

Major Bleeding and Hemorrhagic Stroke  
With Direct Oral Anticoagulants in Patients  
With Renal Failure

Systematic Review and Meta-Analysis of Randomized Trials

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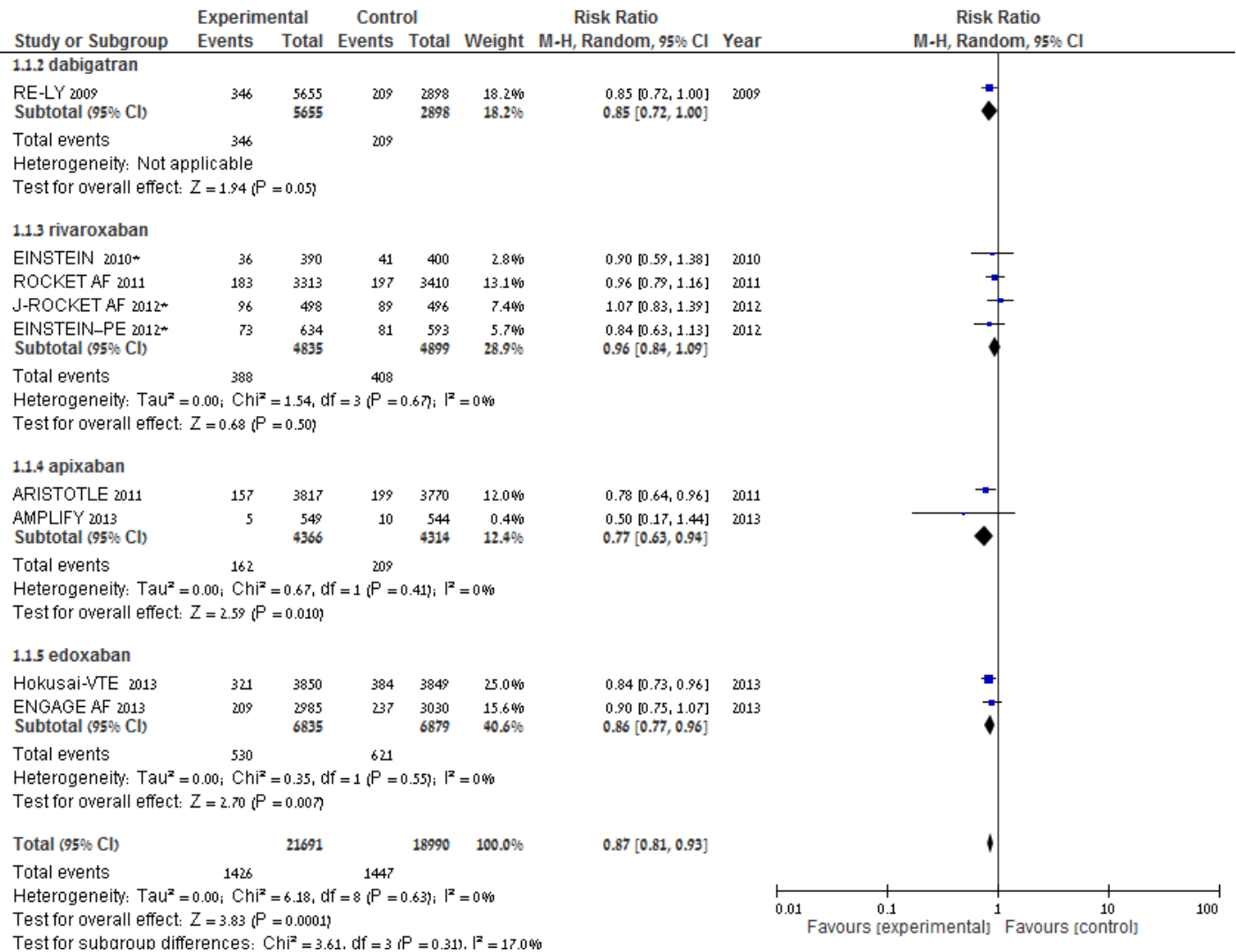
[(apixaban OR rivaroxaban OR dabigatran OR edoxaban OR NOAC) AND (Phase III)] OR [(apixaban OR rivaroxaban OR dabigatran OR edoxaban OR NOAC) AND (Controlled clinical trial OR random\* OR blind)]

