King's Thrombosis Centre

KING'S HEALTH PARTNERS

Pioneering better health for all

Prevention and management of venous thrombosis in patients with cirrhosis

Prof Lara Roberts

Consultant Haematologist &

Honorary Professor of Thrombosis and Haemostasis

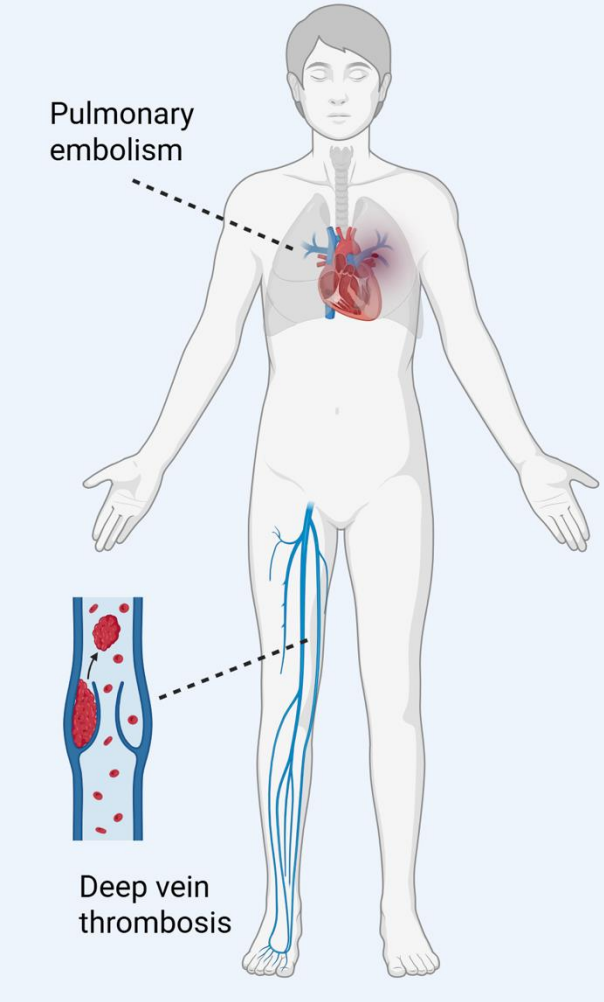
VTE Exemplar Centres

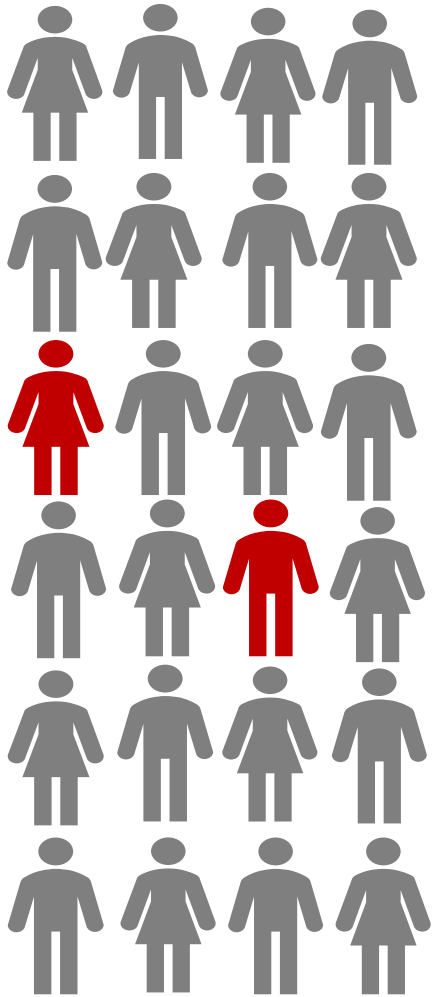
Providing leadership in thrombosis care

Disclosures

- Grants / Research support: Medical Research Council, Synnovis
- Honoraria: Chugai, Hemab, Stago, Viatris
- Patents for drugs or devices: None
- Other: None

