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In vitro anticoagulant and profibrinolytic effects of factor XI inhibitors asundexian, milvexian and abelacimab in patients with liver disease

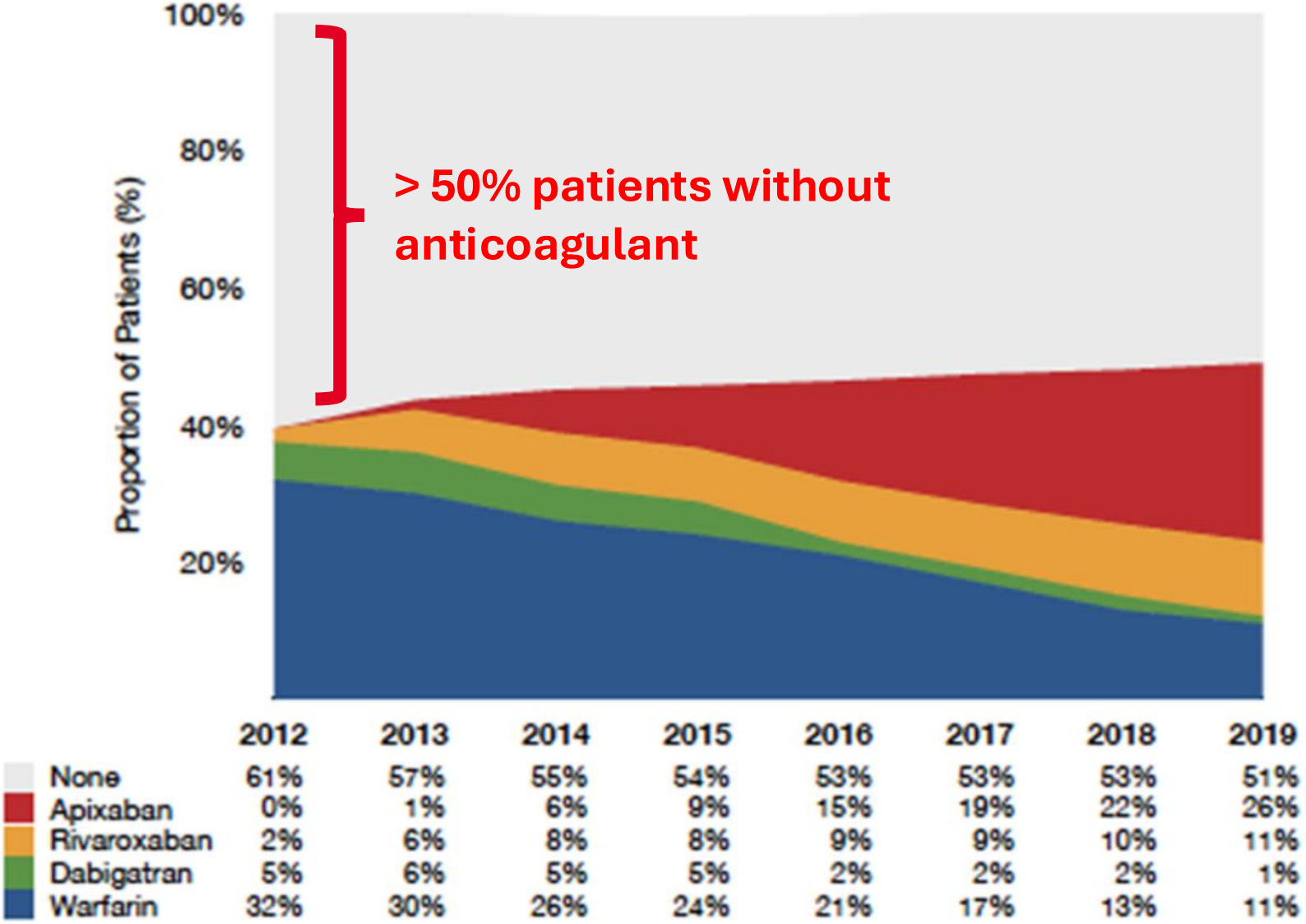
Fynn Elvers, MD

PhD Candidate

