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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INTRODUCCIÓN

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- 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

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- 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

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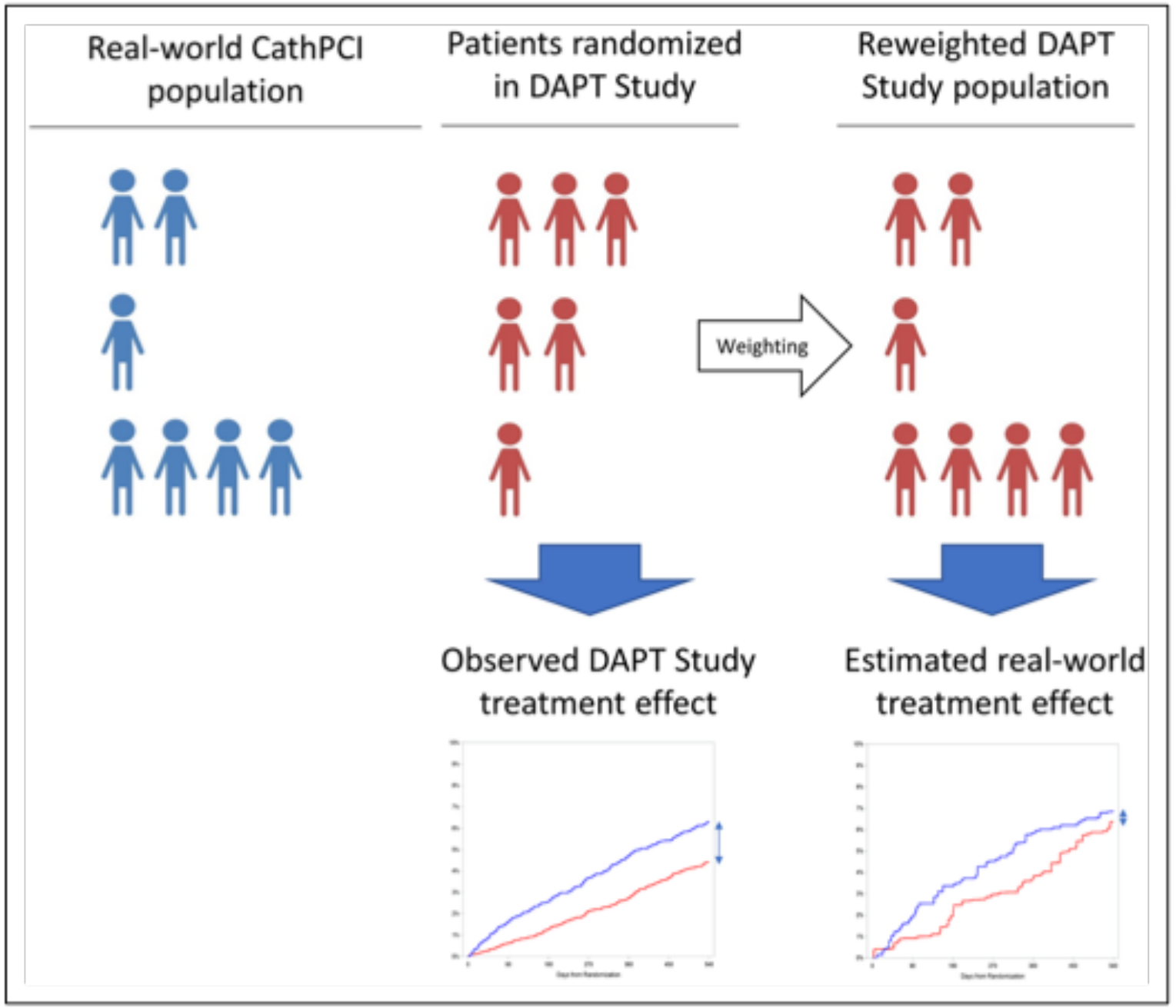
- Recientemente, se han desarrollado métodos estadísticos que permiten cuantificar estas diferencias y estimar cómo los resultados del estudio DAPT pueden jerarquizarse en la población actual de pacientes que reciben una ICP.