Venous thrombosis

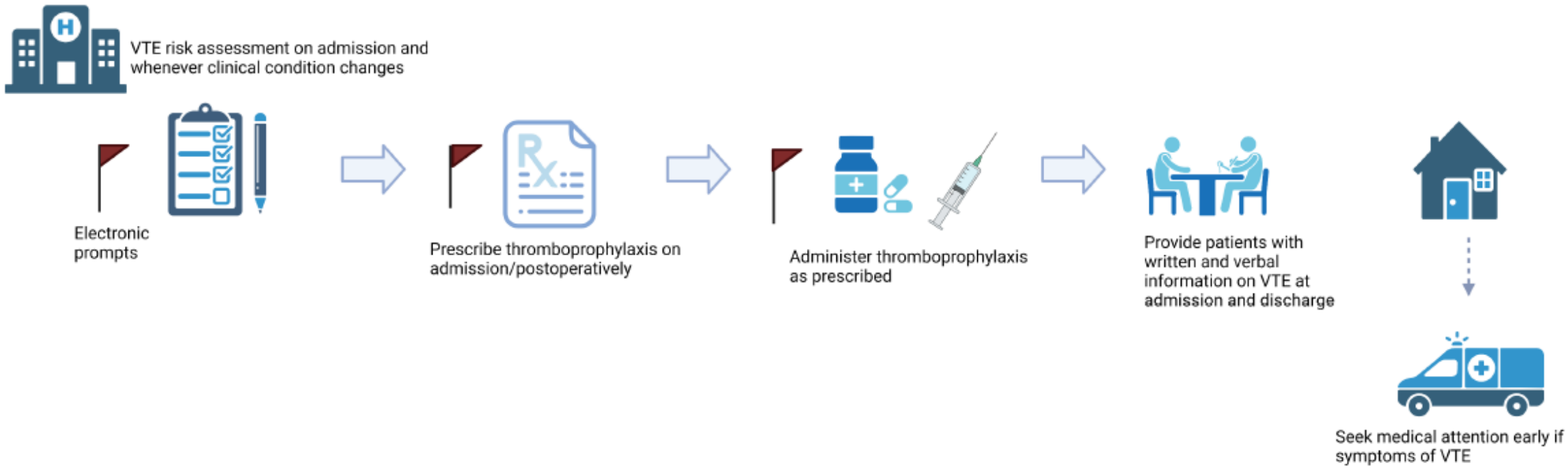




Roberts LN, Arya R and Hunt BJ. *Br J Haematol* 2024

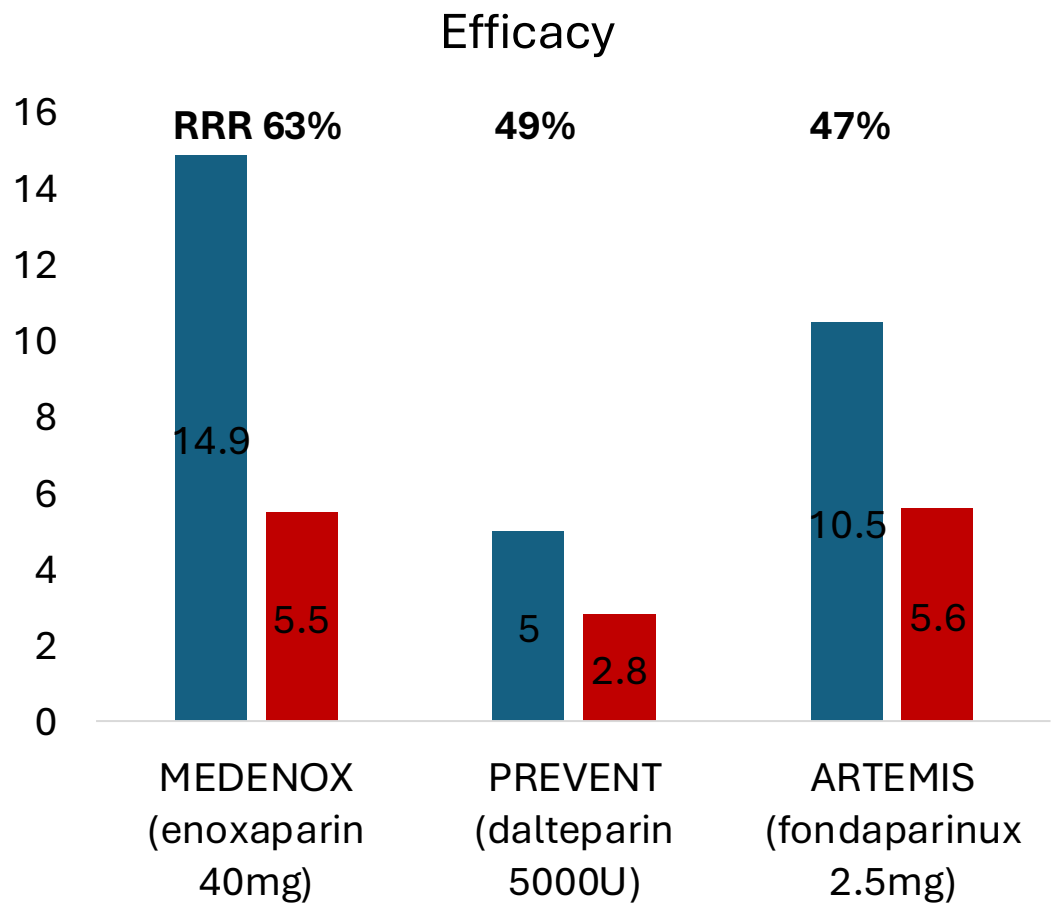
Created in biorender.com

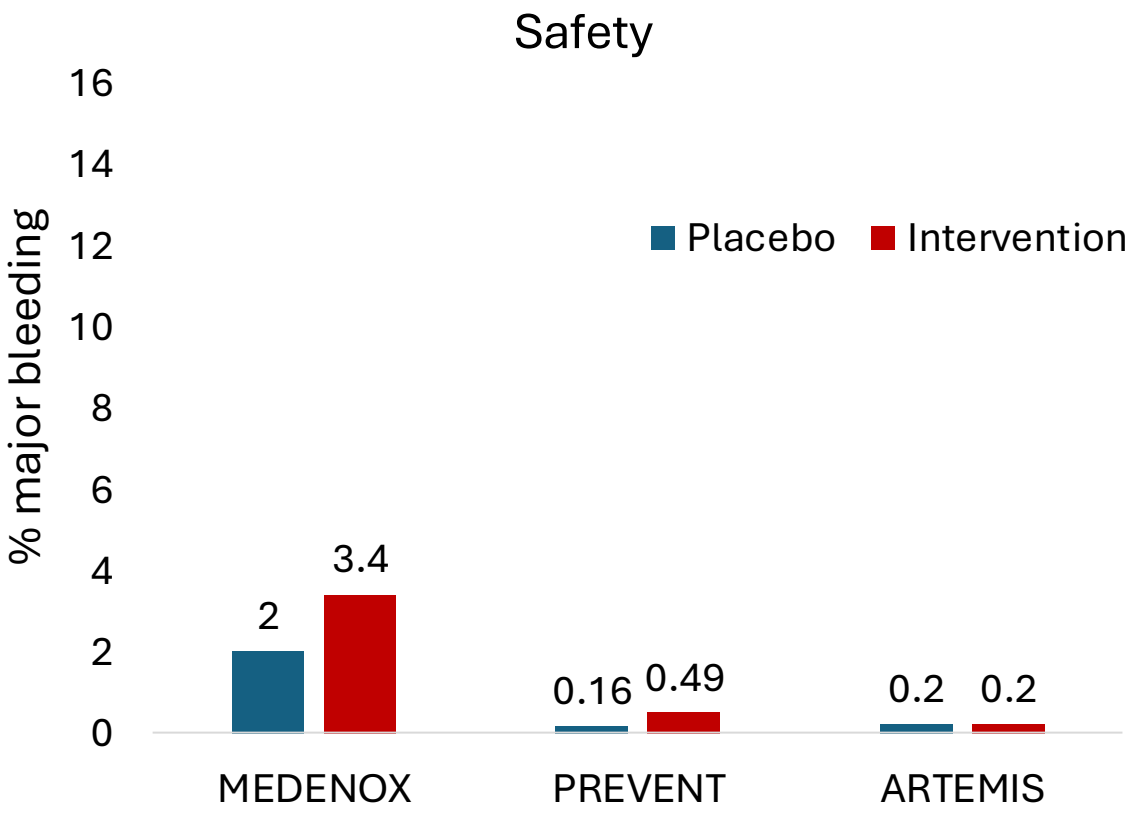
General approach to VTE prevention



Roberts LN *Res Pract Thromb Haemost* 6: e12747.

