (0.130–0.252)
eGFR <60, mL/min/1.73 m^2	6112 (33.1)	724 (43.0)	0.206 (0.156–0.256)	4192 (40.4)	561 (49.0)	0.172 (0.111–0.234)
HbA1c, %	6.1 (5.7–6.8)	6.1 (5.7–7.1)	0.069 (−0.026 to 0.165)	6.2 (5.8–7.0)	6.3 (5.8–7.2)	0.091 (0.007–0.176)
Medication and other interventions						
Diuretics	15 369 (83.2)	1400 (83.2)	0.000 (−0.050 to 0.050)	10342 (86.4)	1148 (89.2)	0.084 (0.027–0.142)
Loop	14 013 (75.8)	1278 (75.9)	0.002 (−0.048 to 0.052)	6692 (64.6)	800 (70.9)	0.134 (0.072–0.195)
Thiazides	1271 (6.9)	120 (7.1)	0.010 (−0.040 to 0.060)	2386 (23.0)	222 (19.7)	0.082 (0.021–0.144)
Digitalis	5216 (28.2)	452 (26.9)	0.031 (−0.019 to 0.081)	1692 (14.1)	210 (16.3)	0.061 (0.003–0.118)
Beta-blocker	17 233 (93.3)	1568 (93.2)	0.004 (−0.046 to 0.054)	8156 (68.2)	889 (69.1)	0.019 (−0.038 to 0.077)
MRA [n,o]	9747 (52.8)	896 (53.2)	0.010 (−0.040 to 0.060)	1942 (18.8)	230 (20.4)	0.041 (−0.021 to 0.102)
ACEI/ARB/ARNI[p]	18 213 (98.6)	1644 (97.7)	0.066 (0.016–0.116)	5548 (94.3)	632 (94.9)	0.027 (−0.053 to 0.107)
CCB	1698 (9.2)	228 (13.5)	0.138 (0.088–0.188)	4294 (35.9)	499 (38.8)	0.060 (0.002–0.117)
Nitrates	3137 (17.0)	301 (17.9)	0.024 (−0.026 to 0.074)	2641 (22.1)	309 (24.0)	0.046 (−0.012 to 0.103)
Statins	10 442 (56.5)	1119 (66.5)	0.206 (0.156–0.256)	4775 (49.7)	631 (59.2)	0.193 (0.130–0.256)
In patients with arterial disease[q]	8374 (71.7)	933 (73.5)	0.041 (−0.017 to 0.099)	3011 (60.7)	419 (65.8)	0.105 (0.023–0.188)
Antiarrhythmics	2077 (11.2)	190 (11.3)	0.002 (−0.048 to 0.051)	1131 (9.5)	135 (10.5)	0.035 (−0.023 to 0.092)
Antiplatelet	10 255 (55.5)	940 (55.9)	0.007 (−0.043 to 0.057)	5102 (42.6)	589 (45.8)	0.063 (0.005–0.120)
Aspirin	9388 (50.8)	828 (49.2)	0.032 (−0.018 to 0.082)	6064 (50.7)	613 (47.6)	0.061 (0.004–0.119)
Anticoagulant	5957 (32.2)	815 (48.4)	0.334 (0.284–0.384)	3143 (26.3)	460 (35.7)	0.206 (0.148–0.263)
Atrial fibrillation/flutter[m]	3240 (74.0)	401 (78.5)	0.105 (0.013–0.196)	1828 (66.6)	259 (69.8)	0.068 (−0.040 to 0.177)
Atrial fibrillation history	4509 (69.4)	603 (75.6)	0.139 (0.066–0.213)	2744 (58.9)	387 (62.4)	0.072 (−0.012 to 0.155)
CHA_2DS_2-VASc score ≥2	5495 (32.6)	815 (48.4)	0.328 (0.277–0.378)	2194 (28.7)	313 (35.2)	0.141 (0.071–0.210)
Alpha adrenoceptor blocker	189 (1.0)	23 (1.4)	0.032 (−0.018 to 0.082)	389 (6.6)	51 (7.7)	0.041 (−0.039 to 0.121)
Insulin of patients with diabetes	1555 (25.2)	182 (27.5)	0.053 (−0.027 to 0.133)	866 (30.8)	126 (33.2)	0.053 (−0.055 to 0.160)
Pacemaker	2186 (11.8)	278 (16.5)	0.135 (0.085–0.185)	1005 (8.4)	135 (10.5)	0.072 (0.014–0.129)

