Circulation

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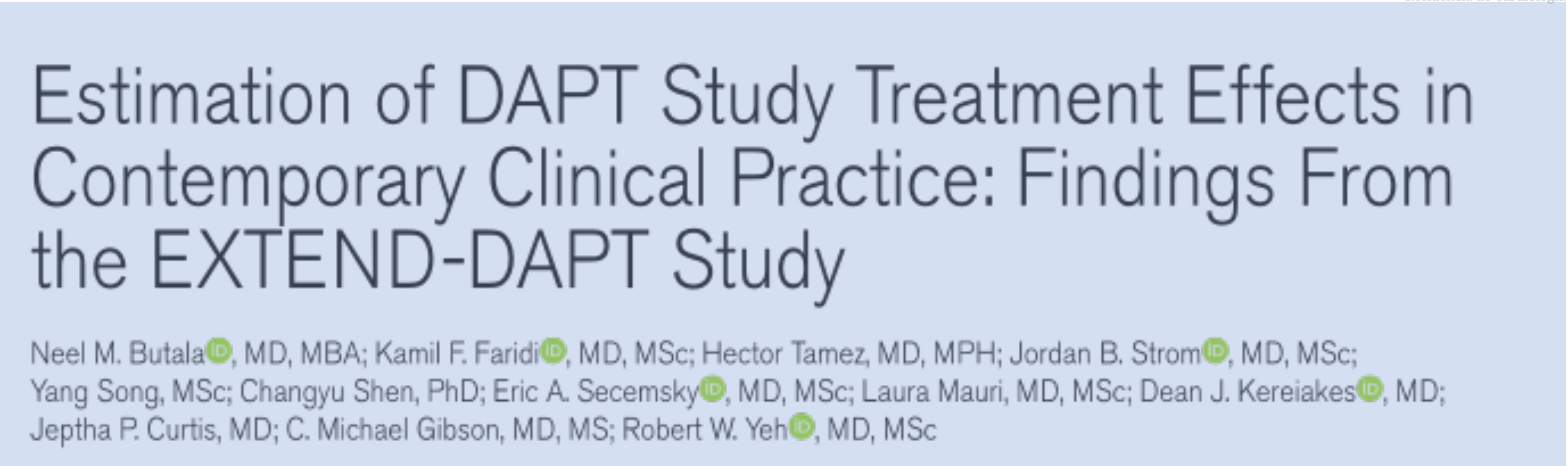
Residencia de Cardiología



Estimation of DAPT Study Treatment Effects in Contemporary Clinical Practice: Findings From the EXTEND-DAPT Study

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INTRODUCCIÓN

- Las diferencias en las **características de los pacientes**, los cambios en los **algoritmos de tratamiento** y los **avances tecnológicos** en la práctica médica podrían influir en los resultados de los ensayos aleatorizados, publicados años previos.

- Además, los participantes de ensayos clínicos, a menudo **no son representativos de las poblaciones del mundo real** en el momento de la inscripción.

INTRODUCCIÓN

- La evidencia sobre la **duración óptima del tratamiento antiplaquetario dual** (DAPT) tras una intervención coronaria percutánea (ICP) sigue siendo un objetivo de estudio.

- La evolución tecnológica de los *stents* y el mayor uso de imágenes intravasculares han reducido el riesgo de trombosis intra- *stent,* pudiendo atenuar el beneficio isquémico de la terapia DAPT prolongada.

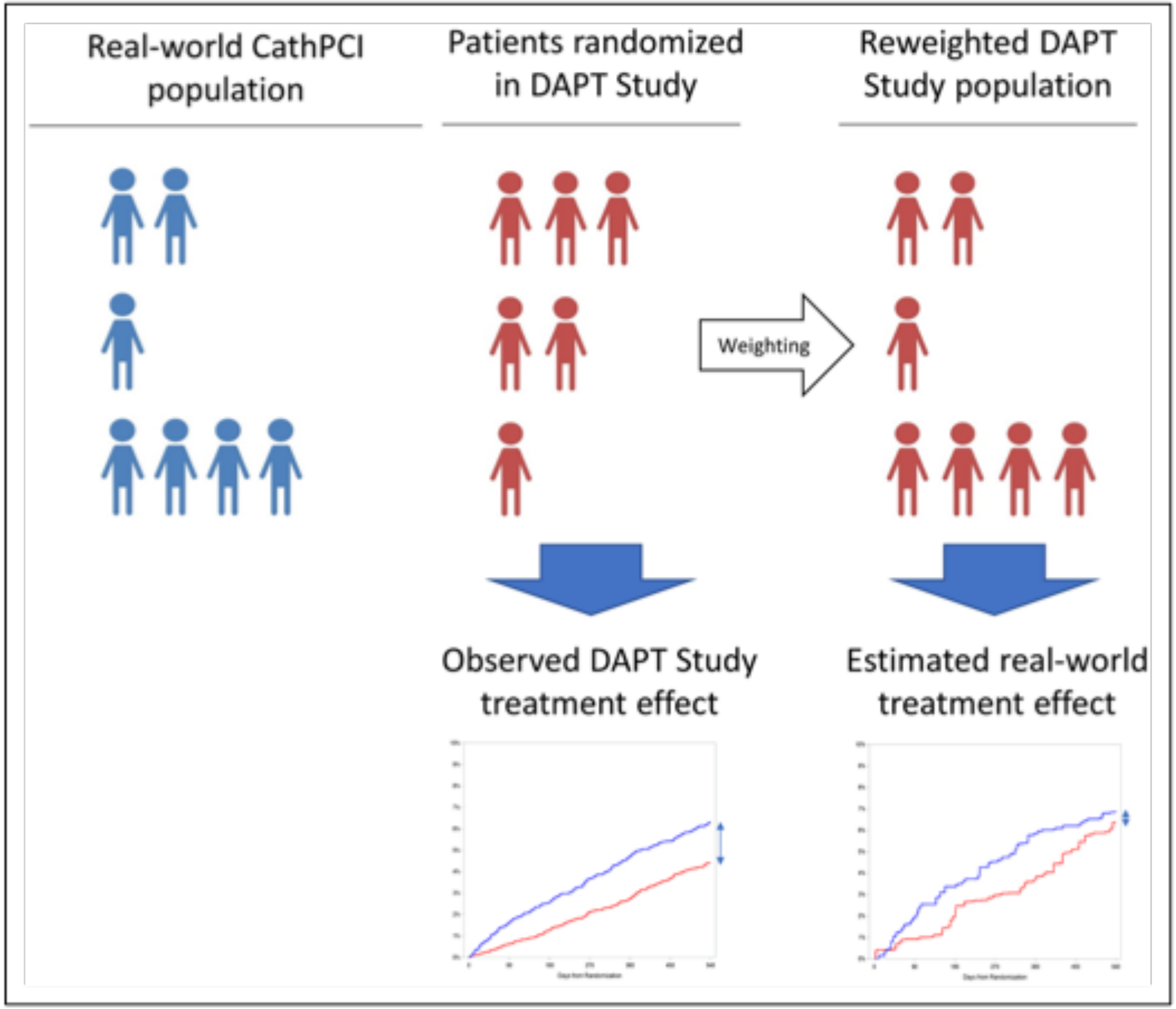
- Sin embargo, ensayos previos describen que el uso de **DAPT más allá de 1 año**, se asocia a un menor número de eventos isquémicos a pesar de mayores eventos hemorrágicos.

INTRODUCCIÓN

- Recientemente, se han desarrollado métodos estadísticos que permiten cuantificar estas diferencias y estimar cómo los resultados del estudio DAPT pueden jerarquizarse en la población actual de pacientes que reciben una ICP.

- Este estudio evaluó la **aplicabilidad del estudio DAPT en la práctica clínica contemporánea** utilizando el Registro Nacional estadounidense de Datos Cardiovasculares (NCDR) *CathPCI Registry*.

DISEÑO DE ESTUDIO


Real-world CathPCI population
Patients randomized in DAPT Study
Reweighted DAPT Study population
Weighting
Observed DAPT Study treatment effect
Estimated real-world treatment effect