VTE prevention: Seminal RCTs in medical patients

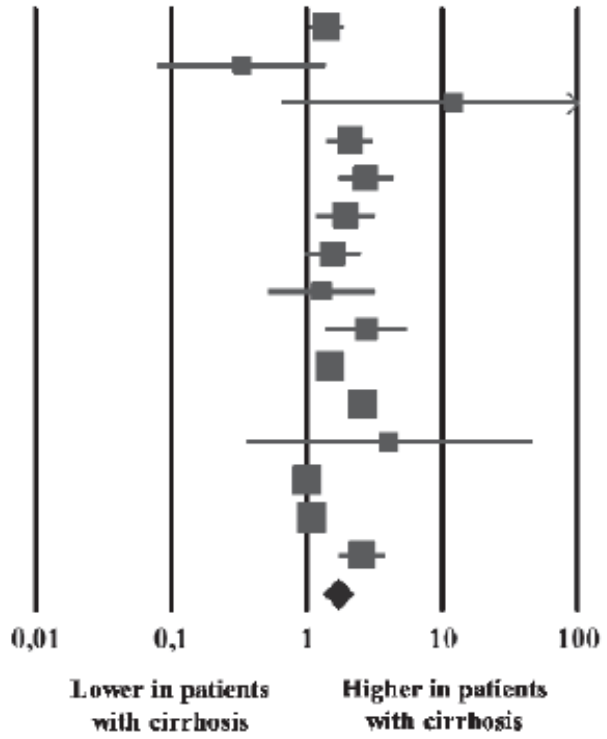




Cohen et al, BMJ 2006
Leizorovicz et al, Circulation 2004
Samama et al, NEJM 1999

DVT/PE in patients with cirrhosis

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Ahmed 2012	1,410	1,045	1,902	2,251	0,024
Al-Dorzi 2013	0,333	0,080	1,392	-1,507	0,132
El Bokl 2014	12,183	0,656	226,356	1,677	0,094
Enger 2014 - DVT	2,090	1,412	3,094	3,683	0,000
Enger 2014 - PE	2,730	1,701	4,382	4,160	0,000
Gulley 2008	1,934	1,173	3,187	2,587	0,010
Ng 2015	1,555	0,969	2,496	1,830	0,067
Ramagopalan 2011 - ORLS1	1,290	0,520	3,200	0,549	0,583
Ramagopalan 2011 - ORLS2	2,760	1,370	5,560	2,841	0,004
Ramagopalan 2011 - England	1,490	1,268	1,751	4,843	0,000
Søgaard 2009	2,578	2,324	2,859	17,909	0,000
Talving 2013	4,067	0,364	45,445	1,139	0,255
Wu 2010 - Compensated LC	1,010	0,961	1,061	0,394	0,694
Wu 2010 - Decompensated LC	1,100	1,028	1,177	2,748	0,006
Yang 2015	2,551	1,724	3,773	4,687	0,000
	1,703	1,333	2,175	4,264	0,000



OR VTE: 1.7 (95% CI 1.3 – 2.3)

OR DVT: 2.0 (1.8 – 2.2)

OR PE: 1.7 (1.0 – 2.6)

Ambrosini et al, Thromb Haemost 2017

VTE risk assessment in patients with cirrhosis

- Limited data to evaluate performance of available risk assessment tools
- PADUA, n = 163 (34% received thromboprophylaxis)
  - High risk, VTE rate 22%; low risk 2%
- IMPROVE, n=98 (76% received thromboprophylaxis)
  - High risk, VTE rate 7.1%; low risk 1.7% (all receiving TP)

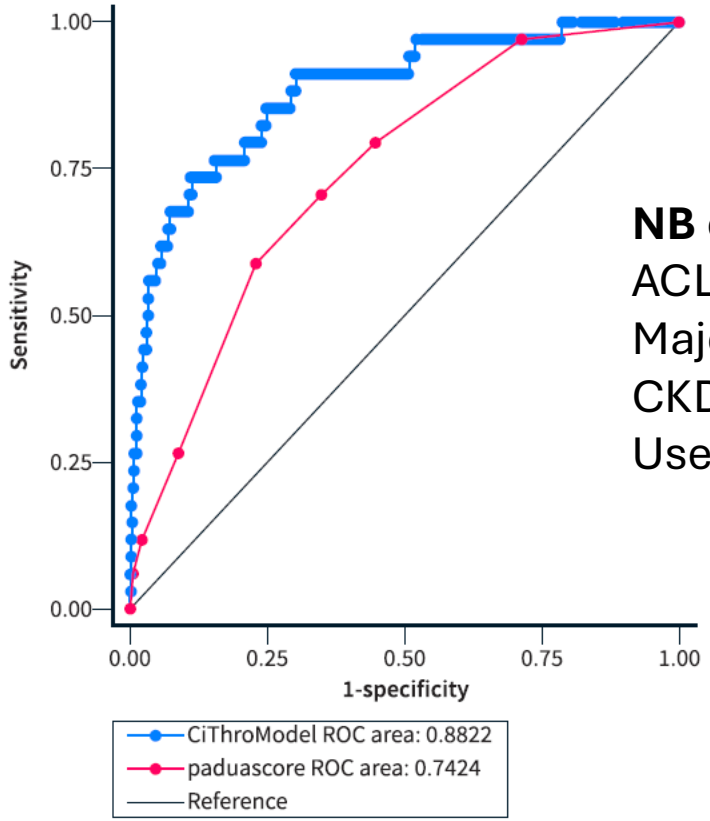
Bogari et al, Thromb Res 2014 ; Davis et al, Eur J Haematol 2020

CiThroModel for VTE risk assessment

n=683, 4.9% DVT/PE during admission

Predictors
Male sex
AKI
Infection
Child Pugh score
Family Hx VTE
Reduced mobility
Admission CRP

majinzin.shinyapps.io/vterisk



NB excluded
ACLF, ICU admission
Major bleeding in prior 30d
CKD, previous VTE, malignancy, HIV,
Use of anticoag/antiplatelets/transfusion in prior 7d

Zanetto et al, United European Gastro J 2025

Baseline characteristics

	VTE (n=34)	No VTE (n=653)	p
MELD score	24 (20-30)	17 (12-23)	<0.001
Child C, %	82	45	<0.001
Bacterial infection, %	61	25	<0.001
Acute kidney injury, %	62	28	<0.001
Hemoglobin, g/dL	8.6 (7.8-10.2)	9.6 (8.1-11.9)	0.02
Creatinine, mmol/L	1.1 (0.7-1.8)	0.8 (0.7-1.3)	0.09
Bilirubin, mg/dL	5.6 (2.6-10.1)	2.4 (1.2-5.2)	<0.001
Albumin, g/L	29.5 (26-33)	31 (27-36)	0.04
Platelet count, $x10^9$/L	73 (48-119)	81 (57-122)	0.2
Thrombocytopenia, %	97	83	0.1
INR	1.8 (1.5-2.2)	1.5 (1.3-1.8)	<0.001
Severe coagulopathy (platelet count <$50x10^9$/L and INR >2), %	15	5	0.009
C-reactive protein, mg/dL	28 (12-48)	9 (3-28)	<0.001

