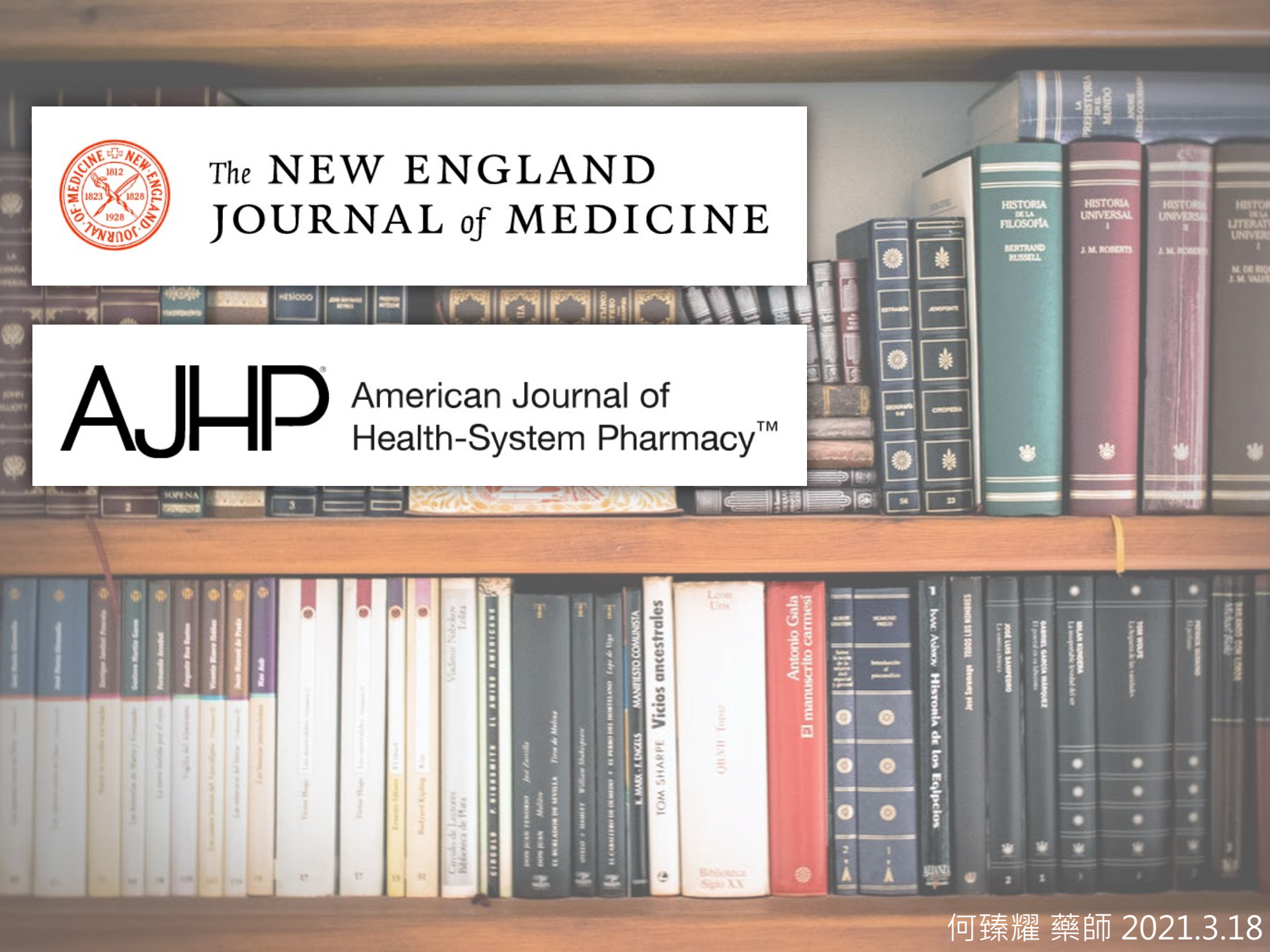
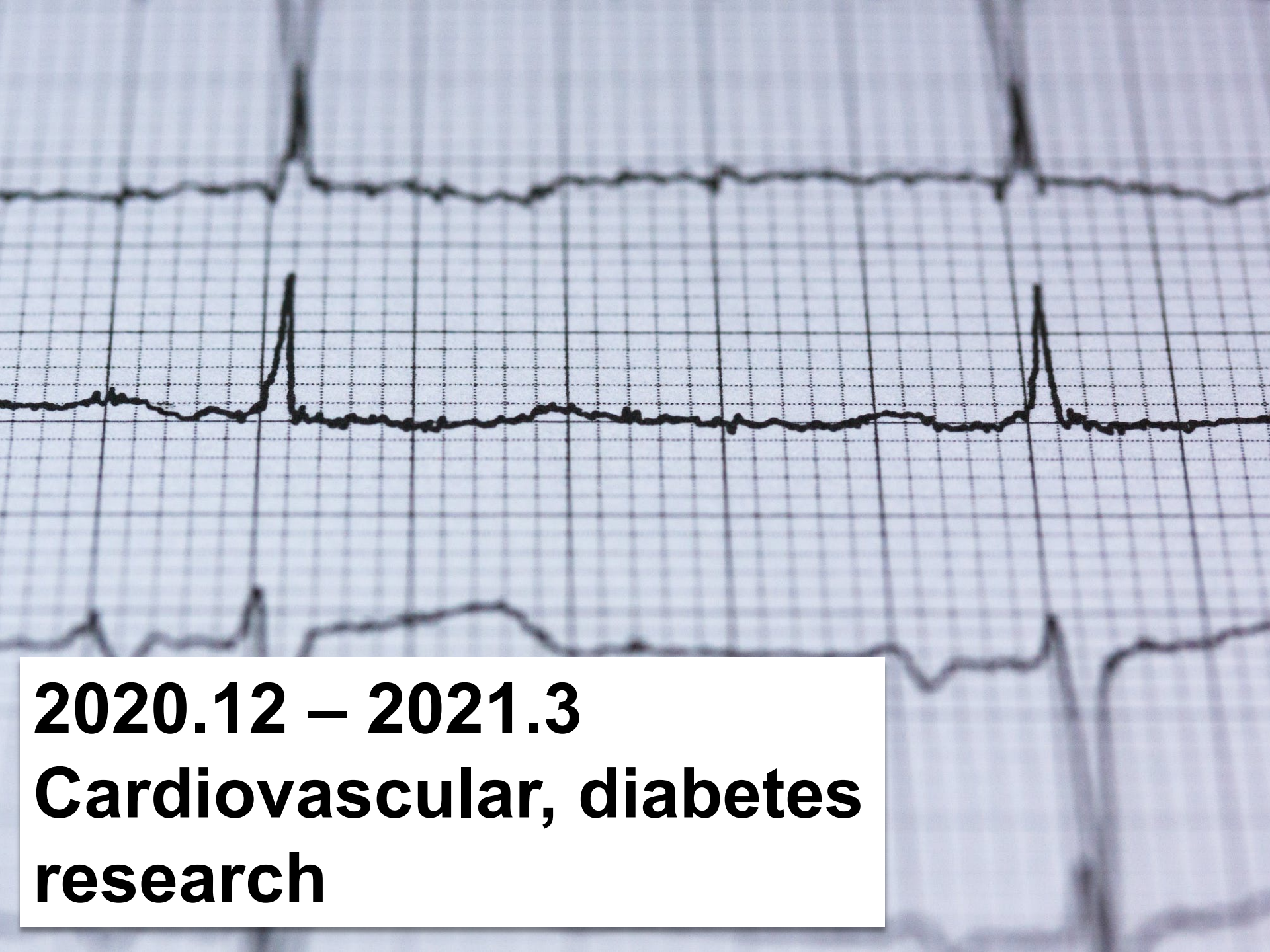


何臻耀 藥師 2021.3.18



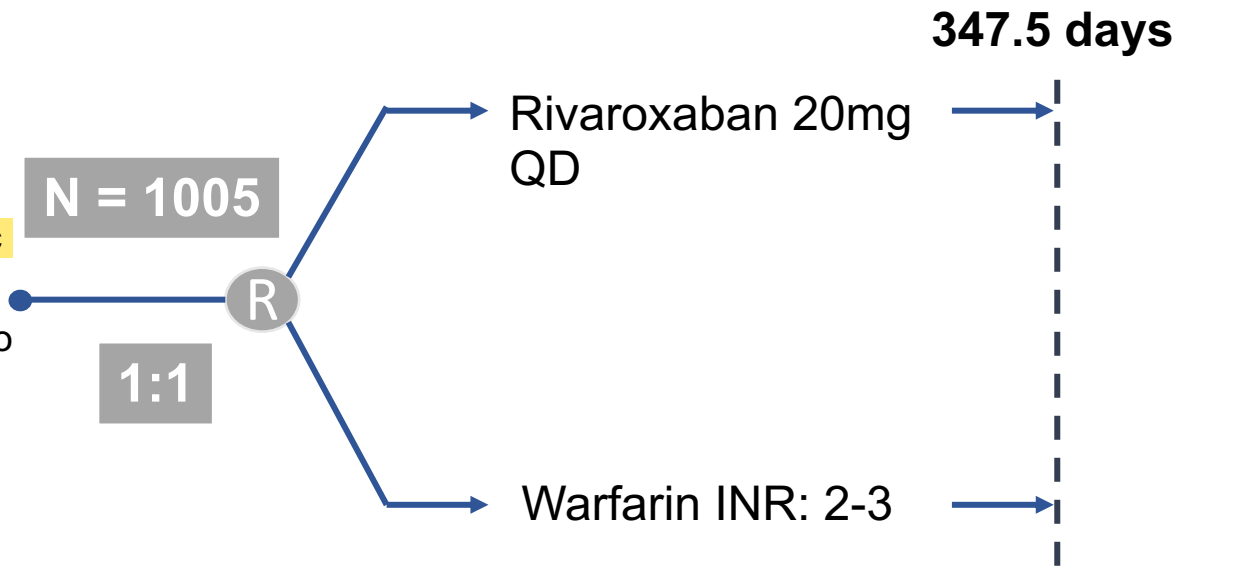
2020.12 – 2021.3
Cardiovascular, diabetes research

Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve

- Design: multicenter trial had a randomized, noninferiority, open-label design

Population:

- Age ≧ 18 years old,
- had permanent, paroxysmal, or persistent atrial fibrillation or flutter and **a bioprosthetic mitral valve**
- Were receiving (or planning to receive) oral anticoagulation
- at least **48 hours** after undergoing mitral-valve surgery



- **Primary outcome:** A composit 12 months.
- **Secondary outcome:** A comp events (stroke, TIA, deep veno systemic embolism not related to the CNS)

Exclusion: Contraindication to either rivaroxaban or warfarin, an extremely high risk of bleeding, transient atrial fibrillation caused by surgery, and the placement of mechanical valves.

Characteristic	Rivaroxaban (N=500)	Warfarin (N=505)	All Patients (N=1005)
Age			
Mean — yr	59.4±2.4	59.2±11.8	59.3±12.1
≥65 yr — no. (%)	179 (35.8)	176 (34.9)	355 (35.3)
Female sex — no. (%)	311 (62.2)	296 (58.6)	607 (60.4)
Medical history — no. (%)			
Diabetes mellitus	74 (14.8)	64 (12.7)	138 (13.7)
Hypertension	308 (61.6)	302 (59.8)	610 (60.7)
Dyslipidemia	176 (35.2)	162 (32.1)	338 (33.6)
Percutaneous valve intervention	39 (7.8)	37 (7.3)	76 (7.5)
Myocardial infarction	24 (4.8)	24 (4.8)	48 (4.7)
Percutaneous coronary intervention	16 (3.2)	16 (3.2)	32 (3.1)
Myocardial revascularization	27 (5.4)	19 (3.8)	46 (4.5)
Stroke	63 (12.6)	66 (13.1)	129 (12.8)
Transient ischemic attack	12 (2.4)	14 (2.8)	26 (2.5)
Peripheral vascular disease	10 (2.0)	6 (1.2)	16 (1.5)
Carotid artery disease	8 (1.6)	7 (1.4)	15 (1.4)
Congestive heart failure	202 (40.4)	188 (37.2)	390 (38.8)
Chronic kidney disease†	7 (1.4)	11 (2.2)	18 (1.7)
Current smoker — no. (%)	16 (3.2)	23 (4.6)	39 (3.8)
Median body-mass index (IQR)‡	26.6 (23.4–29.9)	25.5 (22.8–29.3)	26.0 (23.2–29.7)
Race or ethnic group — no. (%)§			
White	294 (58.8)	270 (53.5)	564 (56.1)
Black	63 (12.6)	69 (13.7)	132 (13.1)
Multiracial	138 (27.6)	159 (31.5)	297 (29.5)
Asian	5 (1.0)	7 (1.4)	12 (1.1)
Type of atrial rhythm — no. (%)			
Paroxysmal fibrillation	114 (22.8)	109 (21.6)	223 (22.2)
Permanent fibrillation	311 (62.2)	310 (61.4)	621 (61.7)
Persistent fibrillation	55 (10.9)	62 (12.3)	117 (11.6)
Flutter	20 (4.0)	24 (4.8)	44 (4.3)
Median serum creatinine (IQR) — mg/dl	0.9 (0.7–1.1)	0.9 (0.7–1.1)	0.9 (0.7–1.1)
Median creatinine clearance (IQR) — ml/min	77.4 (58.8–95.7)	77.7 (59.1–96.8)	77.5 (58.9–96.0)
Mean CHA_2DS_2-VASc score¶	2.7±1.5	2.5±1.3	2.6±1.4
Mean HAS-BLED score‖	1.6±0.6	1.6±0.9	1.6±0.9
Interval between mitral-valve implantation and randomization — no. (%)			
<3 mo	94 (18.8)	95(18.8)	189 (18.8)
3 mo to <1 yr	91 (18.2)	78 (15.4)	169 (16.8)
1 yr to <5 yr	160 (32.0)	164 (32.5)	324 (32.2)
5 yr to <10 yr	148 (29.6)	160 (31.7)	308 (30.6)
Missing data	7 (1.4)	8 (1.6)	15 (1.4)

Medical history

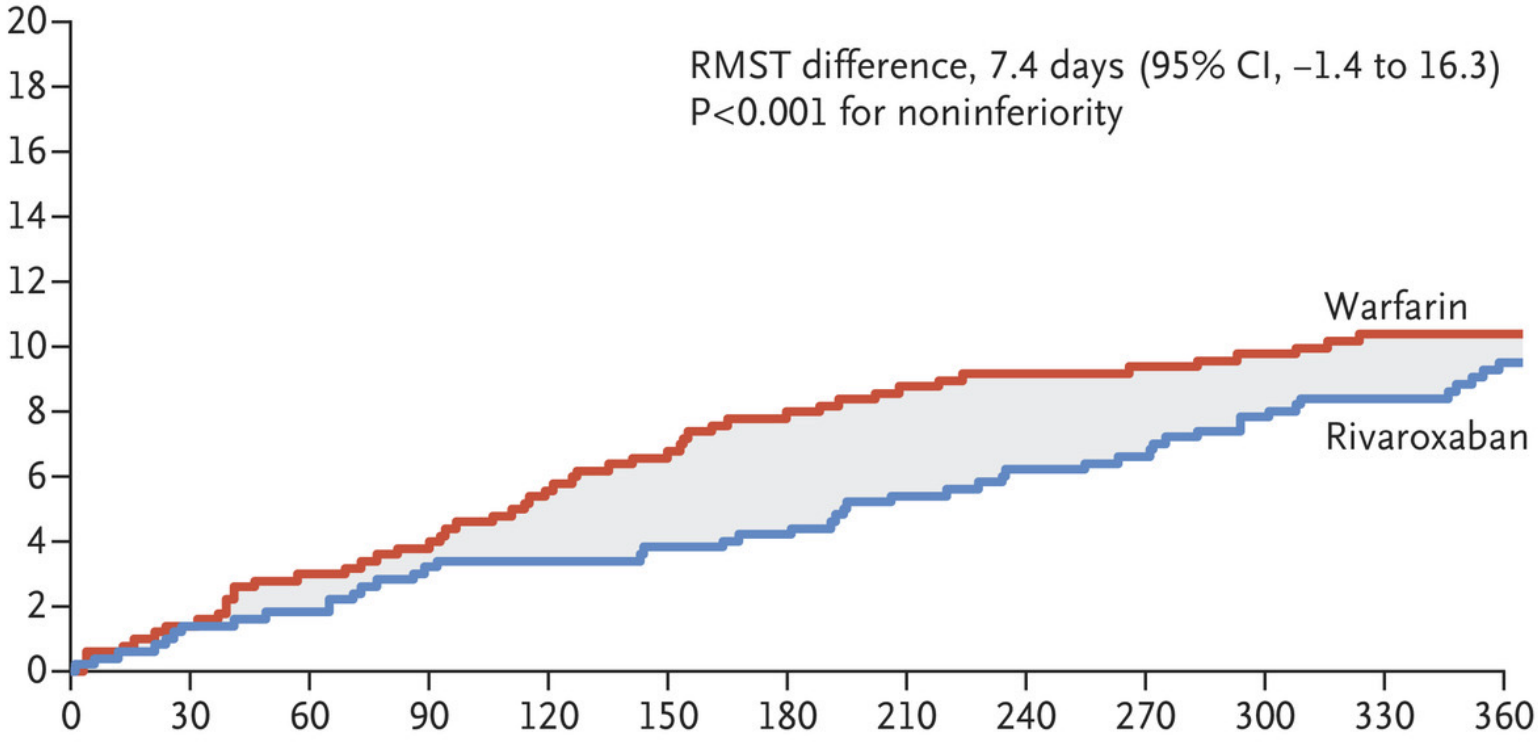
- Hypertension (60.7%)
- Congestive HF (38.8%)

Type of AF

- Permanent (61.7%)
- Paroxysmal (22.2%)
- Persistent (11.6%)

Time from mitral-valve implantation

> 1 year = 62%



- **Primary outcome**： A composite of death, major cardiovascular events, or major bleeding at 12 months(margin = -8 day).
- 處置：**I: 20/15mg QD Rivarxaban ;**
  C: Warfarin INR: 2-3
- 研究結果:
  Restricted mean survival time (RMST) difference: 7.4 days

***RMST: mean time free from an outcome event up to a prespecified time point and thus reflects the area under the survival curve**

Secondary Outcome	Rivaroxaban (N=500)		Warfarin (N=505)		Hazard Ratio (95% CI)†
	no. (%)	*rate per 100 patient-yr*	*no. (%)*	*rate per 100 patient-yr*	
Death from cardiovascular causes or thromboembolic events — no. (%)‡	17 (3.4)	3.53	26 (5.1)	5.44	0.65 (0.35–1.20)
Stroke					
Any	3 (0.6)	0.62	12 (2.4)	2.50	0.25 (0.07–0.88)
Nonfatal	2 (0.4)	0.41	10 (2.0)	2.09	0.20 (0.04–0.91)
Fatal	1 (0.2)	0.20	2 (0.4)	0.39	0.50 (0.05–5.50)
Hemorrhagic	0	0	5 (1.0)	1.03	NA
Ischemic	3 (0.6)	0.62	7 (1.4)	1.45	0.43 (0.11–1.66)
Transient ischemic attack	0	0	1 (0.2)	0.21	NA
Death					
Any	20 (4.0)	4.12	20 (4.0)	4.11	1.01 (0.54–1.87)
From cardiovascular causes	11 (2.2)	2.27	13 (2.6)	2.67	0.85 (0.38–1.90)
Valve thrombosis	5 (1.0)	1.04	3 (0.6)	0.62	1.68 (0.40–7.01)
Non-CNS systemic embolism	0	0	1 (0.2)	0.21	NA
Hospitalization for heart failure	22 (4.4)	4.43	19 (3.8)	3.78	1.15 (0.62–2.13)
Any bleeding	65 (13.0)	14.71	78 (15.4)	17.99	0.83 (0.59–1.15)
Major bleeding	7 (1.4)	1.46	13 (2.6)	2.72	0.54 (0.21–1.35)
Intracranial bleeding	0	0	5 (1.0)	1.03	NA
Fatal bleeding	0	0	2 (0.4)	0.41	NA
Clinically relevant nonmajor bleeding	24 (4.8)	5.12	23 (4.6)	4.87	1.05 (0.60–1.87)
Minor bleeding	37 (7.4)	8.03	49 (9.7)	10.84	0.75 (0.49–1.15)

No significant difference

Cochrane RoB 2.0 of Randomized parallel group trial

Bias arising from the randomization process	✓ Allocation conceal ✓ Allocation sequence random ✓ Baseline balance	**Low risk**
Bias due to deviation from intended intervention	✓ Open-label trial ✓ Balance non-protocol intervention ✓ Implementation and adherence succussed	**Low risk**
Bias due to missing outcome data	✓ 99.4% complete the trial	**Low risk**
Bias in measurement of outcome	✓ Both group RMST outcome measurement ✓ Assessor blinded	**Low risk**
Bias in selection of reported result	✓ No evidence of selection of the reported result	**Low risk**

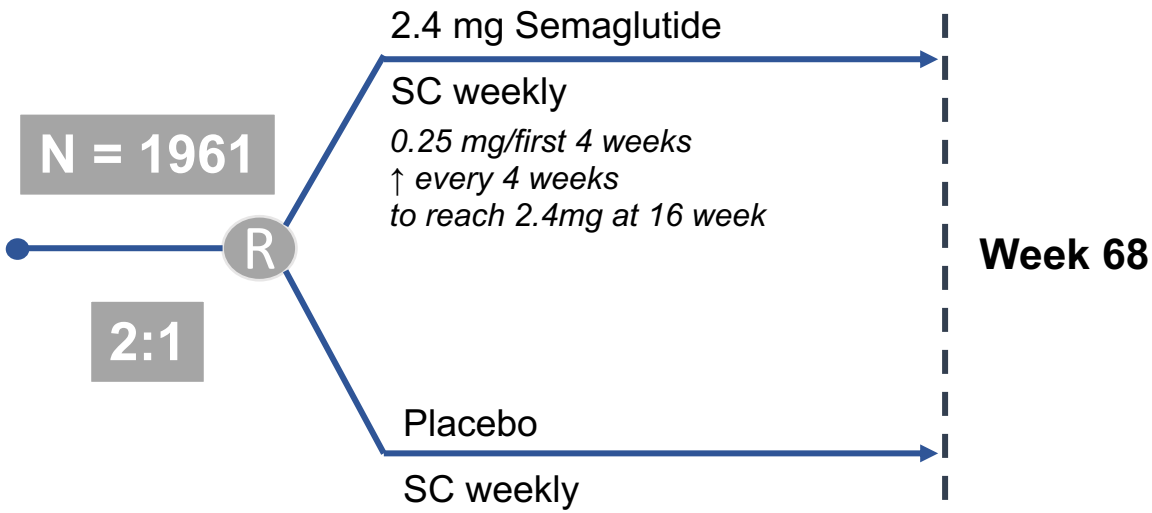
Once-Weekly Semaglutide in Adults with Overweight or Obesity

NEJM

⚕ Design: Randomized, double-blind, placebo-controlled trial

Population:

- ≧ 18 years old
- Self-reported unsuccessful dietary efforts to lose weight
- BMI ≧ 30 **or** BMI ≧ 27 with one or more treated or untreated conditions



Exclusion: **Diabetes**, a glycated hemoglobin level of 48 mmol per mole (6.5%) or greater, a history of **chronic pancreatitis**, **acute pancreatitis within 180 days** before enrollment, previous surgical obesity treatment, and use of **antiobesity medication within 90 days** before enrollment.

- **Primary outcome:** Th… …68 and achievement of a **reduc**… …3
- **Secondary outcome:** A… …**and 15% or more by week 68** and the change from baseline to week 68 in **waist circumference**, systolic blood pressure, physical functioning score on **SF-36**, version 2, and physical function score on the Impact of Weight on **IWQOL-Lite-CT** questionnaire.