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

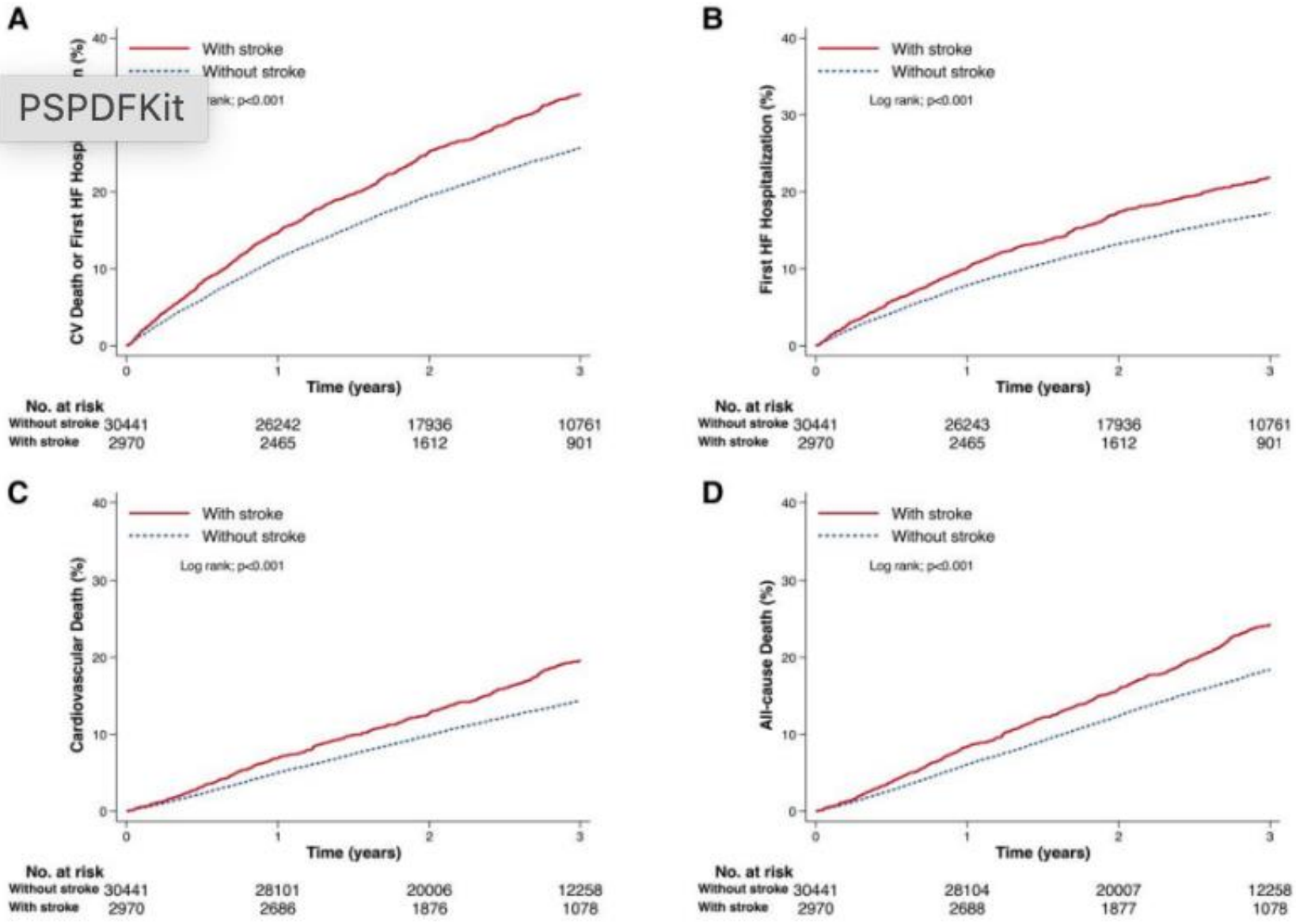
Clinical outcome of HF patients with or without prior stroke