**e-Table 1:** Risk of bias.

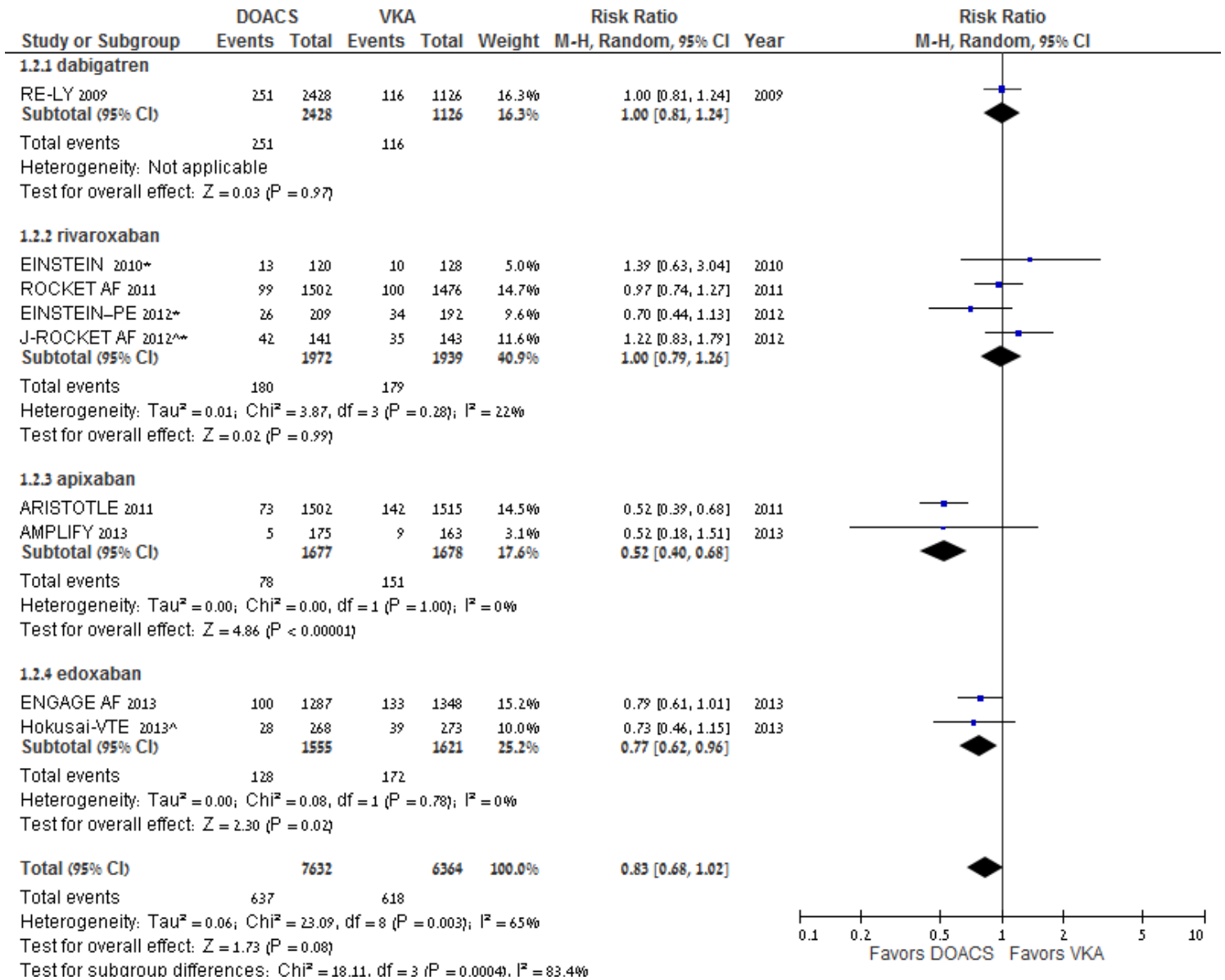
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Rocket AF 2011	+	+	+	+	+	+	+
Einsten 2010	+	+	-	-	+	+	+
Einsten PE 2010	+	+	-	-	+	+	+
J Rocket AF 2012	+	+	+	+	+	+	+
Aristotle 2011	+	+	+	+	+	+	+
Amplify 2013	+	+	+	+	+	+	+
Hokusai VTE 2013	+	+	+	+	+	+	+
Engage AF 2013	+	+	+	+	+	+	+
	random sequence generation	allocation concealment	blinding of participants and personal	blinding of outcome assesment	incomplete outcome data	selective reporting	other bias

**e-Figure 1:** major bleeding in DOAC vs VKA for patients with (A), eCrCl  $r > 50$  to  $< 80$  ml/min ; (B) eCrCl  $< 50$  ml/min:

A.



