Noviembre, 2019

Recomendación de Tratamiento

Informe de búsqueda y síntesis de evidencia de efectos deseables e indeseables

Guía de Práctica Clínica de Endoprótesis total de cadera en personas de 65 años y más con artrosis de cadera con limitación funcional severa - 2019

A. Pregunta clínica

En personas de 65 años y más con endoprótesis total de cadera al momento del alta ¿Se debe "usar tromboprofilaxis con HBPM" en comparación a "usar anticoagulantes orales directos (rivaroxaban, dabigatran o apixaban)"?

Análisis y definición de los componentes de la pregunta en formato PICO

Población: Personas con endoprótesis total de cadera hospitalizados.

Intervención: Usar tromboprofilaxis con HBPM.

Comparación: Usar anticoagulantes orales directos (rivaroxaban o dabigatran o apixaban).

Desenlaces (outcomes): Mortalidad, embolismo pulmonar, trombosis venosa profunda, sangramiento major y adherencia.

B. Métodos

Se realizó una búsqueda general de revisiones sistemáticas sobre cuidados perioperatorios (ver Anexo 1: estrategia de búsqueda). Las bases de datos utilizadas fueron: Cochrane database of systematic reviews (CDSR); Database of Abstracts of Reviews of Effectiveness (DARE); HTA Database; PubMed; LILACS; CINAHL; PsyclNFO; EMBASE; EPPI-Centre Evidence Library; 3ie Systematic Reviews and Policy Briefs Campbell Library; Clinical Evidence; SUPPORT Summaries; WHO institutional Repository for information Sharing; NICE public health guidelines and systematic reviews; ACP Journal Club; Evidencias en Pediatría; y The JBI Database of Systematic Reviews and Implementation Reports. No se aplicaron restricciones en base al idioma o estado de publicación. Dos revisores de manera independiente realizaron la selección de los títulos y los resúmenes, la evaluación del texto completo y la extracción de datos. Un investigador o clínico experimentado resolvió cualquier discrepancia entre los distintos revisores. Finalmente, se seleccionaron las revisiones sistemáticas (y los estudios incluidos en éstas) correspondientes a la temática y se clasificaron en función de las preguntas a las que daban respuesta.

Los resultados de la búsqueda se encuentran alojados en la plataforma Living Overview of the Evidence (L·OVE), sistema que permite la actualización periódica de la evidencia.

C. Resultados

Resumen de la evidencia identificada

Se buscaron revisiones sistemáticas que analizan estudios en pacientes operados por reemplazo de cadera, en los cuales se compara un grupo que recibe profilaxis antitrombótica con HBPM contra un grupo que recibe anticoagulantes orales directos. Se identificaron 40 revisiones sistemáticas que incluyeron 24 estudios primarios, de los cuales todos corresponden a ensayos aleatorizados. Para más detalle ver "*Matriz de evidencia*"[1], en el siguiente enlace: Anticoagulantes orales directos para la prevención de enfermedad tromboembólica post cirugía de cadera.

Tabla 1: Resumen de la evidencia identificada

Revisiones sistemáticas	40 revisiones[1-40]
Estudios primarios	37 ensayos aleatorizados[41-77]

Selección de la evidencia

Se realizó un análisis de la matriz de evidencia, identificándose que todas las revisiones sistemáticas [1-40] y 37 ensayos [41-77] son relevantes para la estimación del efecto, ya que abordan específicamente los componentes de la pregunta priorizada por el panel.