	Total events		Events per 100 person-years (95% CI)		Stroke vs. nonstroke	
	No prior stroke ($n = 30\,441$)	Prior stroke ($n = 2970$)	No prior stroke ($n = 30\,441$)	Prior stroke ($n = 2970$)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
CV death or HF hosp.						
Overall	7578 (24.9)	934 (31.5)	9.97 (9.75–10.20)	13.54 (12.70–14.44)	1.34 (1.26–1.44)	1.18 (1.10–1.27)
HFrEF	4756 (25.7)	521 (31.0)	11.89 (11.55–12.23)	15.66 (14.37–17.06)	1.30 (1.19–1.43)	1.17 (1.07–1.28)
HFpEF	2822 (23.6)	413 (32.1)	7.84 (7.56–8.14)	11.57 (10.51–12.74)	1.46 (1.32–1.62)	1.19 (1.07–1.33)
First HF hosp.						
Overall	4806 (15.8)	586 (19.7)	6.32 (6.15–6.50)	8.50 (7.84–9.21)	1.32 (1.21–1.44)	1.12 (1.03–1.23)
HFrEF	2761(14.9)	307 (18.2)	6.90 (6.65–7.16)	9.23 (8.25–10.32)	1.31 (1.17–1.48)	1.16 (1.03–1.31)
HFpEF	2045 (17.1)	279 (21.7)	5.68 (5.44–5.93)	7.82 (6.95–8.79)	1.35 (1.19–1.53)	1.08 (0.95–1.23)
Cardiovascular death						
Overall	4327 (14.2)	576 (19.4)	5.23 (5.08–5.39)	7.49 (6.90–8.13)	1.44 (1.32–1.57)	1.31 (1.20–1.43)
HFrEF	3024 (16.4)	348 (20.7)	6.98 (6.74–7.24)	9.50 (8.55–10.55)	1.37 (1.22–1.53)	1.23 (1.10–1.37)
HFpEF	1303 (10.9)	228 (17.7)	3.31 (3.13–3.49)	5.67 (4.98–6.45)	1.73 (1.50–1.99)	1.44 (1.25–1.66)
All-cause death						
Overall	5672 (18.6)	740 (24.9)	6.86 (6.68–7.04)	9.62 (8.95–10.34)	1.41 (1.31–1.52)	1.26 (1.17–1.36)
HFrEF	3623 (19.6)	423 (25.1)	8.36 (8.10–8.64)	11.54 (10.49–12.69)	1.39 (1.26–1.54)	1.23 (1.11–1.37)
HFpEF	2049 (17.1)	317 (24.6)	5.20 (4.98–5.43)	7.88 (7.06–8.79)	1.53 (1.36–1.72)	1.28 (1.14–1.45)
Fatal/nonfatal MI						
Overall	1032 (3.4)	148 (5.0)	1.27 (1.19–1.35)	1.97 (1.68–2.32)	1.54 (1.30–1.83)	1.26 (1.06–1.51)
HFrEF	534 (2.9)	59 (3.5)	1.25 (1.15–1.36)	1.64 (1.27–2.12)	1.31 (1.00–1.71)	1.07 (0.82–1.40)
HFpEF	498 (4.2)	89 (6.9)	1.29 (1.18–1.41)	2.28 (1.85–2.80)	1.75 (1.39–2.19)	1.44 (1.15–1.81)
Fatal/nonfatal stroke						
Overall	963 (3.2)	200 (6.7)	1.18 (1.11–1.26)	2.68 (2.34–3.08)	2.27 (1.95–2.64)	2.02 (1.73–2.36)
HFrEF	491 (2.7)	99 (5.9)	1.15 (1.05–1.25)	2.79 (2.29–3.40)	2.44 (1.97–3.03)	2.24 (1.80–2.79)
HFpEF	472 (3.9)	101 (7.9)	1.22 (1.11–1.33)	2.58 (2.13–3.14)	2.12 (1.71–2.63)	1.84 (1.48–2.29)
Fatal/nonfatal MI or stroke						
Overall	1939 (6.4)	329 (11.1)	2.41 (2.31–2.52)	4.51 (4.05–5.02)	1.86 (1.65–2.09)	1.60 (1.42–1.80)
HFrEF	998 (5.4)	148 (8.8)	2.36 (2.22–2.51)	4.24 (3.61–4.98)	1.79 (1.51–2.13)	1.55 (1.30–1.85)
HFpEF	941 (7.9)	181 (14.1)	2.47 (2.32–2.63)	4.75 (4.11–5.50)	1.91 (1.63–2.24)	1.64 (1.39–1.92)
CV death, HF hosp., MI, or stroke						
Overall	8436 (27.7)	1067 (35.9)	11.36 (11.12–11.60)	16.13 (15.19–17.13)	1.40 (1.32–1.50)	1.23 (1.15–1.31)
HFrEF	5159 (27.9)	583 (34.6)	13.12 (12.77–13.48)	18.23 (16.81–19.77)	1.37 (1.26–1.49)	1.22 (1.12–1.33)
HFpEF	3277 (27.4)	484 (37.6)	9.37 (9.06–9.70)	14.16 (12.96–15.48)	1.49 (1.36–1.64)	1.24 (1.12–1.37)