Characteristic	Semaglutide (N=1306)	Placebo (N=655)
Age — yr	46±13	47±12
Female sex — no. (%)	955 (73.1)	498 (76.0)
Body weight — kg	105.4±22.1	105.2±21.5
Body-mass index‡		
Mean	37.8±6.7	38.0±6.5
Distribution — no. (%)		
<30	81 (6.2)	36 (5.5)
≥30 to <35	436 (33.4)	207 (31.6)
≥35 to <40	406 (31.1)	208 (31.8)
≥40	383 (29.3)	204 (31.1)
Coexisting conditions at the time of screening**		
Dyslipidemia — no. (%)	499 (38.2)	226 (34.5)
Hypertension — no. (%)	472 (36.1)	234 (35.7)
Knee osteoarthritis — no. (%)	173 (13.2)	102 (15.6)
Obstructive sleep apnea — no. (%)	159 (12.2)	71 (10.8)
Asthma or chronic obstructive pulmonary disease — no. (%)	147 (11.3)	80 (12.2)
Nonalcoholic fatty liver disease — no. (%)	101 (7.7)	62 (9.5)
Polycystic ovarian syndrome — no./total no. (%)††	62/955 (6.5)	34/498 (6.8)
Coronary artery disease — no. (%)	32 (2.5)	17 (2.6)
No. of coexisting conditions at screening – no. (%)**		
None	328 (25.1)	163 (24.9)
1	337 (25.8)	187 (28.5)
2	298 (22.8)	135 (20.6)
3	183 (14.0)	96 (14.7)
4	96 (7.4)	43 (6.6)
≥5	64 (4.9)	31 (4.7)
SF-36‡‡		
Physical functioning score	51.0±6.9	50.8±7.9
Physical component summary score	51.1±7.3	51.1±7.9
Mental component summary score	55.4±5.7	55.5±5.9
IWQOL-Lite-CT§§		
Physical function score	65.4±24.0	64.0±24.4
Total score	63.6±21.2	63.3±20.9

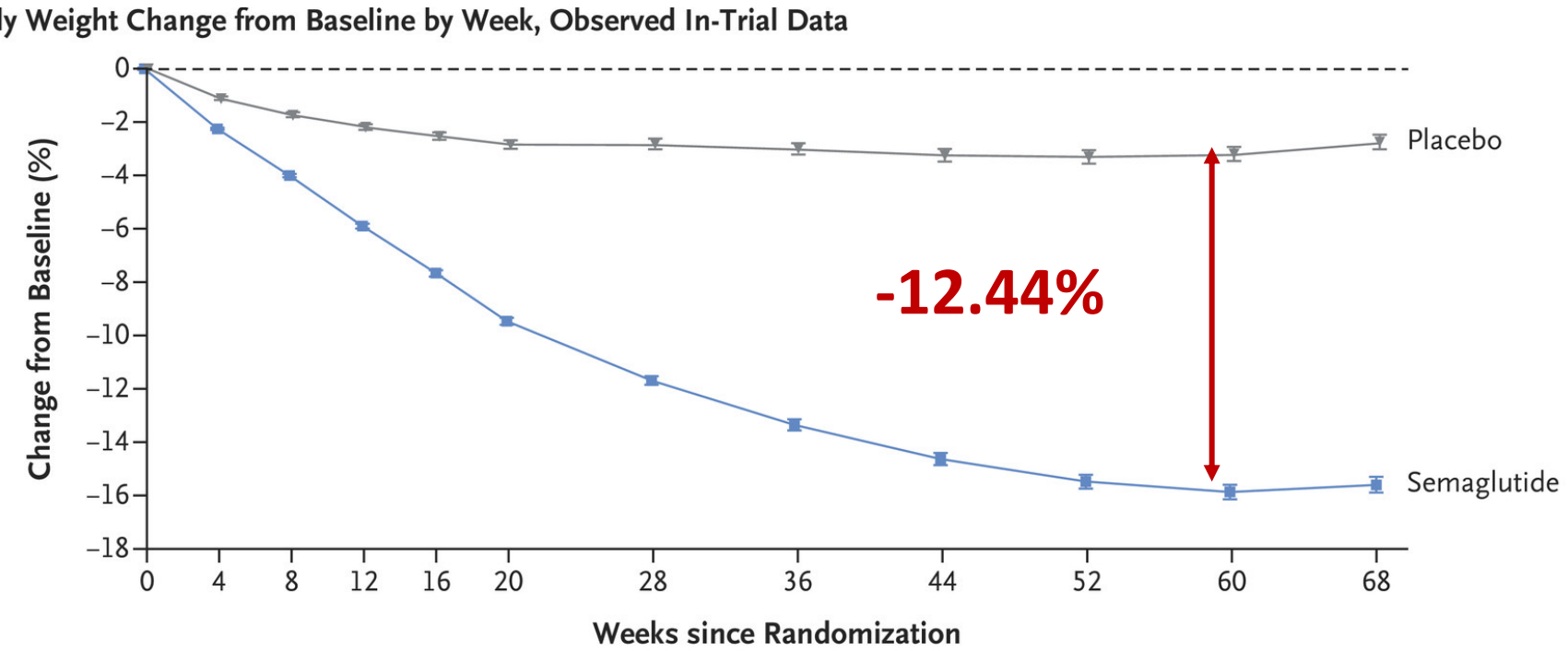
BMI>30 = 94%

HTN+Dyslipidemia = 75%

Without DM

SF-36 = 51-55/100

IWQOL-Lite-CT = 65.4/100



No. at Risk

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

End Point	Semaglutide (N=1306)	Placebo (N=655)	Difference between Semaglutide and Placebo (95% CI)†	Odds Ratio	P Value
Coprimary end points assessed in the overall population					
Percent body-weight change from baseline to wk 68	−14.85	−2.41	−12.44 (−13.37 to −11.51)		<0.001
Participants with body-weight reduction ≥5% at wk 68 — %‡	86.4	31.5		11.2 (8.9 to 14.2)	<0.001

- **Reduction in body weight of 5% or more** from baseline to week 68

  Odd ratio: 11.2 (8.9-14.2)

Confirmatory secondary end points assessed in the overall population					
Participants with body-weight reduction ≥10% at wk 68 — %‡	69.1	12.0		14.7 (11.1 to 19.4)	<0.001
Participants with body-weight reduction ≥15% at wk 68 — %‡	50.5	4.9		19.3 (12.9 to 28.8)	<0.001
Change from baseline to wk 68					
Waist circumference — cm	−13.54	−4.13	−9.42 (−10.30 to −8.53)		<0.001
Systolic blood pressure — mm Hg	−6.16	−1.06	−5.10 (−6.34 to −3.87)		<0.001
SF-36 physical functioning score	2.21	0.41	1.80 (1.18 to 2.42)		<0.001
IWQOL-Lite-CT physical function score	14.67	5.25	9.43 (7.50 to 11.35)		<0.001
Supportive secondary end points assessed in the overall population§					
Participants with body-weight reduction ≥20% at wk 68 — %‡	32.0	1.7			
Change from baseline to wk 68					
Body weight — kg	−15.3	−2.6	−12.7 (−13.7 to −11.7)		
Body-mass index	−5.54	−0.92	−4.61 (−4.96 to −4.27)		
Glycated hemoglobin — percentage points	−0.45	−0.15	−0.29 (−0.32 to −0.26)		
Fasting plasma glucose — mg/dl	−8.35	−0.48	−7.87 (−9.04 to −6.70)		
Diastolic blood pressure — mm Hg	−2.83	−0.42	−2.41 (−3.25 to −1.57)		
Lipid levels, ratio of wk 68 value to baseline¶					
Total cholesterol	0.97	1.00	0.97 (0.95 to 0.98)		
HDL cholesterol	1.05	1.01	1.04 (1.02 to 1.05)		
LDL cholesterol	0.97	1.01	0.96 (0.94 to 0.98)		
VLDL cholesterol	0.78	0.93	0.84 (0.81 to 0.87)		
Free fatty acids	0.83	0.93	0.89 (0.83 to 0.94)		
Triglycerides	0.78	0.93	0.84 (0.81 to 0.87)		
C-reactive protein, ratio of wk-68 value to baseline¶	0.47	0.85	0.56 (0.51 to 0.61)		
Exploratory end-point assessed in the prediabetes subpopulation§‖					
Change in glycated hemoglobin level from baseline to wk 68 — percentage points**	−0.52	−0.17	−0.34 (−0.39 to −0.29)		
Participants with normoglycemia at wk 68 — (%)	84.1	47.8			

BP ↓

QoI ↑

30% (-20% body weight ↑)

Lipid profile

Adverse Event	Semaglutide (N=1306)			Placebo (N=655)		
	No. of participants (%)	No. of events	Events/100 person-yr	No. of participants (%)	No. of events	Events/100 person-yr
Any adverse event	1171 (89.7)	9658	566.1	566 (86.4)	3302	398.0
Serious adverse events	128 (9.8)	164	9.6	42 (6.4)	53	6.4
Adverse events leading to discontinuation of drug or placebo	92 (7.0)	123	7.2	20 (3.1)	23	2.8
Gastrointestinal disorders	59 (4.5)	78	4.6	5 (0.8)	5	0.6
Fatal events†‡	1 (0.1)	1	0.1	1 (0.2)	3	0.3
Adverse events reported in ≥10% of participants§						
Nausea	577 (44.2)	1068	62.6	114 (17.4)	146	17.6
Diarrhea	412 (31.5)	766	44.9	104 (15.9)	138	16.6
Vomiting	324 (24.8)	636	37.3	43 (6.6)	52	6.3
Constipation	306 (23.4)	390	22.9	62 (9.5)	73	8.8
Nasopharyngitis	281 (21.5)	480	28.1	133 (20.3)	216	26.0
Headache	198 (15.2)	387	22.7	80 (12.2)	104	12.5
Dyspepsia	135 (10.3)	179	10.5	23 (3.5)	30	3.6
Abdominal pain	130 (10.0)	175	10.3	36 (5.5)	41	4.9
Upper respiratory tract infection	114 (8.7)	158	9.3	80 (12.2)	116	14.0
Safety focus areas¶						
Gastrointestinal disorders‖	969 (74.2)	4309	252.6	314 (47.9)	739	89.1
Gallbladder-related disorders	34 (2.6)	42	2.5	8 (1.2)	8	1.0
Hepatobiliary disorders‖	33 (2.5)	40	2.3	5 (0.8)	5	0.6
Cholelithiasis	23 (1.8)	24	1.4	4 (0.6)	4	0.5
Hepatic disorders	31 (2.4)	37	2.2	20 (3.1)	24	2.9
Acute pancreatitis**	3 (0.2)	3	0.2	0	—	—
Cardiovascular disorders†	107 (8.2)	134	7.2	75 (11.5)	96	10.5
Allergic reactions	96 (7.4)	108	6.3	54 (8.2)	63	7.6
Injection-site reactions	65 (5.0)	99	5.8	44 (6.7)	82	9.9
Malignant neoplasms†	14 (1.1)	14	0.8	7 (1.1)	7	0.8
Psychiatric disorders‖	124 (9.5)	160	9.4	83 (12.7)	113	13.6
Acute renal failure	3 (0.2)	4	0.2	2 (0.3)	2	0.2
Hypoglycemia	8 (0.6)	15	0.9	5 (0.8)	7	0.8

Cochrane RoB 2.0 of Randomized parallel group trial

Bias arising from the randomization process	✓ Allocation conceal ✓ Allocation sequence random ✓ Baseline balance	**Low risk**
Bias due to deviation from intended intervention	✓ Double-blinded trial ✓ Implementation succussed but **81.1%** adhered to the protocol ✓ Without IPBW method	**High risk**
Bias due to missing outcome data	✓ 94.3% patients complete trail	**Low risk**
Bias in measurement of outcome	✓ Assessor NOT blinded (Self-report) ✓ Assessment of the outcome have been influenced by knowledge of intervention (PN)	**Low risk**
Bias in selection of reported result	✓ No evidence of selection of the reported result	**Low risk**

Polypill with or without Aspirin in Persons without Cardiovascular Disease

- Design: double-blind, randomized, placebo-controlled trial with a 2-by-2-by-2 factorial design

Population:

- Men 50 years of age or older and women 55 years of
- ha
- di
- el
- **Ri**
- **Pri**
- ma
- inc
- **cau**
- **infa**
- **res**
- **art**

Exclusion criteria:

1. Indication, contraindication, preference for or intolerance to statins, beta blockers, angiotensin converting enzyme inhibitors, diuretics, aspirin or clopidogrel in the judgment of the physician.
2. Regular use of vitamin D at doses higher than 400 IU per day.
3. Hypercalcemia, hyperparathyroidism, osteomalacia or other contraindication or indication for vitamin D therapy.
4. Peptic ulcer disease, frequent dyspepsia or bleeding.
5. Expected long term use of anticoagulants
6. Known vascular disease.
7. Systolic BP below 120 mm Hg.
8. Symptomatic hypotension (e.g., dizziness with SBP <110 mm Hg systolic) during the run-in phase.
9. Chronic liver disease or abnormal liver function, i.e. ALT or AST > 3 x ULN.
10. Inflammatory muscle disease or creatine kinase (CK) > 3 x ULN.
11. Severe renal impairment (serum creatinine >264 µmol/L).
12. History of malignancy affecting any organ system, except basal cell carcinoma of the skin, within the previous 5 years.
13. Other serious condition(s) likely to interfere with study participation or with the ability to complete the trial.
14. Concurrent use of any experimental pharmacological agent.
15. Inability to attend follow-up for at least 5 years.

N = 5713

Full dose polypill QD — **4.4 years**

- 40 mg of simvastatin
- 100 mg of atenolol
- 25 mg of HCTZ
- 10 mg of ramipril

acebo QD

pirin 75 mg QD

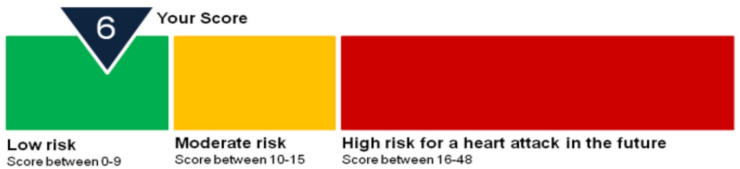
acebo QD

Characteristic	Double Placebo (N=1421)	Aspirin Alone (N=1431)	Polypill Alone (N=1432)	Polypill plus Aspirin (N=1429)
Age — yr	64.1±6.8	63.7±6.7	64.1±6.4	63.8±6.5
Female sex — no. (%)	757 (53.3)	746 (52.1)	777 (54.3)	745 (52.1)
Geographic distribution — no. (%)				
India or Bangladesh	755 (53.1)	760 (53.1)	760 (53.1)	759 (53.1)
Philippines, Malaysia, or Indonesia	479 (33.7)	477 (33.3)	478 (33.4)	479 (33.5)
Colombia	121 (8.5)	122 (8.5)	125 (8.7)	121 (8.5)
Canada	30 (2.1)	35 (2.4)	33 (2.3)	33 (2.3)
Tanzania	10 (0.7)	10 (0.7)	10 (0.7)	9 (0.6)
Tunisia	26 (1.8)	27 (1.9)	26 (1.8)	28 (2.0)
Cardiovascular risk factor — no. (%)				
Reported hypertension or systolic blood pressure >140 mm Hg	1179 (83.0)	1220 (85.3)	1199 (83.7)	1192 (83.4)
Reported diabetes or glucose level >126 mg/dl (7.0 mmol/liter)	527 (37.1)	503 (35.2)	543 (37.9)	522 (36.5)
Impaired fasting glucose ≥110–126 mg/dl (6.1–7.0 mmol/liter)	97 (6.8)	101 (7.1)	109 (7.6)	98 (6.9)
Current smoking	115 (8.1)	138 (9.6)	123 (8.6)	136 (9.5)
INTERHEART Risk Score†	17.9±4.8	17.8±4.7	18.0±4.8	17.9±4.7
Physiological variables				
Heart rate — beats/min	77.1±10.9	77.3±10.5	77.0±10.5	76.6±10.5
Blood pressure — mm Hg				
Systolic	144.4±17.2	144.7±16.8	144.7±16.9	144.3±16.6
Diastolic	83.6±9.6	83.7±9.9	84.2±9.9	84.1±9.4
Cholesterol — mg/dl				
Total	196.4±46.9	196.1±45.1	196.7±45.6	195.5±44.9
LDL	120.7±41.9	120.8±40.1	121.2±40.7	120.0±40.2
HDL	48.2±13.5	47.1±11.9	47.7±13.0	47.9±13.6
Triglycerides — mg/dl	143.2±70.8	148.7±82.8	146.4±70.6	144.7±72.3
Fasting plasma glucose — mg/dl	113.5±43.0	114.4±46.6	114.9±45.5	114.5±44.9
Creatinine — mg/dl	0.9±0.3	0.9±0.3	0.9±0.3	0.9±0.3
Body-mass index‡	25.6±4.6	25.7±4.8	26.1±4.9	25.8±4.6
Waist-to-hip ratio				
Among women	0.91±0.07	0.91±0.07	0.91±0.07	0.91±0.08
Among men	0.96±0.07	0.96±0.06	0.96±0.06	0.96±0.07
Medication use — no. (%)				
Antihypertensive drug	155 (10.9)	156 (10.9)	161 (11.2)	157 (11.0)
Calcium-channel blocker	137 (9.6)	141 (9.9)	153 (10.7)	138 (9.7)
Aspirin or clopidogrel	2 (0.1)	1 (0.1)	0	2 (0.1)
Oral anticoagulant	4 (0.3)	2 (0.1)	2 (0.1)	8 (0.6)
Insulin	35 (2.5)	29 (2.0)	24 (1.7)	29 (2.0)
Oral hypoglycemic agent	302 (21.3)	292 (20.4)	310 (21.6)	314 (22.0)
Statin	0	0	1 (0.1)	0
Other lipid-lowering agent	1 (0.1)	0	0	2 (0.1)

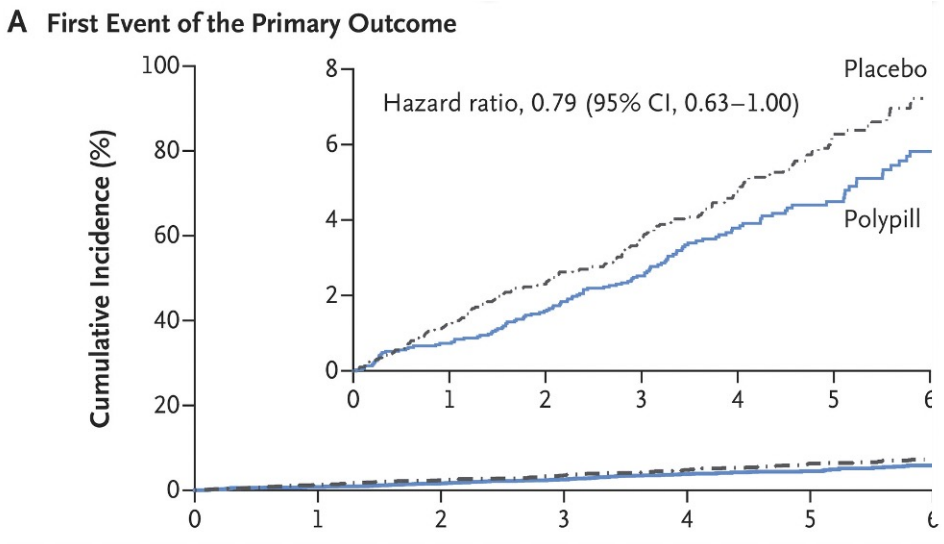
HTN or BP > 140 mmHg: 83%

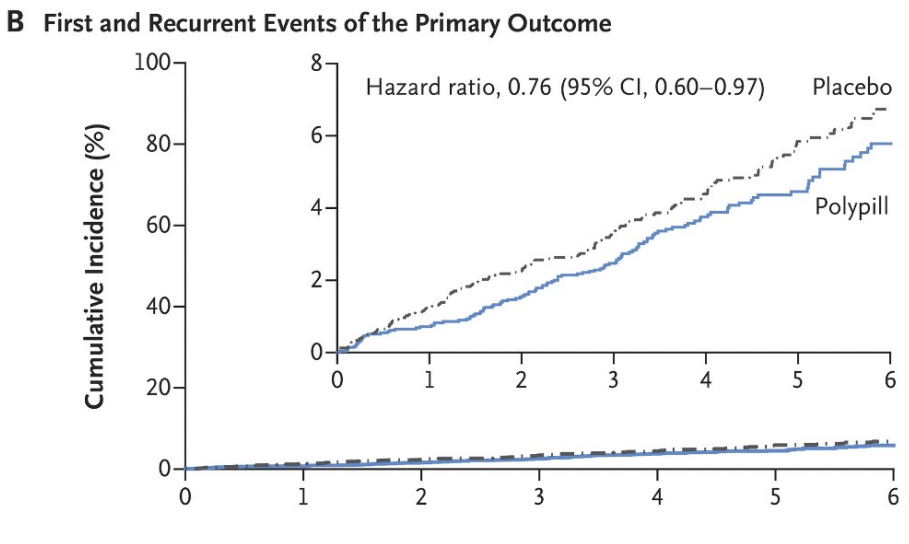
BS > 126 mg/dL: 35%

INTERHEART risk score



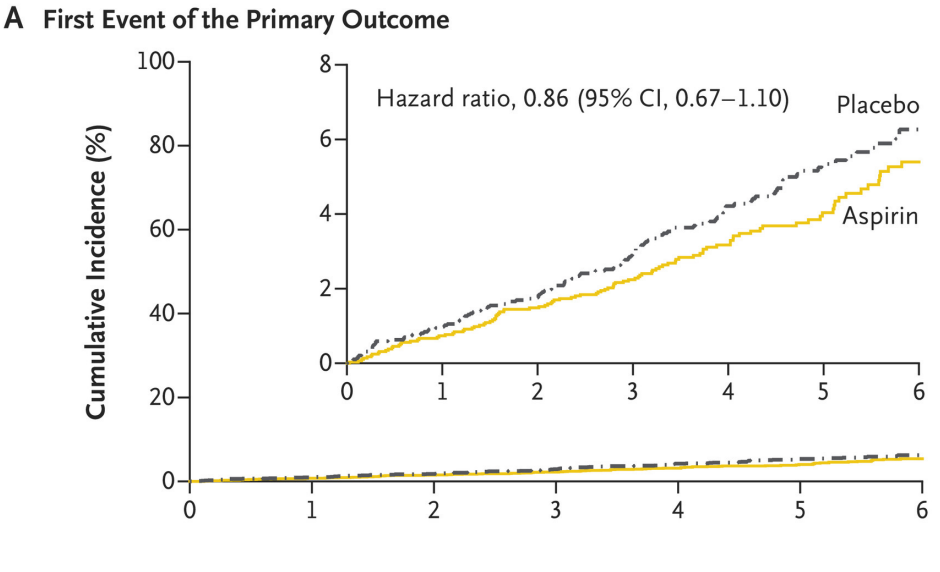
LDL 120±40 mg/dL

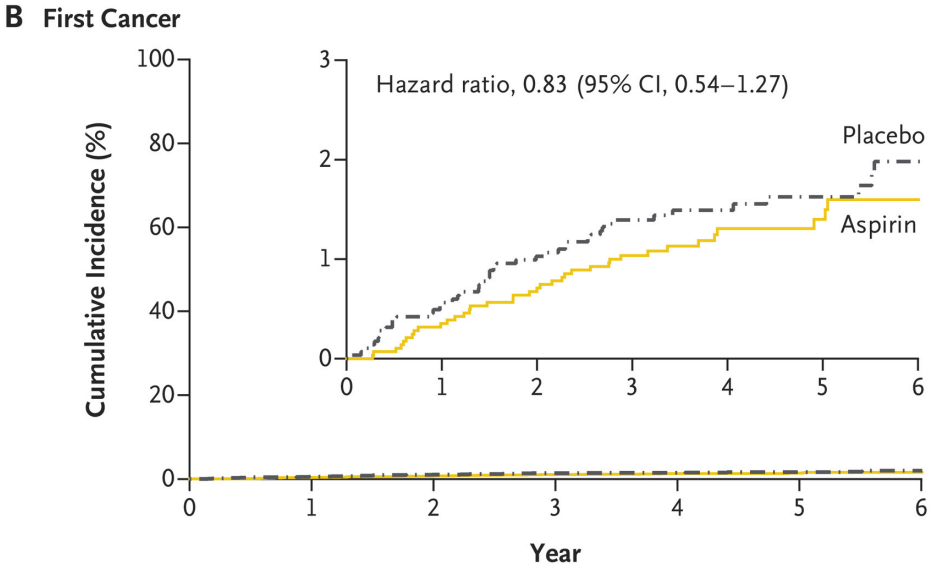




Outcomes	Polypill (N=2861)	Placebo (N=2852)	Hazard Ratio (95% CI)*
Primary outcome			
Death from cardiovascular causes, myocardial infarction, stroke, heart failure, resuscitated cardiac arrest, or arterial revascularization — no. (%)	126 (4.4)	157 (5.5)	0.79 (0.63–1.00)