DISEÑO DE ESTUDIO Y FUENTE DE DATOS

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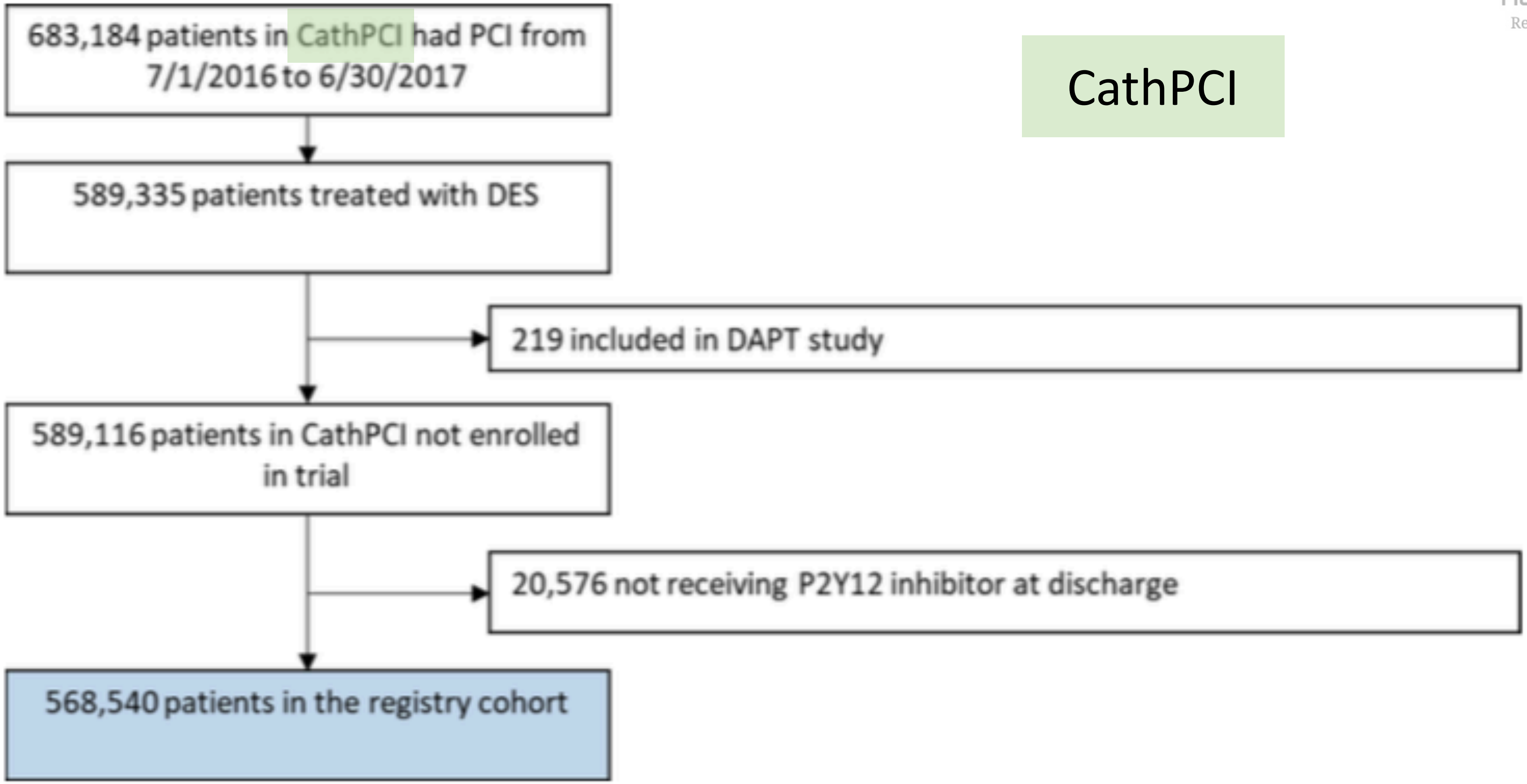
CathPCI



683,184 patients in CathPCI had PCI from 7/1/2016 to 6/30/2017

589,335 patients treated with DES

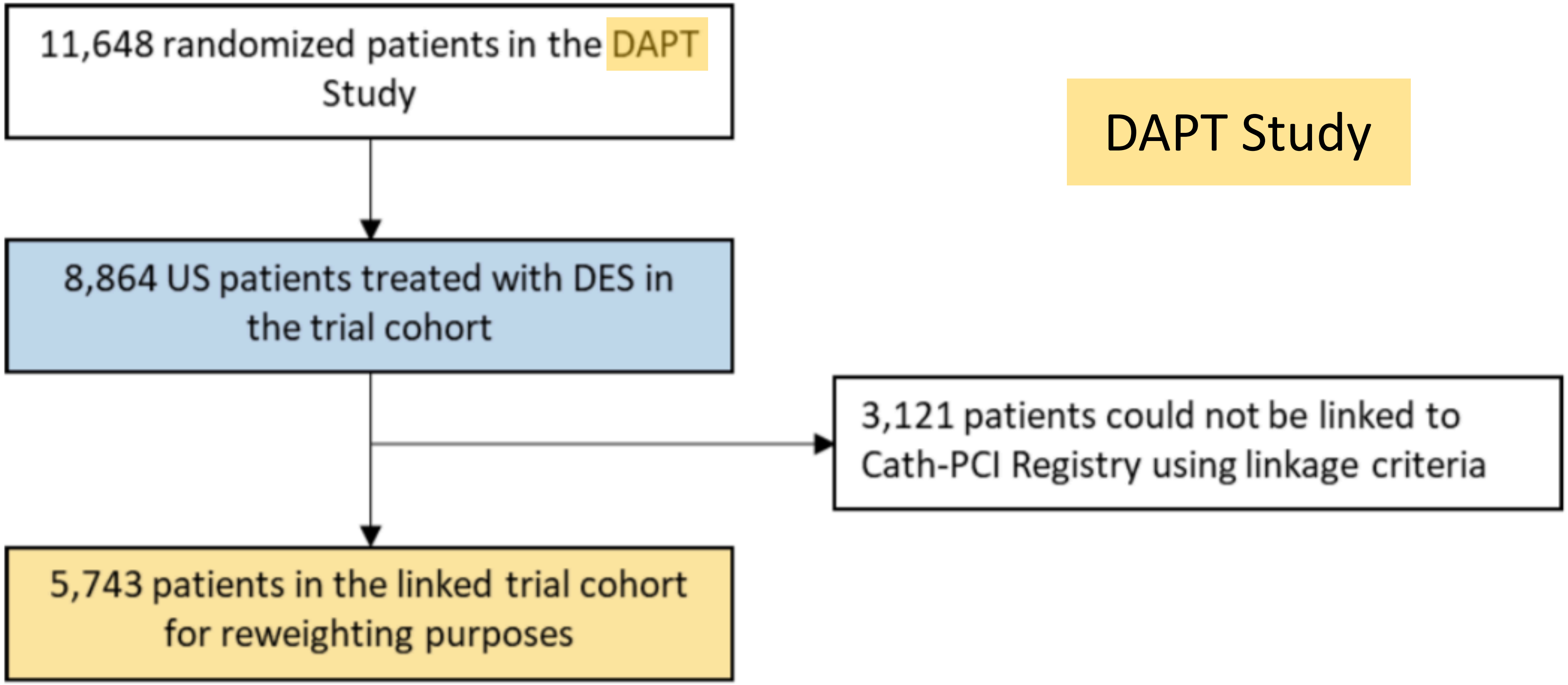
219 included in DAPT study

589,116 patients in CathPCI not enrolled in trial

20,576 not receiving P2Y12 inhibitor at discharge

568,540 patients in the registry cohort

DISEÑO DE ESTUDIO Y FUENTE DE DATOS



11,648 randomized patients in the DAPT Study

8,864 US patients treated with DES in the trial cohort

3,121 patients could not be linked to Cath-PCI Registry using linkage criteria

5,743 patients in the linked trial cohort for reweighting purposes

DAPT Study

MÉTODOS

Objetivos:

- Evaluar la similitud de la población actual de los Estados Unidos que se somete a ICP y aquella incluida en el estudio DAPT.

- Analizar los posibles resultados del estudio DAPT en pacientes representativos de la práctica clínica actual.

MÉTODOS

- Puntos finales:

- Incidencia acumulada de trombosis del *stent* (definitiva o probable).
- Infarto de miocardio (IM).
- Muerte.
- Accidente cerebro vacular (ACV).
- Hemorragias moderadas o graves (GUSTO y BARC).
- MACCE (compuesto de muerte, IM y ACV).

RESULTADOS

CARACTERÍSTICAS BASALES

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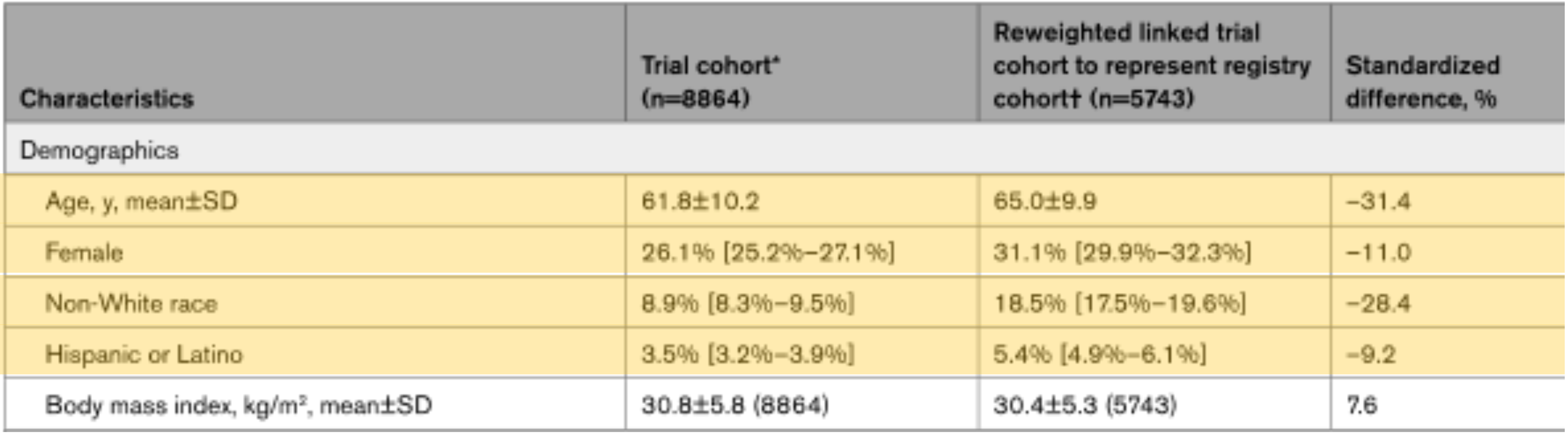

Characteristics	Trial cohort* (n=8864)	Reweighted linked trial cohort to represent registry cohort† (n=5743)	Standardized difference, %
Demographics			
Age, y, mean±SD	61.8±10.2	65.0±9.9	−31.4
Female	26.1% [25.2%–27.1%]	31.1% [29.9%–32.3%]	−11.0
Non-White race	8.9% [8.3%–9.5%]	18.5% [17.5%–19.6%]	−28.4
Hispanic or Latino	3.5% [3.2%–3.9%]	5.4% [4.9%–6.1%]	−9.2
Body mass index, kg/m², mean±SD	30.8±5.8 (8864)	30.4±5.3 (5743)	7.6