Zanetto et al, United European Gastro J 2025

Efficacy of thromboprophylaxis in patients with cirrhosis

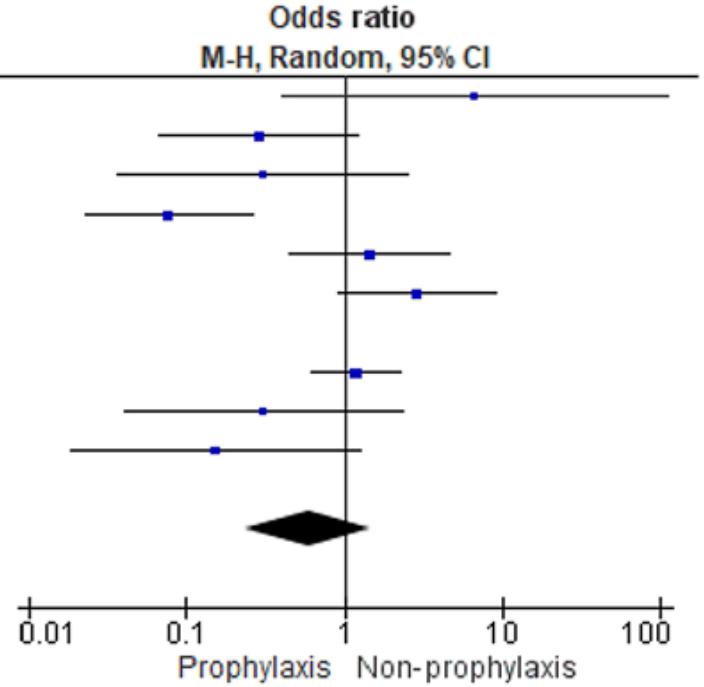
Systematic review and meta-analysis

(B) Forest plot showing odd ratios for VTE occurence

Study or subgroup	Prophylaxis events	Prophylaxis Total	Non-prophylaxis events	Non-prophylaxis Total	Weight	Odds ratio M-H, Random, 95% CI	Year
Aldawood et al.	1	27	1	172	6.5%	6.58 [0.40, 108.41]	2011
Barclay et al.	2	392	21	1189	11.8%	0.29 [0.07, 1.22]	2013
Reichert et al.	1	80	7	176	8.8%	0.31 [0.04, 2.53]	2014
Bogari et al.	3	52	49	111	12.9%	0.08 [0.02, 0.26]	2014
Shatzel et al.	7	296	5	304	13.2%	1.45 [0.45, 4.62]	2015
Moorehead et al.	12	157	4	143	13.2%	2.88 [0.91, 9.13]	2017
Yang et al.	0	61	0	47		Not estimable	2018
Yerke et al.	20	903	17	903	15.5%	1.18 [0.61, 2.27]	2019
Davis et al.	2	74	2	24	9.2%	0.31 [0.04, 2.30]	2019
Alsheikh et al.	1	288	7	313	8.9%	0.15 [0.02, 1.25]	2022
Total (95% CI)		**2330**		**3382**	**100.0%**	**0.59 [0.24, 1.48]**	
Total events	49		113				

Heterogeneity: $\tau^2 = 1.29$; $\chi^2 = 30.35$, $df = 8$ ($P = .0002$); $I^2 = 74\%$

Test for overall effect: $Z = 1.12$ ($P = .26$)



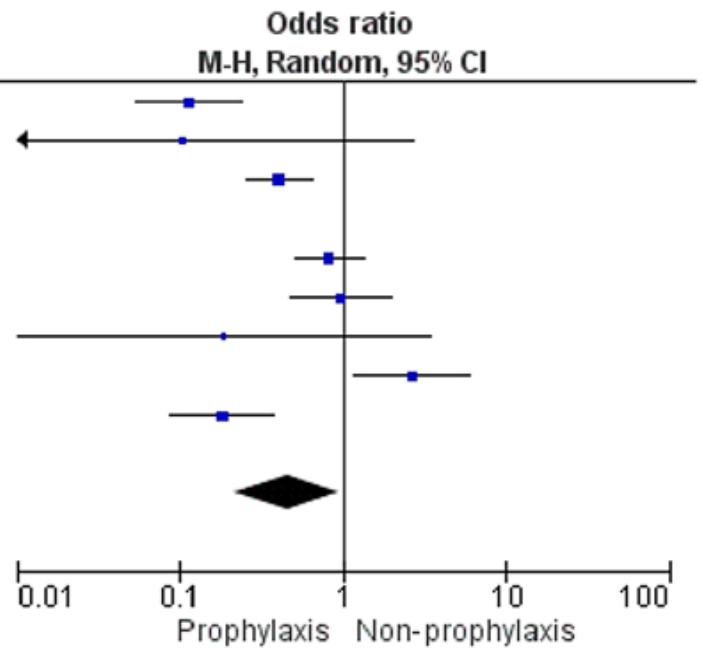
Pasta et al, Liver Int 2023

Safety of thromboprophylaxis in patients with cirrhosis

Study or subgroup	Prophylaxis events	Total	Non-prophylaxis events	Total	Weight	Odds ratio M-H, Random, 95% CI	Year
Alsheikh et al.	8	288	63	313	14.7%	0.11 [0.05, 0.24]	2022
Davis et al.	0	74	1	24	4.1%	0.11 [0.00, 2.67]	2019
Yerke et al.	26	903	62	903	16.1%	0.40 [0.25, 0.64]	2019
Yang et al.	0	61	0	47		Not estimable	2018
Moorehead et al.	47	157	49	143	16.1%	0.82 [0.50, 1.33]	2017
Shatzel et al.	16	296	17	304	15.0%	0.96 [0.48, 1.95]	2015
Bogari et al.	0	52	5	111	4.8%	0.18 [0.01, 3.40]	2014
Reichert et al.	14	80	13	176	14.4%	2.66 [1.19, 5.96]	2014
Barclay et al.	8	392	123	1189	14.8%	0.18 [0.09, 0.37]	2013
Total (95% CI)		**2303**		**3210**	**100.0%**	**0.45 [0.21, 0.96]**	
Total events	119		333				

Heterogeneity: $\tau^2 = 0.86$; $\chi^2 = 49.92$, $df = 7$ ($P < .00001$); $I^2 = 86\%$

Test for overall effect: $Z = 2.06$ ($P = .04$)



Pasta et al, Liver Int 2023

Hospitalisation & risk of portal vein thrombosis

n=623 adm to LITU

Present on adm/<48h

- 13% VTE (85% PVT)

Later (>48h)

- 7.2% VTE (63% PVT)