University Medical Center Groningen

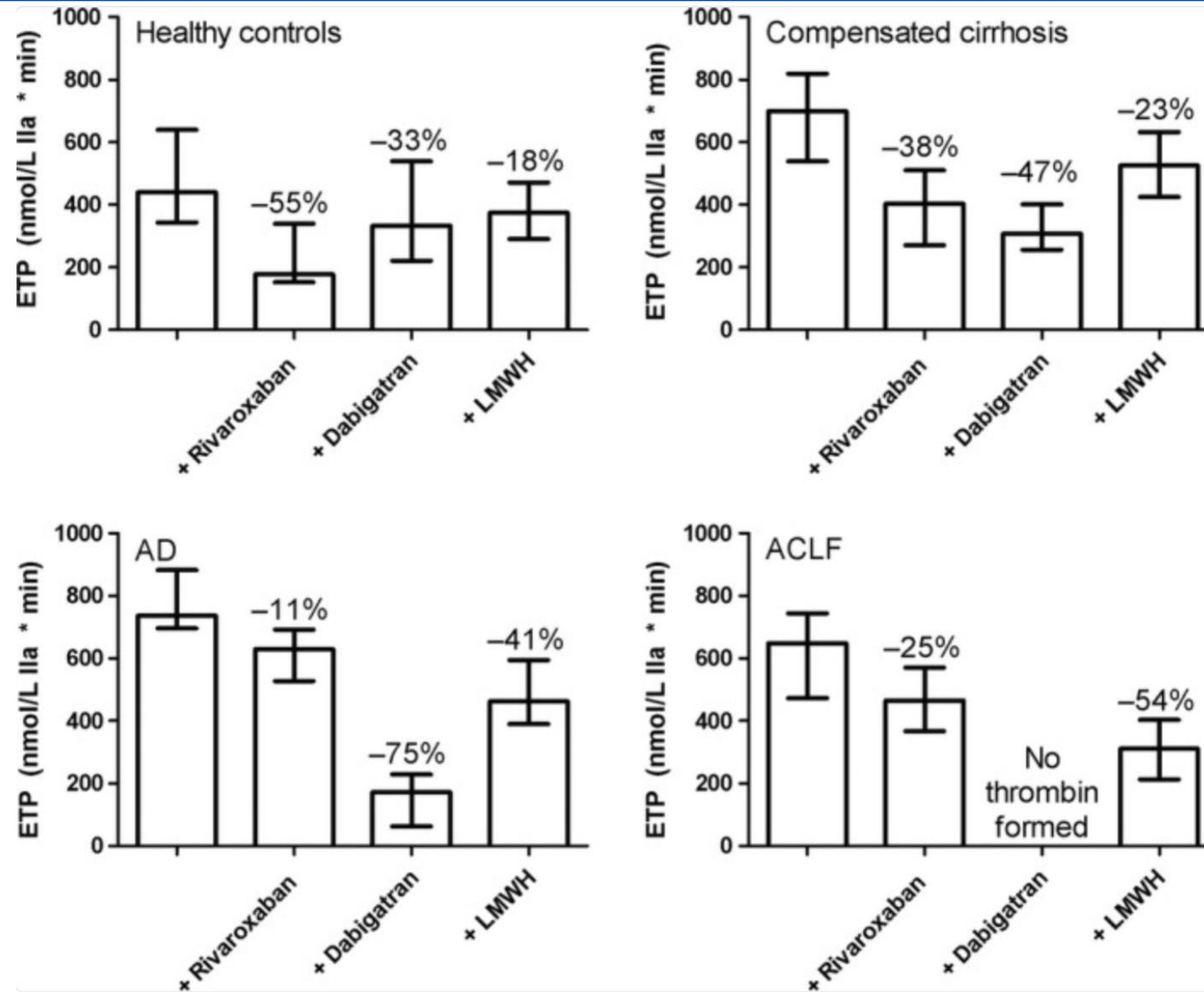


Low anticoagulant prescription rates for thrombosis

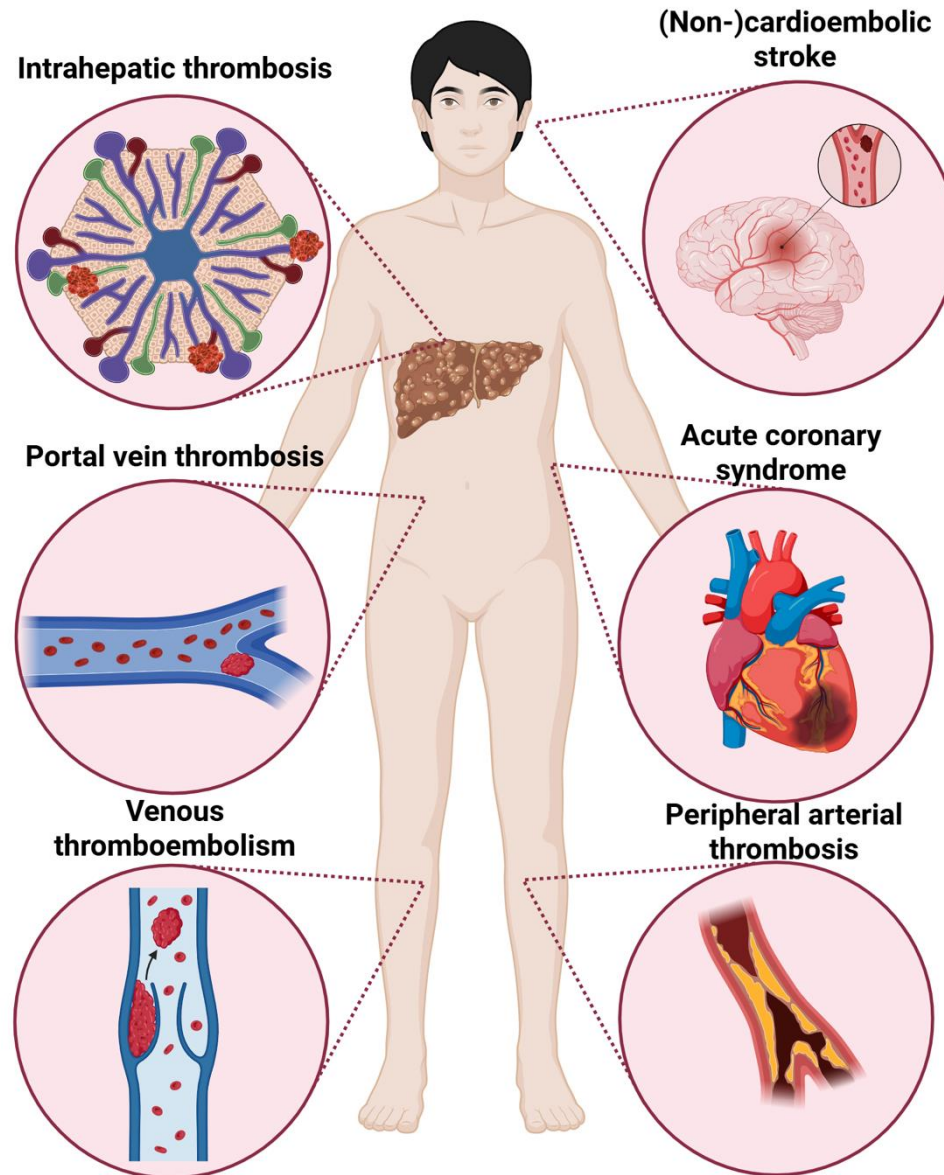


Simon. J Am Heart Assoc. 2023, Fortea. Dig Liver Dis. 2019, Violi. Intern Emerg Med. 2016