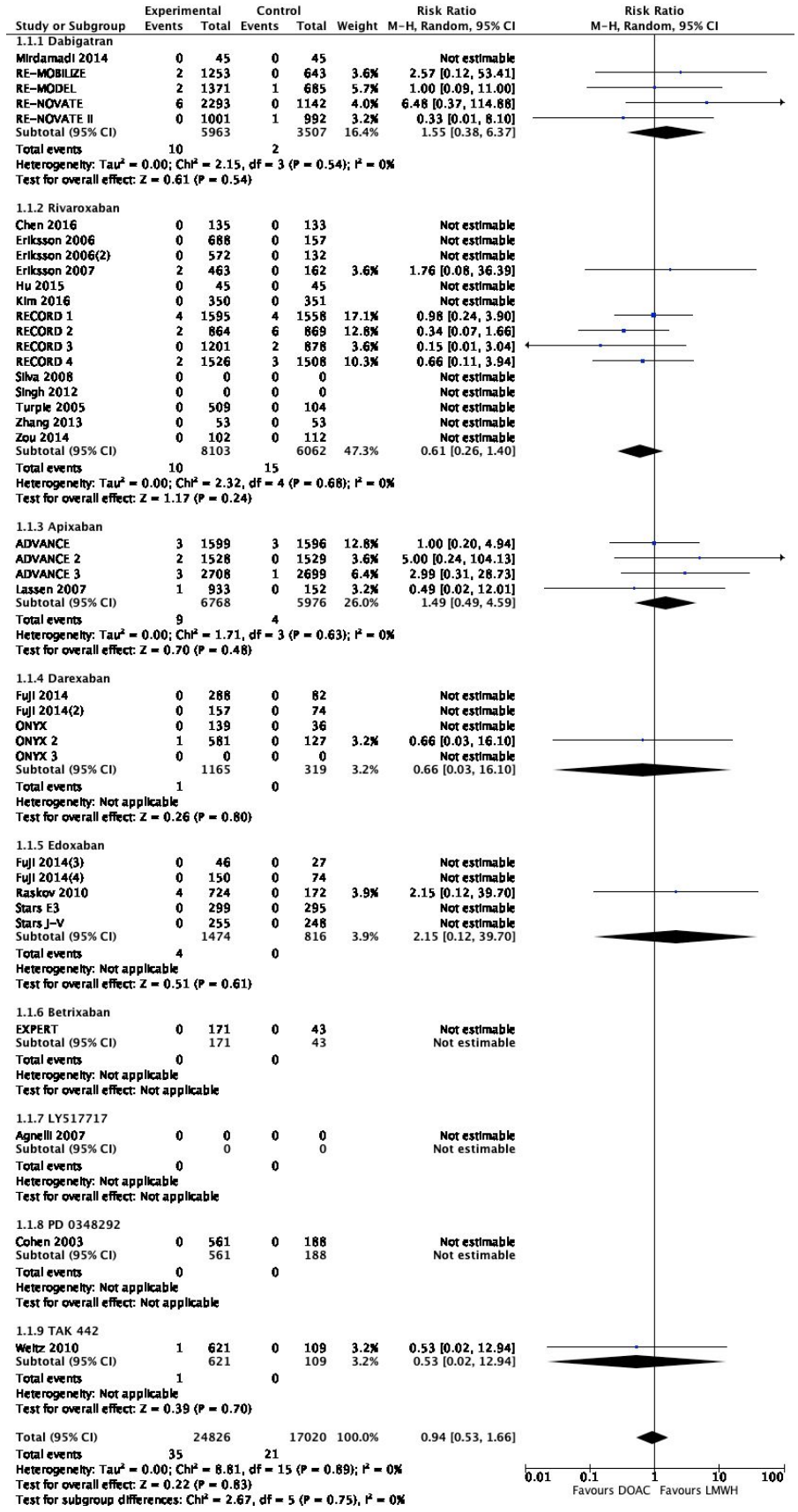
Estimador del efecto

Al analizar la evidencia identificada, se concluyó que ninguna revisión sistemática cumple con todos los requisitos metodológicos establecidos para el presente informe, es decir, incluir los estudios primarios relevantes y entregar un estimador agregado del efecto para los desenlaces de interés. Por lo tanto, se decidió rehacer el metanálisis directamente a partir de los estudios primarios considerados relevantes para construir la tabla de resumen de resultados.