B.

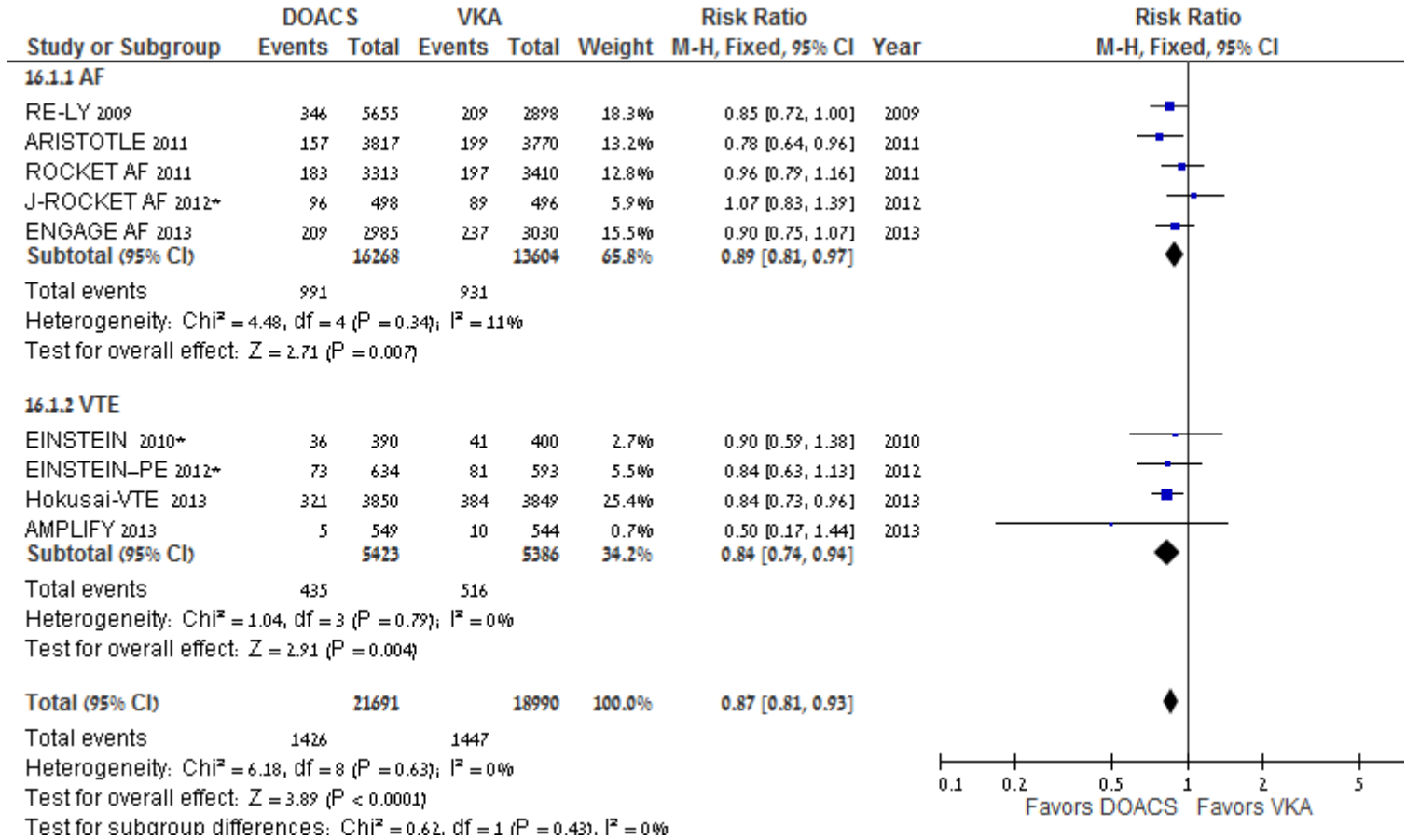


\* major bleeding and clinically relevant non major bleeding

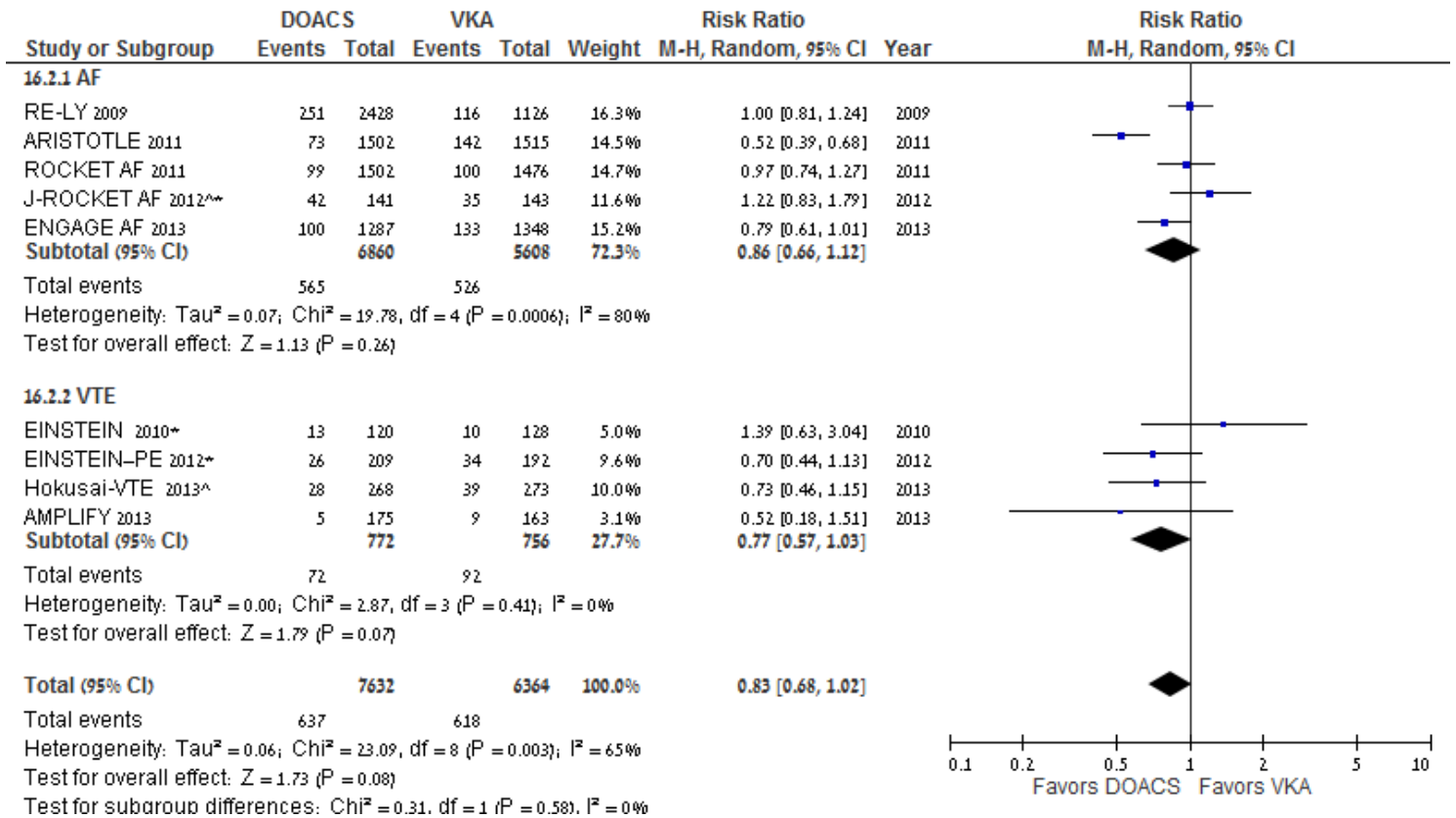
^ eCrCl >50

**e-Figure 2:** sensitivity analysis, DOAC vs VKA for patients with mild renal insufficiency according to treatment indication: (A) eCrCl >50 to <80 ml/min ; (B) eCrCl < 50ml/min:

A.



B.