Abnormal in vitro anticoagulant effects of LMWH and DOACs



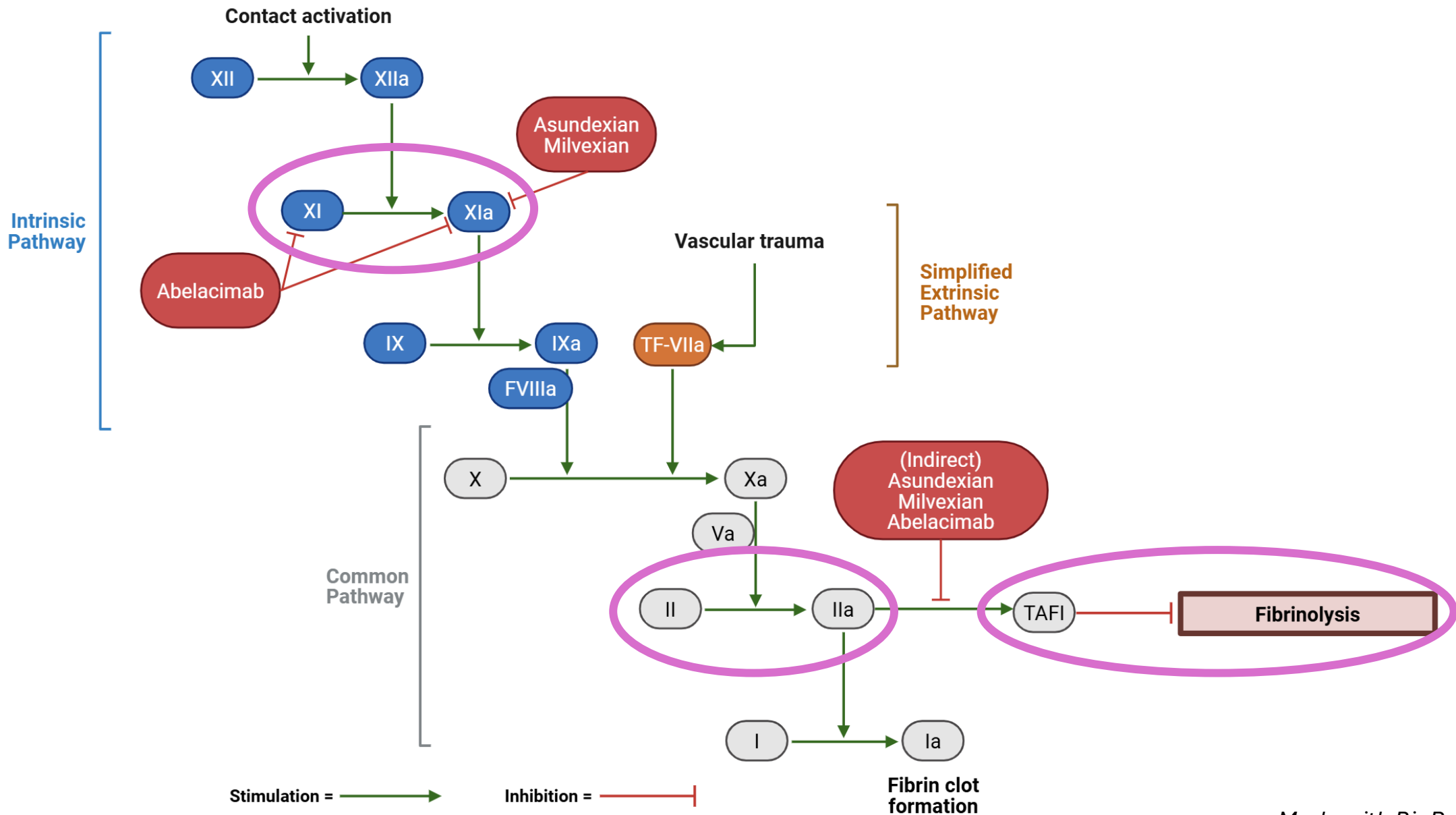
Thrombosis in liver disease requires anticoagulation



Withholding anticoagulants worsens:

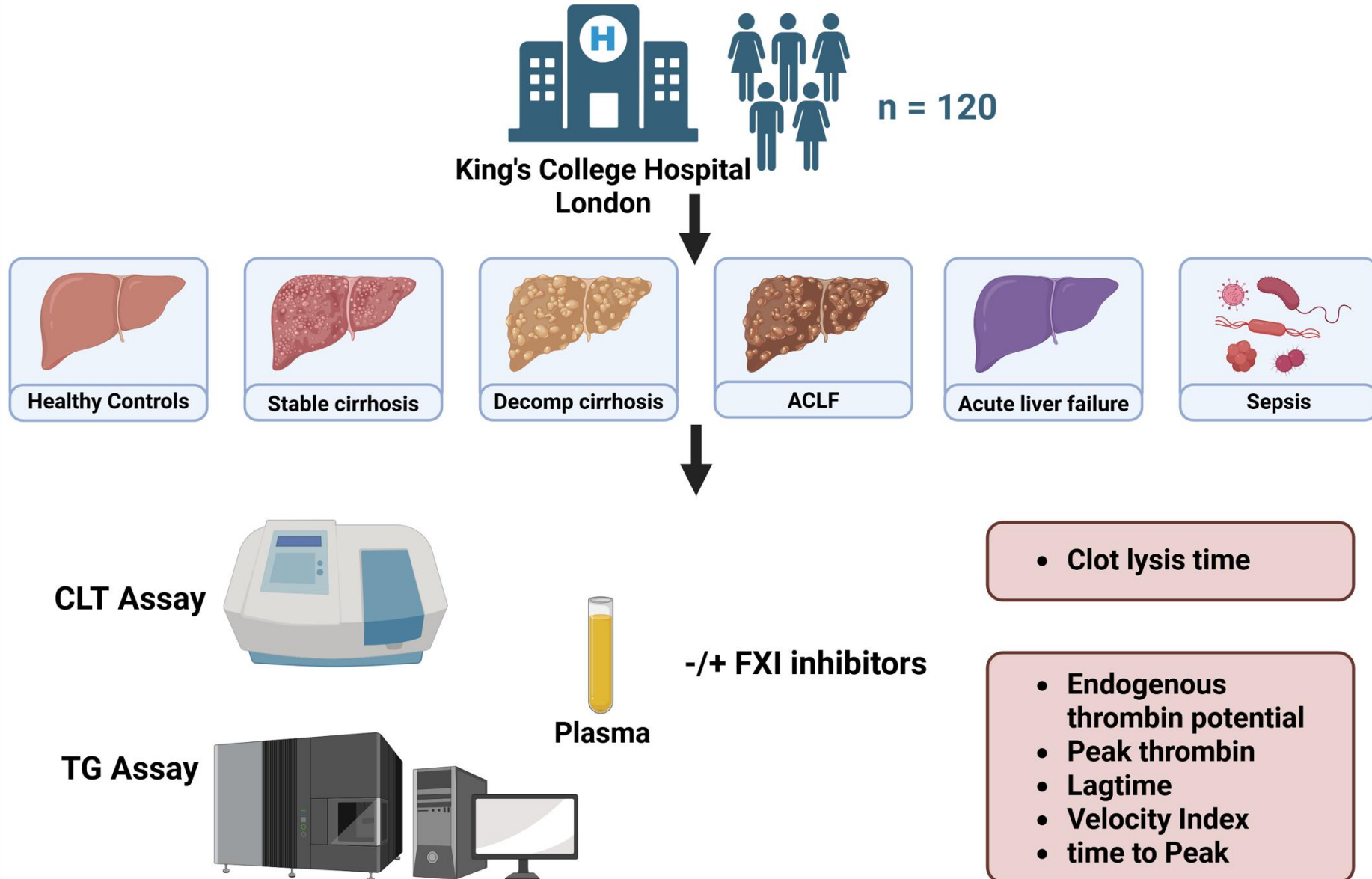
- **Hepatic decompensation**
- **Morbidity**
- **Mortality**