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Kaplan-Meier curves for clinical outcomes in HF patients with or without previous stroke

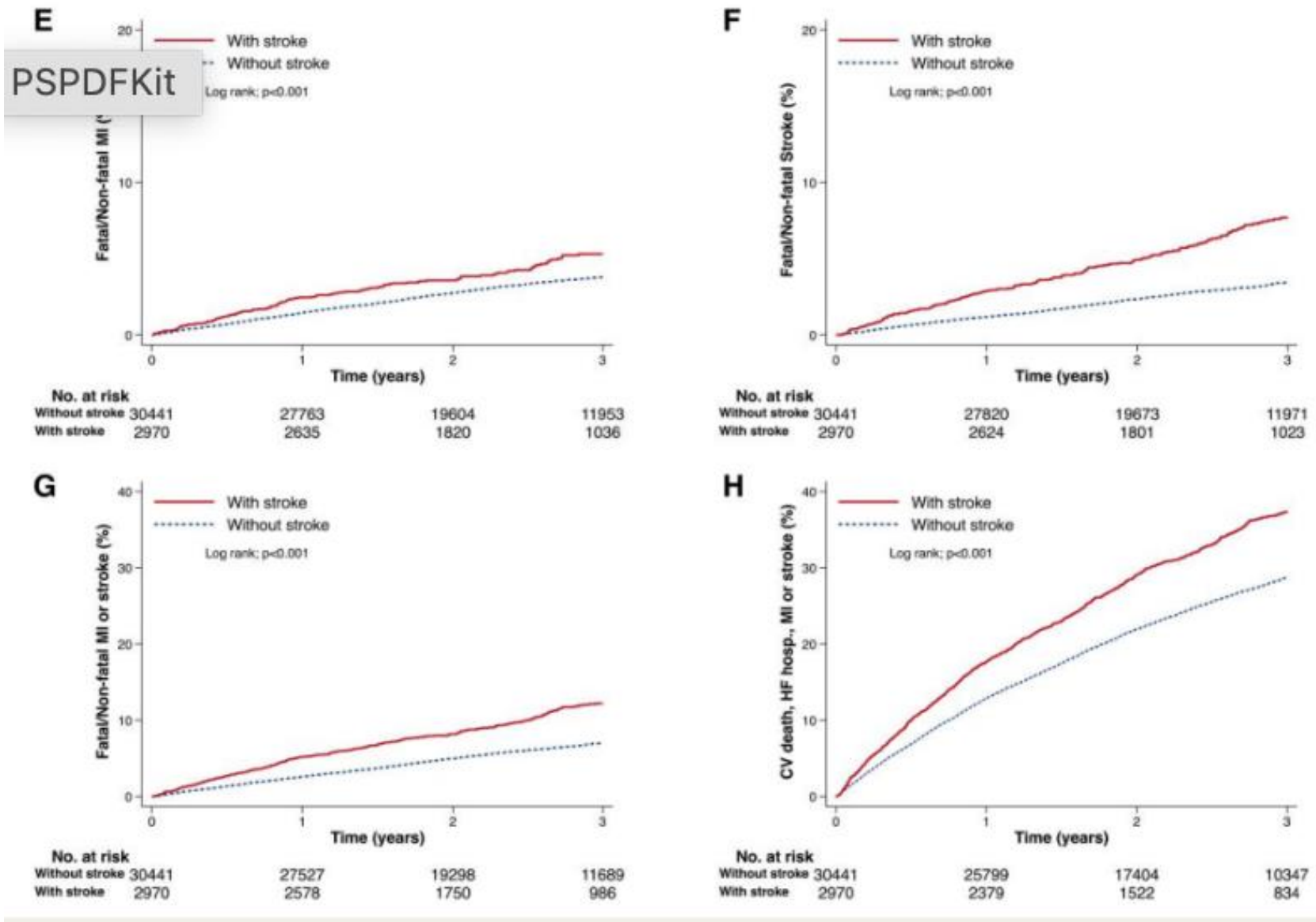
(A) CV death or first hospitalization for HF
(B) hospitalization for HF
(C) CV death
(D) all-cause death