CARACTERÍSTICAS BASALES

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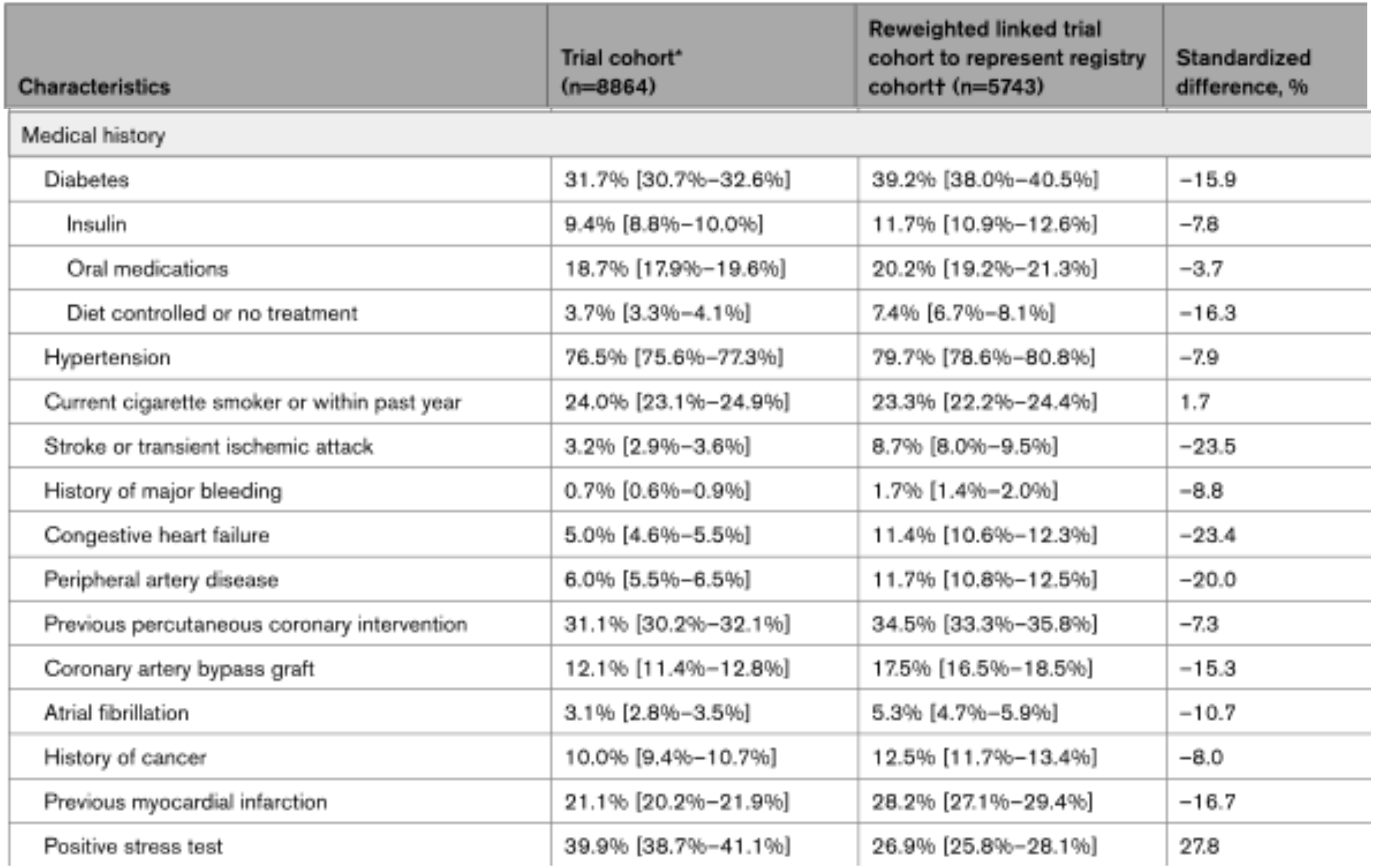
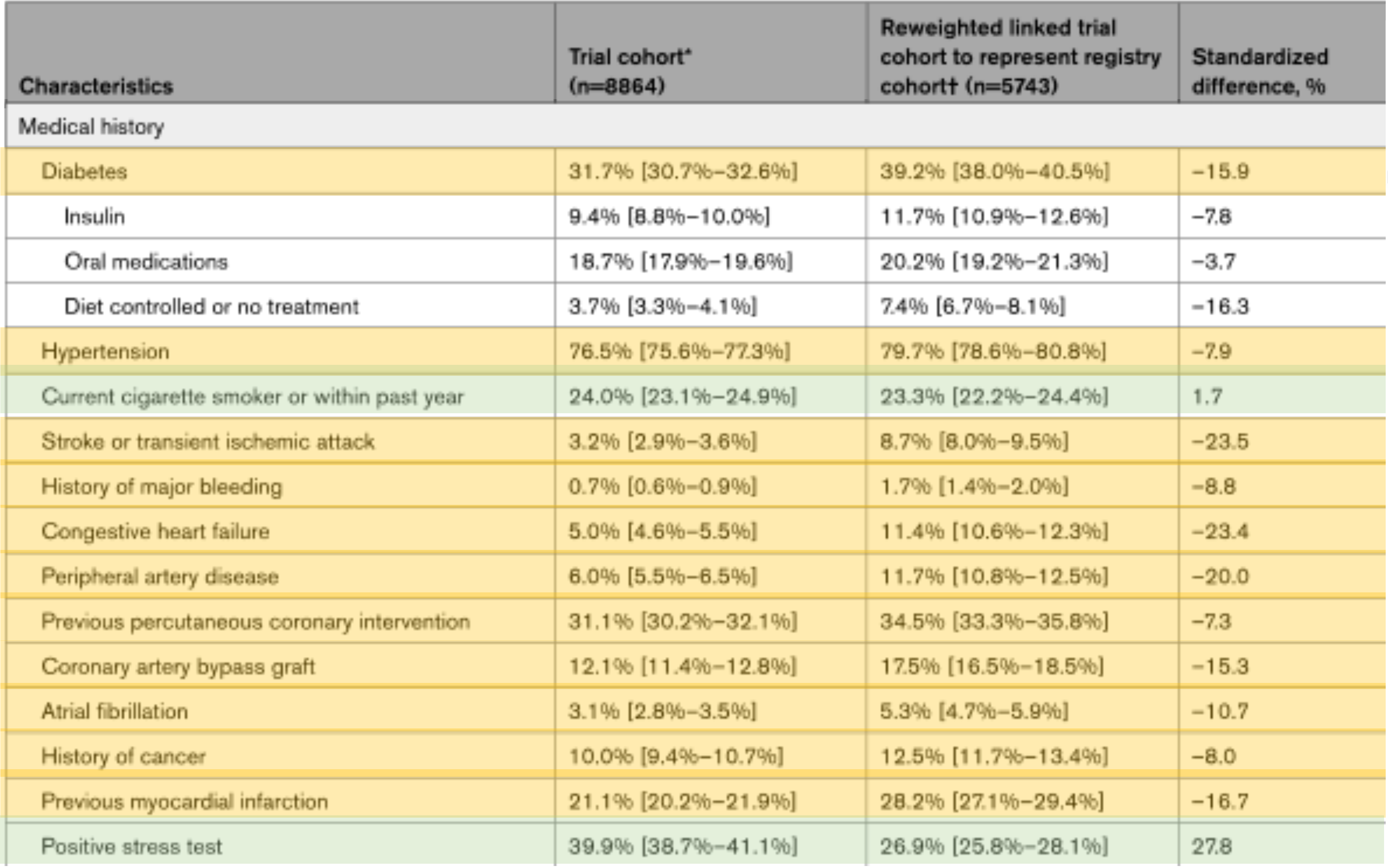


Characteristics	Trial cohort* (n=8864)	Reweighted linked trial cohort to represent registry cohort† (n=5743)	Standardized difference, %
Medical history			
Diabetes	31.7% [30.7%–32.6%]	39.2% [38.0%–40.5%]	−15.9
Insulin	9.4% [8.8%–10.0%]	11.7% [10.9%–12.6%]	−7.8
Oral medications	18.7% [17.9%–19.6%]	20.2% [19.2%–21.3%]	−3.7
Diet controlled or no treatment	3.7% [3.3%–4.1%]	7.4% [6.7%–8.1%]	−16.3
Hypertension	76.5% [75.6%–77.3%]	79.7% [78.6%–80.8%]	−7.9
Current cigarette smoker or within past year	24.0% [23.1%–24.9%]	23.3% [22.2%–24.4%]	1.7
Stroke or transient ischemic attack	3.2% [2.9%–3.6%]	8.7% [8.0%–9.5%]	−23.5
History of major bleeding	0.7% [0.6%–0.9%]	1.7% [1.4%–2.0%]	−8.8
Congestive heart failure	5.0% [4.6%–5.5%]	11.4% [10.6%–12.3%]	−23.4
Peripheral artery disease	6.0% [5.5%–6.5%]	11.7% [10.8%–12.5%]	−20.0
Previous percutaneous coronary intervention	31.1% [30.2%–32.1%]	34.5% [33.3%–35.8%]	−7.3
Coronary artery bypass graft	12.1% [11.4%–12.8%]	17.5% [16.5%–18.5%]	−15.3
Atrial fibrillation	3.1% [2.8%–3.5%]	5.3% [4.7%–5.9%]	−10.7
History of cancer	10.0% [9.4%–10.7%]	12.5% [11.7%–13.4%]	−8.0
Previous myocardial infarction	21.1% [20.2%–21.9%]	28.2% [27.1%–29.4%]	−16.7
Positive stress test	39.9% [38.7%–41.1%]	26.9% [25.8%–28.1%]	27.8