- 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



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DISEÑO DE ESTUDIO Y FUENTE DE DATOS

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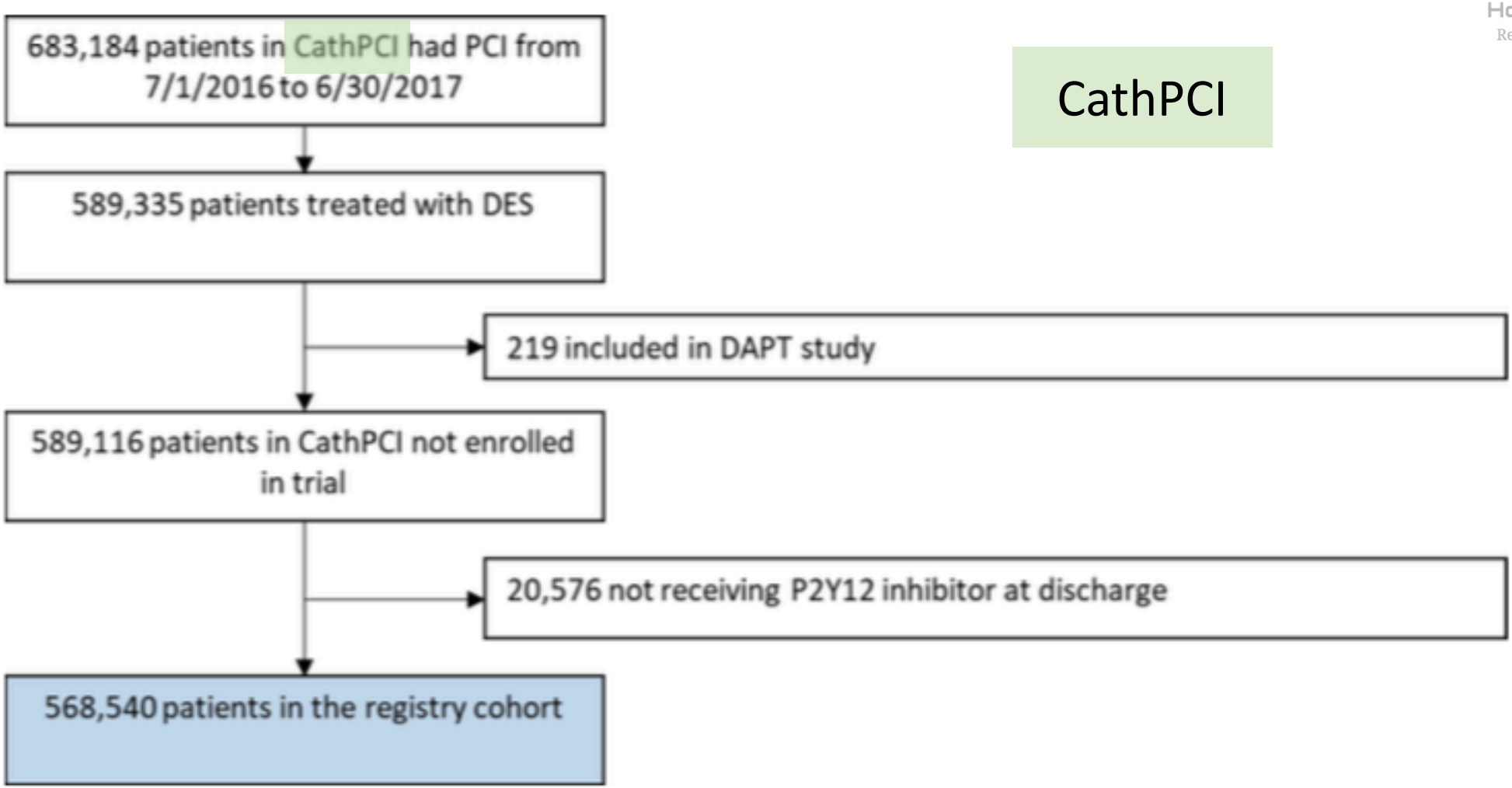