Eur Heart J. 2023 Aug 14;44(31):2998-3013.

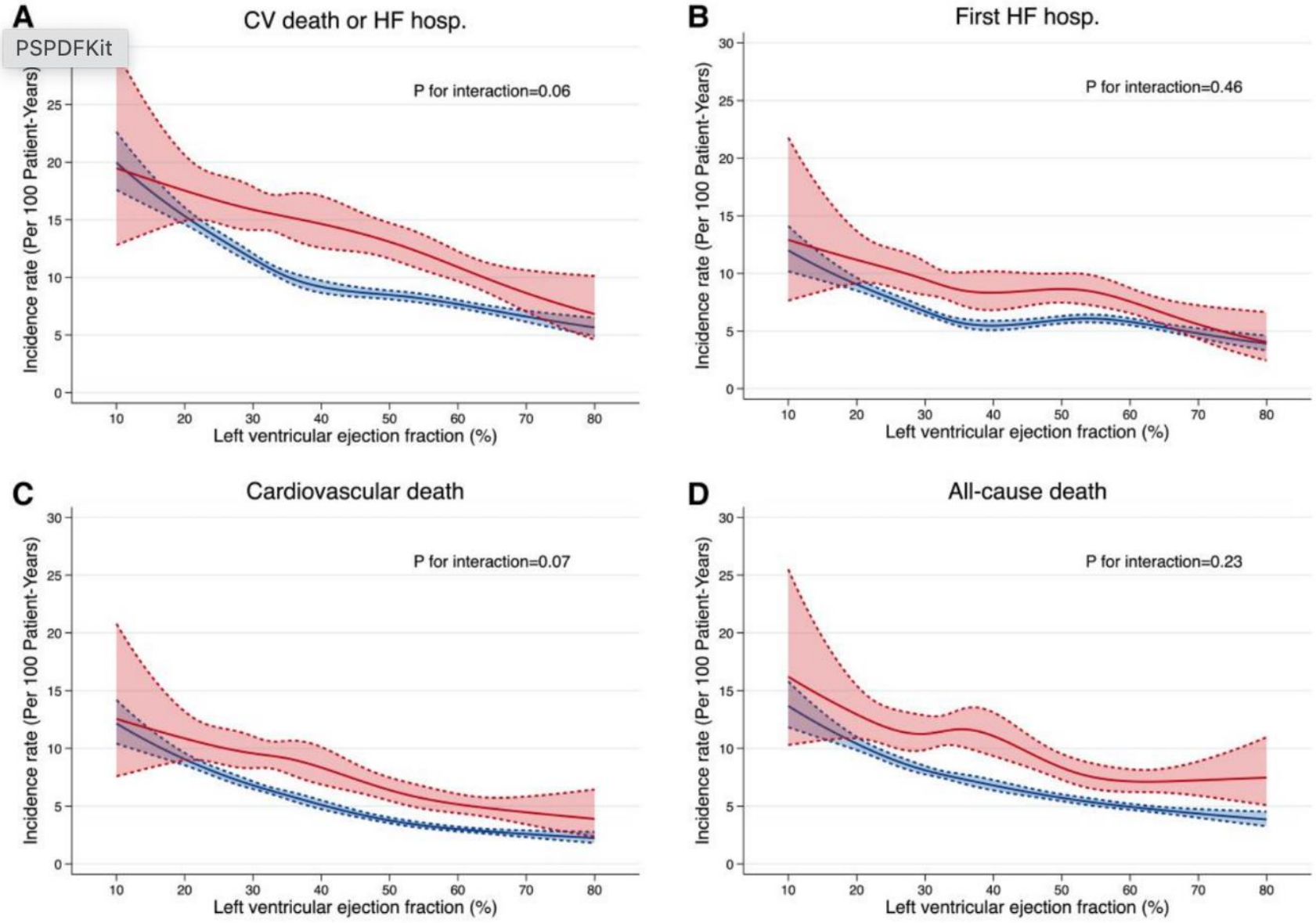
Kaplan-Meier curves for clinical outcomes in HF patients with or without previous stroke