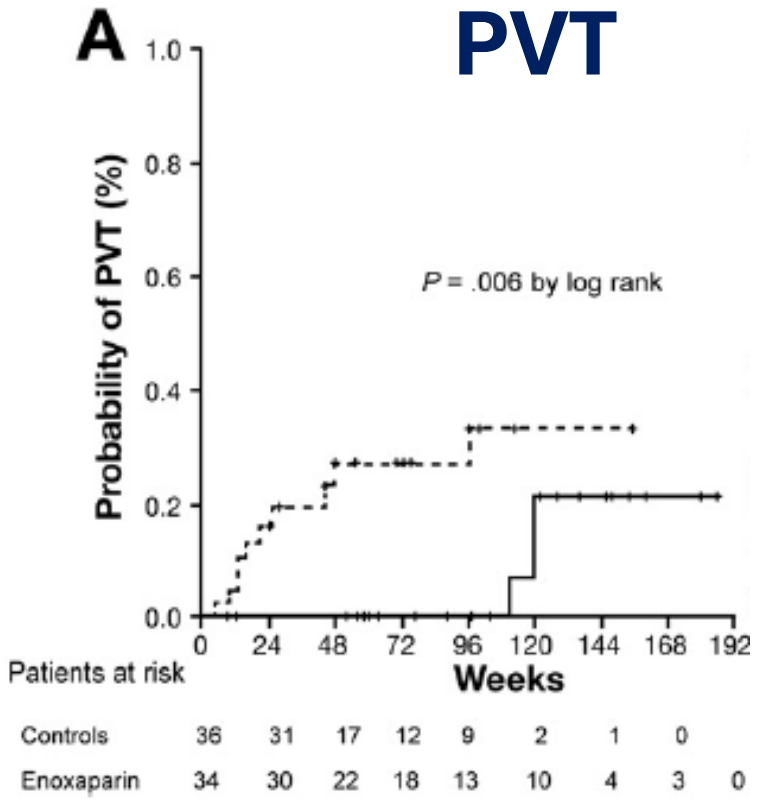
Independent predictor	OR (95% CI)
Non-alcohol aetiology	2.32, 1.39-3.87
HCC	2.79, 1.49 – 5.21

Independent predictor	OR (95% CI)
HCC	2.46, 1.11 – 5.43
Sepsis on adm	2.26, 1.19 – 4.27
Cryoprecipitate recd	2.60, 1.33 – 5.10
Bilirubin	0.995, 0.992 -0.998

Ow et al, Thromb Haemost 2021

PVT prevention in ambulatory patients with cirrhosis

- RCT enoxaparin 40mg od vs nil
- n=70
- Inclusion criteria:
  - CPT B7-C10, no acute decompensation in previous 3m
  - No PVT on imaging prior to entry



Villa et al, NEJM 2012

ISTH SSC clinical recommendations

We recommend:

- Against use of thrombocytopenia/prolonged INR as absolute contraindication to anticoagulant thromboprophylaxis

We suggest:

- Use of anticoagulant thromboprophylaxis in line with local protocols
- Use of LMWH or fondaparinux preferred over UFH
  - LMWH preferred over UFH for patients with renal impairment
  - ACLF/critically ill individualised evaluation of risk/benefit