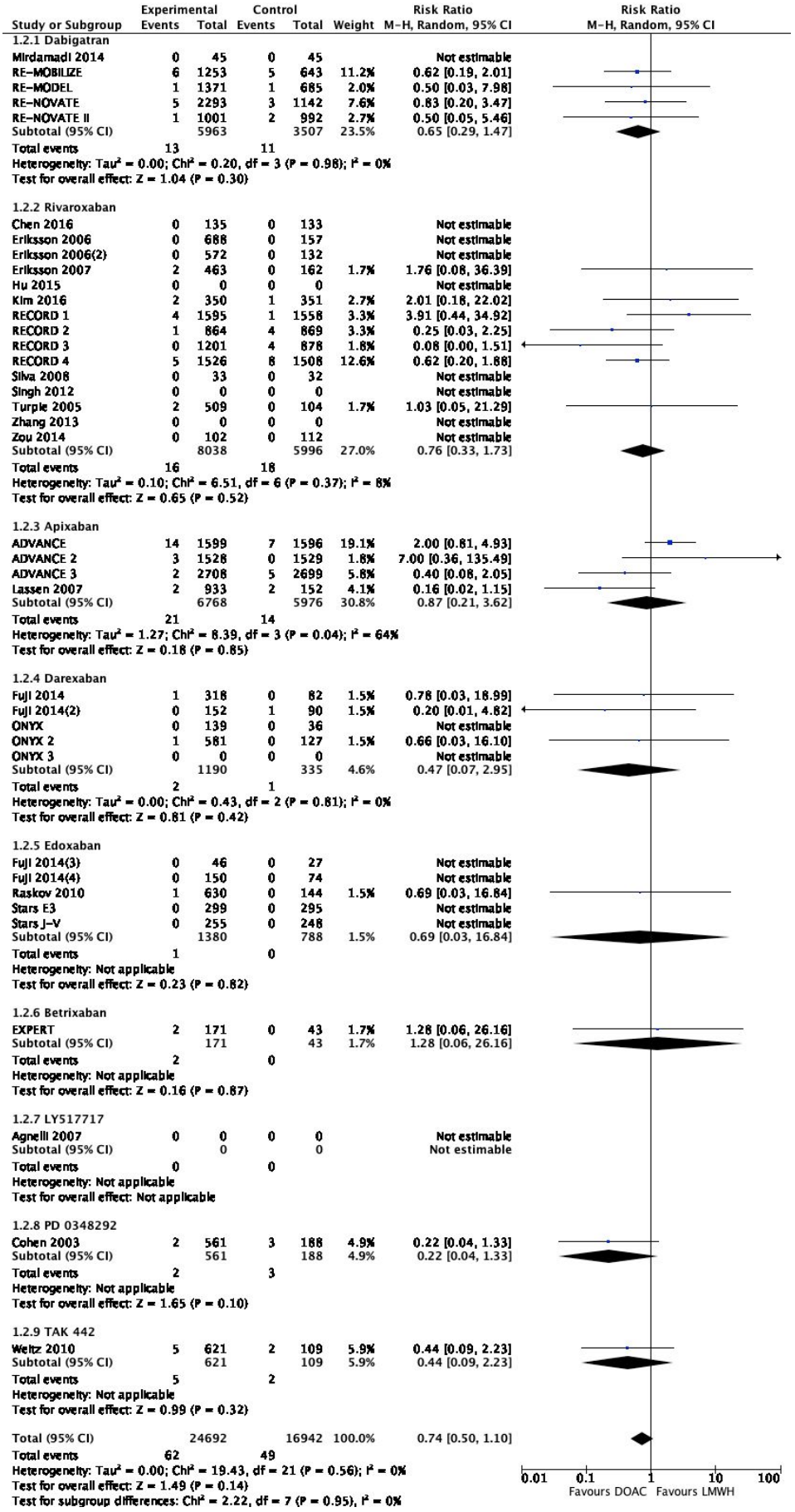
Metanálisis

[1] **Matriz de Evidencia**, tabla dinámica que grafica el conjunto de evidencia existente para una pregunta (en este caso, la pregunta del presente informe). Las filas representan las revisiones sistemáticas y las columnas los estudios primarios que estas revisiones han identificado. Los recuadros en verde corresponden a los estudios incluidos en cada revisión. La matriz se actualiza periódicamente, incorporando nuevas revisiones sistemáticas pertinentes y los respectivos estudios primarios.