(E) fatal/non-fatal MI
(F) fatal/non-fatal stroke
(G) fatal/non-fatal MI or stroke
(H) CV death hospitalization for HF, MI. or stroke.



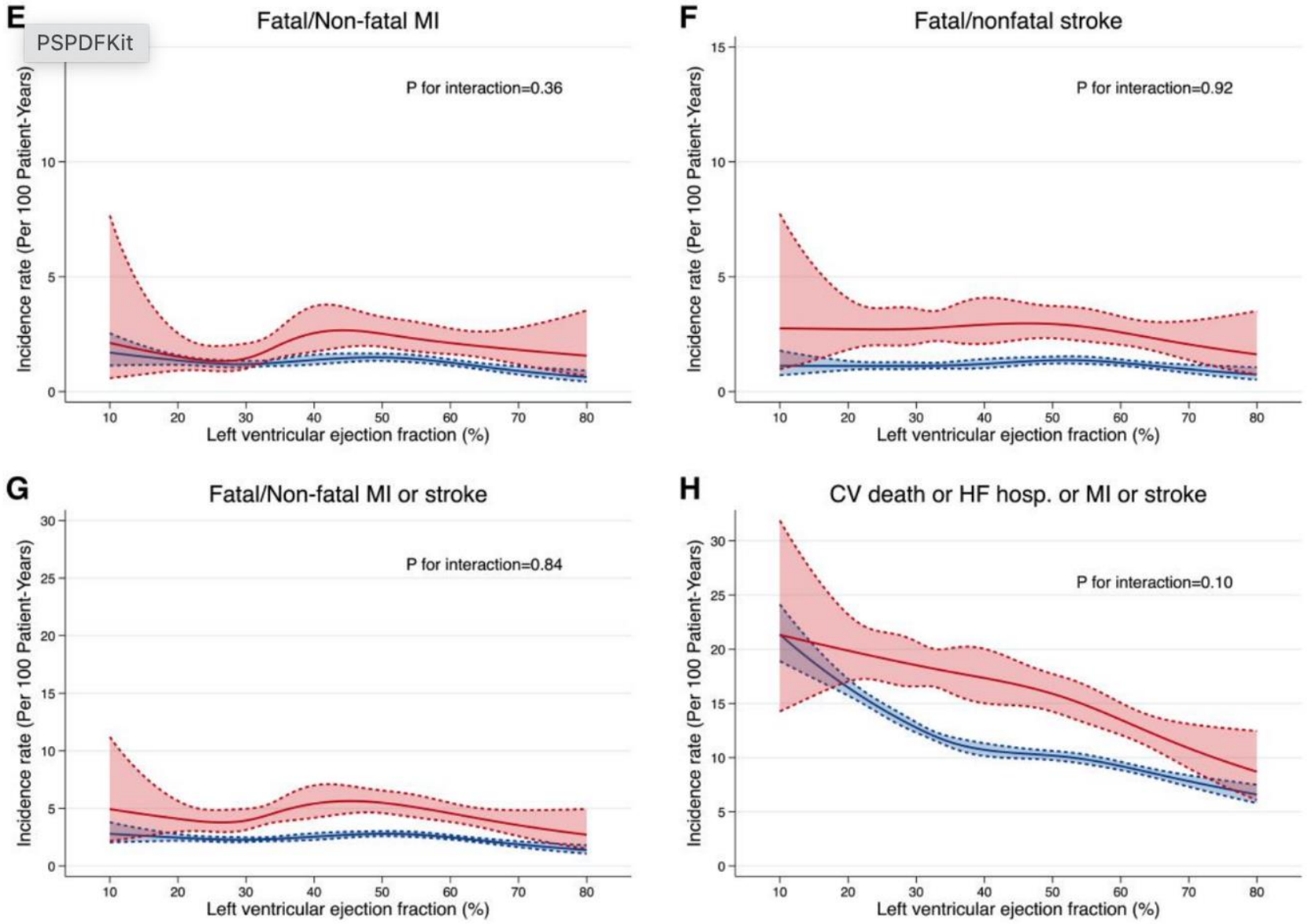
Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Incidence rates of outcomes across LVEF in heart failure patients with (upper lines/red) and without (lower lines/blue) prior stroke



Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Incidence rates of outcomes across LVEF in heart failure patients with (upper lines/red) and without (lower lines/blue) prior stroke



Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Limitations

- The patients analysed were enrolled in clinical trials, i.e. were relatively selected and may not be representative of patients in ordinary clinical practice.
- Ejection fraction could be measured by different methods in the included trials.
- Medical history was based on answers to questions in the trial case report forms, and completion of these may have varied by trial and by country.
- Patients with severe strokes are unlikely to have been enrolled
- No information on type and severity of stroke
- Patients with clinically significant uncorrected primary valvular disease were excluded from the trials analysed, as were patients with uncontrolled arrhythmias. This may have resulted in underestimation of the true prevalence of stroke in a broad real-world population of heart failure due to any cause.

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Conclusions

- About 1 in 11 patients in this pooled heart failure trial database had a history of stroke.
- Their annualized rate of cardiovascular death, hospitalization for heart failure, non-fatal stroke, or non-fatal myocardial infarction was ~18% (compared with 13% in those without a history of stroke); the corresponding rates in patients with HFpEF were 14% and 9%, respectively, and their risk of further stroke was twice as high as in patients without a history of stroke.
- The relatively low rates of use of anticoagulants in patients with atrial fibrillation and statins in patients with arterial disease, along with poor blood pressure control (especially in patients with HFpEF) point to potential therapeutic opportunities to reduce this risk.

Eur Heart J. 2023 Aug 14;44(31):2998-3013.

Stroke in patients with heart failure and reduced or preserved ejection fraction

Population

Individual patient meta-analysis of 7 clinical trials including 20 159 patients with HFrEF and 13 252 patients with HFpEF

Aim

To examine the prevalence of history of prior stroke, characteristics of patients with history of stroke (versus those without) and outcomes related to history of stroke (versus no history)

History of stroke: key findings

Prevalence 8.3% of patients with HFrEF and 9.7% of those with HFpEF

Characteristics Regardless of ejection fraction, patients with a history of stroke had more vascular comorbidity and worse HF

Outcomes The incidence of the composite of cardiovascular death, HF hospitalization, stroke or MI was approximately one-third higher in HFrEF patients with prior stroke versus no prior stroke; in patients with HFpEF it was about 50% higher (see forest plot in panel). Among patients with prior stroke, anticoagulants and statins were underutilized (pie charts). 17% with HFrEF and 38% with HFpEF had systolic BP≥140 mmHg

Conclusion Greater utilization of anticoagulants and statins, and better BP control, may reduce risk in these patients