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Stroke or transient ischemic attack	3.2% [2.9%–3.6%]	8.7% [8.0%–9.5%]	−23.5
History of major bleeding	0.7% [0.6%–0.9%]	1.7% [1.4%–2.0%]	−8.8
Congestive heart failure	5.0% [4.6%–5.5%]	11.4% [10.6%–12.3%]	−23.4
Peripheral artery disease	6.0% [5.5%–6.5%]	11.7% [10.8%–12.5%]	−20.0
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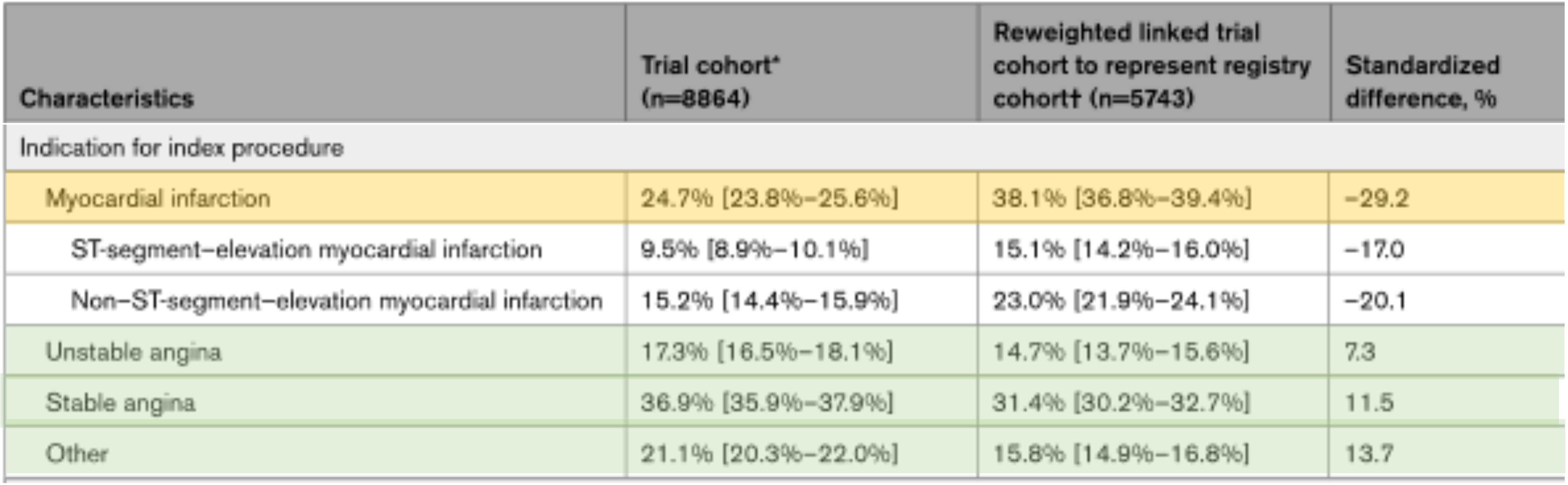
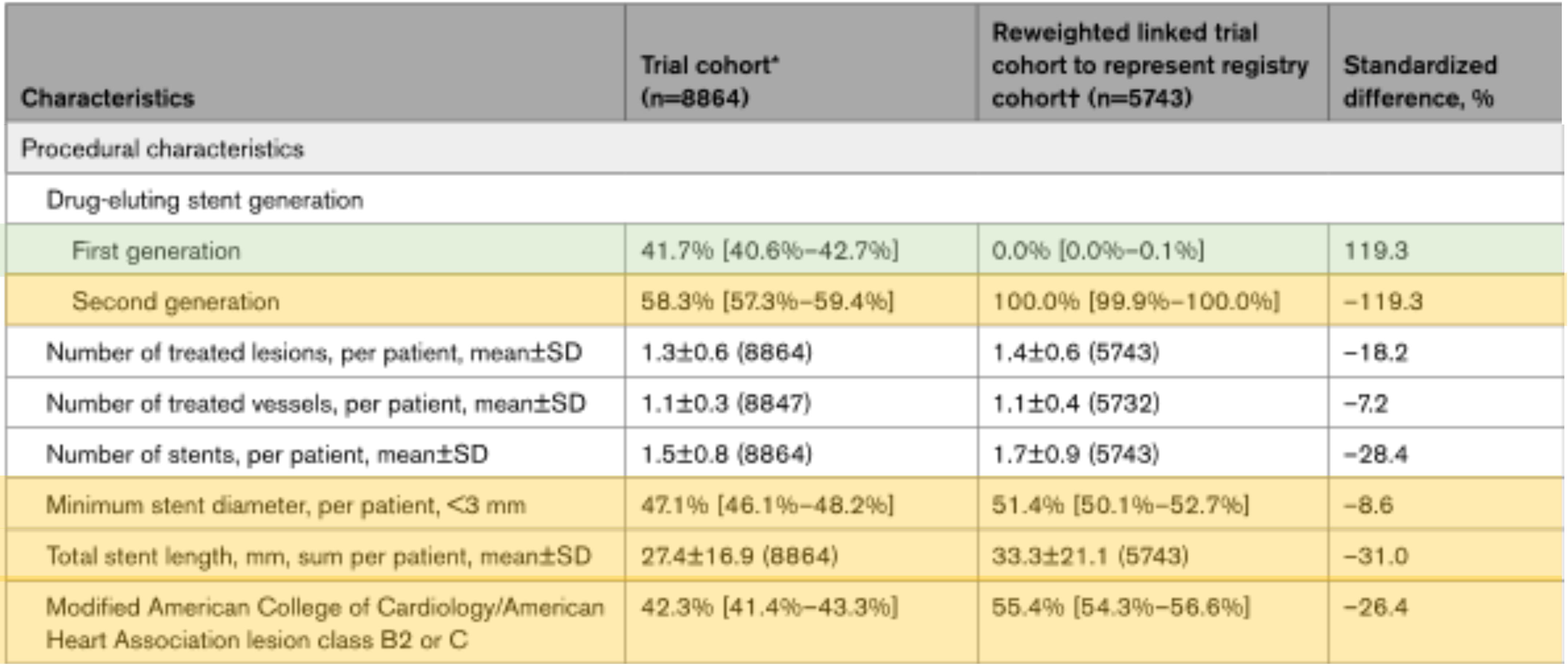
CARACTERÍSTICAS BASALES



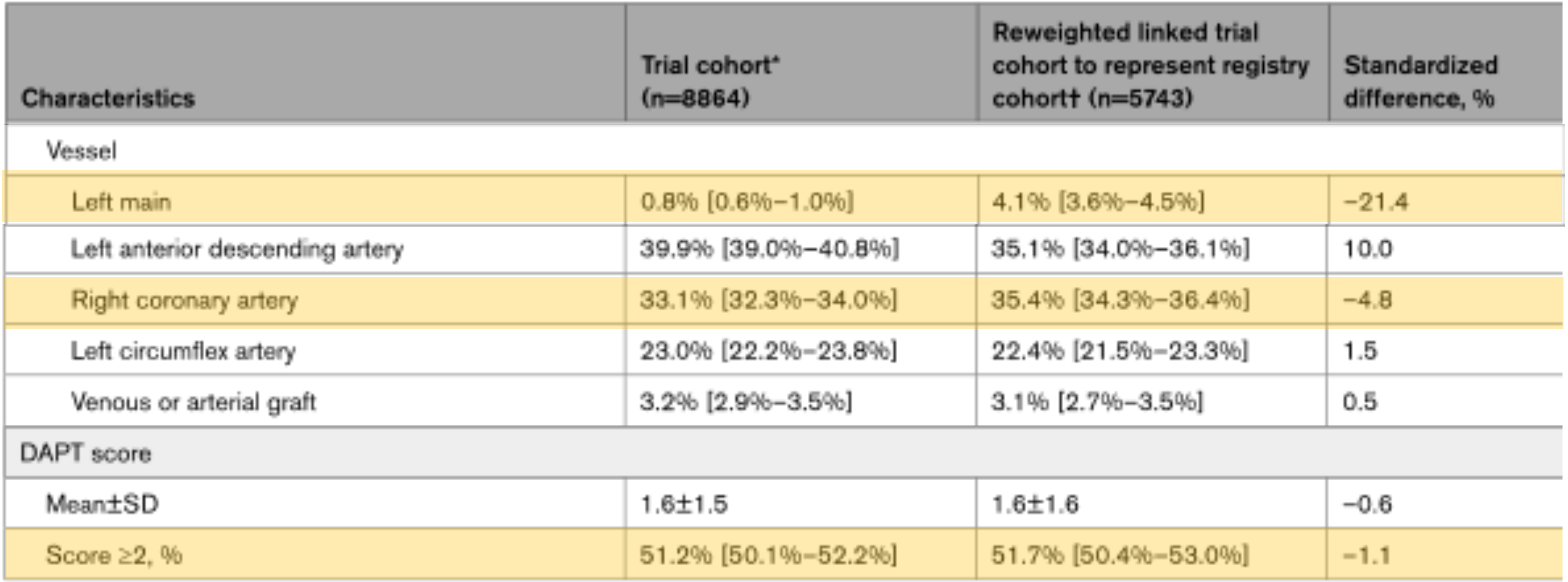
Characteristics	Trial cohort* (n=8864)	Reweighted linked trial cohort to represent registry cohort† (n=5743)	Standardized difference, %
Indication for index procedure			
Myocardial infarction	24.7% [23.8%–25.6%]	38.1% [36.8%–39.4%]	−29.2
ST-segment–elevation myocardial infarction	9.5% [8.9%–10.1%]	15.1% [14.2%–16.0%]	−17.0
Non–ST-segment–elevation myocardial infarction	15.2% [14.4%–15.9%]	23.0% [21.9%–24.1%]	−20.1
Unstable angina	17.3% [16.5%–18.1%]	14.7% [13.7%–15.6%]	7.3
Stable angina	36.9% [35.9%–37.9%]	31.4% [30.2%–32.7%]	11.5
Other	21.1% [20.3%–22.0%]	15.8% [14.9%–16.8%]	13.7