CathPCI

DISEÑO DE ESTUDIO Y FUENTE DE DATOS

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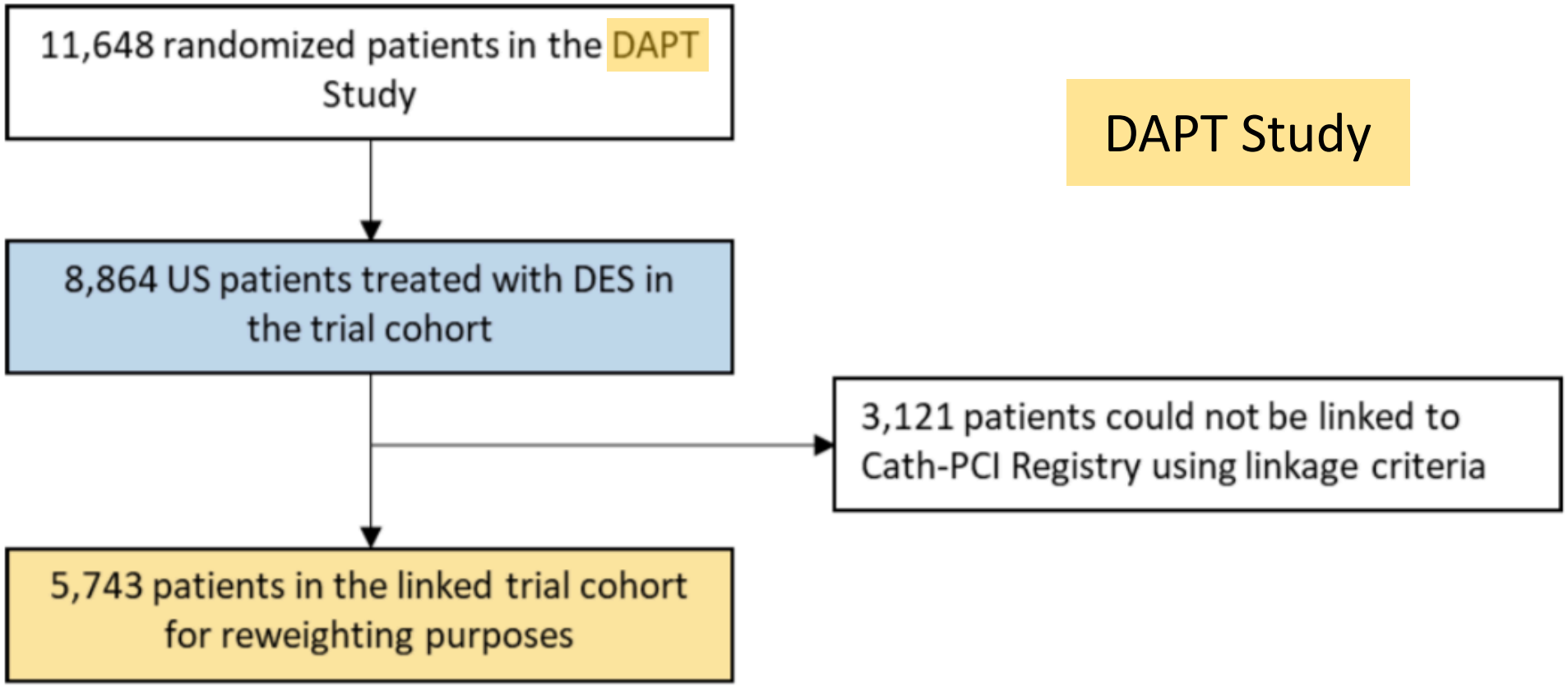

DAPT Study

MÉTODOS

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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

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- <u>Puntos finales:</u>

- 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).