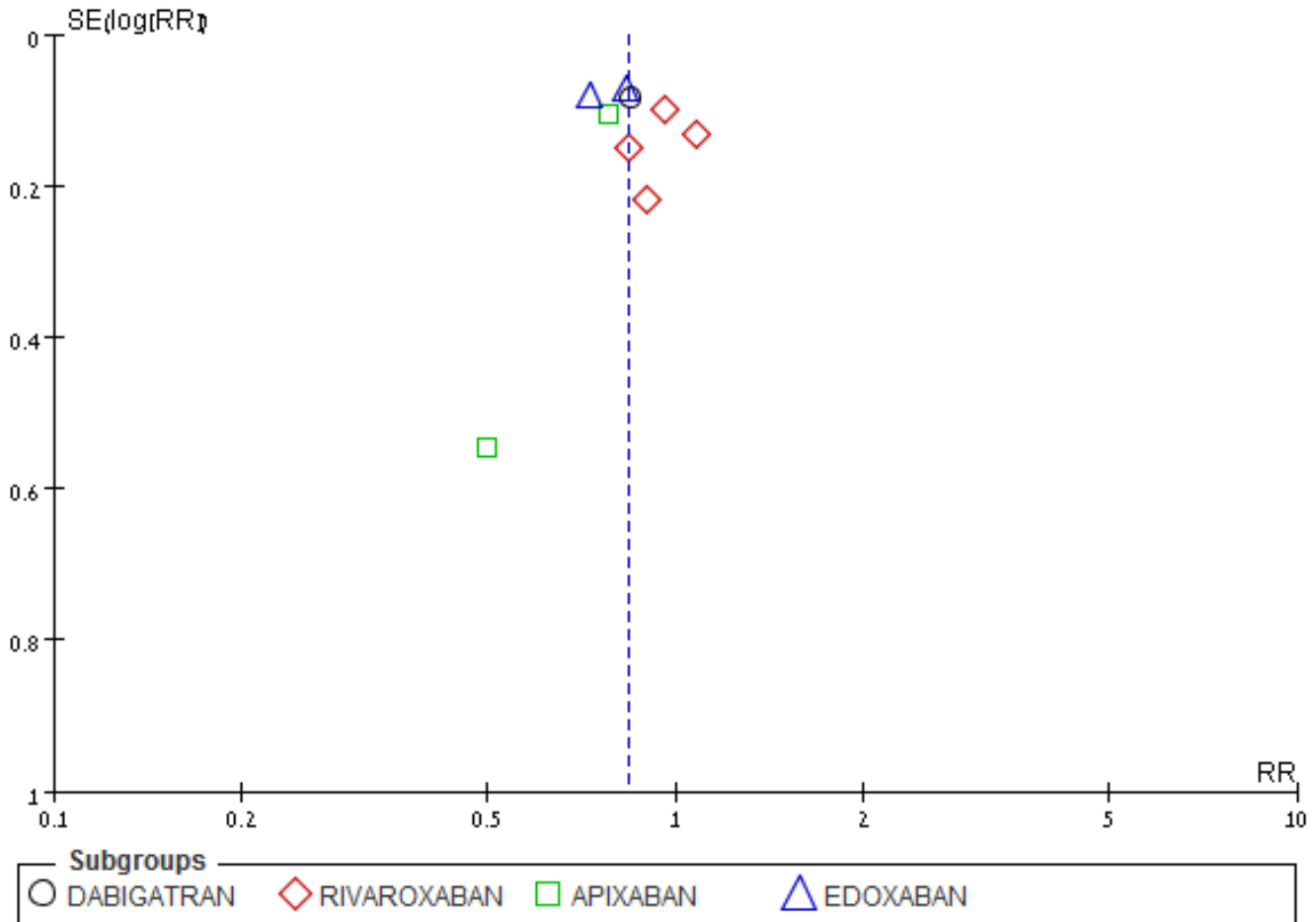
\*major bleeding and clinically relevant non major bleeding.

<sup>^</sup> eCrCl >50

**e-Figure 3:** Assessment of publication bias for each endpoint, the funnel plots displays a measure of study size on the vertical axis as a function of effect size on the horizontal axis.

(A) Comparison of major bleeding in DOAC vs VKAs in patients with eCrCl >50 to <80 ml/min ; (B) eCrCl < 50ml/min

A.



B.