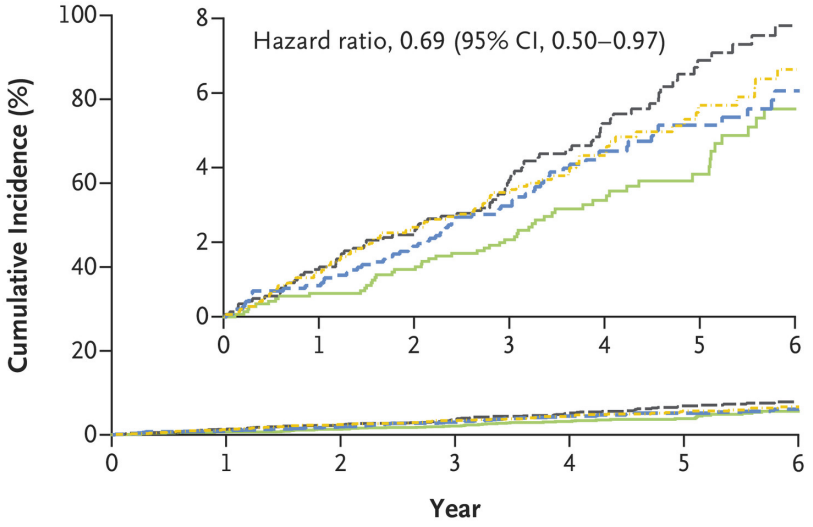
- **Primary outcome**： a composite of major cardiovascular events, which included **death from cardiovascular causes, stroke, myocardial infarction, heart failure, resuscitated cardiac arrest, or arterial revascularization**
- 處置：**I: Polypill 1# PO QD**
  C: Placebo
- 研究結果：**HR: 0.79 (0.63-1.00); HR: 0.76 (0.60-0.97) for recurrent**



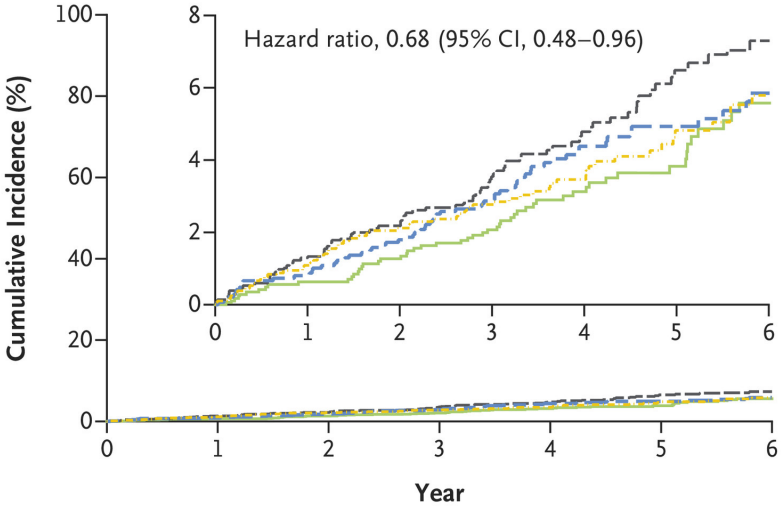


Outcome	Aspirin (N=2860)	Placebo (N=2853)	Hazard Ratio (95% CI)*
Primary outcome			
Death from cardiovascular causes, myocardial infarction, or stroke — no. (%)	116 (4.1)	134 (4.7)	0.86 (0.67–1.10)
Secondary Outcome			
Death from cardiovascular causes, myocardial infarction, stroke, or cancer — no. (%)	153 (5.3)	177 (6.2)	0.86 (0.69–1.07)
Components of the primary and secondary outcomes			
Death from cardiovascular causes — no. (%)†	85 (3.0)	100 (3.5)	0.85 (0.64–1.14)
Myocardial infarction — no. (%)	22 (0.8)	21 (0.7)	1.04 (0.57–1.89)
Stroke — no. (%)	23 (0.8)	39 (1.4)	0.58 (0.35–0.98)
Cancer — no. (%)	38 (1.3)	46 (1.6)	0.83 (0.54–1.27)

A First Event of the Primary Outcome



B First and Recurrent Events of the Primary Outcome



Outcome	Polypill plus Aspirin (N=1429)	Double Placebo (N=1421)	Hazard Ratio (95% CI)*
Primary outcome			
Death from cardiovascular causes, myocardial infarction, stroke, heart failure, resuscitated cardiac arrest, or arterial revascularization — no. (%)	59 (4.1)	83 (5.8)	0.69 (0.50–0.97)
Secondary outcomes			
Death from cardiovascular causes, myocardial infarction, or stroke — no. (%)	52 (3.6)	75 (5.3)	0.68 (0.47–0.96)
Death from cardiovascular causes, myocardial infarction, stroke, heart failure, resuscitated cardiac arrest, arterial revascularization, or angina with evidence of ischemia — no. (%)	61 (4.3)	86 (6.1)	0.69 (0.50–0.96)
Components of the primary and secondary outcomes			
Death from cardiovascular causes — no. (%)†	38 (2.7)	54 (3.8)	0.69 (0.46–1.05)
Myocardial infarction — no. (%)	10 (0.7)	14 (1.0)	0.69 (0.31–1.56)
Stroke — no. (%)	10 (0.7)	23 (1.6)	0.42 (0.20–0.89)
Heart failure — no. (%)	7 (0.5)	3 (0.2)	2.30 (0.60–8.90)
Resuscitated cardiac arrest — no. (%)	0	0	—
Arterial revascularization — no. (%)	5 (0.3)	12 (0.8)	0.40 (0.14–1.14)
Angina with evidence of ischemia — no. (%)	6 (0.4)	10 (0.7)	0.59 (0.22–1.63)

+ angina

Cochrane RoB 2.0 of Randomized parallel group trial

Bias arising from the randomization process	✓ Allocation conceal ✓ Allocation sequence random ✓ Baseline balance	**Low risk**
Bias due to deviation from intended intervention	✓ Double-blinded ✓ 1% withdraw (Run-in period)	**Low risk**
Bias due to missing outcome data	✓ 99% complete trial (57/5713 withdraw)	**Low risk**
Bias in measurement of outcome	✓ Assessor blinded? NI ✓ Outcome was influenced by knowledge of intervention received? PN	**Low risk**
Bias in selection of reported result	✓ Composite outcome and component reported	**Low risk**

SGLT-2 inhibitor

Table 2. Primary End Point and Secondary End Points.*

Table 2. Primary End Point and Secondary End Points.

End Point	Sotagliflozin (N=608)	Placebo (N=614)	Hazard Ratio or Difference (95% CI)*	P Value
Primary end point: deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure — total no. of events (rate)†	245 (51.0)	355 (76.3)	0.67 (0.52 to 0.85)	<0.001
Secondary end points in order of hierarchical testing				
Hospitalizations and urgent visits for heart failure — total no. of events (rate)†	194 (40.4)	297 (63.9)	0.64 (0.49 to 0.83)	<0.001
Deaths from cardiovascular causes — total no. of events (rate)†	51 (10.6)	58 (12.5)	0.84 (0.58 to 1.22)	0.36‡
Deaths from cardiovascular causes, hospitalizations for heart failure, nonfatal myocardial infarctions, and nonfatal strokes — total no. of events (rate)†	247 (51.4)	330 (71.0)	0.72 (0.56 to 0.92)	
Deaths from cardiovascular causes, hospitalizations and urgent visits for heart failure, and events of heart failure during hospitalization — total no. of events (rate)†	263 (54.7)	375 (80.6)	0.68 (0.54 to 0.86)	
Deaths from any cause — total no. of events (rate)†	65 (13.5)	76 (16.3)	0.82 (0.59 to 1.14)	
Least-squares mean change in KCCQ-12 score to month 4	17.7	13.6	4.1 (1.3 to 7.0)	
Least-squares mean change in estimated GFR — ml/min/1.73 m^2	–0.34	–0.18	–0.16 (–1.30 to 0.98)	

* Hazard ratios (sotagliflozin vs. placebo) are shown for all end points except change in KCCQ-12 score to month 4 and change in estimated GFR, for which differences in the least-squares mean values are shown (sotagliflozin minus placebo).
† Rate was calculated as the number of events per 100 person-years of follow-up.
‡ The hierarchical analysis was stopped after the first P value indicating nonsignificance.

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

Variable	Omecamtiv Mecarbil (N=4120)		Placebo (N=4112)		Hazard Ratio or Difference (95% CI)†	P Value
	Value	Events	Value	Events		

Trial Group	No. of Patients	Change from Baseline in LDL Cholesterol Level	Difference vs. Placebo (95% CI)	P Value
		percent	*percentage points*	
Subcutaneous regimen				
Evinacumab				
450 mg weekly	40	−47.2±6.2	−56.0±9.0 (−73.7 to −38.3)	<0.001
300 mg weekly	42	−44.0±6.3	−52.9±9.0 (−70.7 to −35.1)	<0.001
300 mg every 2 wk	39	−29.7±6.4	−38.5±9.1 (−56.5 to −20.6)	<0.001
Placebo, weekly	39	8.8±6.4	—	—
Intravenous regimen				
Evinacumab				
15 mg/kg every 4 wk	38	−49.9±6.1	−50.5±9.0 (−68.4 to −32.6)	<0.001
5 mg/kg every 4 wk	35	−23.5±6.6	−24.2±9.3 (−42.6 to −5.7)†	—
Placebo, every 4 wk	33	0.6±6.6	—	—
Exploratory outcome				
Heart-failure event — no. (%)	1177 (28.6)	18.7	1236 (30.1)	20.3	0.93 (0.86 to 1.00)	NA

tolerated dose, with or without ezetimibe.

placebo

2020.12 – 2021.3
COVID-19 research

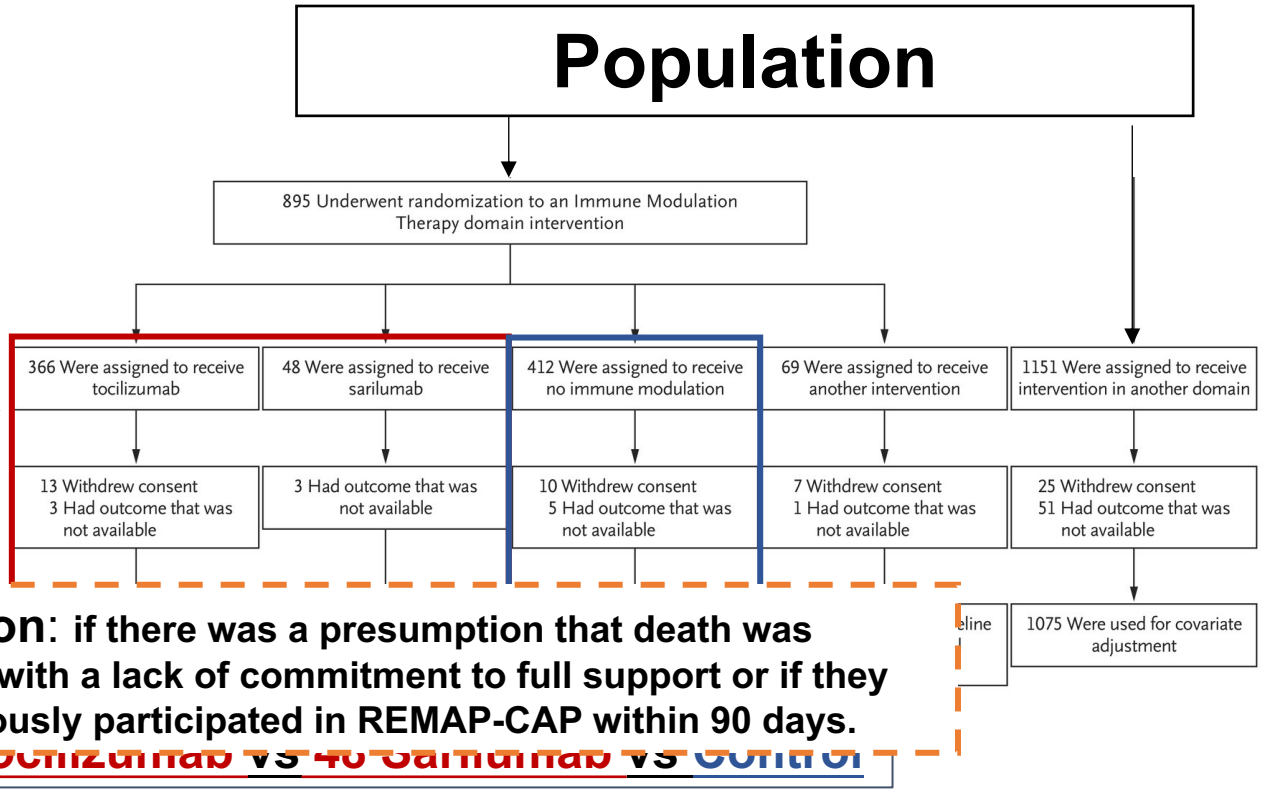
Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

NEJM

⚕ Design: International, adaptive platform trial

Population:

- Critically ill patients,
- ≧18 years of age clinically suspected or microbiologically confirmed Covid-19 who were admitted to an **intensive care unit (ICU)** and **receiving respiratory** or **cardiovascular organ support**



- **Primary outcome:** The number of respiratory and cardiovascular organ support–free days up to day 21.

Characteristic	Tocilizumab (N=353)	Sarilumab (N=48)	Control (N=402)†	All Patients (N=865)‡
APACHE II score‖				
Patients evaluated	337	42	381	820
Median (IQR)	13 (8–19)	10 (7–16)	12 (8–18)	12 (8–19)
Confirmed SARS-CoV-2 infection — no./total no. (%)**	284/345 (82)	44/47 (94)	334/394 (85)	715/847 (84)
Median time to enrollment (IQR)				
From hospital admission — days	1.2 (0.8–2.8)	1.4 (0.9–2.8)	1.2 (0.8–2.8)	1.2 (0.8–2.8)
From ICU admission — hr	13.1 (6.6–19.0)	16.0 (11.4–20.8)	14.0 (6.8–19.5)	13.6 (6.6–19.4)
Acute respiratory support — no./total no. (%)				
None or supplemental oxygen only	1/353 (<1)	0/48	2/402 (<1)	3/865 (<1)
High-flow nasal cannulae	101/353 (29)	17/48 (35)	110/402 (27)	249/865 (29)
Noninvasive ventilation only	147/353 (42)	23/48 (48)	169/402 (42)	359/865 (42)
Invasive mechanical ventilation	104/353 (29)	8/48 (17)	121/402 (30)	254/865 (29)

- **APACHE II score**

Mortality 15%

APACHE II Score	Nonoperative	Postoperative
0-4	4%	1%
5-9	8%	3%
10-14	15%	7%
15-19	25%	12%
20-24	40%	30%
25-29	55%	35%
30-34	73%	73%
>34	85%	88%

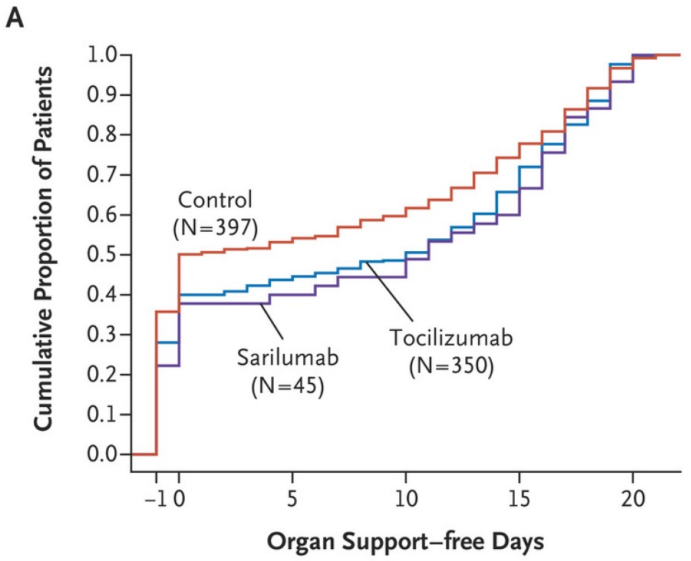
- **Confirmed infection**

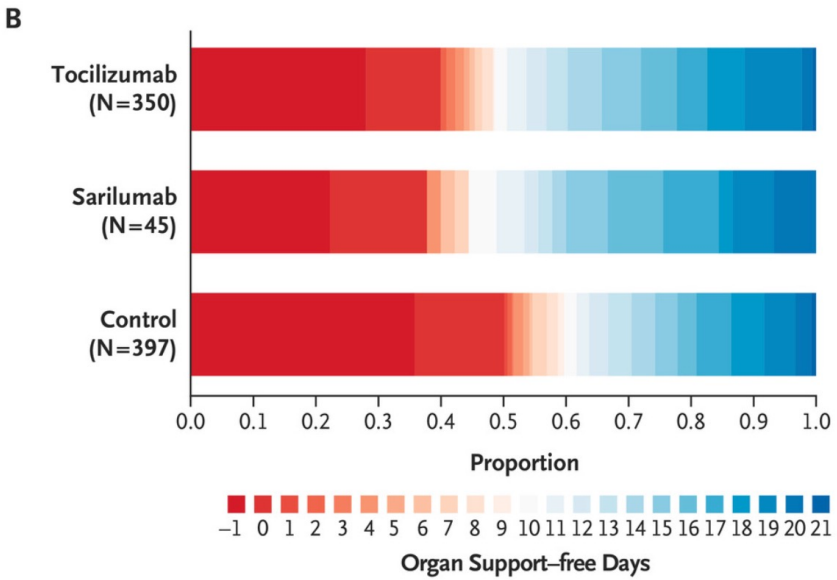
80%↑

- **None or supplemental oxygen only**

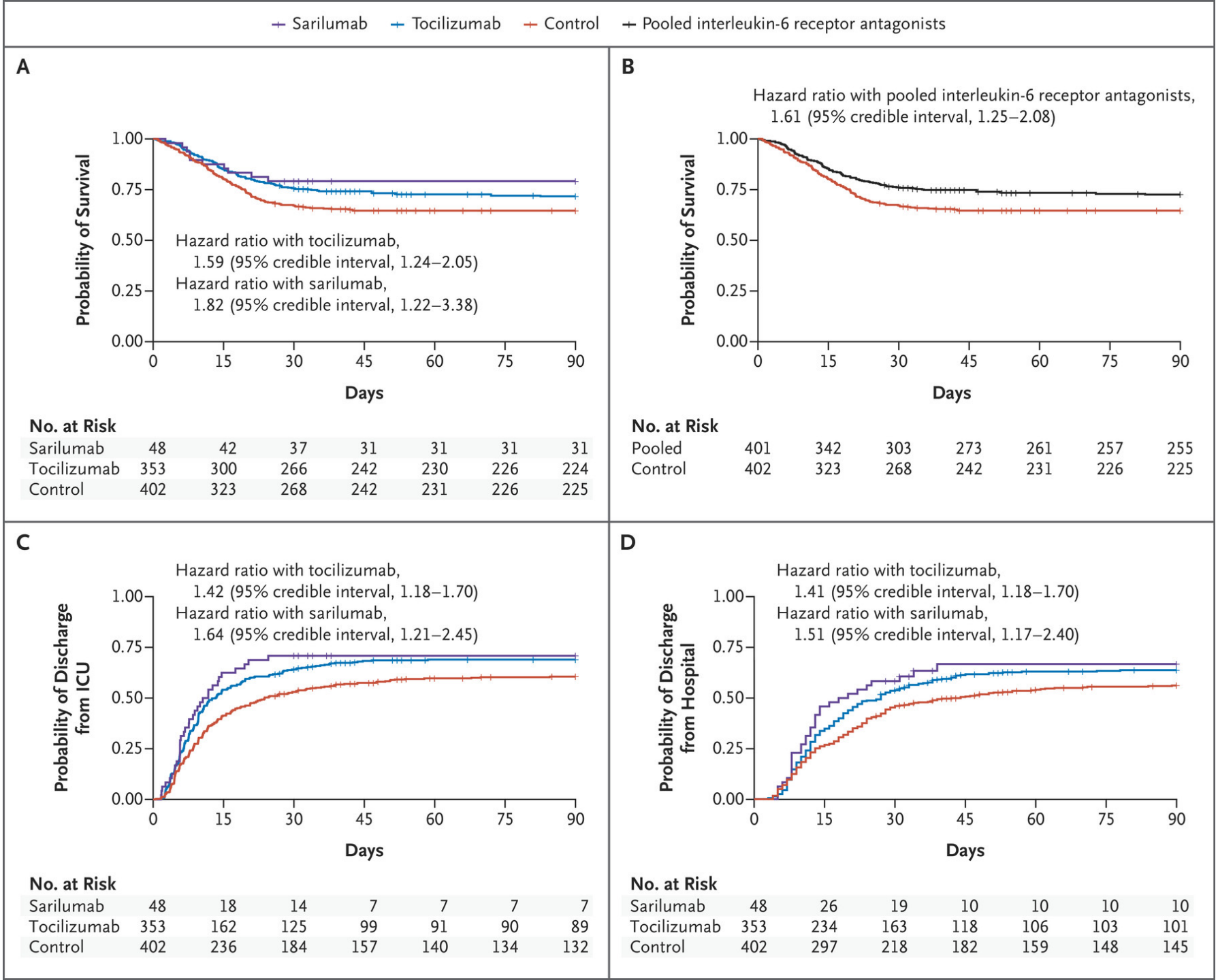
<1%

Outcome or Analysis	Tocilizumab (N=353)	Sarilumab (N=48)	Control (N=402)
Primary outcome			
Organ support–free days			
Median (IQR)	10 (–1 to 16)	11 (0 to 16)	0 (–1 to 15)
Adjusted odds ratio			
Mean	1.65±0.23	1.83±0.44	1
Median (95% credible interval)	1.64 (1.25 to 2.14)	1.76 (1.17 to 2.91)	1
Probability of superiority to control — %	>99.9	99.5	—
Subcomponents of organ support–free days			
In-hospital death — no./total no. (%)	98/350 (28)	10/45 (22)	142/397 (36)
Concurrent with tocilizumab randomization	—	—	127/355 (36)†
Concurrent with sarilumab randomization	—	—	19/63 (30)†
Median no. of days free of organ support in survivors (IQR)	14 (7 to 17)	15 (6 to 17)	13 (4 to 17)