Decoupling thrombosis from hemostasis with Factor XI inhibitors

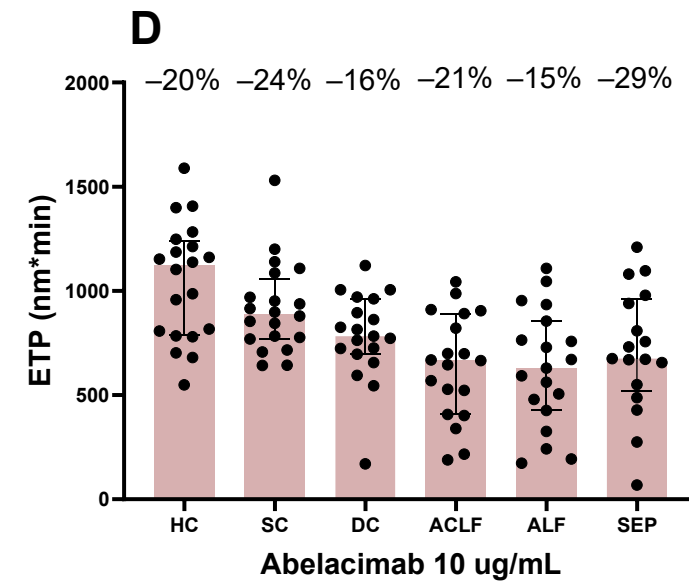
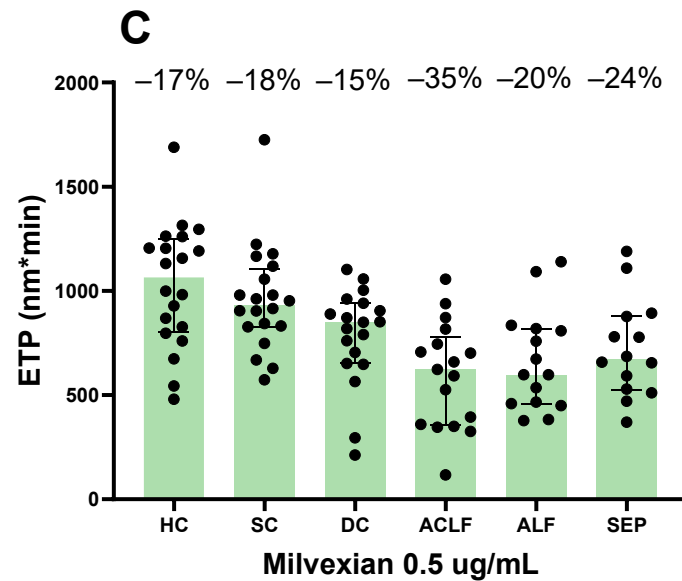
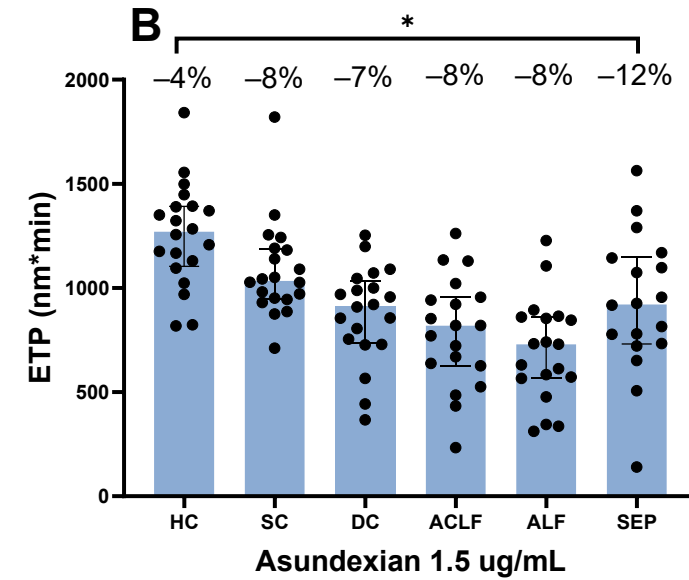
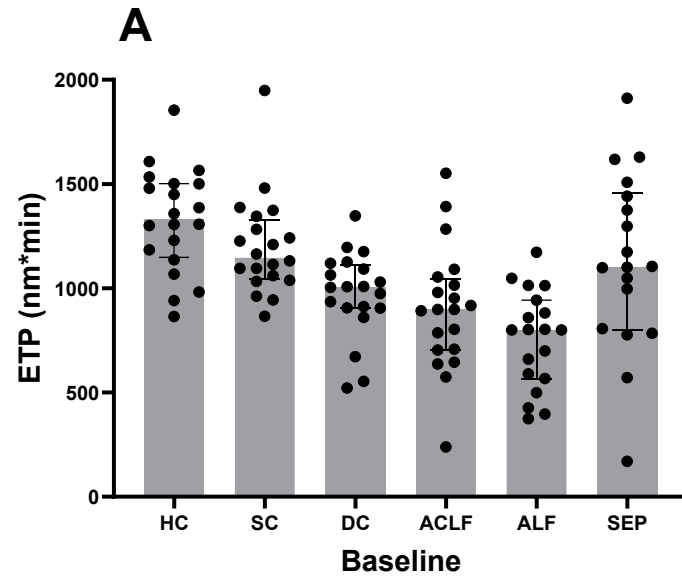