CARACTERÍSTICAS BASALES



Characteristics	Trial cohort* (n=8864)	Reweighted linked trial cohort to represent registry cohort† (n=5743)	Standardized difference, %
Procedural characteristics			
Drug-eluting stent generation			
First generation	41.7% [40.6%–42.7%]	0.0% [0.0%–0.1%]	119.3
Second generation	58.3% [57.3%–59.4%]	100.0% [99.9%–100.0%]	−119.3
Number of treated lesions, per patient, mean±SD	1.3±0.6 (8864)	1.4±0.6 (5743)	−18.2
Number of treated vessels, per patient, mean±SD	1.1±0.3 (8847)	1.1±0.4 (5732)	−7.2
Number of stents, per patient, mean±SD	1.5±0.8 (8864)	1.7±0.9 (5743)	−28.4
Minimum stent diameter, per patient, <3 mm	47.1% [46.1%–48.2%]	51.4% [50.1%–52.7%]	−8.6
Total stent length, mm, sum per patient, mean±SD	27.4±16.9 (8864)	33.3±21.1 (5743)	−31.0
Modified American College of Cardiology/American Heart Association lesion class B2 or C	42.3% [41.4%–43.3%]	55.4% [54.3%–56.6%]	−26.4

CARACTERÍSTICAS BASALES



Characteristics	Trial cohort* (n=8864)	Reweighted linked trial cohort to represent registry cohort† (n=5743)	Standardized difference, %
Vessel			
Left main	0.8% [0.6%–1.0%]	4.1% [3.6%–4.5%]	−21.4
Left anterior descending artery	39.9% [39.0%–40.8%]	35.1% [34.0%–36.1%]	10.0
Right coronary artery	33.1% [32.3%–34.0%]	35.4% [34.3%–36.4%]	−4.8
Left circumflex artery	23.0% [22.2%–23.8%]	22.4% [21.5%–23.3%]	1.5
Venous or arterial graft	3.2% [2.9%–3.5%]	3.1% [2.7%–3.5%]	0.5
DAPT score			
Mean±SD	1.6±1.5	1.6±1.6	−0.6
Score ≥2, %	51.2% [50.1%–52.2%]	51.7% [50.4%–53.0%]	−1.1

DAPT EXTENDIDO: RESULTADOS

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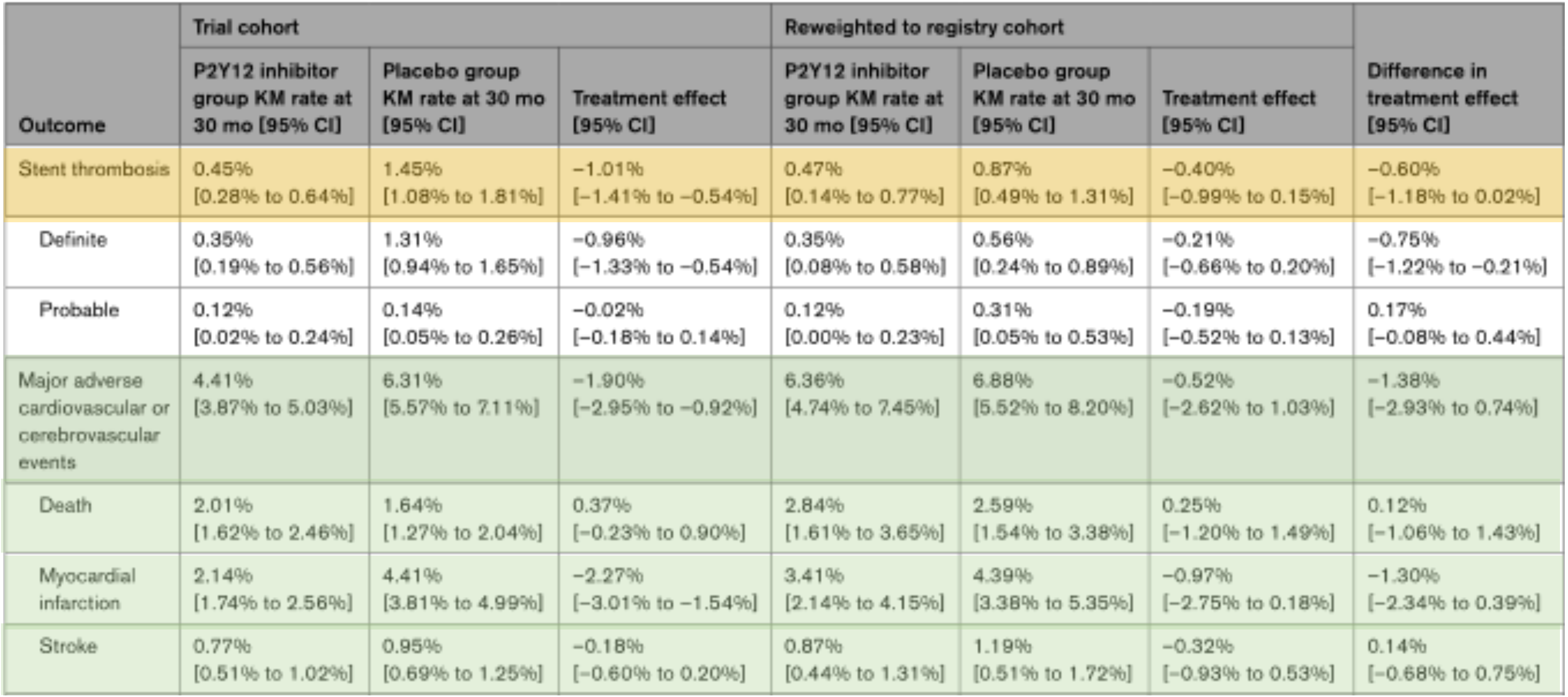

Outcome	Trial cohort			Reweighted to registry cohort			Difference in treatment effect [95% CI]
	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment effect [95% CI]	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment effect [95% CI]	
Stent thrombosis	0.45% [0.28% to 0.64%]	1.45% [1.08% to 1.81%]	−1.01% [−1.41% to −0.54%]	0.47% [0.14% to 0.77%]	0.87% [0.49% to 1.31%]	−0.40% [−0.99% to 0.15%]	−0.60% [−1.18% to 0.02%]
Definite	0.35% [0.19% to 0.56%]	1.31% [0.94% to 1.65%]	−0.96% [−1.33% to −0.54%]	0.35% [0.08% to 0.58%]	0.56% [0.24% to 0.89%]	−0.21% [−0.66% to 0.20%]	−0.75% [−1.22% to −0.21%]
Probable	0.12% [0.02% to 0.24%]	0.14% [0.05% to 0.26%]	−0.02% [−0.18% to 0.14%]	0.12% [0.00% to 0.23%]	0.31% [0.05% to 0.53%]	−0.19% [−0.52% to 0.13%]	0.17% [−0.08% to 0.44%]
Major adverse cardiovascular or cerebrovascular events	4.41% [3.87% to 5.03%]	6.31% [5.57% to 7.11%]	−1.90% [−2.95% to −0.92%]	6.36% [4.74% to 7.45%]	6.88% [5.52% to 8.20%]	−0.52% [−2.62% to 1.03%]	−1.38% [−2.93% to 0.74%]
Death	2.01% [1.62% to 2.46%]	1.64% [1.27% to 2.04%]	0.37% [−0.23% to 0.90%]	2.84% [1.61% to 3.65%]	2.59% [1.54% to 3.38%]	0.25% [−1.20% to 1.49%]	0.12% [−1.06% to 1.43%]
Myocardial infarction	2.14% [1.74% to 2.56%]	4.41% [3.81% to 4.99%]	−2.27% [−3.01% to −1.54%]	3.41% [2.14% to 4.15%]	4.39% [3.38% to 5.35%]	−0.97% [−2.75% to 0.18%]	−1.30% [−2.34% to 0.39%]
Stroke	0.77% [0.51% to 1.02%]	0.95% [0.69% to 1.25%]	−0.18% [−0.60% to 0.20%]	0.87% [0.44% to 1.31%]	1.19% [0.51% to 1.72%]	−0.32% [−0.93% to 0.53%]	0.14% [−0.68% to 0.75%]