Outcome or Analysis	Tocilizumab (N=353)	Sarilumab (N=48)	Control (N=402)
Primary in-hospital survival			
Adjusted odds ratio			
Mean	1.66±0.31	2.25±0.96	1
Median (95% credible interval)	1.64 (1.14 to 2.35)	2.01 (1.18 to 4.71)	1
Probability of superiority to control — %	99.6	99.5	—
Secondary analysis of primary outcome			
Adjusted odds ratio			
Mean	1.68±0.24	1.84±0.44	1
Median (95% credible interval)	1.66 (1.26 to 2.18)	1.77 (1.18 to 2.90)	1
Probability of superiority to control — %	>99.9	99.6	—
Secondary analysis of primary in-hospital survival			
Adjusted odds ratio			
Mean	1.67±0.31	2.24±0.94	1
Median (95% credible interval)	1.65 (1.15 to 2.34)	2.00 (1.17 to 4.69)	1
Probability of superiority to control — %	99.6	99.4	—


Sarilumab
Tocilizumab
Control
Pooled interleukin-6 receptor antagonists
A
Probability of Survival
1.00
0.75
0.50
0.25
0.00
0
15
30
45
60
75
90
Days
Hazard ratio with tocilizumab,
1.59 (95% credible interval, 1.24–2.05)
Hazard ratio with sarilumab,
1.82 (95% credible interval, 1.22–3.38)
No. at Risk
Sarilumab 48 42 37 31 31 31 31
Tocilizumab 353 300 266 242 230 226 224
Control 402 323 268 242 231 226 225
B
Hazard ratio with pooled interleukin-6 receptor antagonists,
1.61 (95% credible interval, 1.25–2.08)
Probability of Survival
Days
No. at Risk
Pooled 401 342 303 273 261 257 255
Control 402 323 268 242 231 226 225
C
Hazard ratio with tocilizumab,
1.42 (95% credible interval, 1.18–1.70)
Hazard ratio with sarilumab,
1.64 (95% credible interval, 1.21–2.45)
Probability of Discharge from ICU
Days
No. at Risk
Sarilumab 48 18 14 7 7 7 7
Tocilizumab 353 162 125 99 91 90 89
Control 402 236 184 157 140 134 132
D
Hazard ratio with tocilizumab,
1.41 (95% credible interval, 1.18–1.70)
Hazard ratio with sarilumab,
1.51 (95% credible interval, 1.17–2.40)
Probability of Discharge from Hospital
Days
No. at Risk
Sarilumab 48 26 19 10 10 10 10
Tocilizumab 353 234 163 118 106 103 101
Control 402 297 218 182 159 148 145

A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19

✢ Design: open-label, cluster-randomized trial

• ≧18 years of age • Had a recent history of close-contact exposure to a PCR-confirmed case patient with Covid-19 • With either a negative or positive PCR test at baseline to assess the prophylactic and preemptive effect of hydroxychloroquine treatment, respectively	Hydroxychloroquine (Dolquine) at a dose of 800 mg on day 1, followed by 400 mg once daily for 6 days	Standard care	• The primary outcome was the onset of a PCR-confirmed, symptomatic Covid-19 episode, defined as symptomatic illness (at least one of the following symptoms: fever, cough, difficulty breathing, myalgia, headache, sore throat, new olfactory or taste disorder, or diarrhea

Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19

✢ Design: randomized, controlled, open-label platform trial

• Hospitalized patients were eligible for the trial if they had clinically-suspected or laboratory- confirmed SARS-CoV-2 infection and no medical history	**2:1:1** • Standard of care • Standard of care + Hydroxychloroquine (Loading 800mg; 400mg Q12h to day 9) • Other available treatment	• The primary outcome was all-cause mortality within 28 days after randomization

Vaccination

- **mRNA 疫苗(mRNA-1273/BNT162)**

mRNA 全名為信使 RNA（message RNA），可將特定蛋白質的製造指示送至細胞核糖體（ribosomes）進行生產。mRNA 疫苗會將能製造新冠病毒棘狀蛋白的 mRNA 送至人體內，並不斷製造棘狀蛋白，藉此驅動免疫系統攻擊與記憶此類病毒蛋白，增加人體對新冠病毒的免疫力，最終 mRNA 將被細胞捨棄。

- **病毒載體疫苗 (Ad.26.COV2.S)**

病毒載體疫苗通常會用腺病毒（adenovirus）傳遞至人體。製造病毒載體疫苗首先得將病毒載體的自我複製能力消除，再將一段製造病毒棘狀蛋白的 RNA 或 DNA 放入腺病毒基因序列中，最後將之遞送至人體細胞，製造抗原刺激免疫系統。

- **蛋白質次單元疫苗 (NVX-CoV2373)**

蛋白質次單元（protein subunit）疫苗能以更直接的方式刺激免疫系統。將結合類病毒奈米粒子的蛋白質傳遞至患者體內，免疫系統即可迅速產生抗體，相比透過 mRNA 或其他核酸來製造棘狀蛋白還直接。以下為 2 家蛋白質次單元疫苗藥廠。

節錄自：https://geneonline.news/4-covid-vac

Name

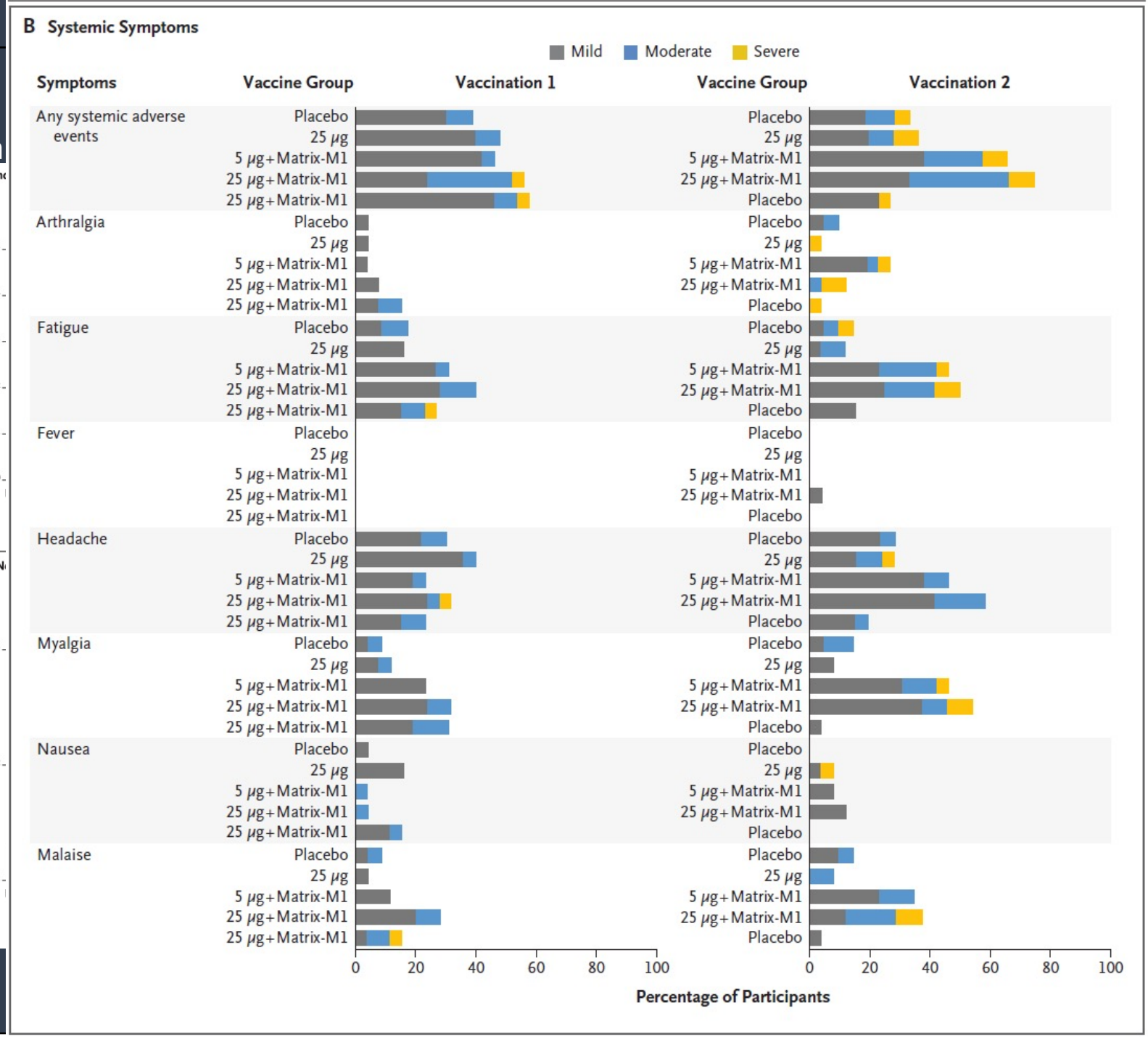
Type & Mechanism

Trial

Proced

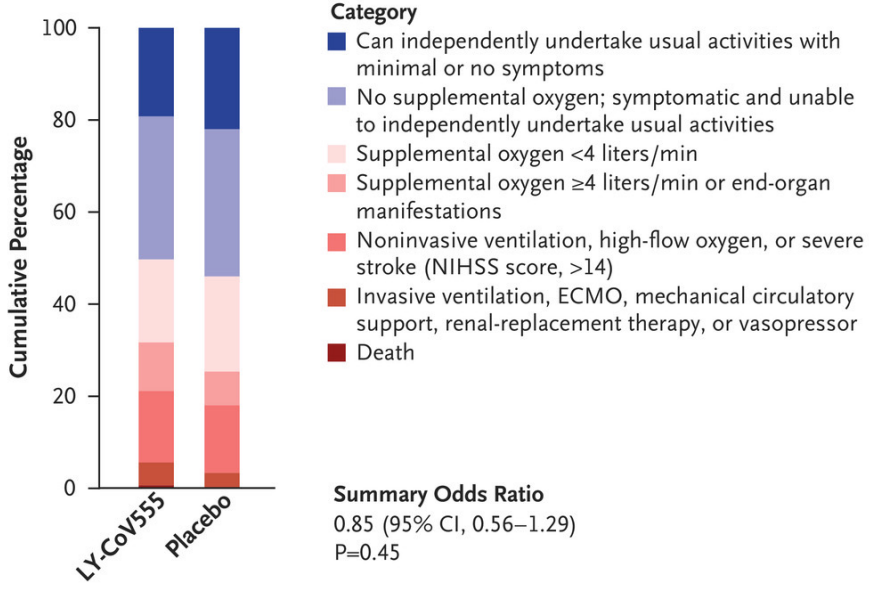
Efficacy

Safety

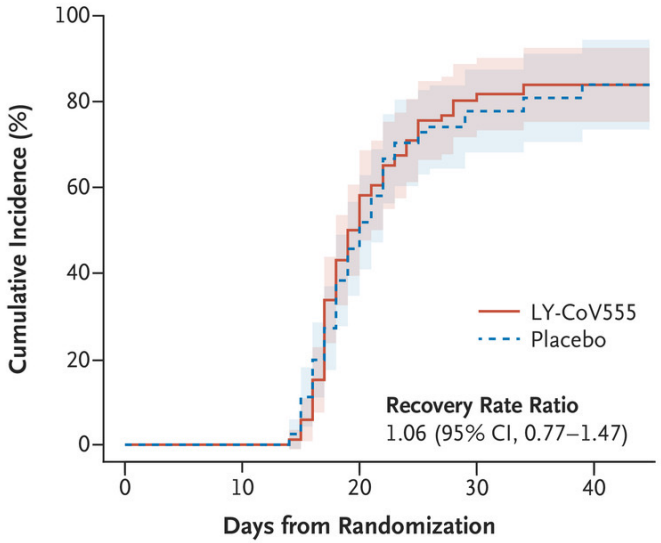


A Pulmonary Ordinal Outcome on Day 5

Category		LY-CoV555	Placebo
		no. of patients (%)	
Better	1	31 (19.3)	33 (22.0)
	2	50 (31.1)	48 (32.0)
	3	29 (18.0)	31 (20.7)
	4	17 (10.6)	11 (7.3)
	5	25 (15.5)	22 (14.7)
	6	8 (5.0)	5 (3.3)
Worse	7	1 (0.6)	0 (0.0)

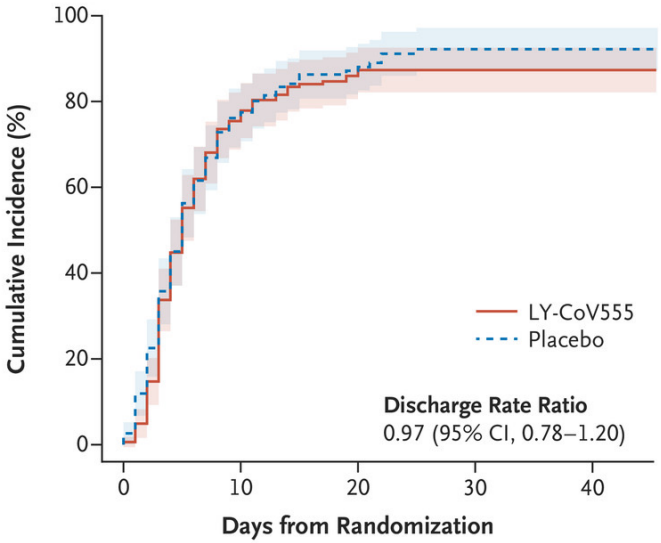


B Time to Sustained Recovery



No. at Risk					
LY-CoV555	87	86	41	9	3
Placebo	81	81	41	10	4

C Time to Hospital Discharge



No. at Risk					
LY-CoV555	163	38	17	6	3
Placebo	151	36	13	6	4

Name

Type

Mild Moderate

A Local Events

100 90 83 16–55

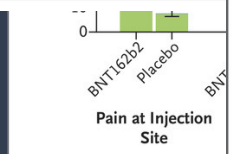
Table 2. Vaccine Efficac

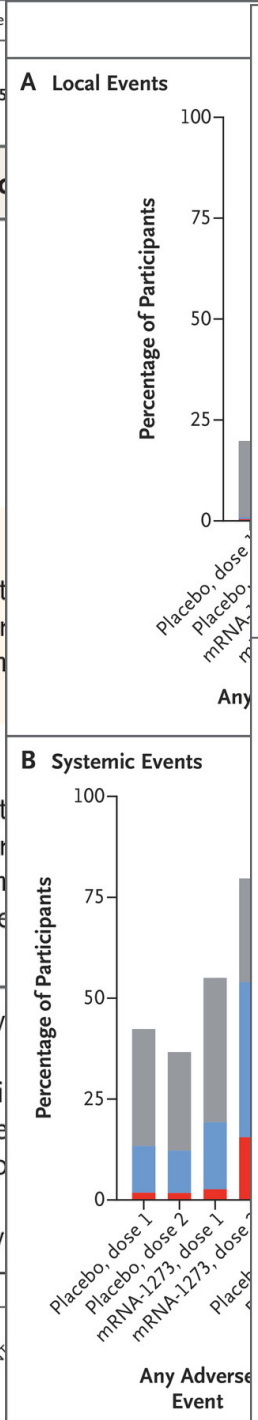
Efficacy End Point	
Covid-19 occurrence at days after the secon in participants with dence of infection	9999
Covid-19 occurrence at days after the secon in participants with those without evide infection	9999

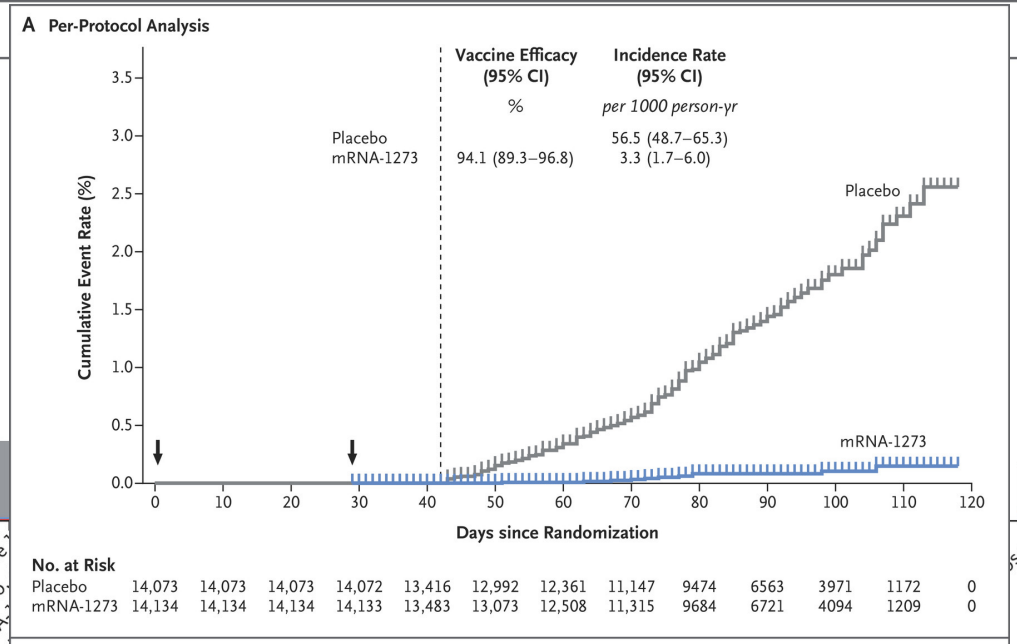
* The total population w tion was 40,137.
† The surveillance time i end point. The time pe
‡ The credible interval fo surveillance time.
§ Posterior probability w

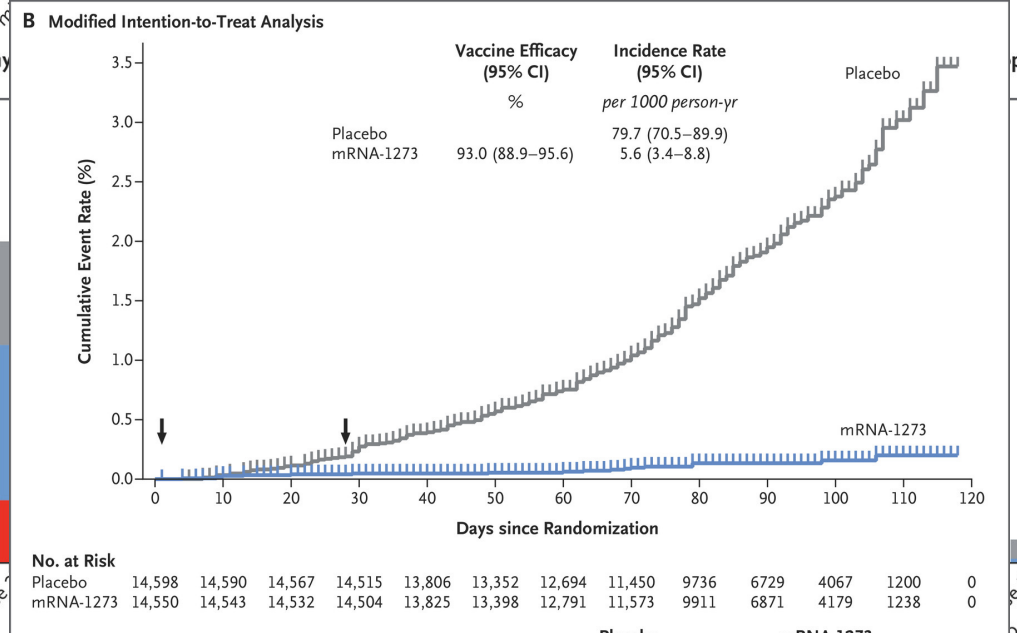
terior ability e Efficacy 0%)§

e of infec-
k for the
ed for the
nce time.

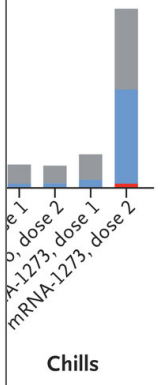








Covid-19 Onset	Placebo (N=14,598)	mRNA-1273 (N=14,550)
Randomization to 14 days after dose 1	11	5
14 Days after dose 1 to dose 2	35	2
Dose 2 to 14 days after dose 2	19	0
Starting 14 days after dose 2	204	12
Total (any time after randomization)	269	19

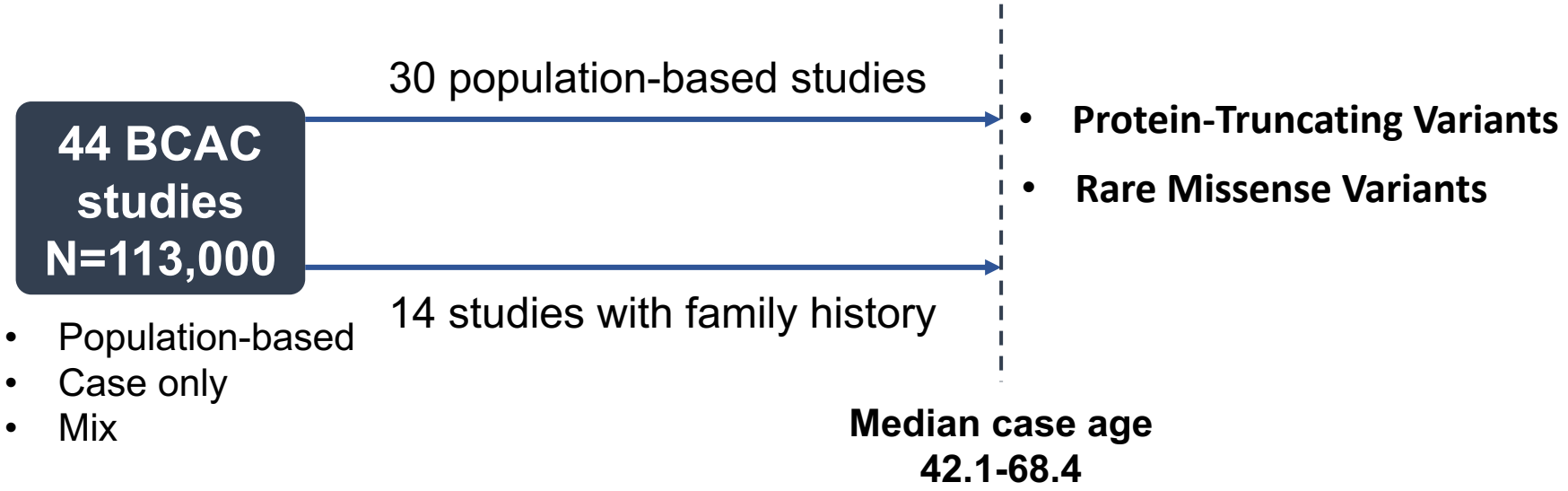


2020.12 – 2021.3
Cancer research

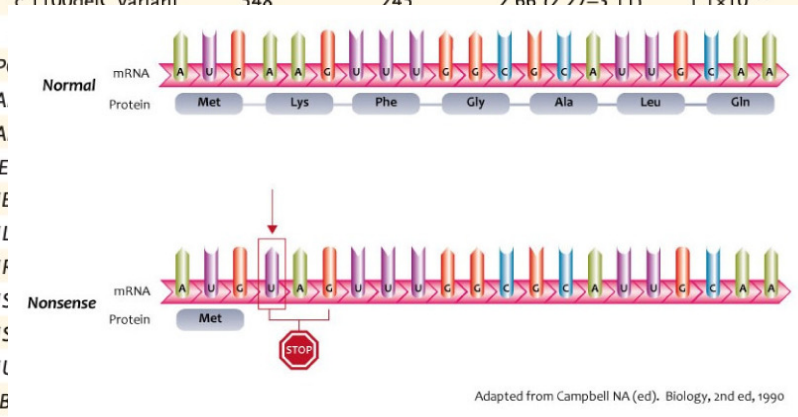
Breast Cancer Risk Genes — Association Analysis in More than 113,000 Women