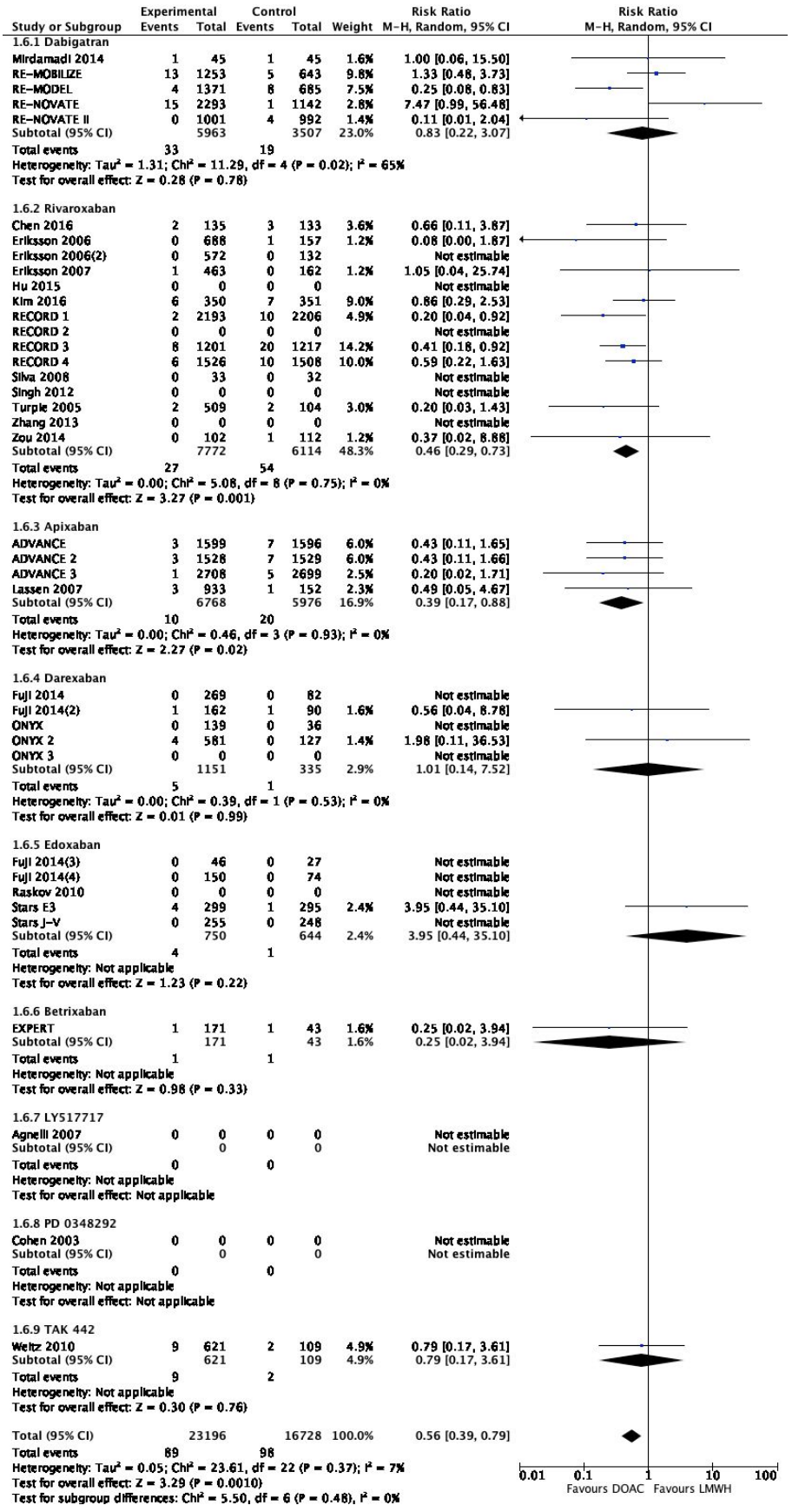
Mortalidad



Embolismo pulmonar


Experimental
Control
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
1.2.1 Dabigatran
Mirdamadi 2014 0 45 0 45 Not estimable
RE-MOBILIZE 6 1253 5 643 11.2% 0.62 [0.19, 2.01]
RE-MODEL 1 1371 1 685 2.0% 0.50 [0.03, 7.98]
RE-NOVATE 5 2293 3 1142 7.6% 0.83 [0.20, 3.47]
RE-NOVATE II 1 1001 2 992 2.7% 0.50 [0.05, 5.46]
Subtotal (95% CI) 5963 3507 23.5% 0.65 [0.29, 1.47]
Total events 13 11
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 3 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.04 (P = 0.30)
1.2.2 Rivaroxaban
Chen 2016 0 135 0 133 Not estimable
Eriksson 2006 0 688 0 157 Not estimable
Eriksson 2006(2) 0 572 0 132 Not estimable
Eriksson 2007 2 463 0 162 1.7% 1.76 [0.08, 36.39]
Hu 2015 0 0 0 0 Not estimable
Kim 2016 2 350 1 351 2.7% 2.01 [0.18, 22.02]
RECORD 1 4 1595 1 1558 3.3% 3.91 [0.44, 34.92]
RECORD 2 1 864 4 869 3.3% 0.25 [0.03, 2.25]
RECORD 3 0 1201 4 878 1.8% 0.08 [0.00, 1.51]
RECORD 4 5 1526 8 1508 12.6% 0.62 [0.20, 1.88]
Silva 2008 0 33 0 32 Not estimable
Singh 2012 0 0 0 0 Not estimable
Turpie 2005 2 509 0 104 1.7% 1.03 [0.05, 21.29]
Zhang 2013 0 0 0 0 Not estimable
Zou 2014 0 102 0 112 Not estimable
Subtotal (95% CI) 8038 5996 27.0% 0.76 [0.33, 1.73]
Total events 16 18
Heterogeneity: Tau² = 0.10; Chi² = 6.51, df = 6 (P = 0.37); I² = 8%
Test for overall effect: Z = 0.65 (P = 0.52)
1.2.3 Apixaban
ADVANCE 14 1599 7 1596 19.1% 2.00 [0.81, 4.93]
ADVANCE 2 3 1528 0 1529 1.8% 7.00 [0.36, 135.49]
ADVANCE 3 2 2708 5 2699 5.8% 0.40 [0.08, 2.05]
Lassen 2007 2 933 2 152 4.1% 0.16 [0.02, 1.15]
Subtotal (95% CI) 6768 5976 30.8% 0.87 [0.21, 3.62]
Total events 21 14
Heterogeneity: Tau² = 1.27; Chi² = 8.39, df = 3 (P = 0.04); I² = 64%