DAPT EXTENDIDO: RESULTADOS

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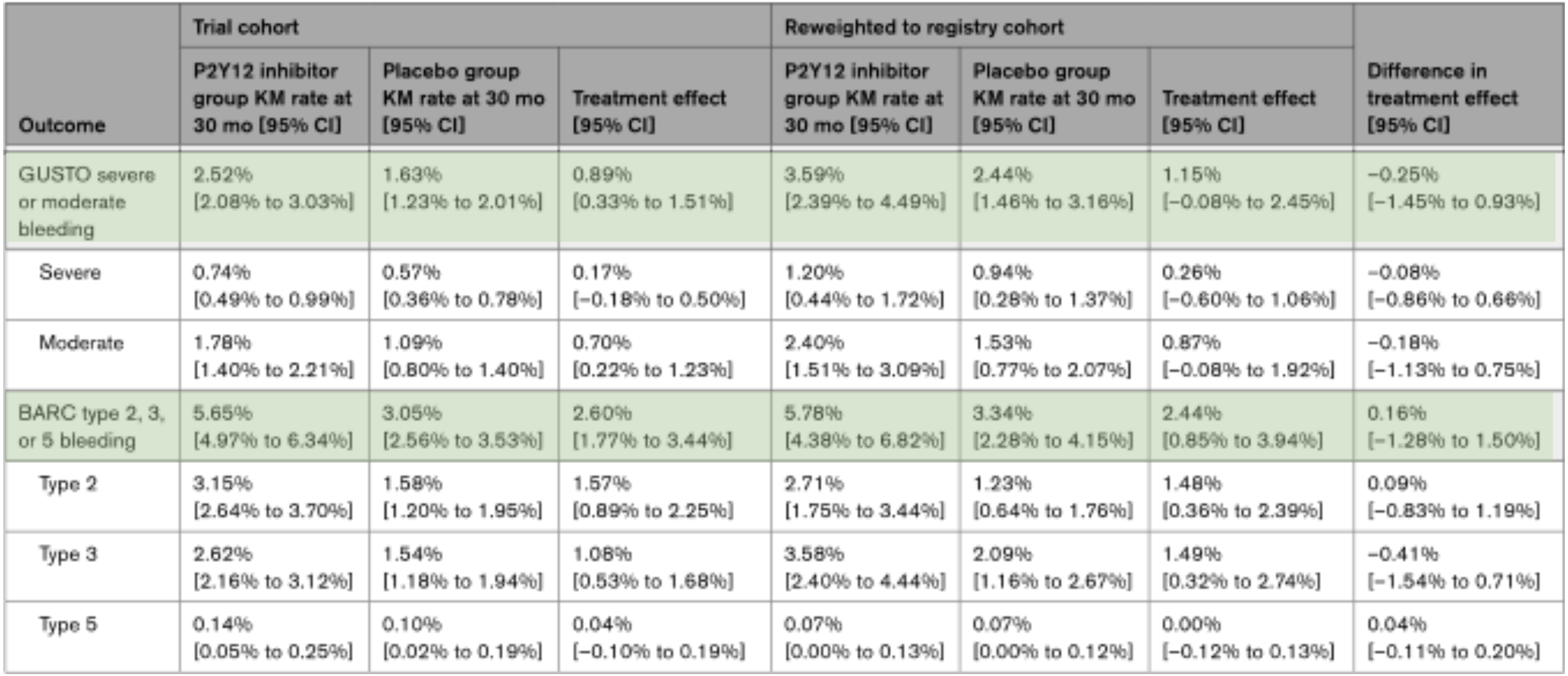
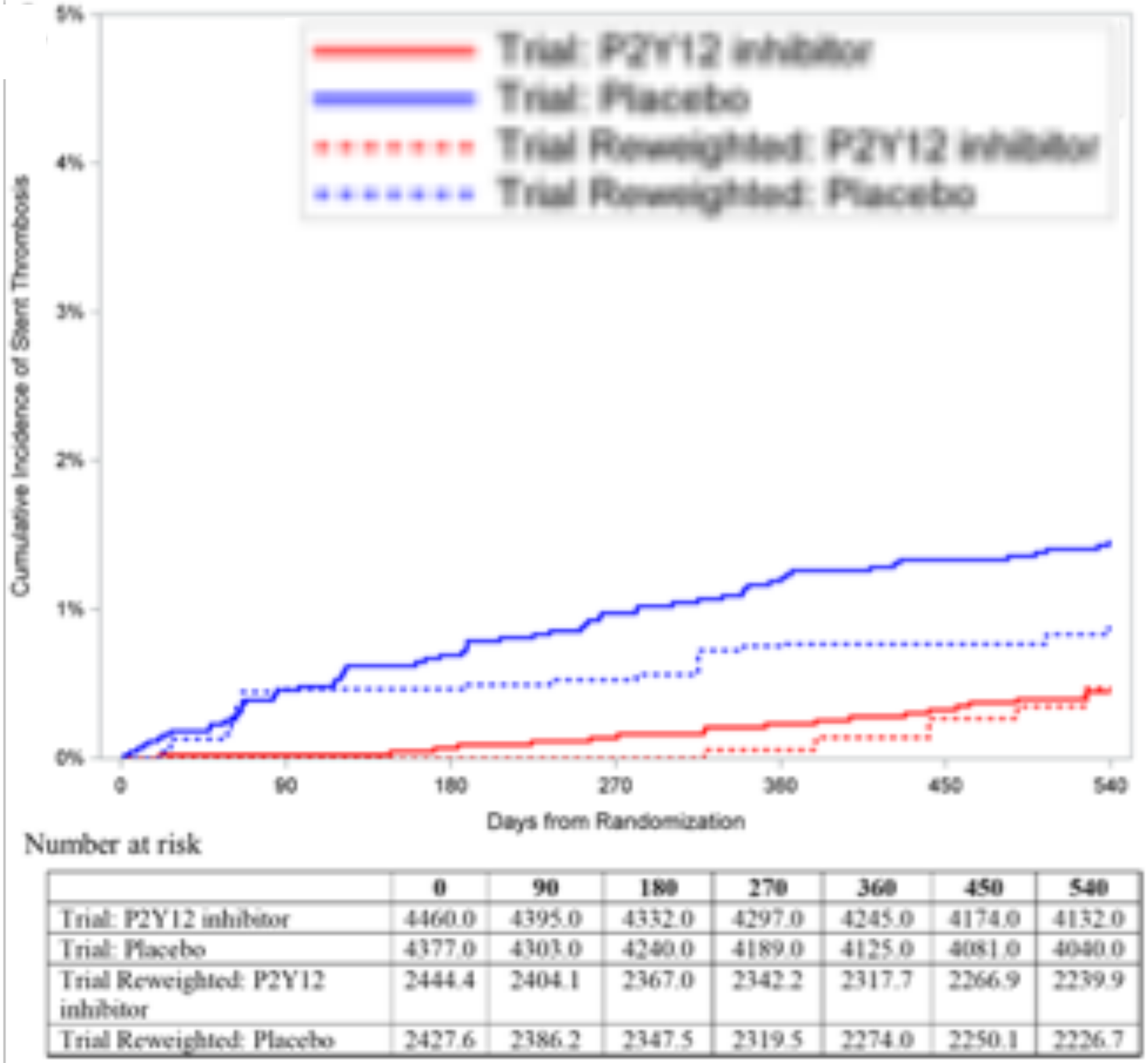


Outcome	Trial cohort			Reweighted to registry cohort			Difference in treatment effect [95% CI]
	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment effect [95% CI]	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment effect [95% CI]	
GUSTO severe or moderate bleeding	2.52% [2.08% to 3.03%]	1.63% [1.23% to 2.01%]	0.89% [0.33% to 1.51%]	3.59% [2.39% to 4.49%]	2.44% [1.46% to 3.16%]	1.15% [−0.08% to 2.45%]	−0.25% [−1.45% to 0.93%]
Severe	0.74% [0.49% to 0.99%]	0.57% [0.36% to 0.78%]	0.17% [−0.18% to 0.50%]	1.20% [0.44% to 1.72%]	0.94% [0.28% to 1.37%]	0.26% [−0.60% to 1.06%]	−0.08% [−0.86% to 0.66%]
Moderate	1.78% [1.40% to 2.21%]	1.09% [0.80% to 1.40%]	0.70% [0.22% to 1.23%]	2.40% [1.51% to 3.09%]	1.53% [0.77% to 2.07%]	0.87% [−0.08% to 1.92%]	−0.18% [−1.13% to 0.75%]
BARC type 2, 3, or 5 bleeding	5.65% [4.97% to 6.34%]	3.05% [2.56% to 3.53%]	2.60% [1.77% to 3.44%]	5.78% [4.38% to 6.82%]	3.34% [2.28% to 4.15%]	2.44% [0.85% to 3.94%]	0.16% [−1.28% to 1.50%]
Type 2	3.15% [2.64% to 3.70%]	1.58% [1.20% to 1.95%]	1.57% [0.89% to 2.25%]	2.71% [1.75% to 3.44%]	1.23% [0.64% to 1.76%]	1.48% [0.36% to 2.39%]	0.09% [−0.83% to 1.19%]
Type 3	2.62% [2.16% to 3.12%]	1.54% [1.18% to 1.94%]	1.08% [0.53% to 1.68%]	3.58% [2.40% to 4.44%]	2.09% [1.16% to 2.67%]	1.49% [0.32% to 2.74%]	−0.41% [−1.54% to 0.71%]
Type 5	0.14% [0.05% to 0.25%]	0.10% [0.02% to 0.19%]	0.04% [−0.10% to 0.19%]	0.07% [0.00% to 0.13%]	0.07% [0.00% to 0.12%]	0.00% [−0.12% to 0.13%]	0.04% [−0.11% to 0.20%]