NEJM

Design: Observational study

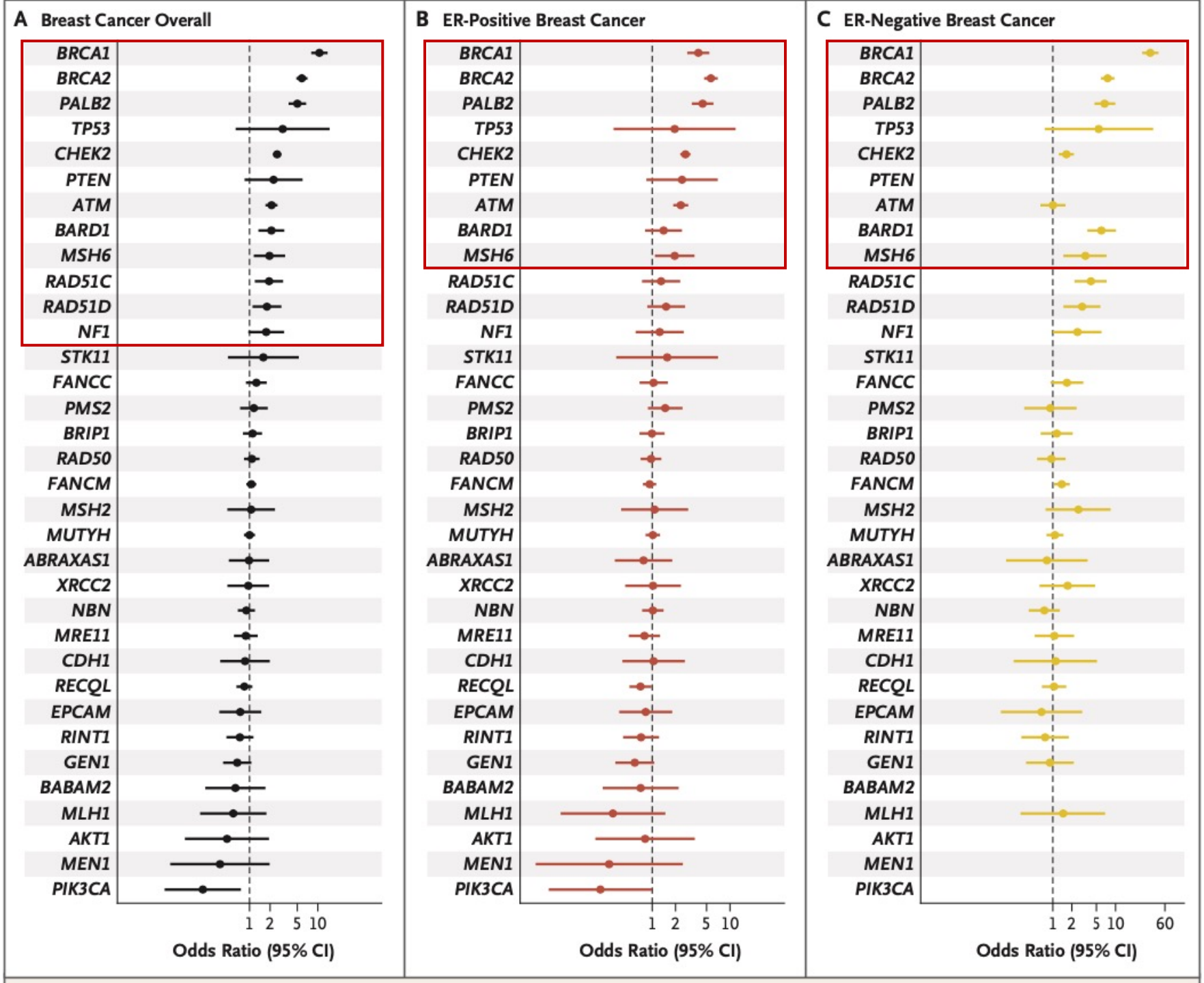


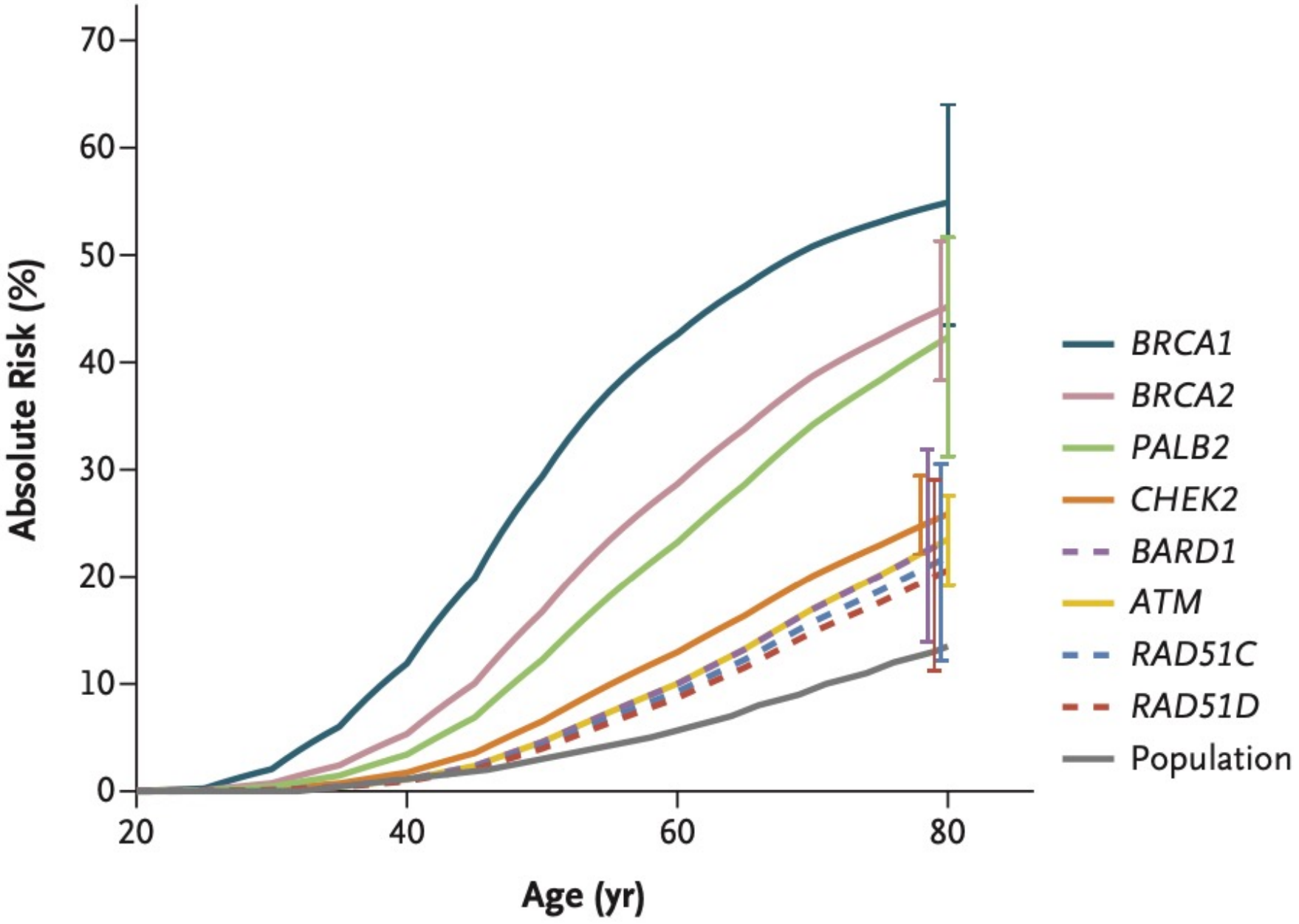
Gene	Population-Based Studies (48,826 patients and 50,703 controls)†				All Studies (60,466 patients and 53,461 controls)†	Prior Probability‡	BFDP
	No. of Carriers of Protein-Truncating Variants		Odds Ratio (95% CI)	P Value	P Value		
	Women with Breast Cancer	Controls					
ABRAXAS1	17	19	0.98 (0.50–1.94)	0.96	0.93	0.1	0.98
AKT1	3	6	0.47 (0.12–1.93)	0.29	0.14	0.1	0.94
ATM	294	150	2.10 (1.71–2.57)	9.2×10^{-13}	5.5×10^{-20}	0.8	1.3×10^{-18}
BABAM2	7	9	0.62 (0.23–1.71)	0.36	0.34	0.1	0.95
BARD1	62	32	2.09 (1.35–3.23)	0.00098	0.00011	0.2	0.0076
BRCA1	515	58	10.57 (8.02–13.93)	1.1×10^{-62}	3.7×10^{-65}	0.99	1.5×10^{-64}
BRCA2	754	135	5.85 (4.85–7.06)	2.2×10^{-75}	8.4×10^{-77}	0.99	3.1×10^{-76}
BRIP1	86	75	1.11 (0.80–1.53)	0.54	0.54	0.2	0.85
CDH1	11	12	0.86 (0.37–1.98)	0.72	0.58	0.2	0.94
CHEK2	704	315	2.54 (2.21–2.91)	3.1×10^{-39}	3.2×10^{-61}	0.99	1.3×10^{-60}
c.1100delC variant	548	245	2.66 (2.27–3.11)	1.1×10^{-33}	5.3×10^{-53}		
					7.4×10^{-10}		
EP					0.13	0.1	0.95
FA					0.20	0.1	0.87
FA					0.28	0.1	0.96
GE					0.18	0.1	0.95
ME					0.64	0.1	0.95
ML					0.55	0.1	0.95
MR					0.34	0.1	0.98
MS					0.80	0.1	0.92
MS					0.021	0.1	0.55
MU					0.88	0.1	1.00
NB					0.65	0.2	0.95
NF1	31	17	1.76 (0.96–3.21)	0.068	0.011	0.2	0.25
PALB2	274	55	5.02 (3.73–6.76)	1.6×10^{-26}	1.1×10^{-32}	0.99	2.9×10^{-32}
PIK3CA	3	12	0.21 (0.06–0.75)	0.016	0.19	0.1	0.94
PMS2	40	36	1.16 (0.73–1.85)	0.53	0.37	0.1	0.92
PTEN	14	6	2.25 (0.85–6.00)	0.10	0.0040	0.2	0.14
RAD50	120	121	1.08 (0.83–1.40)	0.57	0.45	0.1	0.95
RAD51C	54	26	1.93 (1.20–3.11)	0.0070	0.00026	0.3	0.0090
RAD51D	51	25	1.80 (1.11–2.93)	0.018	0.0018	0.3	0.044
RECQL	103	120	0.84 (0.64–1.10)	0.21	0.89	0.1	0.95
RINT1	32	49	0.72 (0.46–1.14)	0.17	0.31	0.1	0.96
STK11	6	5	1.60 (0.48–5.28)	0.44	0.50	0.2	0.70
TP53	7	2	3.06 (0.63–14.91)	0.17	0.015	0.8	0.033
XRCC2	15	18	0.96 (0.47–1.93)	0.90	0.81	0.1	0.98



BFDP: Bayesian false-discovery probability

- **Protein-Truncating Variants**
  - **ATM**
    - Leukemia, lymphoma
  - **BARD1**
  - **BRCA1**
    - Ovary
  - **BRCA2**
    - Ovary, prostate, pancreas, male breast, leukemia, brain tumors, Wilms' tumor
  - **CHEK2**
  - **PALB2**
    - Pancreas
  - **RAD51C**
    - Ovary

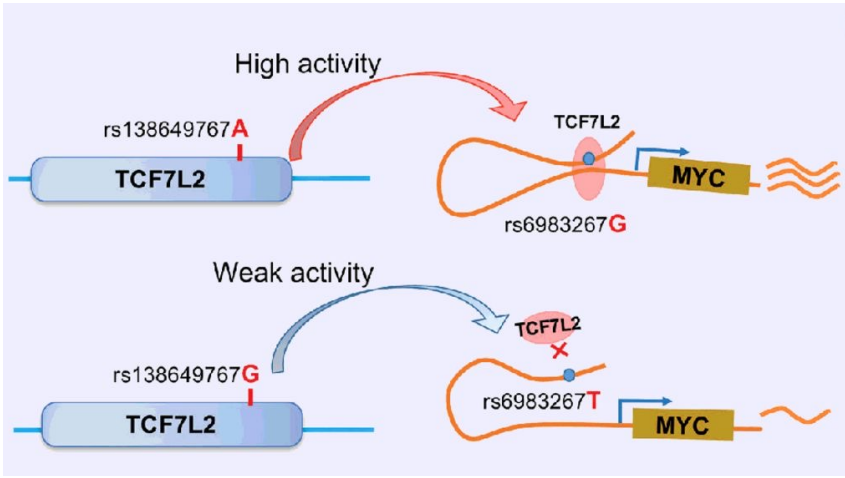

A Breast Cancer Overall
B ER-Positive Breast Cancer
C ER-Negative Breast Cancer
BRCA1
BRCA2
PALB2
TP53
CHEK2
PTEN
ATM
BARD1
MSH6
RAD51C
RAD51D
NF1
STK11
FANCC
PMS2
BRIP1
RAD50
FANCM
MSH2
MUTYH
ABRAXAS1
XRCC2
NBN
MRE11
CDH1
RECQL
EPCAM
RINT1
GEN1
BABAM2
MLH1
AKT1
MEN1
PIK3CA
1 2 5 10
1 2 5 10
1 2 5 10 60
Odds Ratio (95% CI)
Odds Ratio (95% CI)
Odds Ratio (95% CI)



protein-truncating variants

Gene	Population-Based Studies (48,826 patients and 50,703 controls)*				All Studies (60,466 patients and 53,461 controls)*
	No. of Carriers of Rare Missense Variants		Odds Ratio (95% CI)	P Value	P Value
	Women with Breast Cancer	Controls			
ABRAXAS1	233	242	1.04 (0.86–1.25)	0.70	0.40
AKT1	142	156	0.96 (0.76–1.21)	0.72	0.63
ATM	2411	2471	1.06 (1.00–1.13)	0.051	0.0010
BABAM2	167	170	1.01 (0.81–1.26)	0.91	0.63
BARD1	591	616	1.00 (0.89–1.12)	0.94	0.41
BRCA1	1393	1300	1.11 (1.02–1.20)	0.010	0.027
BRCA2	2831	3038	0.98 (0.93–1.04)	0.50	0.58
BRIP1	868	961	0.95 (0.86–1.04)	0.25	0.54
CDH1	682	668	1.10 (0.98–1.23)	0.096	0.042
CHEK2	895	697	1.42 (1.28–1.58)	2.5×10^{-11}	2.9×10^{-18}
EPCAM	290	328	0.97 (0.82–1.14)	0.69	0.43
FANCC	597	620	0.95 (0.85–1.07)	0.42	0.80
FANCM	1434	1566	0.95 (0.88–1.02)	0.17	0.85
GEN1	701	707	1.05 (0.94–1.17)	0.38	0.25
MEN1	109	130	0.86 (0.66–1.12)	0.25	0.81
MLH1	677	711	1.02 (0.91–1.13)	0.78	0.68
MRE11	552	611	0.94 (0.84–1.06)	0.33	0.93
MSH2	908	1024	0.92 (0.84–1.01)	0.093	0.12
MSH6	1088	1155	1.00 (0.92–1.09)	0.98	0.74
MUTYH	659	702	1.00 (0.90–1.12)	1.00	0.58
NBN	665	725	0.95 (0.85–1.06)	0.37	0.71
NF1	816	899	0.94 (0.85–1.03)	0.19	0.53
PALB2	805	892	0.96 (0.87–1.06)	0.39	1.00
PIK3CA	170	205	0.83 (0.67–1.02)	0.080	0.33
PMS2	934	963	0.95 (0.87–1.05)	0.31	0.62
PTEN	68	70	1.08 (0.76–1.53)	0.65	0.48
RAD50	1046	1089	0.99 (0.91–1.08)	0.83	0.44
RAD51C	196	206	0.93 (0.76–1.14)	0.49	0.60
RAD51D	224	212	1.05 (0.86–1.27)	0.64	0.57
RECQL	656	627	1.12 (1.00–1.26)	0.047	0.036
RINT1	732	762	1.01 (0.91–1.12)	0.89	0.18
STK11	114	139	0.83 (0.64–1.07)	0.15	0.16
TP53	257	244	1.10 (0.91–1.31)	0.32	0.00080
XRCC2	207	213	1.03 (0.84–1.25)	0.80	0.53

- **Rare Missense Variants**



BRCA1、CHEK2、TP53

Nivolun … -Cell Carcino…

+ Desig…

- Adults … int was treated … survival …

- …
- …

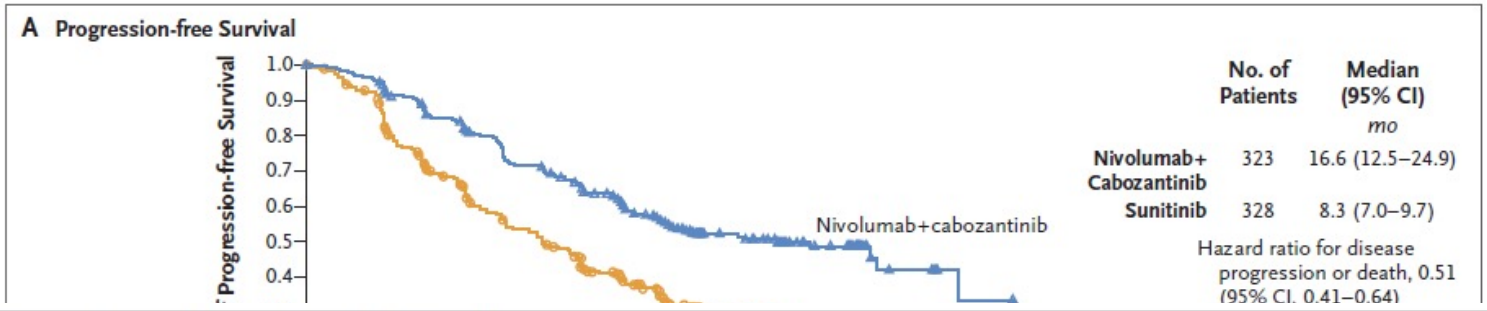
L… C…

+ …

- …

at leas…

lesion …



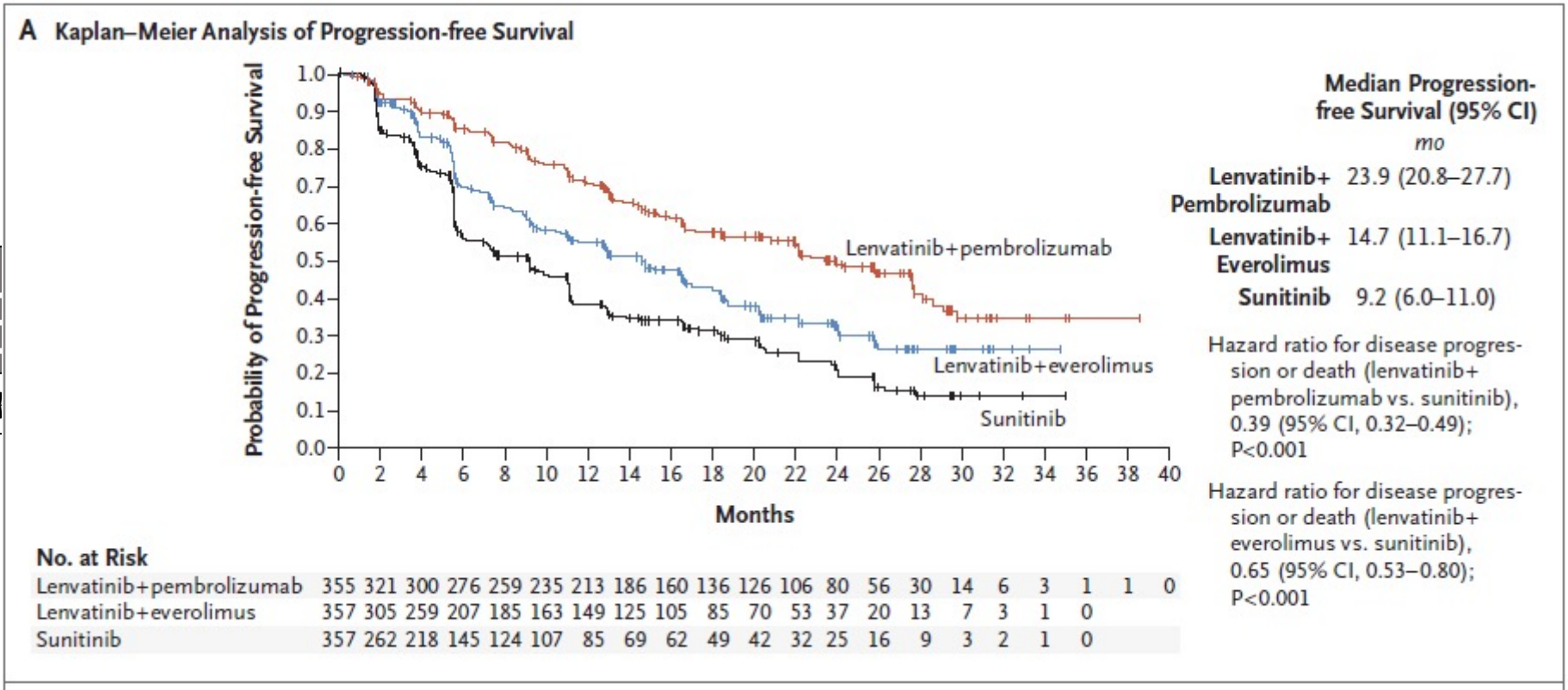


Figure 1. Progression-free and Overall Survival in the Intention-to-Treat Population.

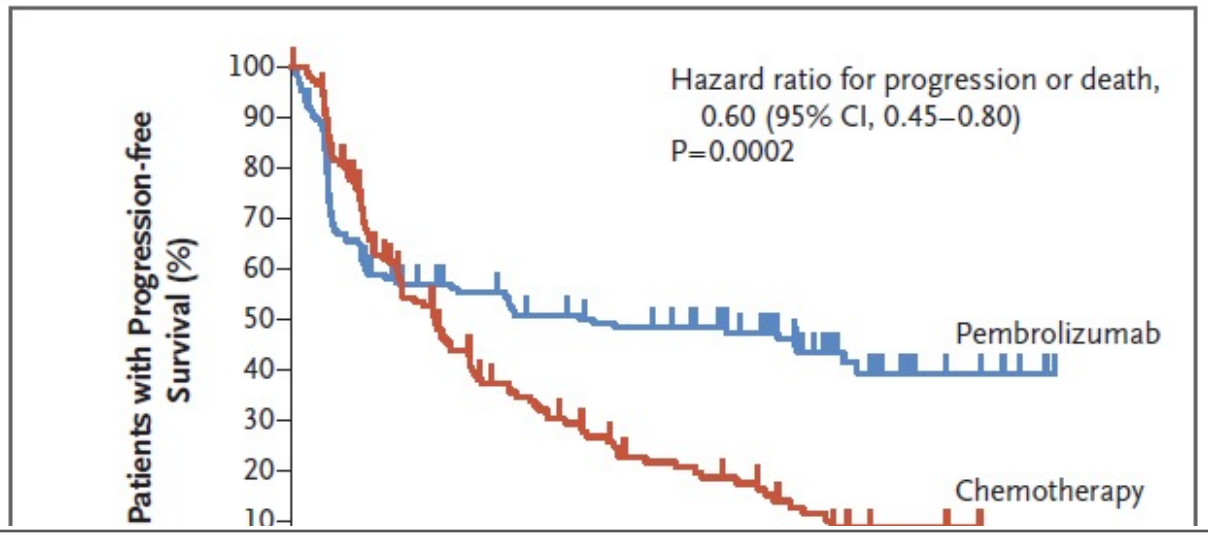
The intention-to-treat population included all the patients who underwent randomization. Shown are Kaplan–Meier estimates of progression-free survival (Panel A) and overall survival (Panel B). Progression-free survival was assessed according to Response Evaluation Criteria in Solid Tumors, version 1.1, by blinded independent central review of radiologic imaging. NE denotes could not be estimated, and NR not reached.