What are the in vitro anticoagulant and profibrinolytic effects of clinically relevant concentrations of asundexian, milvexian and abelacimab in patients with liver disease?

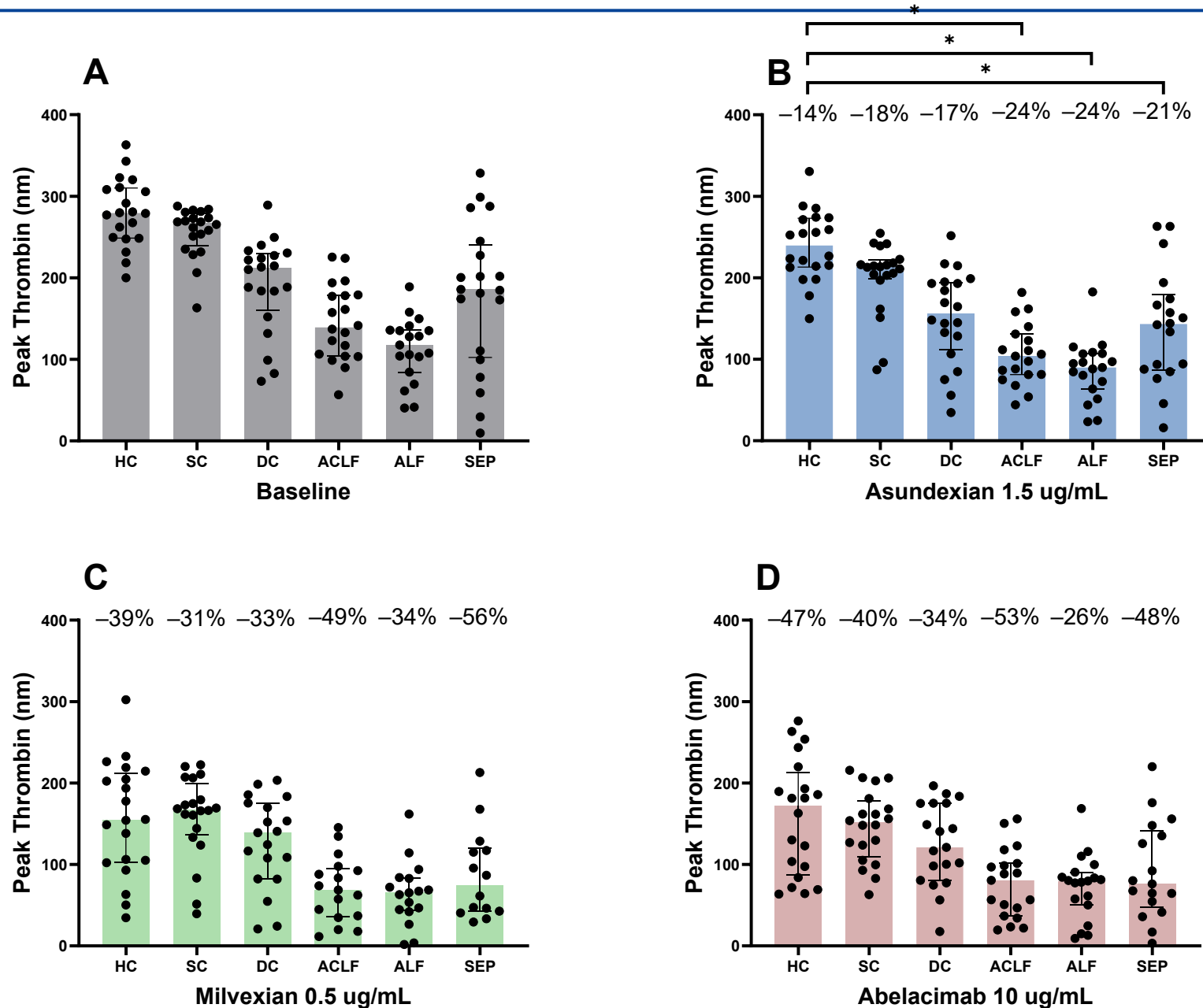
Methods



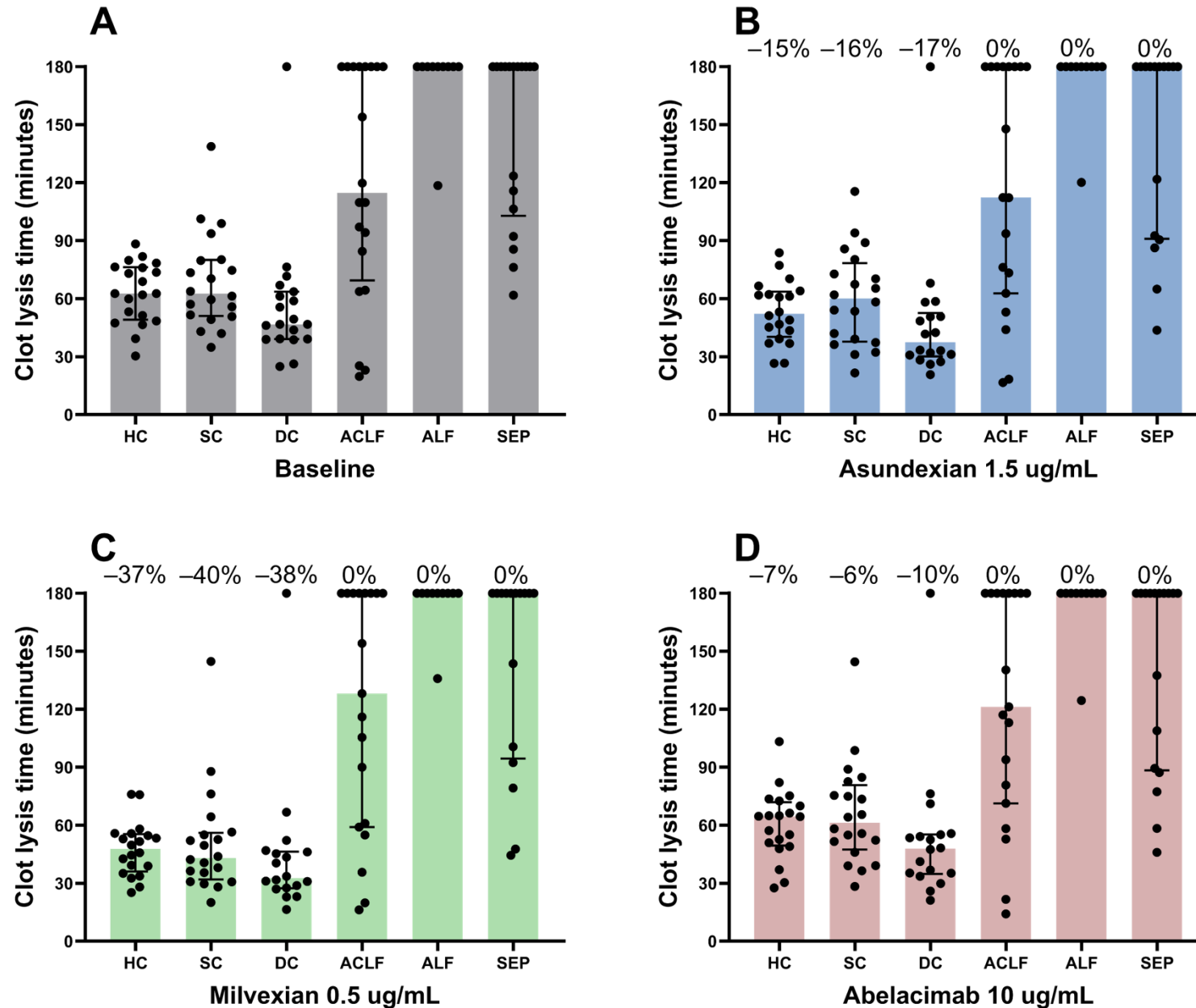
Similar ETP reduction by FXI inhibitors in controls and liver disease



Similar peak thrombin reduction by FXI inhibitors in controls and liver disease



Similar profibrinolytic effects of FXI inhibitors in controls and liver disease



Limitations

- Not accounted for cellular components
- Altered drug metabolism in liver disease
- CLT in ACLF, ALF and sepsis not captured

In summary

1. Similar in vitro anticoagulant and profibrinolytic effects of asundexian, milvexian & abelacimab in stable and decompensated cirrhosis- contrasting current anticoagulants
2. Slightly lower and enhanced anticoagulant effects of FXI inhibitors in ACLF, ALF and sepsis - cautious use
3. More predictable anticoagulation in liver disease with FXI inhibitors – in vivo studies to confirm