Roberts et al, J Thromb Haemost 2022

Management of VTE

Ideal anticoagulant

Proven efficacy

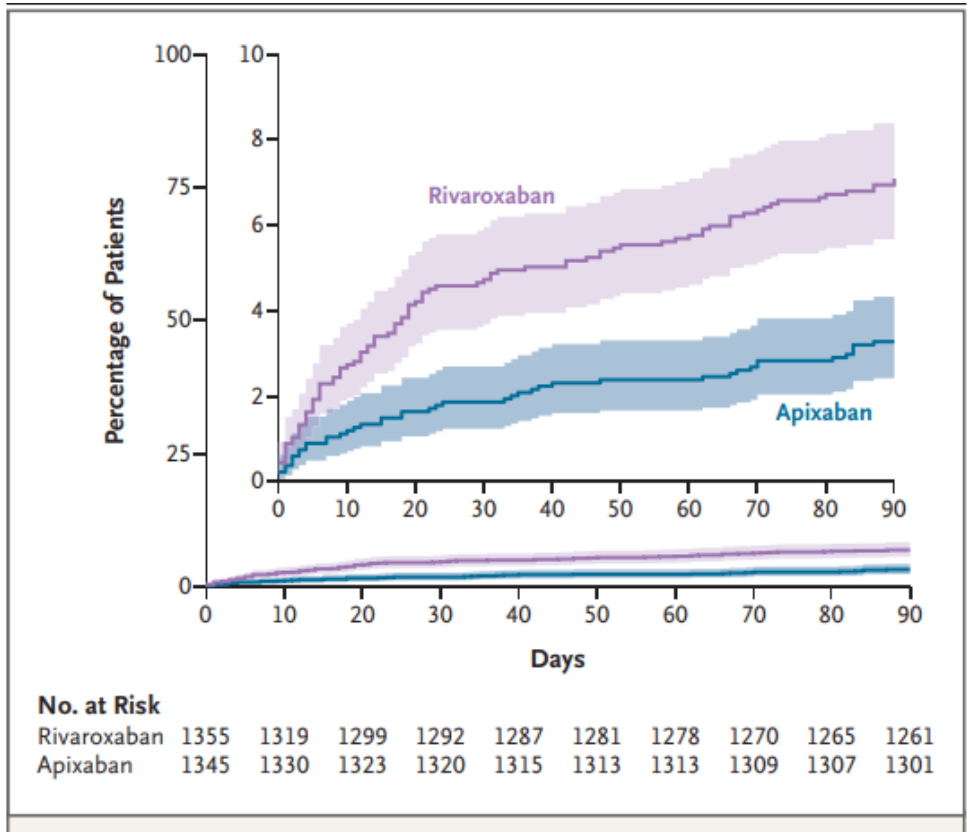
Safety

Generally DOAC > VKA

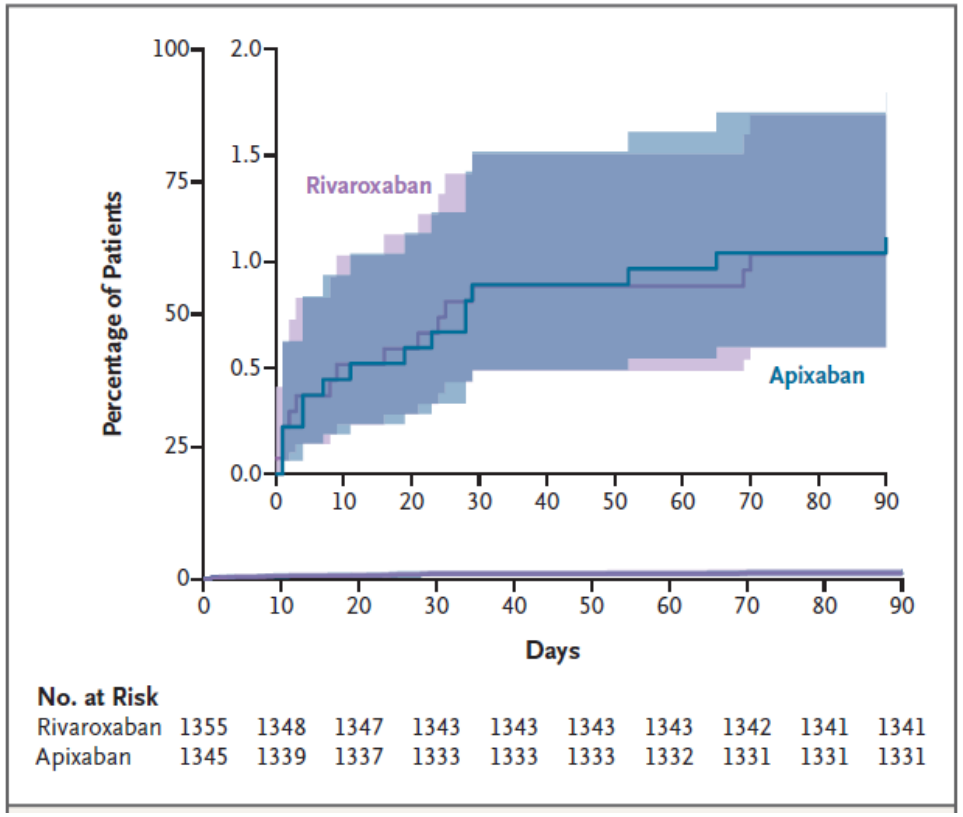
Created in biorender.com

COBRRA trial: apixaban vs rivaroxaban for VTE

Clinically relevant bleeding



Recurrent VTE



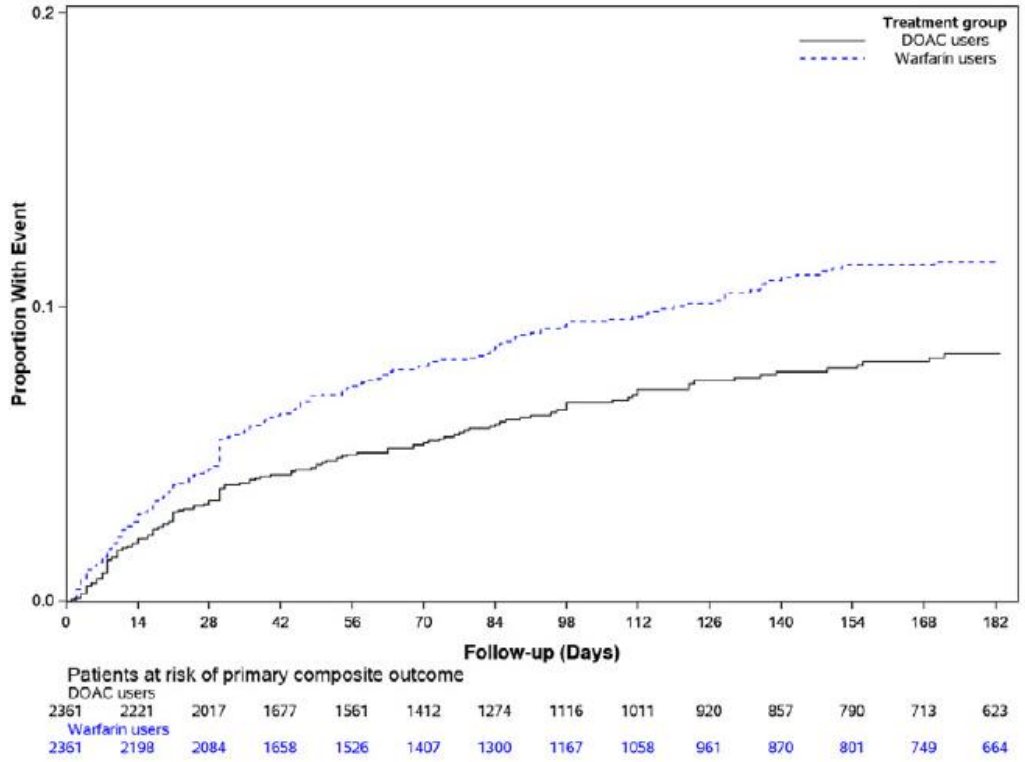
Lower adherence with apixaban 65.7% vs. 75.1%

Castellucci et al, NEJM 2026

Efficacy and safety of DOACs for DVT/PE in CLD

- US Optum database
- Patients with chronic liver disease within 12m of VTE index date
- n=8477 (cirrhosis, n=2449)
  - Warfarin, 5377
  - Rivaroxaban, 2161
  - Apixaban, 895
  - Dabigatran, 83
  - Edoxaban, n=1

1º outcome = composite of hospitalisation with rVTE or MB



Lawal et al, RPTH 2024

Incidence of outcome measures, rate/100py

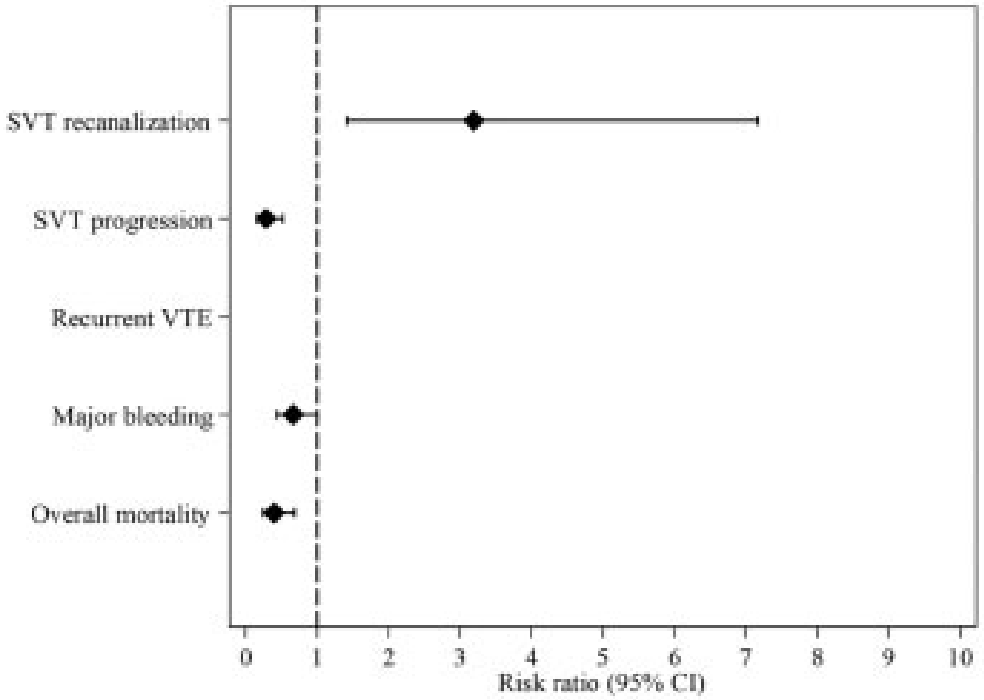
	DOACs*, n= 2361	Warfarin, n=2361	HR (95% CI)
Primary outcome	22.5	32.6	0.72 (0.61-0.85)
Recurrent VTE	6.9	8.5	0.81 (0.59-1.12)
All-cause mortality	29.1	26.8	1.09 (0.92-1.30)
Major bleeding	16.6	29.2	0.69 (0.57-0.84)