Pembrolizum
Colorectal Ca

- Design: multic

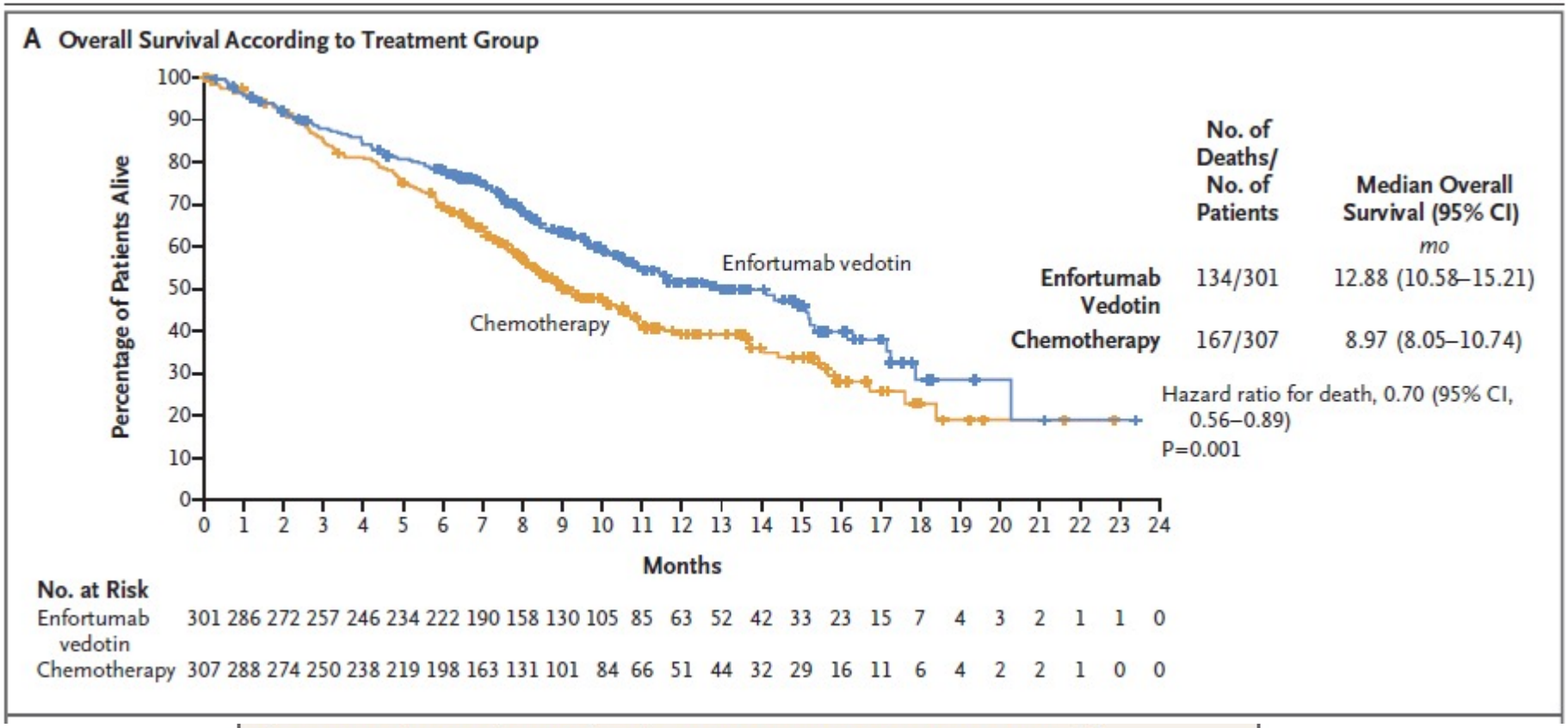
- 18 years of ag
  and had MSI-H
  stage IV colore
  with measurab

id points were
urvival and overall



En

-



Oral Azaci… Remissio…

✛ Design: p…

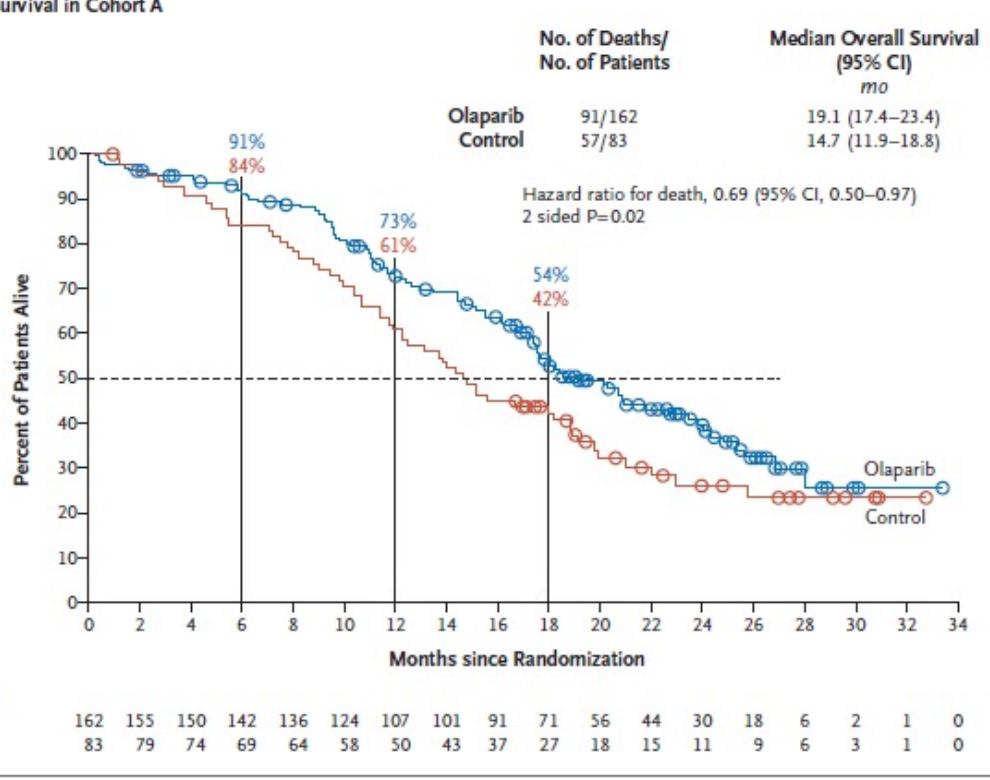
- At least 5… and to hav… diagnosed… (i.e., AML … anteceder… disorder) … AML and i… poor-risk … characteris… diagnosis

Survival w…

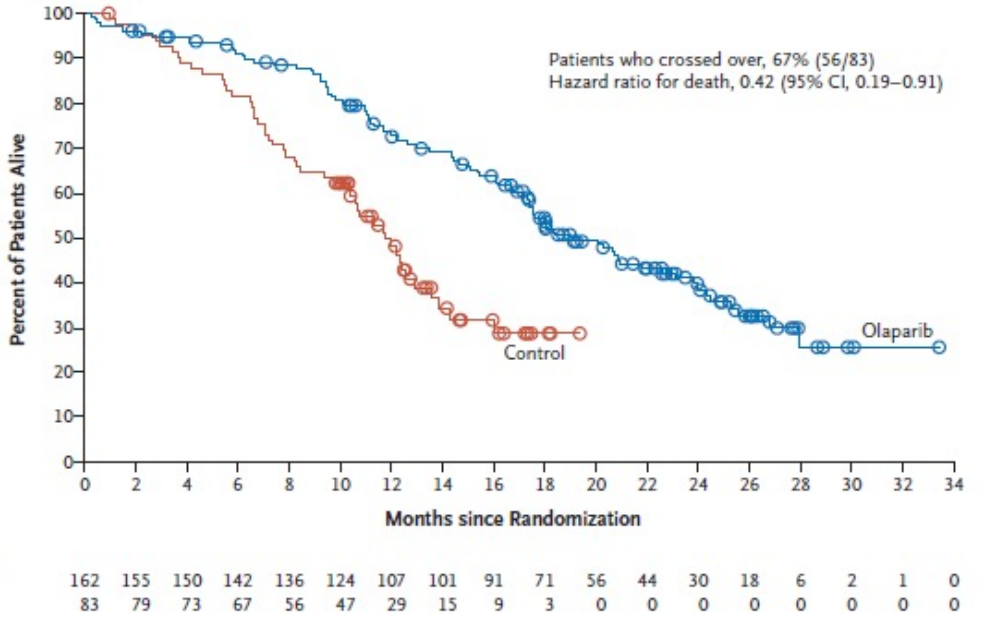
✛ Design: C…

- Metastatic… resistant p… whose dis… progresse… previous t… enzalutam… or both. Pr… chemother… allowed

A Overall Survival in Cohort A



B Crossover-Adjusted Analysis of Overall Survival in Cohort A



…ia in First …

…l point was defined as …ndomization …y cause.

72 78

1 0
1 0

…e Cancer

(defined as …ndomization …y cause …ether the … from the …y or received …cer therapy) …a key alpha- …ndary end

72

0

…ization.
…0.15 months


Miscellaneous

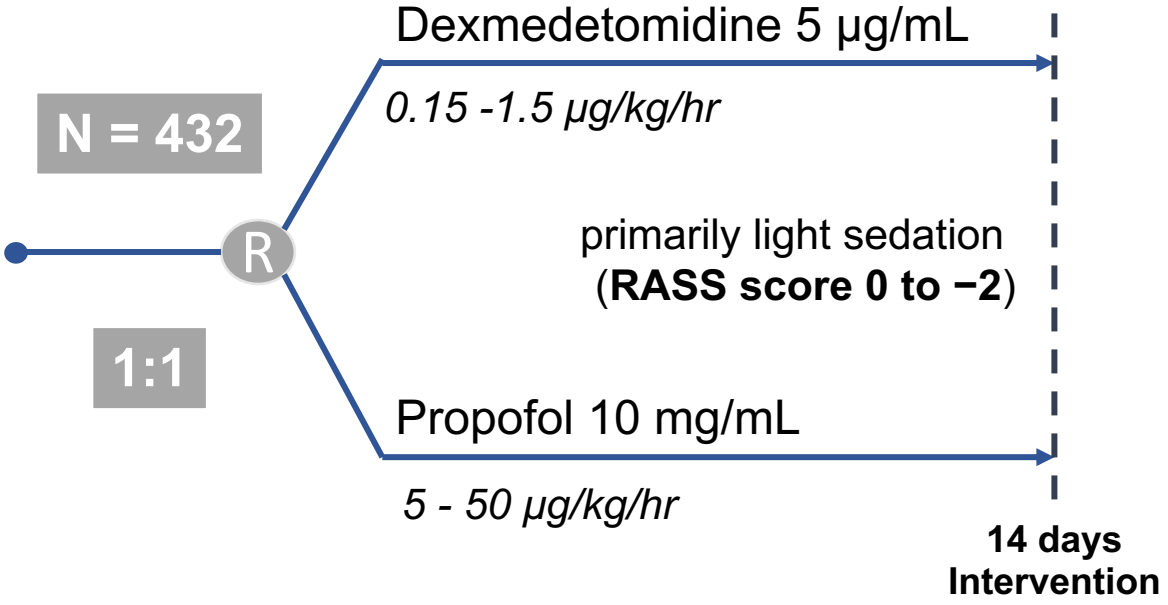
Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis

NEJM

Design: randomized, controlled, double-blind trial

Population:

- Admitted to a medical or surgical ICU, had **suspected or known infection**, and were treated with continuous sedation for invasive mechanical ventilation.

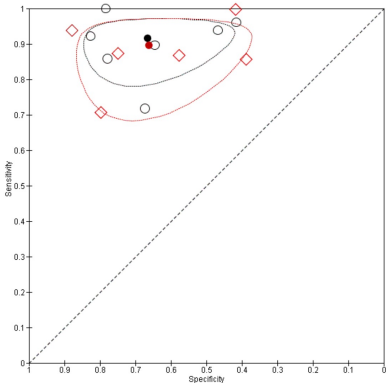


- **Primary outcome:** The number of calendar days alive without delirium or coma during the 14-day intervention period
- **Secondary/Safety outcome:** Ventilator-free days at 28 days, death at 90 days, and global cognition at 6 months using the age-adjusted TICS total score (TICS-T score)

Median IQCODE-SF score (IQR)§	3.06 (3.00–3.23)	3.00 (3.00–3.25)
Median Charlson Comorbidities Index score (IQR)¶	2 (1–4)	2 (1–4)
Admitted to surgical ICU — no. (%)	76 (36)	72 (35)
Median APACHE II score at ICU admission (IQR)‖	27 (21–32)	27 (22–32)
Median days from ICU admission to trial enrollment (IQR)	1.21 (0.67–1.95)	1.17 (0.68–1.94)
Median days of mechanical ventilation before trial enrollment (IQR)	0.98 (0.58–1.36)	0.97 (0.61–1.54)
Median total SOFA score at trial enrollment (IQR)**	10 (8–13)	10 (8–12)
Shock, receiving vasopressor, at enrollment — no. (%)	119 (56)	102 (49)
Known or suspected source of infection — no. (%)		
Blood	92 (43)	79 (38)
Lung	116 (54)	133 (64)
Abdomen	19 (9)	20 (10)
Urinary tract	46 (21)	55 (26)
Skin or wound	23 (11)	26 (12)
Stool	12 (6)	12 (6)
Other	24 (11)	21 (10)
Infection status — no. (%)		
Infection confirmed by culture	146 (68)	132 (63)
Infection suspected but not confirmed by culture	58 (27)	68 (33)
Infection ruled out	10 (5)	8 (4)
Dexmedetomidine before enrollment — no. (%)	35 (16)	25 (12)
Propofol before enrollment — no. (%)	131 (61)	129 (62)
Benzodiazepine before enrollment — no. (%)	62 (29)	73 (35)
Opioid before enrollment — no. (%)	144 (67)	147 (71)
Antipsychotic agent before enrollment — no. (%)	24 (11)	27 (13)
Delirium at enrollment — no. (%)††	75 (35)	91 (44)
Level of arousal closest to the time of randomization — no. (%)‡‡		
Coma: RASS –5 or –4	81 (38)	74 (36)
Deep sedation: RASS –3	29 (14)	38 (18)
Light sedation: RASS –2 or –1	85 (40)	75 (36)
Awake and calm: RASS 0	13 (6)	14 (7)
Agitated: RASS +1 to +4	6 (3)	7 (3)

IQCODE-SF score

Threshold 3.3



APACHE II score

Mortality 30-50%

APACHE II Score	Nonoperative	Postoperative
0-4	4%	1%
5-9	8%	3%
10-14	15%	7%
15-19	25%	12%
20-24	40%	30%
25-29	55%	35%
30-34	73%	73%
>34	85%	88%

SOFA score

Initial score: 10
50% mortality

Outcome	Dexmedetomidine N = 214	Propofol N = 208
Median hours from meeting inclusion criteria to drug initiation (IQR)	22.4 (13.4–31.3)	22.1 (12.8–33.7)
Median hours from randomization to drug initiation (IQR)	1.3 (0.9–2.2)	1.3 (0.8–2.1)
Trial drug administration		
Median days of receipt of drug (IQR)	3.0 (2.0–5.0)	4.0 (2.0–6.0)
Median days from first meeting trial criteria to initiation of drug (IQR)	1.00 (0.00–1.00)	1.00 (0.00–1.00)
Median daily volume on days administered (IQR) — ml	119 (46–243)	131 (67–229)
Median daily dose on days administered (IQR)	0.27 μg/kg/hr (0.11–0.61)	10.2 μg/kg/min (5.5–18.4)
Median total no. of drug adjustments per patient (IQR)	9 (5–15.8)	11.5 (5.8–25)
Drug temporarily held — no. (%)*	60 (28)	57 (27)
Median no. of times drug temporarily held per patient (IQR)	1 (1–1)	1 (1–2)
Drug permanently discontinued — no. (%)	25 (12)	23 (11)
Trial or clinical team aware of the drug used — no. (%)	27 (13)	31 (15)
Withdrawal from trial during hospitalization — no. (%)	10 (5)	9 (4)
Median RASS score while receiving drug (IQR)	−2.00 (−3.00 to −1.00)	−1.95 (−3.03 to −0.98)
Percent time at target sedation level while receiving drug	57	60
Median CPOT score while receiving drug (IQR)†	0.33 (0.00–0.83)	0.31 (0.00–0.87)

Percent of days with adherence to ABCDE bundle‡		
Spontaneous awakening trial	98	98
Spontaneous breathing trial	93	95
Coordination of awakening and breathing trials	86	84
Nondrug delirium interventions	99	99
Early mobilization	91	92
Median daily fentanyl dose on days administered (IQR) — μg/hr	68 (28–119)	56 (20–95)
Midazolam exposure		
Ever used — no. (%)	114 (53)	90 (43)
Median days among users (IQR)	2.0 (1.0–4.0)	1.0 (1.0–2.0)
Median daily dose on days administered (IQR) — mg per day	3.8 (2.0–10.9)	4.0 (2.0–10.8)
Antipsychotic exposure		
Ever used — no. (%)	90 (42)	87 (42)
Median days among users (IQR)	5.0 (2.0–7.8)	4.0 (2.0–8.0)
Median daily dose on days administered (IQR) — mg§	2.2 (1.0–6.4)	3.6 (1.0–6.3)
Open-label propofol exposure		
Ever used — no. (%)	27 (13)	16 (8)
Median days among users (IQR)	2.0 (1.0–3.0)	1.5 (1.0–2.0)
Median daily dose on days administered (IQR) — μg/kg/min	10.8 (4.9–17.4)	4.8 (3.4–6.6)
Open-label dexmedetomidine exposure		
Ever used — no. (%)	9 (4)	6 (3)
Median days among users (IQR)	1.0 (1.0–2.0)	1.0 (1.0–3.2)
Median daily dose on days administered (IQR) — μg/kg/hr	0.24 (0.04–0.30)	0.26 (0.07–0.7)

End Point	Dexmedetomidine (N=214)	Propofol (N=208)
Primary end point		
Days alive without delirium or coma at 14 days		
Unadjusted no. of days — median (IQR)	8.0 (1.0–12.8)	7.5 (1.8–11.2)
Adjusted no. of days — median (95% CI)	10.7 (8.5–12.5)	10.8 (8.7–12.6)
Adjusted odds ratio (95% CI)	0.96 (0.74–1.26)	Reference
Secondary end points		
Ventilator-free days at 28 days		
Unadjusted no. of days — median (IQR)	20.9 (0.0–26.1)	19.9 (4.2–24.9)
Adjusted no. days — median (95% CI)	23.7 (20.5–25.4)	24.0 (20.9–25.4)
Adjusted odds ratio (95% CI)	0.98 (0.63–1.51)	Reference
Death at 90 days		
Unadjusted no. of patients (%)	81 (38)	82 (39)
Adjusted hazard ratio (95% CI)	1.06 (0.74–1.52)	Reference
TICS-T score at 6 mo†		
Unadjusted score — median (IQR)	39 (28–48)	38 (30–46)
Adjusted score — median (95% CI)	40.9 (33.6–47.1)	41.4 (34.0–47.3)
Adjusted odds ratio (95% CI)	0.94 (0.66–1.33)	Reference

- **TICS-T score <35 indicates cognitive impairment**

Cochrane RoB 2.0 of Randomized parallel group trial

Bias arising from the randomization process	✓ Allocation conceal ✓ Allocation sequence random ✓ Baseline balance	**Low risk**
Bias due to deviation from intended intervention	✓ Double-blinded ✓ Crossover intervention ✓ Multivariate regression model but not IPBW analysis	**High risk**
Bias due to missing outcome data	✓ >50% missing data (died in hospital) ✓ In time-to-event analyses, participants' follow up is censored when they stop or change their assigned intervention	**High risk**
Bias in measurement of outcome	✓ Assessor blinded? PY	**Low risk**
Bias in selection of reported result	✓ No evidence of selection of the reported result	**Low risk**

Trial of Dexamethasone for Chronic Subdural Hematoma

NEJM

⚕ Design: multicenter, randomized trial

Population:

- 18 years or age and older and were admitted to a participating neurosurgical unit with symptomatic chronic subdural hematoma had been confirmed cranial imaging.

N = 748

R

tapering 2-week course of oral dexamethasone

8 mg BID on days 1 - 3,
6 mg BID on days 4 - 6,
4 mg BID on days 7 - 9
2 mg BID on days 10 - 12

Exclusion: Had conditions for which glucocorticoids are **contraindicated** (e.g., active systemic infection, recent peptic ulceration or gastrointestinal bleeding), were **receiving** (or had been receiving within 1 month before screening) **oral or intravenous glucocorticoids** on a regular basis, were previously enrolled in this trial for a separate chronic subdural hematoma episode, had a cerebrospinal fluid shunt, had severe **lactose intolerance or a known hypersensitivity to dexamethasone** or other excipient, had a **history of psychotic disorders**, or were unwilling to take products containing gelatin.

nths
w-up

- **Primary outcome:** a
  randomization
- **Secondary/Safety ou**
  neurosurgical unit and

from the

Characteristic	Dexamethasone (N=375)	Placebo (N=373)
Age — yr	74.5±11.8	74.3±11
Male sex — no./total no. (%)	268/375 (71.5)	286/373 (76.7)
Symptoms at presentation — no./total no. (%)†		
Headache	211/373 (56.6)	214/373 (57.4)
Gait disturbance	171/373 (45.8)	170/373 (45.6)
Cognitive impairment	129/373 (34.6)	128/373 (34.3)
Hemiparesis	105/373 (28.2)	107/373 (28.7)
Speech disturbance	81/373 (21.7)	94/373 (25.2)
Seizure	11/373 (2.9)	10/373 (2.7)
Other	54/373 (14.5)	66/373 (17.7)
Modified Rankin scale score at admission — no./total no. (%)‡		
1–3	186/310 (60.0)	182/304 (59.9)
4–5	124/310 (40.0)	122/304 (40.1)
Glasgow Coma Scale score at admission — no./total no. (%)§		
13–15	350/371 (94.3)	350/371 (94.3)
9–12	15/371 (4.0)	15/371 (4.0)
3–8	6/371 (1.6)	6/371 (1.6)
Known head trauma — no./total no. (%)	253/373 (67.8)	267/373 (71.6)
Main coexisting medical conditions — no./total no. (%)		
Atrial fibrillation	88/375 (23.5)	68/373 (18.2)
Diabetes	55/375 (14.7)	54/373 (14.5)
Ischemic heart disease	58/375 (15.5)	50/373 (13.4)
Previous stroke	34/375 (9.1)	39/373 (10.5)
Any antithrombotic medication — no./total no. (%)	178/370 (48.1)	166/368 (45.1)
Midline shift on admission scan — no./total no. (%)		
0–5 mm	68/314 (21.7)	74/318 (23.3)
6–10 mm	126/314 (40.1)	115/318 (36.2)
>10 mm	120/314 (38.2)	129/318 (40.6)

Baseline Rankin scale

No symptoms at all	0
No significant disability despite symptoms; able to carry out all usual duties and activities	+1
Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance	+2
Moderate disability; requiring some help, but able to walk without assistance	+3
Moderately severe disability; unable to walk and attend to bodily needs without assistance	+4
Severe disability; bedridden, incontinent and requiring constant nursing care and attention	+5
Dead	+6

Variable	Dexamethasone	Placebo	Measure of Effect†	Difference or Odds or Rate Ratio (95% CI)	P Value
Primary outcome					
Modified Rankin scale score at 6 mo — no./ total no. (%)					
Dichotomous outcomes					
0–3: Primary outcome	286/341 (83.9)	306/339 (90.3)	Percentage-point difference	–6.4 (–11.4 to –1.4)	0.01
4–6	55/341 (16.1)	33/339 (9.7)			
Ordinal outcomes					
0: No symptoms	163/341 (47.8)	164/339 (48.4)			
1: No clinically significant disability	49/341 (14.4)	55/339 (16.2)			
2: Slight disability	14/341 (4.1)	21/339 (6.2)			
3: Moderate disability	60/341 (17.6)	66/339 (19.5)			
4: Moderately severe disability	10/341 (2.9)	9/339 (2.7)			
5: Severe disability	15/341 (4.4)	7/339 (2.1)			
6: Dead	30/341 (8.8)	17/339 (5.0)			