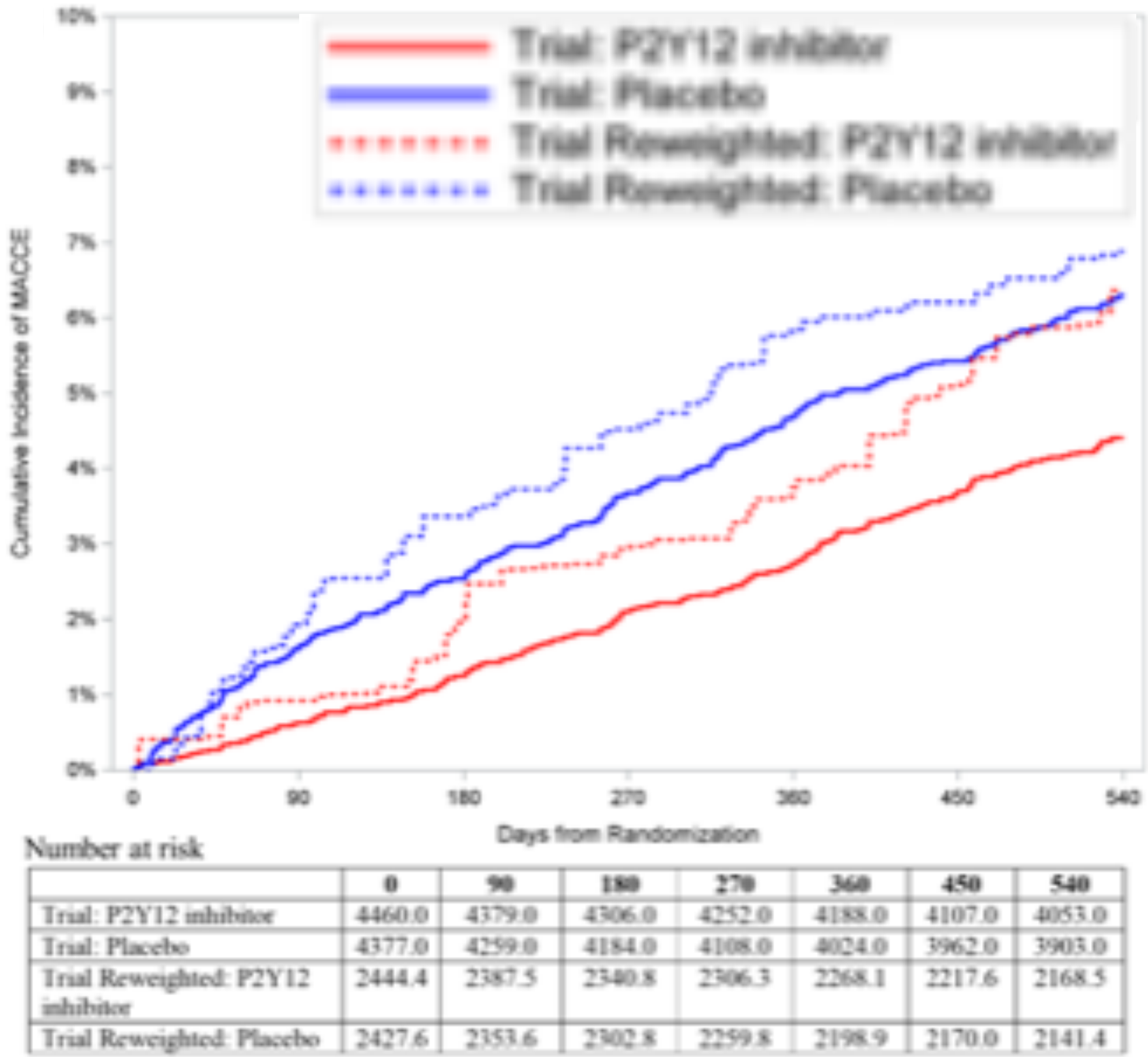
INCIDENCIA DE TROMBOSIS INTRA-STENT



Number at risk

	0	90	180	270	360	450	540
Trial: P2Y12 inhibitor	4460.0	4395.0	4332.0	4297.0	4245.0	4174.0	4132.0
Trial: Placebo	4377.0	4303.0	4240.0	4189.0	4125.0	4081.0	4040.0
Trial Reweighted: P2Y12 inhibitor	2444.4	2404.1	2367.0	2342.2	2317.7	2266.9	2239.9
Trial Reweighted: Placebo	2427.6	2386.2	2347.5	2319.5	2274.0	2250.1	2226.7

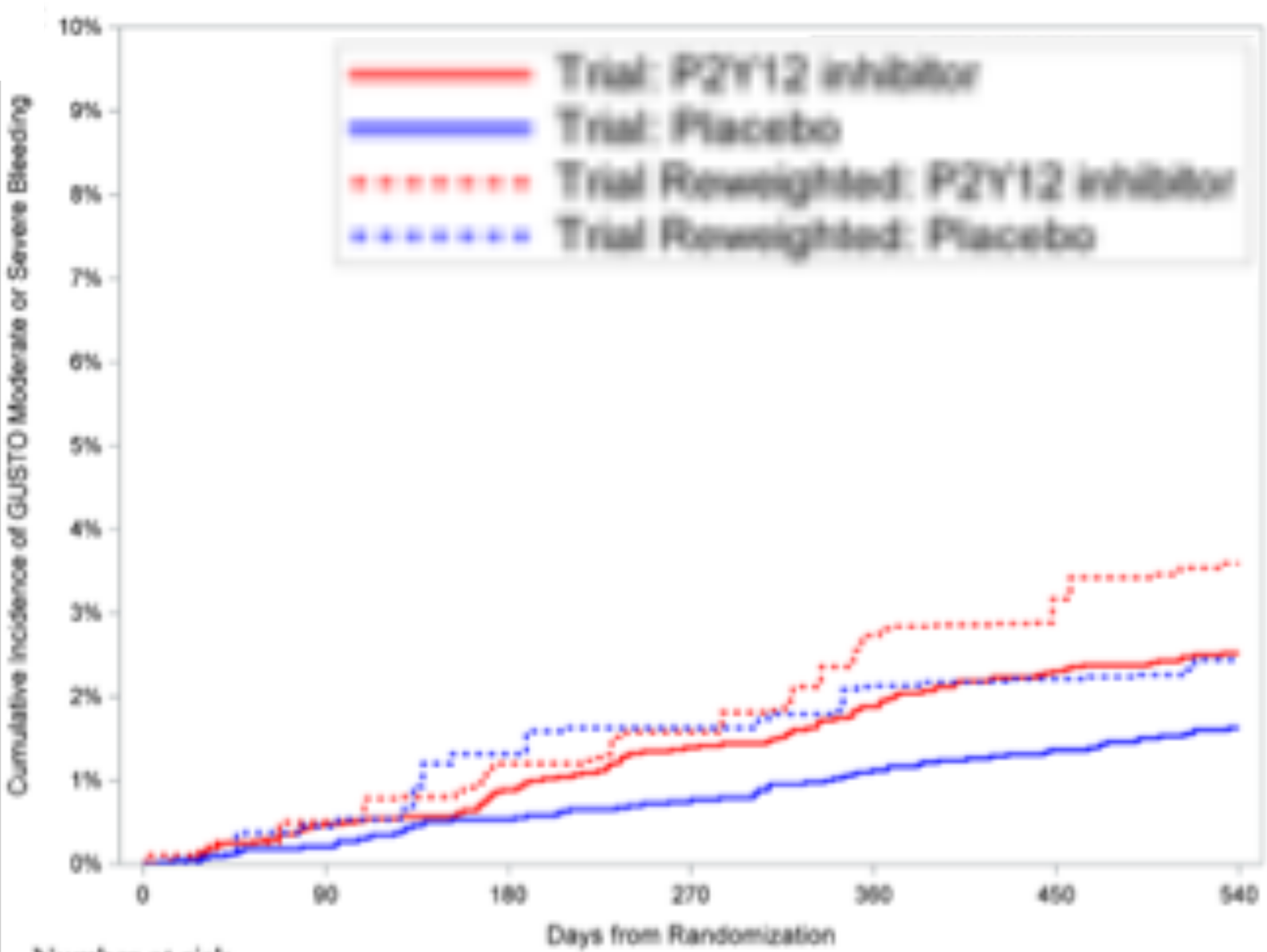
INCIDENCIA DE MACCE



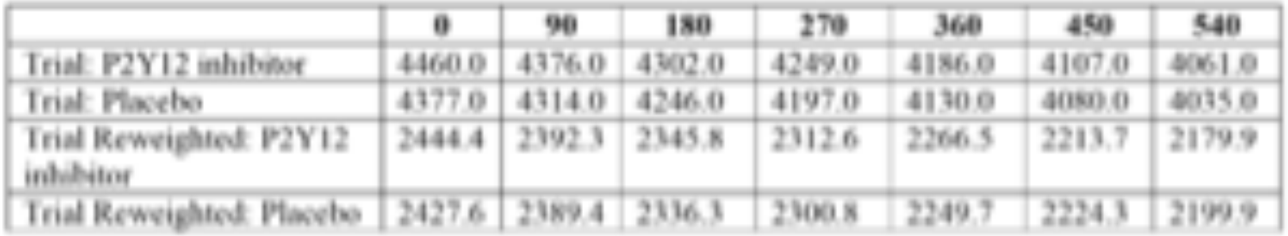
Number at risk

	0	90	180	270	360	450	540
Trial: P2Y12 inhibitor	4460.0	4379.0	4306.0	4252.0	4188.0	4107.0	4053.0
Trial: Placebo	4377.0	4259.0	4184.0	4108.0	4024.0	3962.0	3903.0
Trial Reweighted: P2Y12 inhibitor	2444.4	2387.5	2340.8	2306.3	2268.1	2217.6	2168.5
Trial Reweighted: Placebo	2427.6	2353.6	2302.8	2259.8	2198.9	2170.0	2141.4