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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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Oral medications	18.7% [17.9%–19.6%]	20.2% [19.2%–21.3%]	−3.7
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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
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History of cancer	10.0% [9.4%–10.7%]	12.5% [11.7%–13.4%]	−8.0
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Positive stress test	39.9% [38.7%–41.1%]	26.9% [25.8%–28.1%]	27.8

CARACTERÍSTICAS BASALES

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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

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Residencia de Cardiología

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

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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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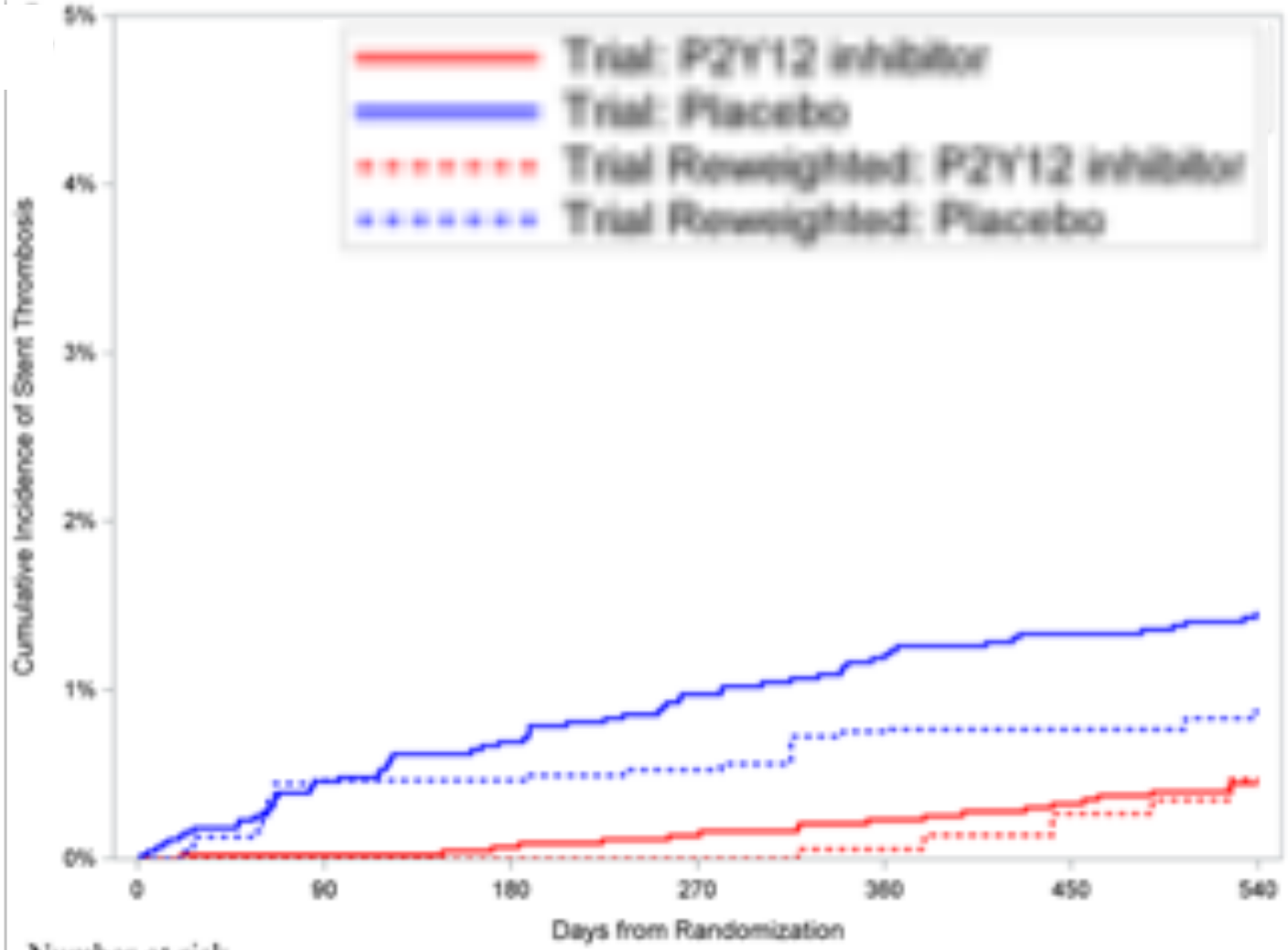
Outcome	Trial cohort			Reweighted to registry cohort			Difference in treatment effect [95% CI]
	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment effect [95% CI]	P2Y12 inhibitor group KM rate at 30 mo [95% CI]	Placebo group KM rate at 30 mo [95% CI]	Treatment 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%]