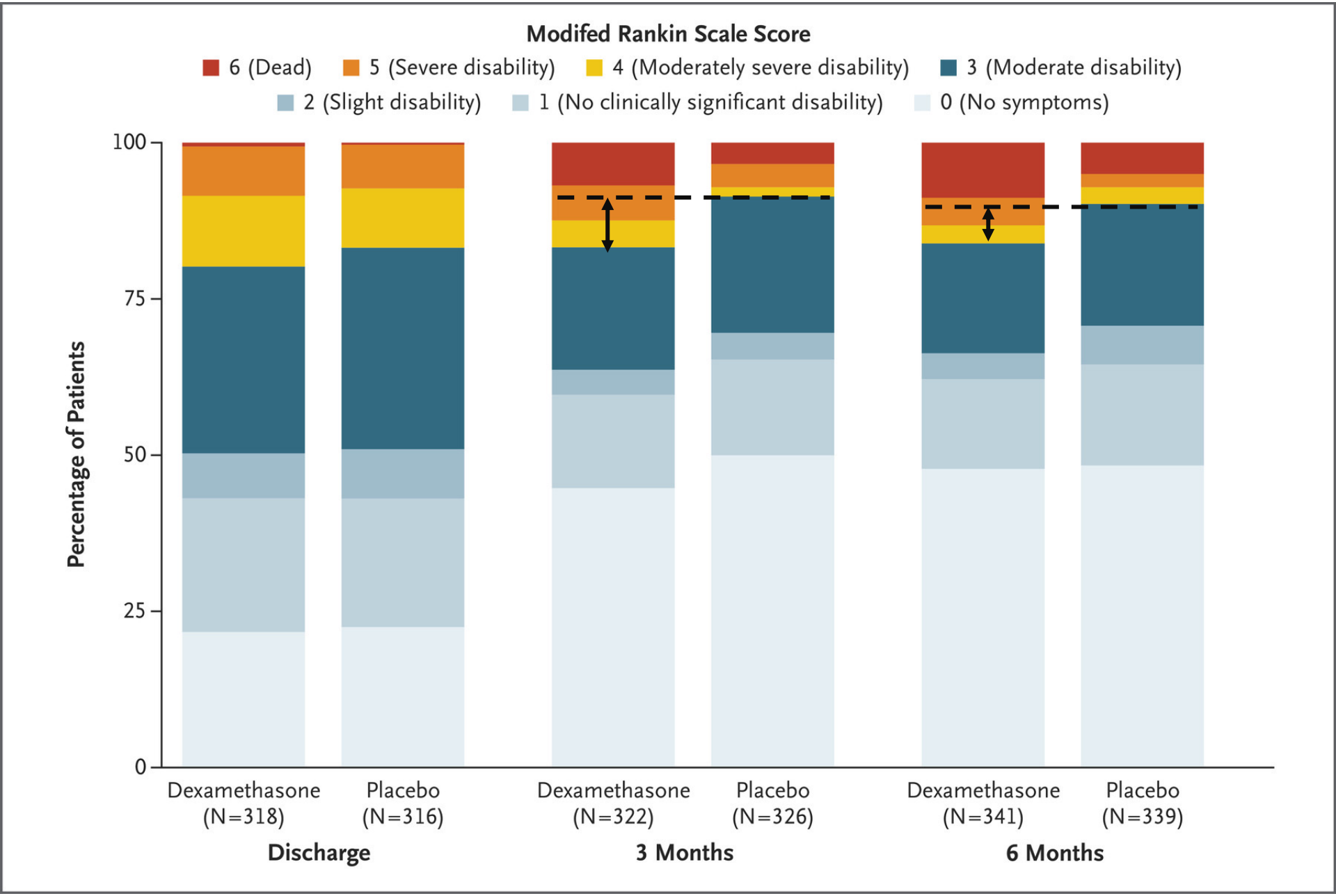
- **Primary outcome**： score of **0 to 3 on the modified Rankin scale** at 6 months after randomization.
- 處置：**I: Tapering dexamethasone**
  C: Placebo
- 研究結果：**Percentage-point difference: -6.4 (-11.4 to -1.4)**

Secondary, tertiary, and safety outcomes					
Modified Rankin scale score at 3 mo — no./total no. (%)					
0–3	268/322 (83.2)	298/326 (91.4)	Percentage-point difference	−8.2 (−13.3 to −3.1)	
4–6	54/322 (16.8)	28/326 (8.6)			
Modified Rankin scale score at discharge — no./total no. (%)					
0–3	255/318 (80.2)	263/316 (83.2)	Percentage-point difference	−3.0 (−9.1 to 3.0)	
4–6	63/318 (19.8)	53/316 (16.8)			
Mortality at 30 days — no./total no. (%)	8/375 (2.1)	2/373 (0.5)	Odds ratio	4.08 (1.01 to 27.2)	
Mortality at 6 mo — no./total no. (%)	30/341 (8.8)	17/339 (5.0)	Odds ratio	1.83 (0.99 to 3.45)	
One operation during index admission — no./total no. (%)	341/372 (91.7)	330/370 (89.2)	Rate ratio‡	0.97 (0.83 to 1.12)	
Operations during subsequent admissions — no./total no. (%)	19/372 (5.1)	28/370 (7.6)	Rate ratio‡	0.90 (0.72 to 1.11)	
Repeat surgery for recurrence of chronic subdural hematoma — no./total (%)§	[illegible]	[illegible]	Percentage-point difference	−5.4 (−8.7 to −2.5)	
Mean EQ-5D-5L utility index score¶					
At discharge	0.697	0.727	Difference	−0.03 (−0.07 to 0.01)	
At 3 mo	0.707	0.773	Difference	−0.07 (−0.12 to −0.02)	
At 6 mo	0.733	0.766	Difference	−0.03 (−0.09 to 0.02)	
Adverse events of special interest up to day 30 — no./total no. (%)‖	41/375 (10.9)	12/373 (3.2)	Odds ratio	3.40 (1.81 to 6.85)	<0.001
Serious adverse events up to day 30 — no./total no. (%)‖	60/[illegible]	[illegible]	Odds ratio	2.49 (1.54 to 4.15)	<0.001

Favor placebo

Favor dexamethasone

Favor placebo


Modifed Rankin Scale Score
6 (Dead)
5 (Severe disability)
4 (Moderately severe disability)
3 (Moderate disability)
2 (Slight disability)
1 (No clinically significant disability)
0 (No symptoms)
Percentage of Patients
100
75
50
25
0
Dexamethasone (N=318)
Placebo (N=316)
Dexamethasone (N=322)
Placebo (N=326)
Dexamethasone (N=341)
Placebo (N=339)
Discharge
3 Months
6 Months

Cochrane RoB 2.0 of Randomized parallel group trial

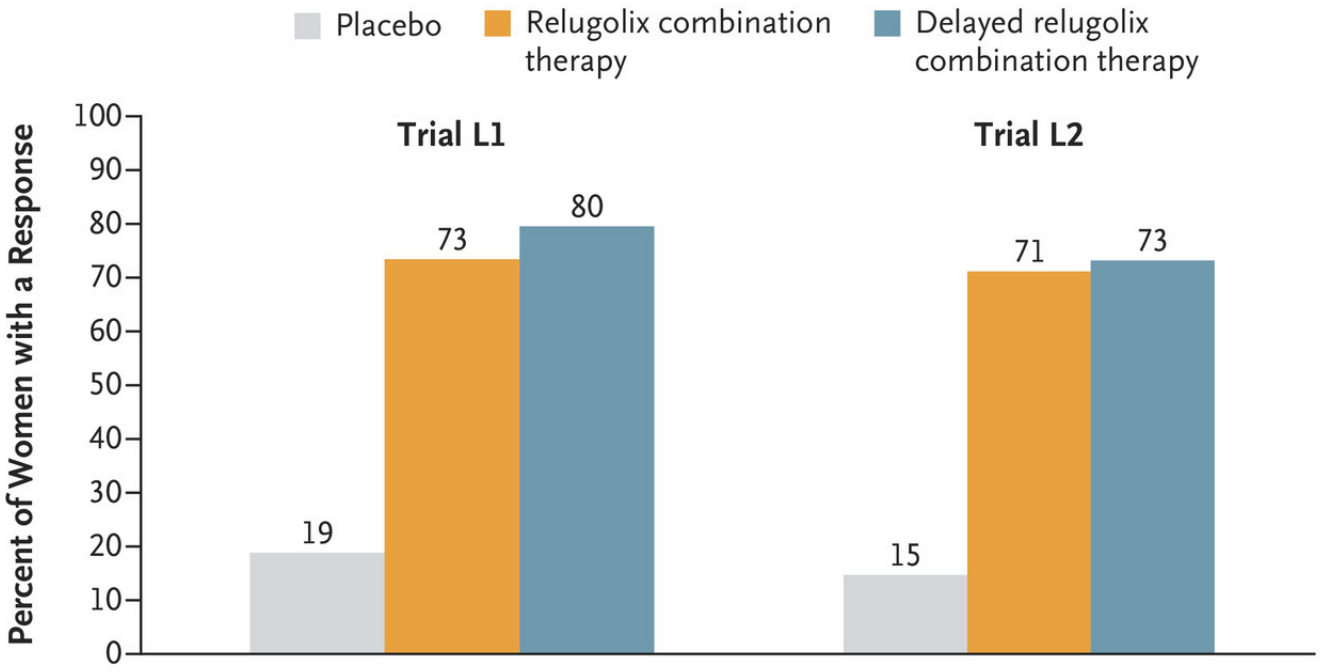
Bias arising from the randomization process	✓ Allocation conceal ✓ Allocation sequence random ✓ Baseline balance	**Low risk**
Bias due to deviation from intended intervention	✓ Open-label ✓ Balance non-protocol intervention ✓ Implementation and adherence succussed	**Low risk**
Bias due to missing outcome data	✓ >90% complete trial	**Low risk**
Bias in measurement of outcome	✓ Self reported assessment ✓ Could assessment of the outcome have been influenced by knowledge of intervention received? PY	**Some concerns**
Bias in selection of reported result	✓ No evidence of selection of the reported result	**Low risk**

Table 2. Efficacy Measures (Mo

Efficacy Measure†					P Value
Primary end point					
Least-squares mean change fro					<0.001†

Table 3. Adverse Events and Safety during the Treatment Period (Safety Population).*

Variable	Xanomeline–Trospium (N=89)	Placebo (N=90)
Any adverse event — no (%)	48 (54)	39 (43)
Serious adverse event — no. (%)†	1 (1)	0
Severe adverse event — no. (%)‡	1 (1)	1 (1)



	Trial L1			Trial L2		
No. of Patients	127	128	132	129	125	127
Difference vs. Placebo — percentage points (95% CI)		55 (44–65)	61 (51–70)		56 (46–66)	58 (49–68)
P Value vs. Placebo		<0.001			<0.001	

for the primary end point of se

‡ The effect size (0.75) was calcu eline at week 5 between the xanomeline–trosp group difference.

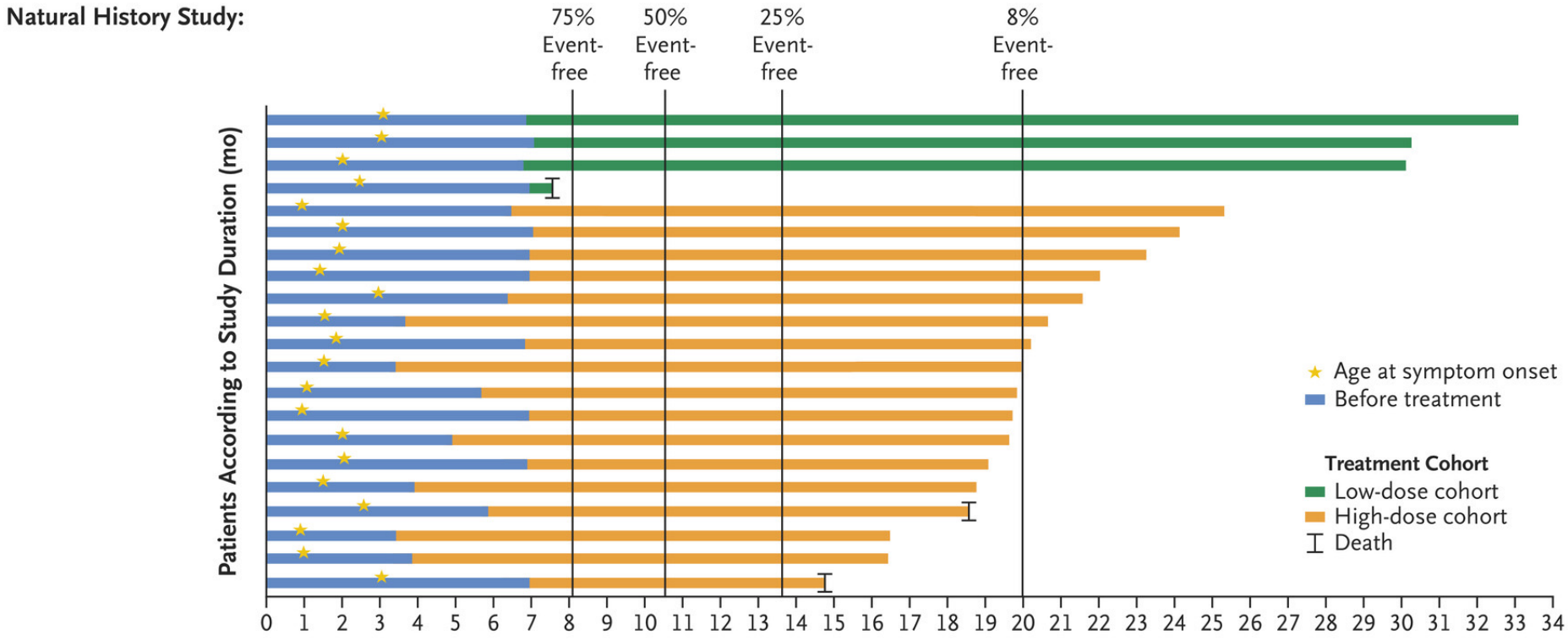
§ Secondary end points are prese

incapacity.

‡ A severe adverse event was defined as any event that was incapacitating or caused an inability to perform normal activities of daily living.

§ Scores on the Simpson–Angus Scale range from 0 to 40; higher scores indicate greater severity of drug-induced parkinsonian symptoms.

¶ Scores on the Barnes Akathisia Rating Scale range from 0 to 14; higher scores indicate greater symptoms of akathisia.



End Point	Avacopan (N=166)	Prednisone (N=164)	Difference (95% CI)
Primary end points			
Remission at wk 26 — no. (%)†	120 (72.3)	115 (70.1)	3.4 (–6.0 to 12.8)‡§
Sustained remission at wk 52 — no. (%)¶	109 (65.7)	90 (54.9)	12.5 (2.6 to 22.3)‡‖

remission at week 26 and at week 52 and no receipt of glucocorticoids for 4 weeks before week 52.

Impact of a multidisciplinary workflow on safety and management of patients with heparin-induced thrombocytopenia

- Design: Medication error reports and a retrospective review

Postimplementation workflow

Suspicion for HIT based on clinical assessment

Clinician:

1. Access the "HIT Management Order Panel" in EHR
   a. Place order for appropriate HIT laboratory test combination
   b. Place order for alternate anticoagulant when appropriate
   c. Place order for pharmacy consult
   d. Place nursing order for heparin allergy precautions

Decentralized Clinical Pharmacist:

1. Review pharmacist consult order in in-basket
2. Screen medication profile and discontinue all heparin-containing products
3. Add temporary heparin allergy to EHR
4. Recommend alternate anticoagulant to provider when appropriate
5. Write "HIT Initial Pharmacy Note" in EHR, which includes the 4Ts score calculated with the clinician

Nursing:

1. Review heparin allergy precautions order placed by provider
2. Place heparin allergy sign on patient's door
3. Use normal saline flushes only

HIT laboratory testing finalized

Impact of a multidisciplinary workflow on safety and management of patients with heparin-induced thrombocytopenia

HIT laboratory testing finalized

Laboratory Staff:*
1. Page Pharmacy Resident On-Call to review HIT testing results

Pharmacy Resident On-Call:*
1. Develop a treatment plan using "HIT Management Guideline" based on results
2. Page decentralized clinical pharmacist and review results and treatment plan

Decentralized Clinical Pharmacist:
1. Review results and treatment plan with clinician
2. Update or delete pending heparin allergy in EHR based on results
3. Write "HIT Follow-up Pharmacy Note" in EHR
4. Provide discharge counseling and allergy card to HIT positive patients ***(in collaboration with nursing)***

HIT Stewardship Pharmacist:
1. Review finalized testing weekly using report generated from EHR

Clinician:
1. Finalize treatment plan using "HIT Management Guideline"
2. Update nursing order for heparin allergy precautions based on results

Impact of a multidisciplinary workflow on safety and management of patients with heparin-induced thrombocytopenia

No. of HIT test combinations completed[a]	590	350	
Heparin/PF4 ELISA only, no. (%)	31 (5.3)	88 (25.1)	<0.001
Negative	28 (90.3)	87 (98.9)	
Positive	0	0	
Indeterminate	3 (9.7)	1 (1.1)	
Heparin/PF4 ELISA + aggregation, No. (%)	524 (88.8)	219 (62.6)	<0.001
Negative	485 (92.6)	195 (89.0)	
Positive	31 (5.9)	19 (8.7)	
Indeterminate	8 (1.5)	5 (2.3)	
Heparin/PF4 ELISA + aggregation + SRA, No. (%)	31 (5.3)	37 (10.5)	0.004
Negative	26 (83.9)	34 (91.9)	
Positive	5 (16.1)	3 (8.1)	
Indeterminate	0	0	
Heparin/PF4 ELISA + SRA, No. (%)	0	3 (0.9)	0.051
Negative	0	2 (66.7)	
Positive	0	1 (33.3)	
Indeterminate	0	0	

SRA: Serotonin release assay

Impact of a multidisciplinary workflow on safety and management of patients with heparin-induced thrombocytopenia

Table 2. Heparin Administration by HIT Testing Status

Testing Status	Preimplementation Group (*n* = 590)	Postimplementation Group (*n* = 350)	*P* Value
HIT testing ongoing	320 (54.2)	70 (20.0)	<0.001
HIT testing positive	6/36 (16.6)	2/23 (8.7)	0.464
HIT testing indeterminate	6/11 (54.5)	0/6 (0)	0.043

Abbreviation: HIT, heparin-induced thrombocytopenia.
[a]All data are number (percentage) or fraction (percentage) of documented laboratory test combinations (denoted by *n*).

Table 3. Appropriate Heparin Allergy Documentation After Testing Finalization, by Study Group[a]

	Preimplementation Group (*n* = 464)[b]	Postimplementation Group (*n* = 316)	*P* Value
Correct documentation	441 (95.0)	316 (100)	<0.001
HIT diagnosis confirmed	26/28 (92.9)	23/23 (100)	0.495
HIT diagnosis ruled out	413/433 (95.4)	290/290 (100)	<0.001
Test results indeterminate	2/3 (66.7)	3/3 (100)	>0.99

Abbreviation: HIT, heparin-induced thrombocytopenia.
[a]Data are number (percentage) or fraction (percentage) of patients.
[b]Excludes patients who expired prior to finalization of testing results.

Reduction of phone interruptions post implementation of a central call center in community pharmacies of an academic health system

- Design: 2-phase pre-post cohort study

Pharmacy services call center
PSCC

Answer simple and repetitive calls

- Prescription readiness
- Refill status

Reduction of phone interruptions post implementation of a central call center in community pharmacies of an academic health system

Table 1. Observational Data Collected Before and After Call Center Implementation, Overall and by Pharmacy Size and Employee Type

	Observation Hours	Rx Touched	Phone BIT	Rx Touched per Hour	Change After PSCC Implemented	Phone BIT per Hour	Change After PSCC Implemented	Phone BIT per Rx Touched	Change After PSCC Implemented
All Evaluated Pharmacies									
Overall (7 pharmacies)	414	5,511	910	13.3		2.2		0.17	
Summary PRE	210	3,217	597	15.3		2.8		0.19	
Pharmacists	84	1,991	161	23.7		1.9		0.08	
Technicians	126	1,226	436	9.7		3.5		0.36	
Summary POST	204	2,294	313	11.2	–26.8%	1.5	–46.4%	0.14	–26.3%
Pharmacists	78	1,268	109	16.3		1.4		0.09	
Technicians	126	1,026	204	8.1		1.6		0.20	
Small Pharmacies (<10 FTEs)									
Summary PRE	120	1,259	236	10.5		2.0		0.19	
Pharmacists	48	801	73	16.7		1.5		0.09	
Technicians	72	458	163	6.4		2.3		0.36	
Summary POST	114	899	159	7.9	–24.8%	1.4	–30.0%	0.18	–5.3%
Pharmacists	42	485	51	11.5		1.2		0.11	
Technicians	72	414	108	5.8		1.5		0.26	
Large Pharmacies (>10 FTEs)									
Summary PRE	90	1,958	361	21.8		4.0		0.18	
Pharmacists	36	1,190	88	33.1		2.4		0.07	
Technicians	54	768	273	14.2		5.1		0.36	
Summary POST	90	1,395	154	15.5	–28.9%	1.7	–57.5%	0.11	–38.9%
Pharmacists	36	783	58	21.8		1.6		0.07	
Technicians	54	612	96	11.3		1.8		0.16	

Abbreviations: FTE, full-time equivalent; POST, postimplementation; PRE, preimplementation; PSCC, pharmacy services call center.

Reduction of phone interruptions post implementation of a central call center in community pharmacies of an academic health system

Table 2. Observational Data on Dispensing and Nondispensing Tasks, Overall and by Pharmacy Size and Employee Type

	Dispensing Tasks	Nondispensing Tasks	Ratio of Nondispensing to Dispensing Tasks	Change After PSCC Implemented
All Evaluated Pharmacies				
Overall (7 pharmacies)	1,801	1,104	0.61	
Summary PRE	925	586	0.63	
Pharmacists	408	220	0.54	
Technicians	517	366	0.71	
Summary POST	876	518	0.59	–6.3%
Pharmacists	371	210	0.57	5.6%
Technicians	505	308	0.61	–14.1%
Small Pharmacies (<10 FTEs)				
Summary PRE	410	284	0.69	
Pharmacists	172	106	0.62	
Technicians	238	178	0.75	
Summary POST	520	313	0.60	–13.0%
Pharmacists	198	126	0.64	3.2%
Technicians	322	187	0.58	–22.7%
Large Pharmacies (>10 FTEs)				
Summary PRE	515	302	0.59	
Pharmacists	236	114	0.48	
Technicians	279	188	0.67	
Summary POST	356	205	0.58	–1.7%
Pharmacists	173	84	0.49	2.1%
Technicians	183	121	0.66	–1.5%

Abbreviations: FTE, full-time equivalent; POST, postimplementation; PRE, preimplementation; PSCC, pharmacy services call center.
[a]All data are counts (*n*) unless indicated otherwise.

Reduction of phone interruptions post implementation of a central call center in community pharmacies of an academic health system

Table 3. Observational Data on Breaks in Task, Overall and by Pharmacy Size and Employee Type

Location	Phone BIT	Nonphone BIT	Ratio of Phone BIT to Nonphone BIT	Change After PSCC Implemented
All Evaluated Pharmacies				
Overall (7 pharmacies)	910	2,357	0.39	
Summary PRE	597	1,195	0.50	
Pharmacists	161	488	0.33	
Technicians	436	707	0.62	
Summary POST	313	1,162	0.27	–46.0%
Pharmacists	109	507	0.21	–36.4%
Technicians	204	655	0.31	–50.0%
Small Pharmacies (<10 FTEs)				
Summary PRE	236	588	0.40	
Pharmacists	73	244	0.30	
Technicians	163	344	0.47	
Summary POST	159	715	0.22	–45.0%
Pharmacists	51	321	0.16	–46.7%
Technicians	108	394	0.27	–42.6%
Large Pharmacies (>10 FTEs)				
Summary PRE	361	607	0.59	
Pharmacists	88	244	0.36	
Technicians	273	363	0.75	
Summary POST	154	447	0.34	–42.4%
Pharmacists	58	186	0.31	–13.9%
Technicians	96	261	0.37	–50.7%

Abbreviations: BIT, breaks in task; FTE, full-time equivalent; POST, postimplementation; PRE, preimplementation; PSCC, pharmacy services call center.
[a]All data are counts (*n*) unless indicated otherwise.