Acknowledgments

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Jelle Adelmeijer
Ton Lisman

King's College Hospital

Marilena Stamouli
William Bernal
Vishal C. Patel



References



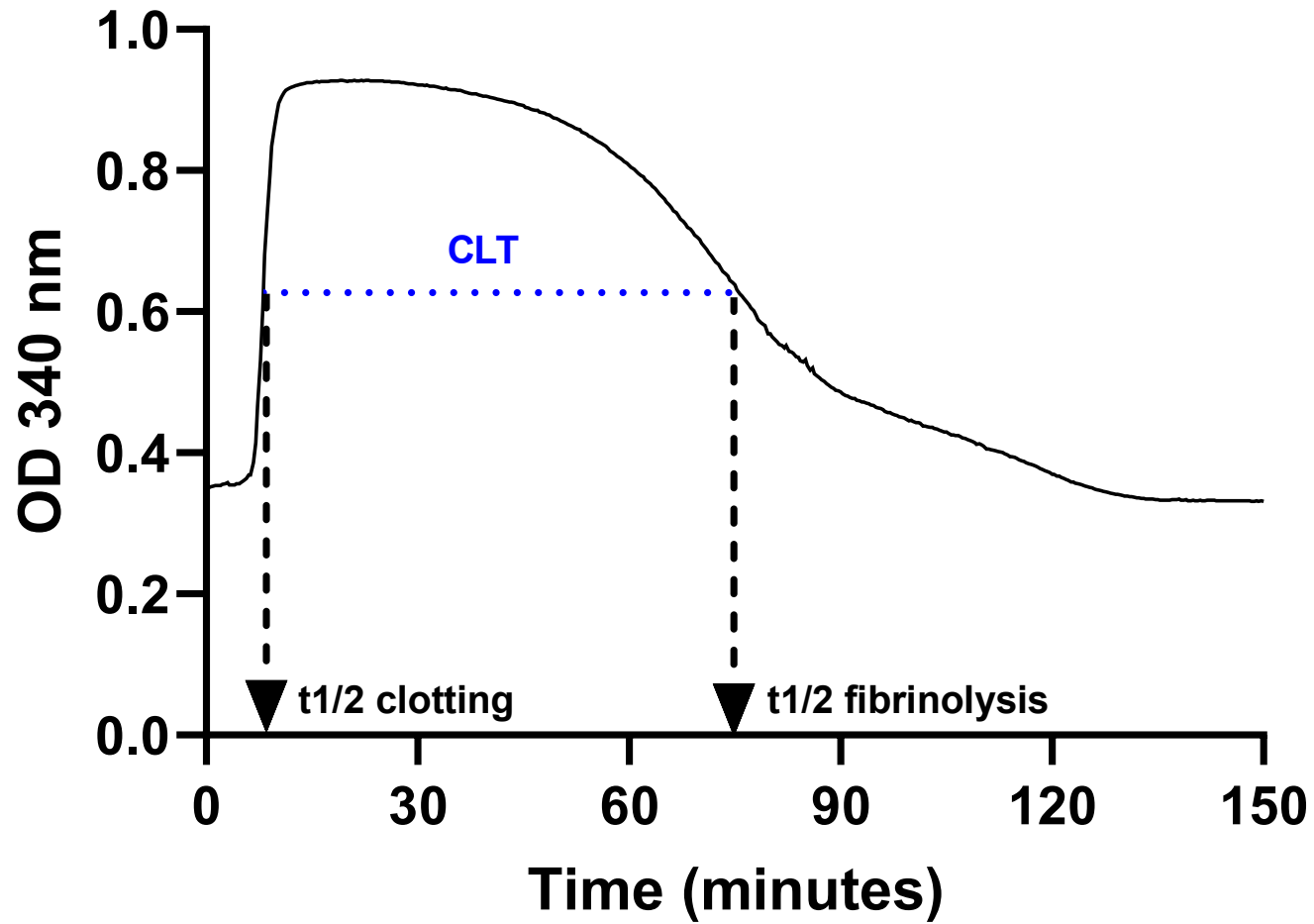
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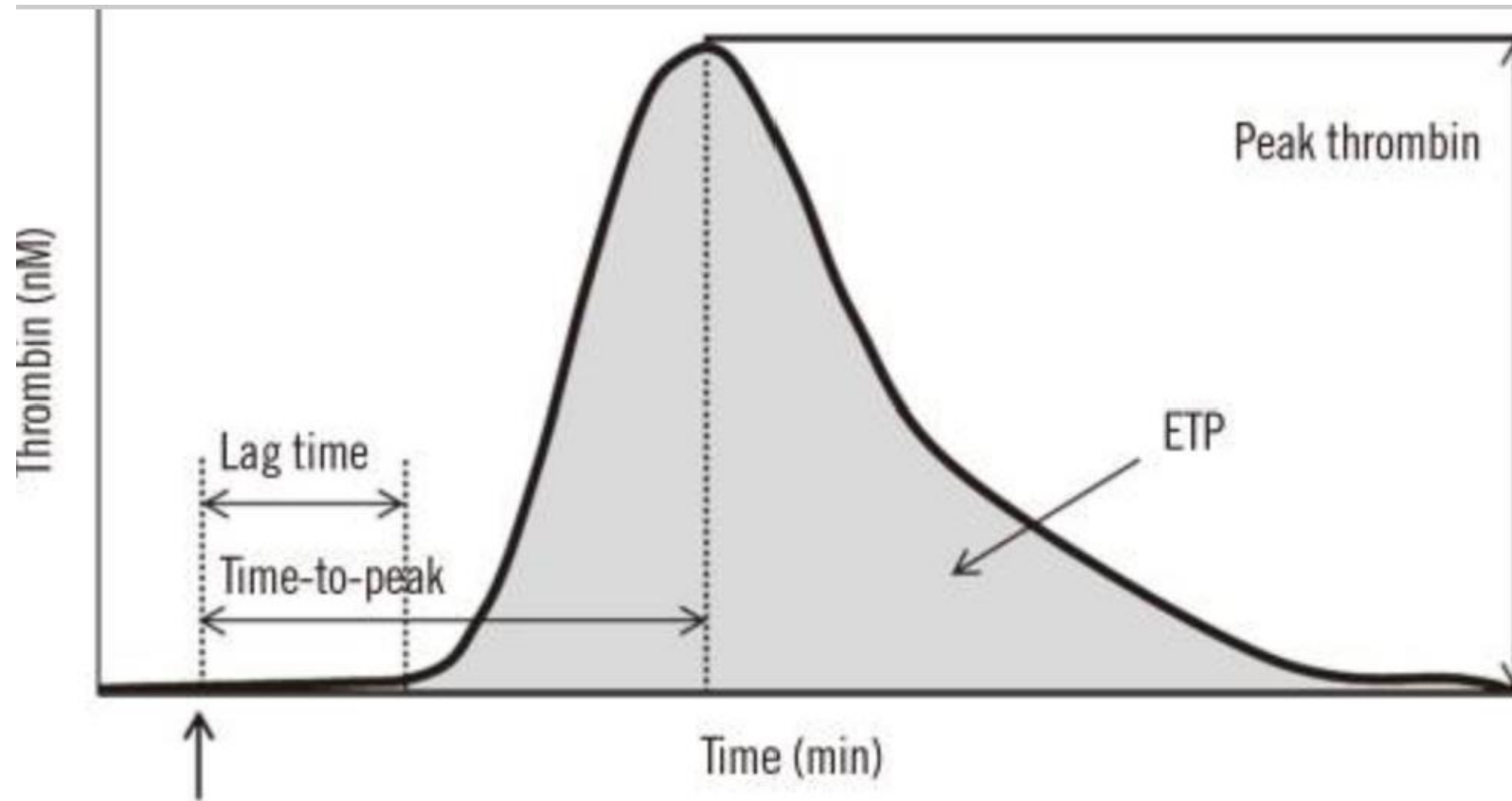
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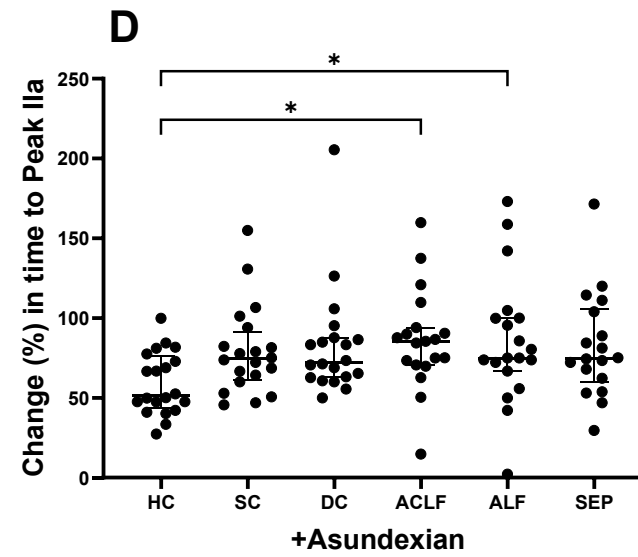
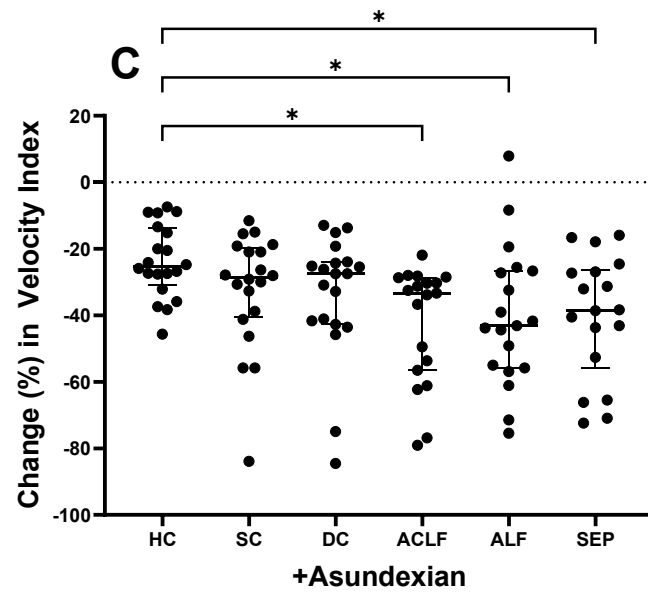
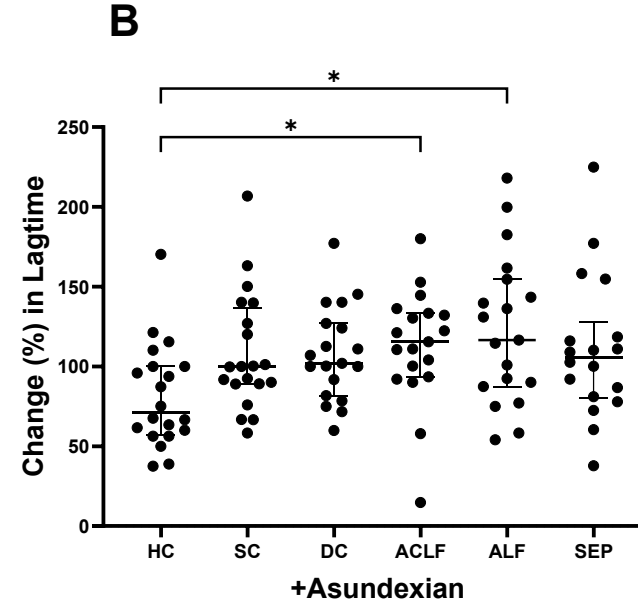
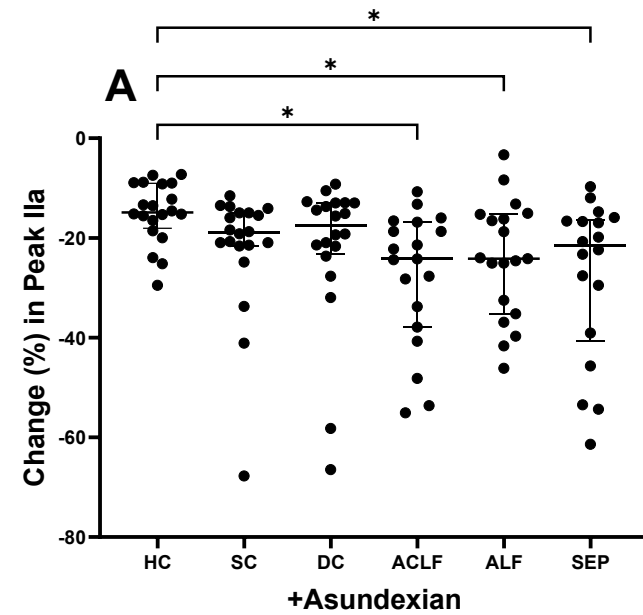
Plasma-based clot lysis time assay



Calibrated automated thrombin generation assay



Enhanced anticoagulant efficacy of asundexian in ACLF, ALF and sepsis



Clinical Trial > Clin Pharmacokinet. 2024 Nov;63(11):1631-1648.

doi: 10.1007/s40262-024-01435-7. Epub 2024 Nov 7.

Effect of Age, Sex, Renal Impairment and Hepatic Impairment on the Safety, Pharmacokinetics and Pharmacodynamics of Asundexian

Christine Brase ¹, Sebastian Schmitz ², Katharina Sommer ³, Atef Halabi ⁴, Friederike Kanefendt ⁵

Clinical Trial > Clin Pharmacokinet. 2022 Jun;61(6):857-867. doi: 10.1007/s40262-022-01110-9.

Epub 2022 Mar 9.

Single-Dose Pharmacokinetics of Milvexian in Participants with Mild or Moderate Hepatic Impairment Compared with Healthy Participants

Vidya Perera ¹, Grigor Abelian ², Danshi Li ², Zhaoqing Wang ², Liping Zhang ³, Susan Lubin ², Wei Chen ², Akintunde Bello ², Bindu Murthy ²