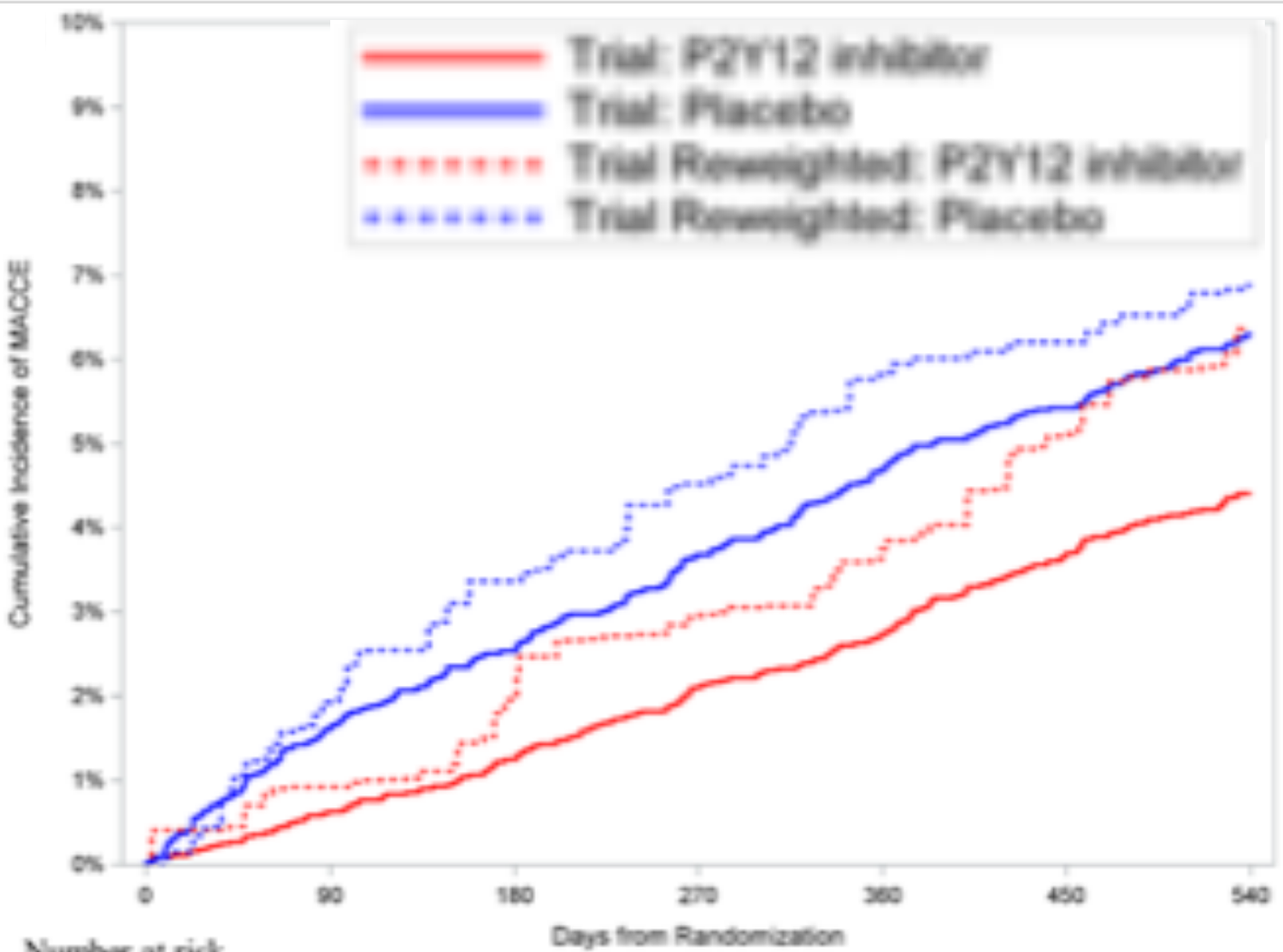
INCIDENCIA DE TROMBOSIS INTRA-STENT



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