Test for overall effect: Z = 0.18 (P = 0.85)
1.2.4 Darexaban
Fuji 2014 1 318 0 82 1.5% 0.78 [0.03, 18.99]
Fuji 2014(2) 0 152 1 90 1.5% 0.20 [0.01, 4.82]
ONYX 0 139 0 36 Not estimable
ONYX 2 1 581 0 127 1.5% 0.66 [0.03, 16.10]
ONYX 3 0 0 0 0 Not estimable
Subtotal (95% CI) 1190 335 4.6% 0.47 [0.07, 2.95]
Total events 2 1
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.81 (P = 0.42)
1.2.5 Edoxaban
Fuji 2014(3) 0 46 0 27 Not estimable
Fuji 2014(4) 0 150 0 74 Not estimable
Raskov 2010 1 630 0 144 1.5% 0.69 [0.03, 16.84]
Stars E3 0 299 0 295 Not estimable
Stars J-V 0 255 0 248 Not estimable
Subtotal (95% CI) 1380 788 1.5% 0.69 [0.03, 16.84]
Total events 1 0
Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)
1.2.6 Betrixaban
EXPERT 2 171 0 43 1.7% 1.28 [0.06, 26.16]
Subtotal (95% CI) 171 43 1.7% 1.28 [0.06, 26.16]
Total events 2 0
Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)
1.2.7 LY517717
Agnelli 2007 0 0 0 0 Not estimable
Subtotal (95% CI) 0 0 Not estimable
Total events 0 0
Heterogeneity: Not applicable
Test for overall effect: Not applicable
1.2.8 PD 0348292
Cohen 2003 2 561 3 188 4.9% 0.22 [0.04, 1.33]
Subtotal (95% CI) 561 188 4.9% 0.22 [0.04, 1.33]
Total events 2 3
Heterogeneity: Not applicable
Test for overall effect: Z = 1.65 (P = 0.10)
1.2.9 TAK 442
Weitz 2010 5 621 2 109 5.9% 0.44 [0.09, 2.23]
Subtotal (95% CI) 621 109 5.9% 0.44 [0.09, 2.23]
Total events 5 2
Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)
Total (95% CI) 24692 16942 100.0% 0.74 [0.50, 1.10]
Total events 62 49
Heterogeneity: Tau² = 0.00; Chi² = 19.43, df = 21 (P = 0.56); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Chi² = 2.22, df = 7 (P = 0.95), I² = 0%
0.01 0.1 1 10 100
Favours DOAC Favours LMWH