*apixaban and rivaroxaban

Lawal et al, RPTH 2024

Anticoagulation for PVT

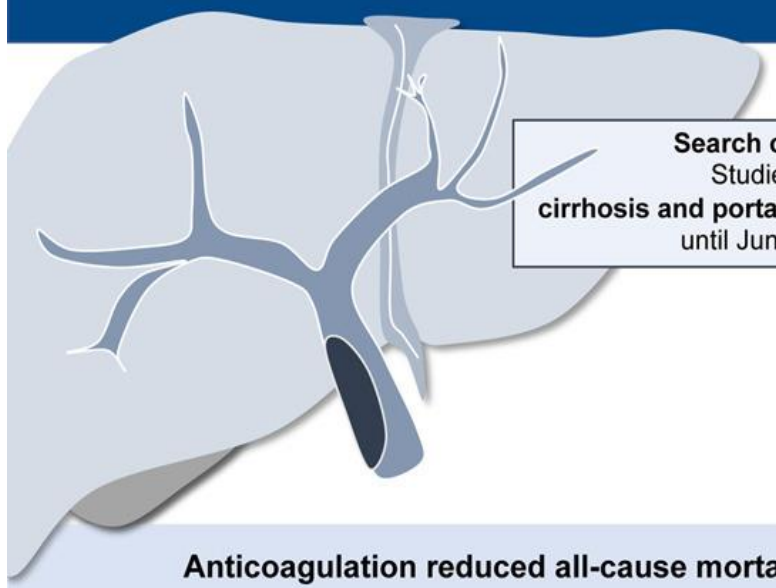
26 studies, 1475 patients



Outcome	Anticoagulated: events (n/N, %)	Untreated: events (n/N, %)	Studies (n)	I^2 (%)	RR (95% CI)
SVT recanalization	195/305 (63.9%)	79/282 (28.0%)	9	80	3.19 (1.42-7.17)
SVT progression	16/224 (7.1%)	44/181 (24.3%)	8	0	0.28 (0.15-0.52)
Recurrent VTE	8/92 (8.7%)	10/57 (17.5%)	1	-	-
Major bleeding	14/218 (6.4%)	20/179 (11.2%)	6	0	0.52 (0.28-0.97)
Overall mortality	21/230 (9.1%)	39/186 (21.0%)	6	0	0.42 (0.24-0.73)

Valeriani et al, Thromb Haemost 2021

The IMPORTAL competing-risk individual patient data meta-analysis



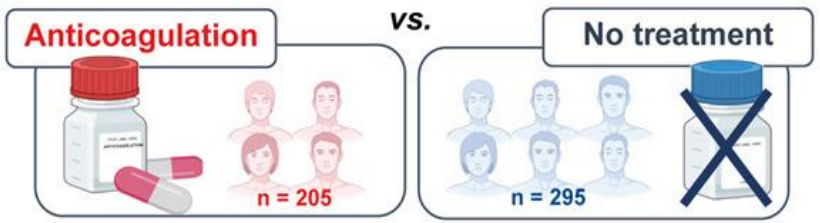
Search criteria:
Studies of
cirrhosis and portal vein thrombosis
until June 2020

Selection
✓ 5 studies
✓ 500 patients

Primary outcome:
All-cause mortality

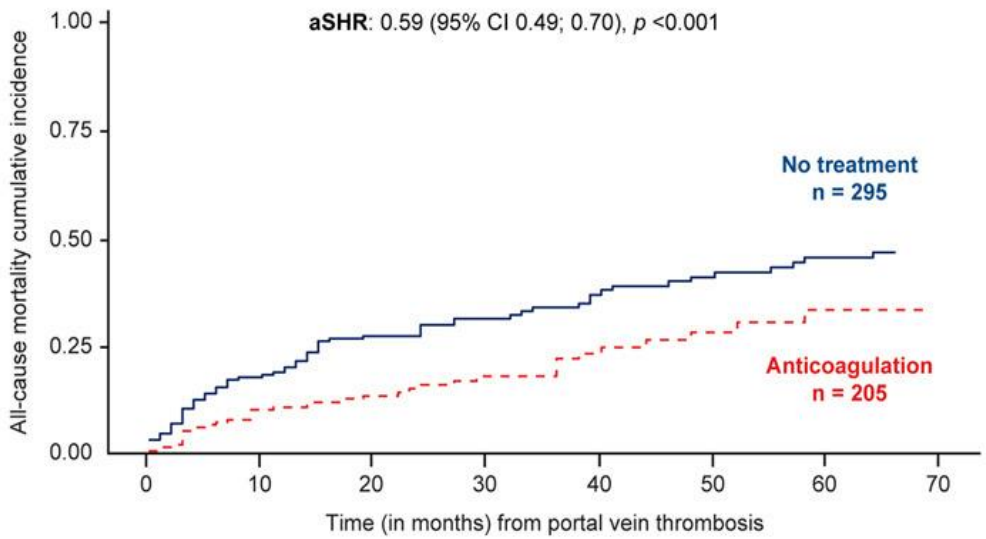
Method:
One-step meta-analysis
Competing-risk model with liver transplantation