INCIDENCIA DE SANGRADO: GUSTO



Number at risk



	0	90	180	270	360	450	540
Trial: P2Y12 inhibitor	4460.0	4376.0	4302.0	4249.0	4186.0	4107.0	4061.0
Trial: Placebo	4377.0	4314.0	4246.0	4197.0	4130.0	4080.0	4035.0
Trial Reweighted: P2Y12 inhibitor	2444.4	2392.3	2345.8	2312.6	2266.5	2213.7	2179.9
Trial Reweighted: Placebo	2427.6	2389.4	2336.3	2300.8	2249.7	2224.3	2199.9

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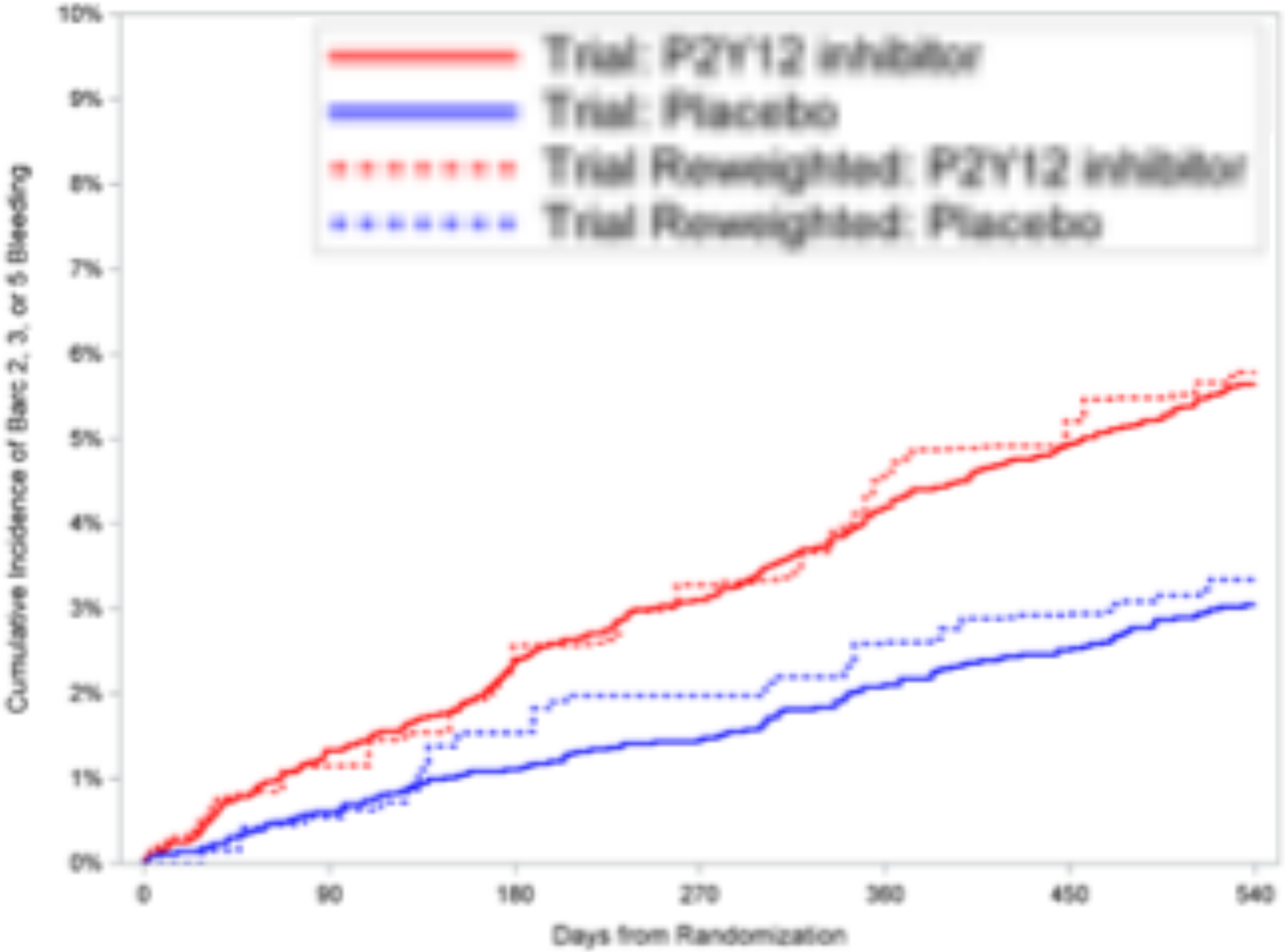
INCIDENCIA DE SANGRADO: BARC



Number at risk

	0	90	180	270	360	450	540
Trial: P2Y12 inhibitor	4458.0	4339.0	4237.0	4175.0	4088.0	3996.0	3930.0
Trial: Placebo	4376.0	4296.0	4220.0	4167.0	4090.0	4033.0	3979.0
Trial Reweighted: P2Y12 inhibitor	2439.8	2377.7	2314.3	2272.9	2230.3	2172.6	2135.3
Trial Reweighted: Placebo	2427.6	2385.0	2329.0	2290.6	2238.8	2208.0	2179.7

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DISCUSIÓN

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- Este sub-análisis evaluó la **vigencia del DAPT *trial* a 30 meses**, de una población estadounidense con angioplastia coronaria con colocación de *stent* liberador de droga (DES), en una población más actual.

- Se observó que en aquellos pacientes contemporáneos que recibieron tratamiento prolongado presentaron **aumento de hemorragias, sin demostrar los beneficios en cuanto al MACCE, trombosis del *stent* e infarto de miocardio evidenciados en el estudio DAPT.**

DISCUSIÓN

- Estas diferencias se deben a las **mejoras en la tecnología** de los *stents* y a los cambios en las **características basales** de los pacientes.

LIMITACIONES

- Es posible que la selección de muestra de pacientes inicialmente inscritos en el DAPT *trial* pueda afectar a las estimaciones del efecto del tratamiento en el mundo real.

- Los intervalos de confianza para las diferencias estimadas son amplios, lo que dificulta detectar **diferencias estadísticamente significativas**.

- El Registro Nacional estadounidense de Datos Cardiovasculares (NCDR) ***CathPCI Registry*** recopiló datos hasta el **2017**.

CONCLUSIONES

- Las diferencias entre pacientes y *stents* utilizados en la práctica clínica contemporánea en comparación con el DAPT *trial* **se asociaron a una disminución en los beneficios y mayores efectos adversos atribuibles al uso prolongado de la doble terapia anti-plaquetaria.**

PICOTS

- **P:** 8,864 ptes EEUU, DAPT *trial* con colocación DES. 5,743 ptes con criterio de inclusión CathPCI. Edad promedio 62 años. Sexo masculino (74%) e HTA (77%).
- **I:** sub-análisis del estudio DAPT. Ensayo prospectivo, aleatorizado y doble ciego.
- **C:** los puntos finales primarios del uso de DAPT prolongado (30 meses) en la población estadounidense del DAPT *trial* que recibieron DES *versus* un subgrupo con características de inclusión al registro CathPCI.
- **O:** no se observaron beneficios significativos en el uso de DAPT prolongado en la reducción de trombosis del *stent,* en efectos adversos cardio y cerebrovasculares mayores y en infarto de miocardio; evidenciándose un aumento de eventos hemorrágicos.
- **T:** desde agosto de 2009 hasta julio de 2011.
- **S:** multicéntrico, en 178 centros de Estados Unidos.

Circulation

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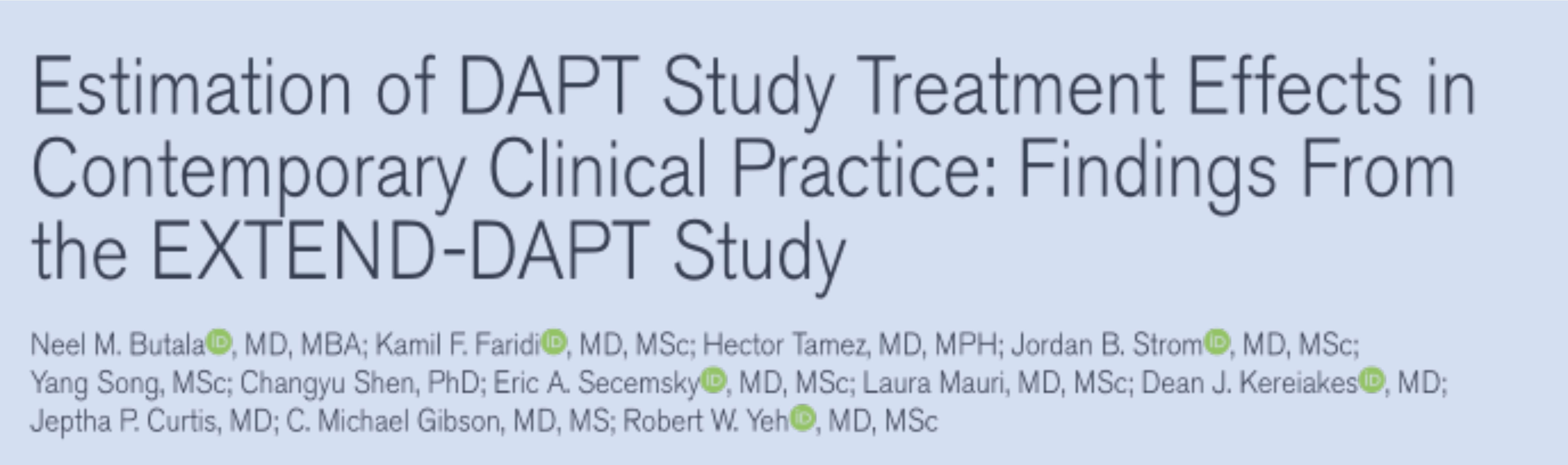

Estimation of DAPT Study Treatment Effects in Contemporary Clinical Practice: Findings From the EXTEND-DAPT Study

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