Trombosis venosa profunda sintomática



Sangrado mayor

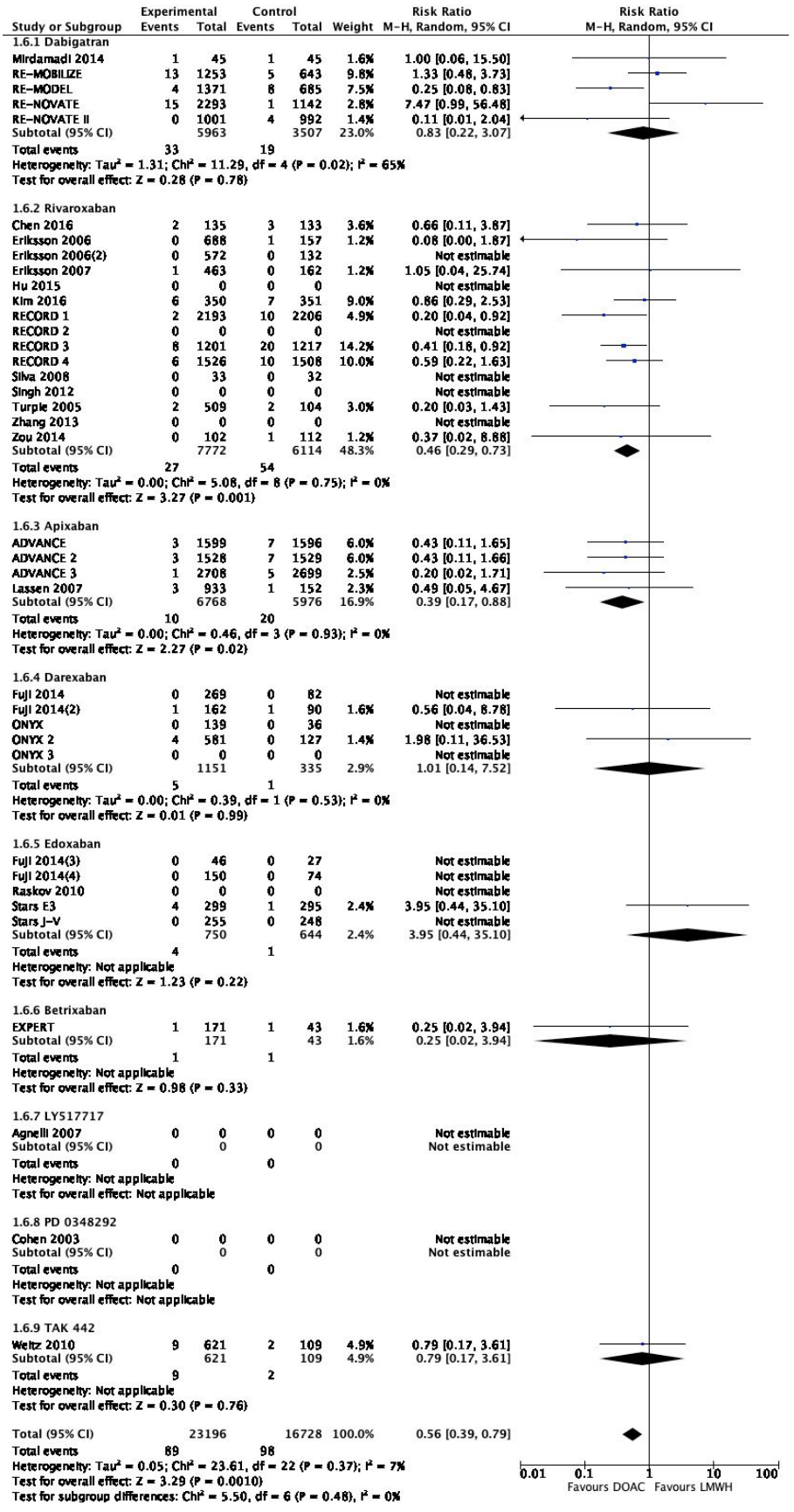


Tabla de Resumen de Resultados (Summary of Findings)