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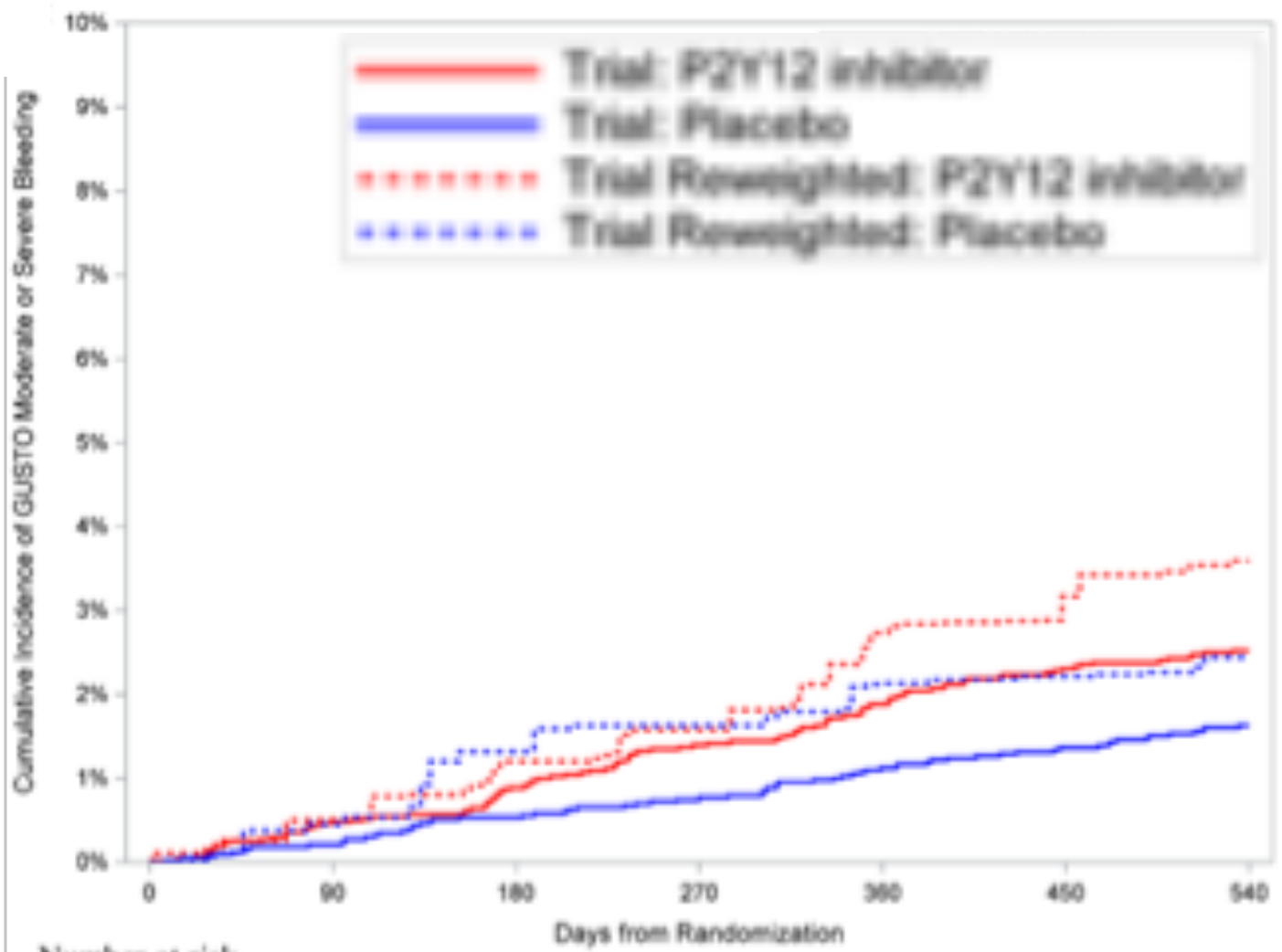
INCIDENCIA DE SANGRADO: GUSTO