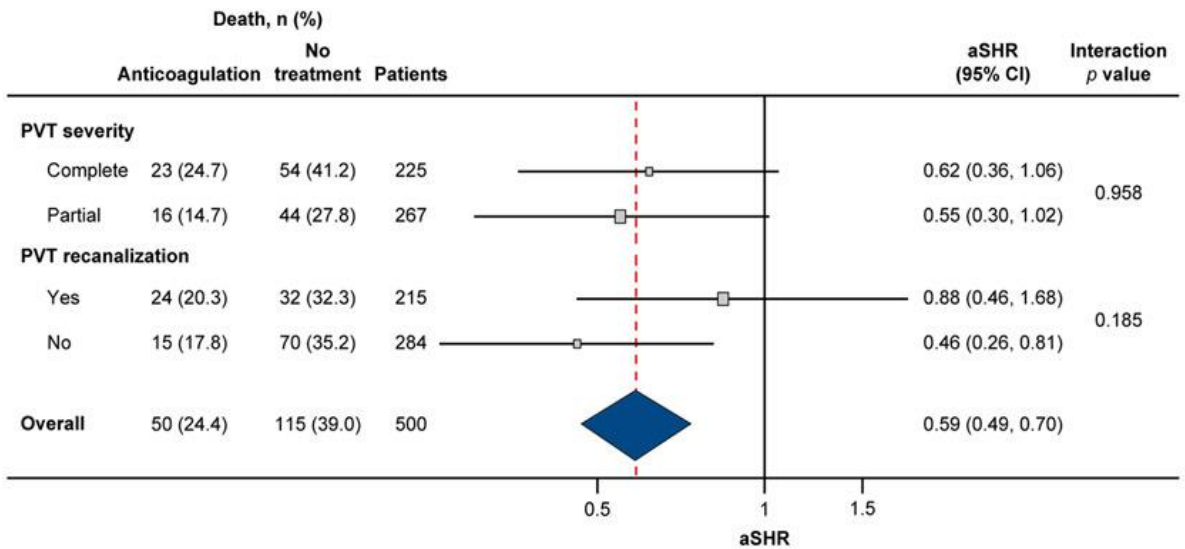
Anticoagulation *vs.* **No treatment**



Anticoagulation reduced all-cause mortality…

…independently of thrombosis severity and recanalization





Guerrero *et al. Journal of Hepatology* 2023 7969-78

IMPORTAL – bleeding events

	Anticoagulant treatment (n=205)	No treatment (n=295)	P
Total bleeding events, N (%)	39 (19.0)	46 (15.6)	0.315
Portal hypertension related bleedings, N (%)	19 (9.3)	41 (13.9)	0.120
Non-portal hypertension related bleedings, N (%)	20 (9.7%)	5 (1.7%)	<0.001

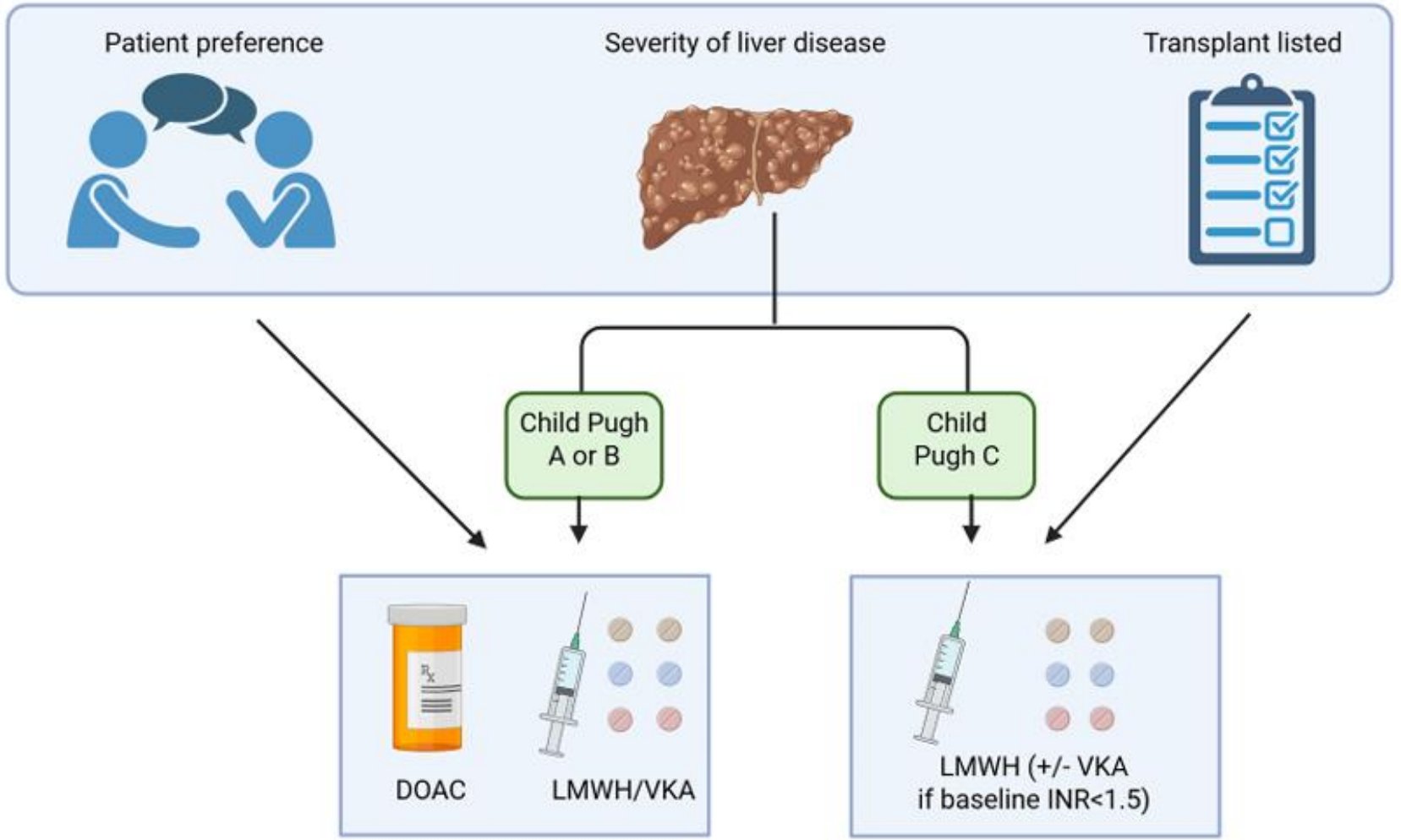
Guerrero *et al*. *Journal of Hepatology* 2023 7969-78DOI: (10.1016/j.jhep.2023.02.023)

Guideline recommendations

Guideline	EASL 2025	ISTH 2024	Baveno VII 2022	AASLD 2021	ACG 2020
Treatment indications	LT candidates - Any PVT Non-LT candidates - >50-100% occlusion - Progression of <50% occlusive PVT or if SMV involved	- Symptomatic & asympt with progression - Treat for ≥ 6 months - Continue long-term for LT candidates - Case by case extension for non-LT candidates	-Recent (<6 mth) thrombosis of PV trunk -Symptomatic PVT -Potential LT candidate -Minimally occlusive PV that is rapidly progressing or with SMV compromise	-Recent (<6 mth) main PVT or SMV thrombosis -Ischemic symptoms	-Acute PVT with complete occlusion -Patients awaiting liver transplant -Chronic PVT with: 1. Progression or SMV involvement 2. Hx of bowel ischemia 3. Inherited thrombophilia

Carlin et al, JTH 2024 ; de Franchis R. J Hepatol 2022;
Northup PG. Hepatology 2021; O'Leary et al, Gastroenterology 2020; Rautou et al, J Hepatol 2025.

Suggested approach to anticoagulation for PVT



Created in BioRender.com

Bell et al, J Thromb Haemost 2026