TROMBOPROFILAXIS CON HBPM EN PERSONAS CON ENDOPRÓTESIS DE CADERA HOSPITALIZADOS.						
Pacientes	Personas con endoprótesis total de cadera hospitalizados.					
Intervención	Usar anticoagulantes orales directos (ACOD) (rivaroxaban, dabigatran o apixaban).					
Comparación	Usar tromboprofilaxis con HBPM					
Desenlaces	**Efecto relativo (IC 95%) -- Pacientes/ estudios**	**Efecto absoluto estimado***			**Certeza de la evidencia (GRADE)**	**Mensajes clave en términos sencillos**
		CON HBPM	**CON ACOD**	**Diferencia (IC 95%)**		
Mortalidad	RR 0,94 (0,53 a 1,66) -- 41.816 pacientes/ 37 ensayos	1 por 1000	1 por 1000	0 más (1 menos a 1 más)	⨁⨁⨁⨁ Alta	En personas sometidas a una artroplastia total de cadera con endoprotesis, usar ACOD en comparación a HBPM no cambia la mortalidad
Tromboembolismo pulmonar	RR 0,74 (0,50 a 1,10) -- 41.634 pacientes/ 37 ensayos	3 por 1000	3 por 1000	1 menos (1 menos a 0 más)	⨁⨁⨁⨁ Alta	En personas sometidas a una artroplastia total de cadera con endoprotesis, usar ACOD en comparación a HBPM no cambia el riesgo de tromboembolismo pulmonar
Trombosis venosa profunda	RR 0,56 (0,39 a 0,79) -- 39.994 pacientes/ 37 ensayos	6 por 1000	3 por 1000	3 menos (4 a 1 menos)	⨁⨁⨁⨁ Alta	En personas sometidas a una artroplastia total de cadera con endoprotesis, usar ACOD en comparación a HBPM reduce el riesgo de trombosis venosa profunda
Evento de sangrado mayor	RR 1,03 (0,79 a 1,35) -- 46.382 pacientes/ 37 ensayos	8 por 1000	8 por 1000	0 menos (2 menos a 3 más)	⨁⨁⨁⨁ Alta	En personas sometidas a una artroplastia total de cadera con endoprotesis, usar ACOD en comparación a HBPM no cambia el riesgo de sangrado mayor
Adherencia al tratamiento	No fue medido en los estudios.				--	--

IC 95%: Intervalo de confianza del 95%.
RR: Riesgo relativo.
GRADE: Grados de evidencia *Grading of Recommendations Assessment, Development and Evaluation*.
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Fecha de elaboración de la tabla: Noviembre, 2019.

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Anexo 1: estrategia de búsqueda

#1 (((hip* OR acetabular* OR femoral) AND (arthroplast* OR replace* OR prosthe* OR implant*)) OR THA OR THR)

#2 (((direct* OR new* OR target* OR "non-vitamin K" OR "non vitamin K") AND (anticoag* OR "anti-coagulant" OR "anti-coagulants") AND oral*) OR doac OR doacs OR noac OR noacs OR tsoac OR tsoacs) OR (oral* AND (direct AND thrombin)) OR ximelagatran* OR Exanta OR Exarta OR dabigatran* OR Pradaxa OR ((direct* OR oral*) AND ("factor xa" OR fxa)) OR rivaroxaban* OR Xarelto OR apixaban* OR Eliquis OR edoxaban* OR DU176b OR "DU-176b" OR "DU 176b" OR Savaysa OR Lixiana OR betrixaban* OR PRT054021 OR PRT064445 OR Bevyxxa OR darexaban* OR ym150 OR "ym-150" OR "ym 150" OR letaxaban* OR TAK442 OR "TAK-442" OR "TAK 442" OR eribaxaban* OR PD0348292 OR "PD-0348292" OR "PD 0348292"

#3 #1 AND #2