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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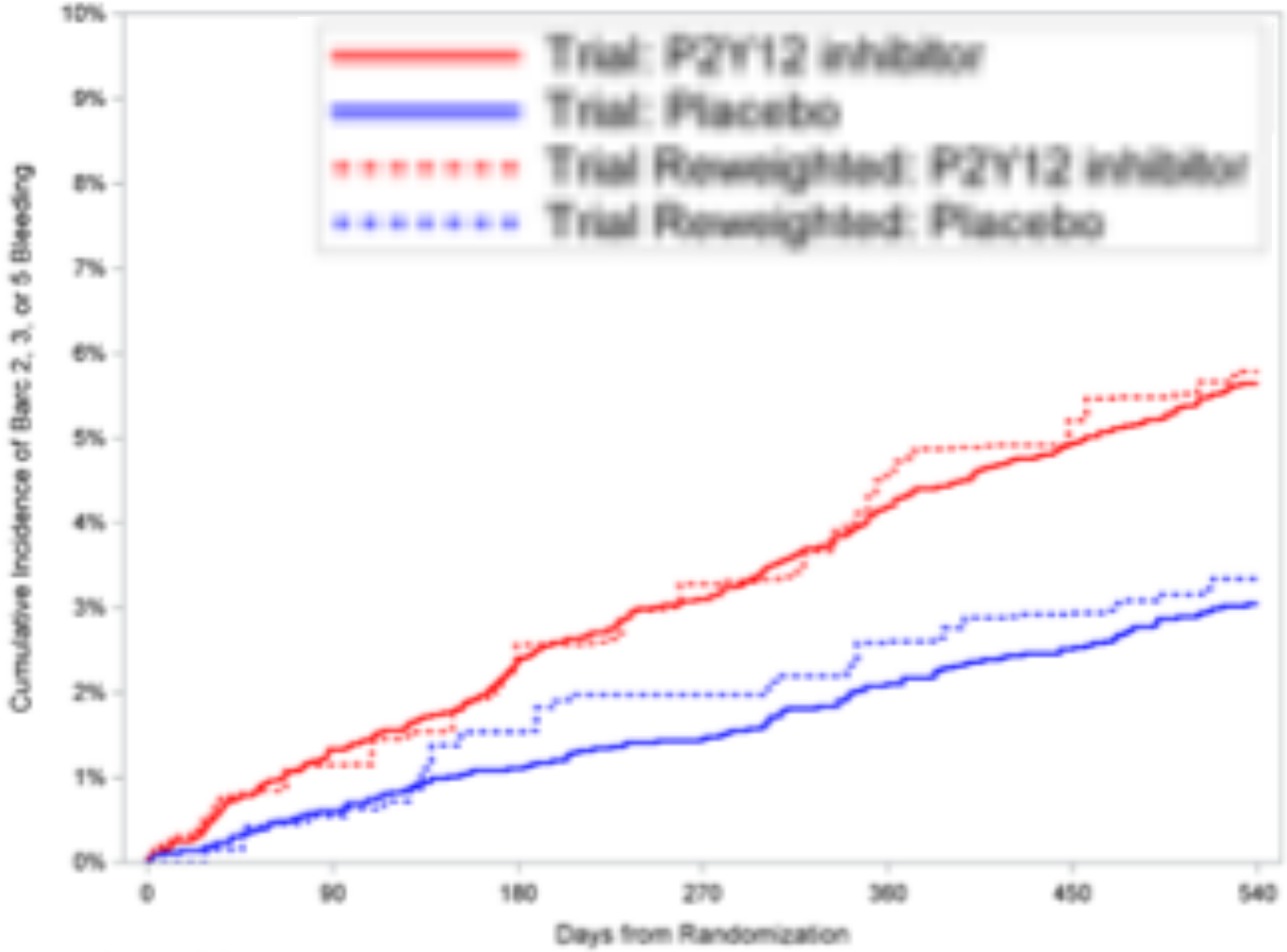
INCIDENCIA DE SANGRADO: BARC



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

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- 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

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- 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

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- 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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