Comparison of intermittent audit vs daily documentation of pharmacist interventions

Design: 2-phase pre-post cohort study

Table 1. Numbers and Types of Pharmacist Interventions

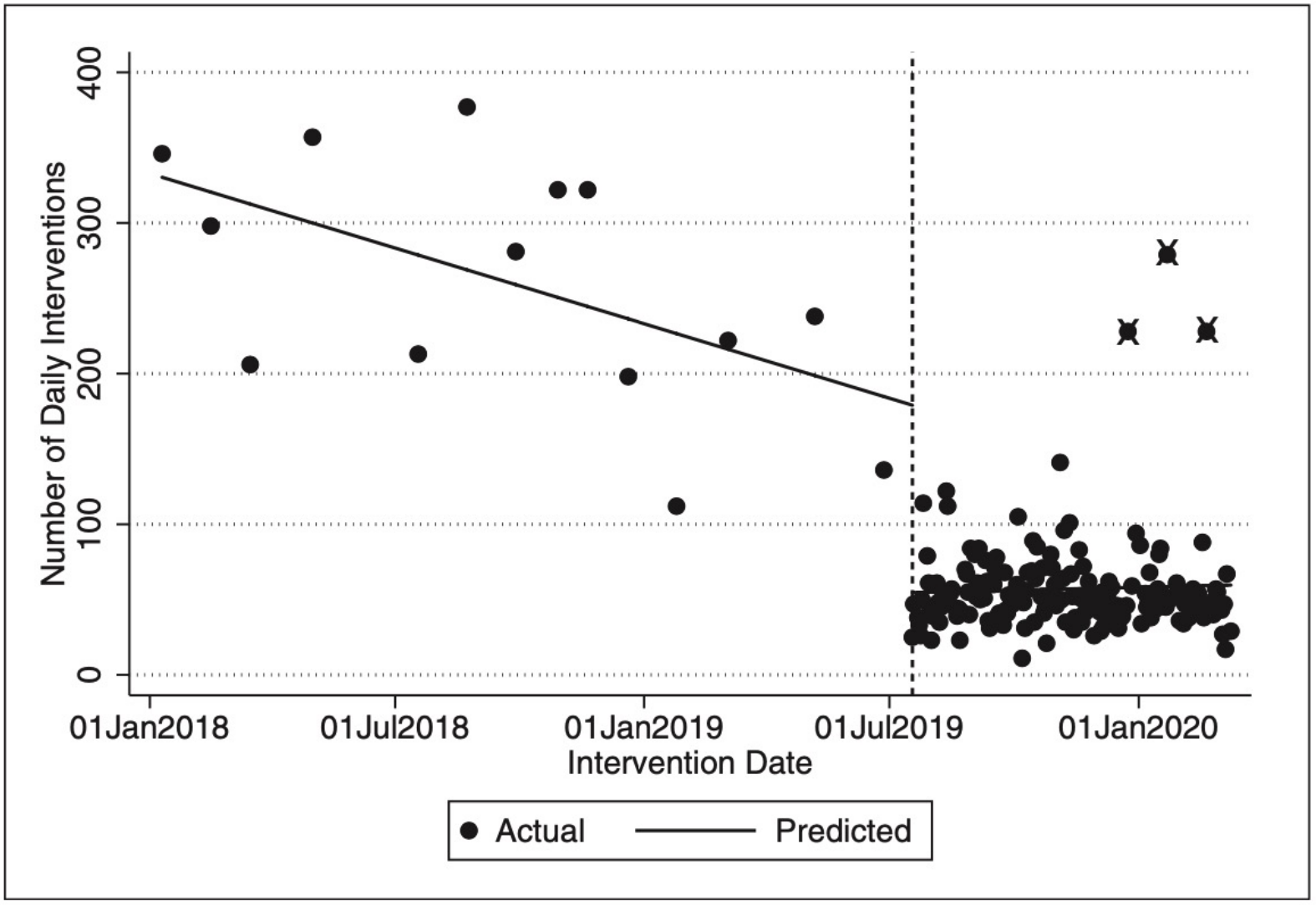
Type	No. per Day, Mean (SD)		*P* Value
	Before Daily Documentation	With Daily Documentation	
Process interventions			
Clinical review	154.2 (54.6)	36.6 (24.0)	<0.001
Patient counseling	12.9 (6.1)	5.2 (3.0)	<0.001
Drug information	24.7 (10.3)	0.6 (0.9)	<0.001
Community liaison	22.2 (12.8)	0.7 (1.5)	<0.001
Drug therapy interventions			
Drug changed	5.1 (2.7)	0.9 (0.9)	<0.001
Drug ceased	5.8 (3.5)	1.2 (1.4)	<0.001
Route changed	0.7 (0.7)	0.1 (0.3)	<0.001
Dose changed	9.5 (3.3)	2.6 (2.3)	<0.001
Frequency changed	4.1 (2.5)	0.8 (1.0)	<0.001
Omitted drug started	9.0 (3.1)	2.3 (1.9)	<0.001
Drug monitoring changed	2.3 (1.9)	0.7 (1.4)	<0.001
Drug administration changed	0.8 (0.7)	0.2 (0.7)	0.006
Drug duplication avoided	2.5 (2.3)	0.7 (0.9)	<0.001
Other changes	5.2 (2.8)	1.4 (4.5)	0.002

Abbreviation: SD, standard deviation.

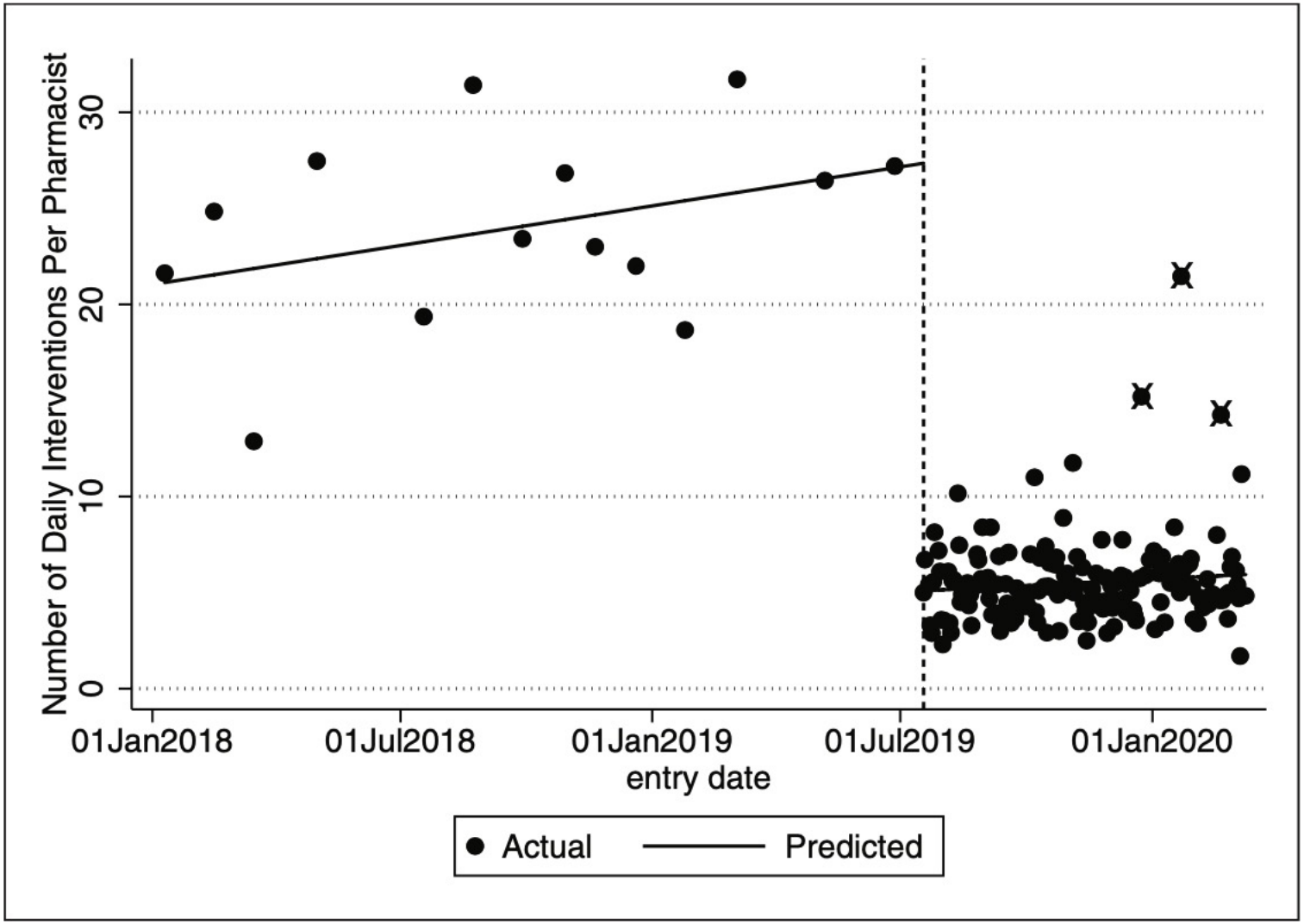
Pre-phase
Intermittent audit (monthly)

Post-phase
Daily documentation

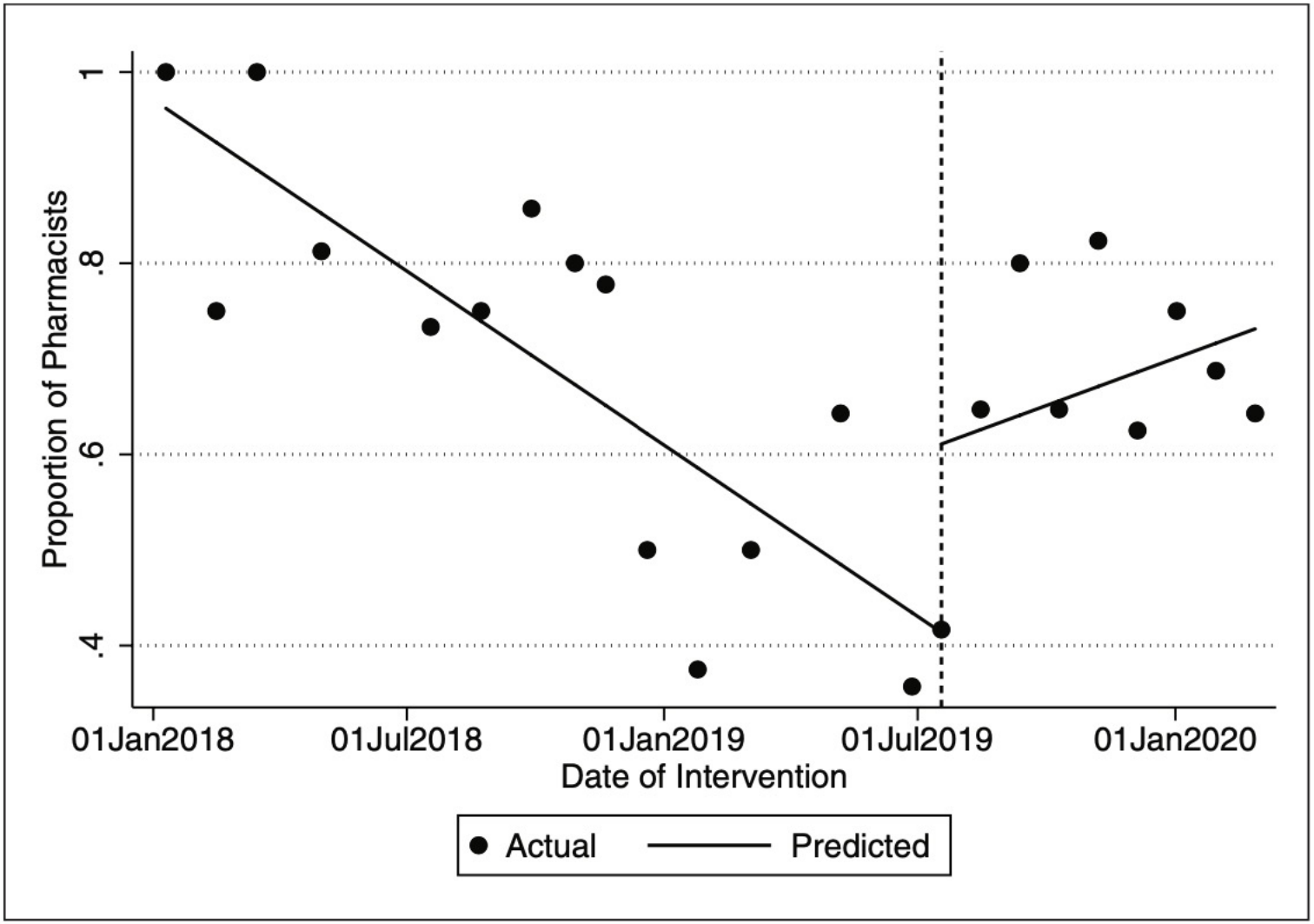
Comparison of intermittent audit vs daily documentation of pharmacist interventions



Comparison of intermittent audit vs daily documentation of pharmacist interventions



Comparison of intermittent audit vs daily documentation of pharmacist interventions

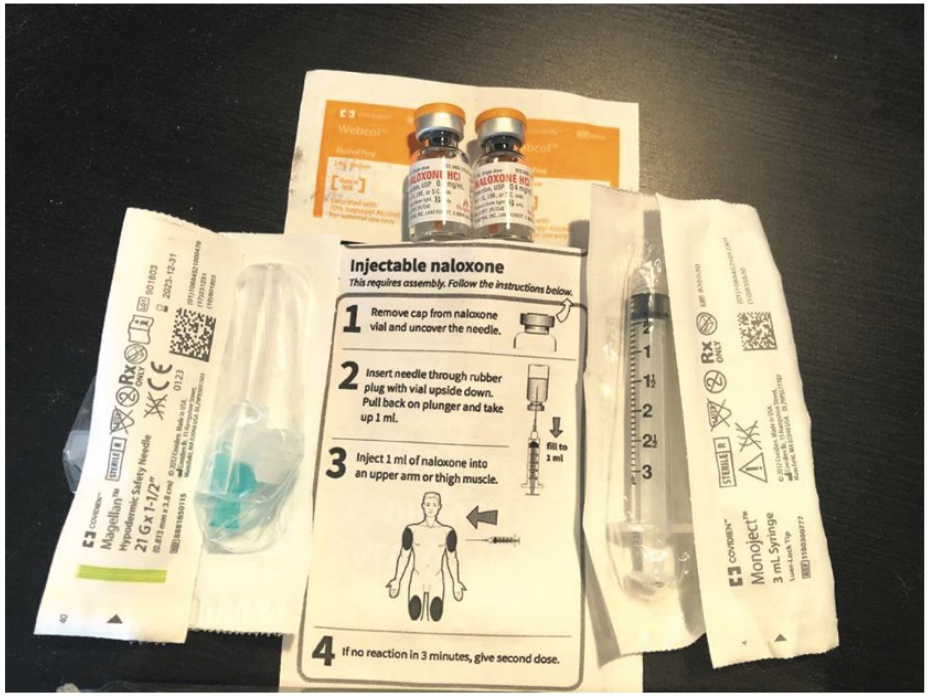


Point-of-care naloxone distribution in the emergency department: A pilot study

- Design: Pilot study

Inclusion Criteria	Exclusion Criteria
Illicit opioid use (eg, heroin)	Age of <18 years
Methadone use at home	Current trauma-related presentation or psychiatry-related complaint
Buprenorphine use at home	Current psychiatric presentation
Fentanyl use at home	Active malignancy
Opioid and benzodiazepine coprescription at home	Receiving hospice care
Current ED presentation for opioid overdose	Active suicidal ideation
History of prior overdose	Lack of mental capacity to receive education
Recent release from incarceration, mandatory detoxification, or substance treatment program	Planned admission to hospital
Friend or family member thought to be at risk for opioid overdose	

Point-of-care naloxone distribution in the emergency department: A pilot study



Box 1. Take-home Naloxone Kit Contents

Naloxone vial (0.4 mg/1 mL) x 2

Syringe (3 mL) x 2

Safety needle (21 gauge) x 2

Isopropyl alcohol wipe x 2

Instructional card

- **Rate of obtainment**

87.3% rate of obtainment (<50% other studies)

- **Facilitators of ED OEND**

1.Immediate support from stakeholder
2.OEND team
3.Naloxon dispense status

- **Role of pharmacist**

1. Formula and price comparison
2. Dispensing workflow implementation
3. Training clinician
4. Screening
5. Data abstraction

AJHP American Journal of Health-System Pharmacy™

Abstract

Clinical pharmacy and obstetrics

✢ Frontline pharmacist

- **The practice site**
- **Developing a clinical pharmacy shift in obstetrics**
- **Expanding pharmacy services to a new population**
- **Quality improvement**
- **Barriers overcome and future directions**
- **Training future obstetric pharmacists.**

The innovative role of an “opioid overdose prevention pharmacist” at a mental health teaching hospital

✢ Frontline pharmacist

- **Organization-wide naloxone training:** 1on1 patient training with clinician
- **Online module: e-training**
- **Standardized assessment and documentation:** Validity approach
- **Educational materials for internal and external stakeholders:** Facilitate guideline development (Cheklist for Naloxone training)
- **Full-time permanent pharmacist position:** Naloxone distribution and educations

Comparison of IV oncology infusions compounded via robotics and gravimetrics-assisted workflow processes

✢ **Retrospective analysis**

- **IV gravimetric technology–assisted workflow (TAWF) vs IV robotics system**
- **Dosage accuracy/Dose precision**
- **4 error:** operator/wrong-diluent/wrong-drug/preparation errors.

Economic and workload impact of therapeutic interchange of inhaler medications and nebulizer solutions

✢ **Retrospective observational study**

- P: 18 years of age or older who received respiratory medications and were admitted to the hospital, placed in observation status, or seen in the ED during the study periods.
- I: Ordered Inhaler Therapy
- C: Interchanged NEB Therapy
- O: (1)**mean cost of respiratory medications** (2)**mean number of RCP visits per hospital stay** (3)**mean cost of wasted doses**

Bempedoic acid: Review of a novel therapy in lipid management

- **Clinical revie**
- **Mechanism**
- **Phase 3 trial**
- **Safety:** Incre
- **Clinical impl**

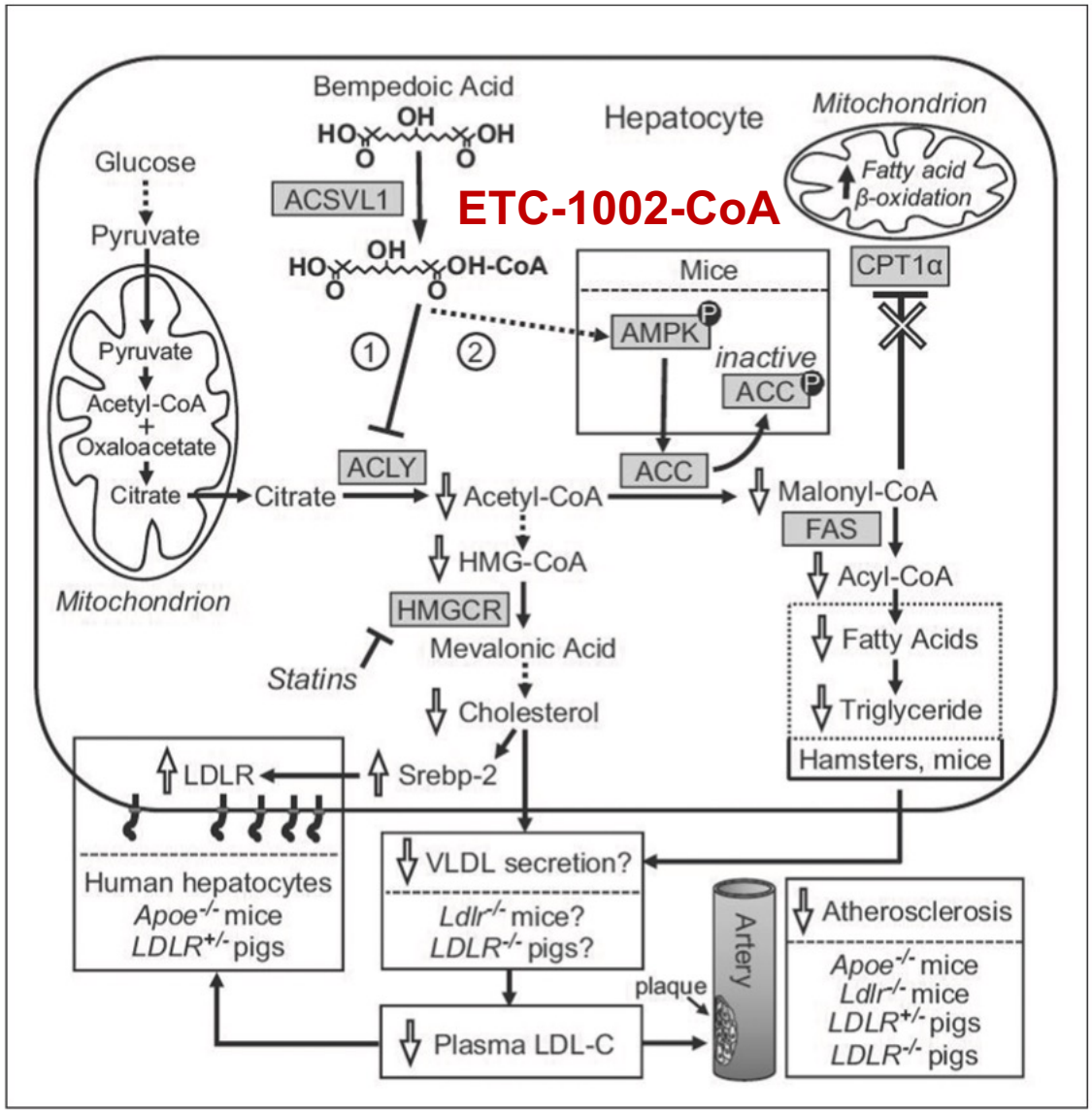


Table 2. Summary of Publish

Study Name or Identifier (Other ID)		Results
CLEAR Harmony (ECT-1002-040)[33,a]	ASCVD maxir statin ≥ 70	No difference in overall rates of adverse effects ($P = 0.91$); incidence of new-onset or worsening diabetes lower with bempedoic acid vs placebo (3.3% vs 5.4%, $P = 0.02$)
CLEAR Wisdom (ECT-1002-047)[35]	ASCVD maxir statin of ≥1	Mean LDL-C reduction of 15.1% with bempedoic acid, compared to increase of 2.4% with placebo ($P < 0.001$)
CLEAR Serenity (ECT-1002-046)[36]	History ance itiona	Mean LDL-C reduction from baseline of 23.6% with bempedoic acid vs 1.3% with placebo ($P < 0.001$)
CLEAR Tranquility (ECT-1002-048)[37]	History ance itiona	Mean LDL-C reduction of 23.5% with bempedoic acid, compared to mean increase of 5.0% in placebo group ($P < 0.001$)
NCT03337308 (1002FDC-053)[39]	High ris cular and/c	Mean LDL-C reduction significantly lower with FDC (36.2%) vs bempedoic acid monotherapy (17.2%) or ezetimibe (23.2%) ($P < 0.001$ for all comparisons)

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; FDC, fixed-dose combination.
[a]Open-label extension trial is ongoing.
[b]Bempedoic acid 180 mg and ezetimibe 10 mg.