Crossing the Threshold: VTE Care from Pediatrics to Adulthood



Dr. Marieke Kruip, internist-hematologist Erasmus MC Dr. Irene Klaassen, pediatric hematologist Amsterdam UMC

Disclosure belangen spreker – Irene Klaassen			
Nederlands Trombose Congres – 16 mei 2025			
(potentiële) Belangenverstrengeling			
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Geen		
 Sponsoring of onderzoeksgeld 	Geen		
 Honorarium of andere (financiële) vergoeding 			
Aandeelhouder			
 Andere relatie, namelijk: 			



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Introduction

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SUCCESSFUL TRANSITION IS ESSENTIAL FOR QUALITY CARE

Background



Chalmers E. Epidemiology of venous thromboembolism in neonates and children. Thromb Res. 2006;118(1):3-12.

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Background

BIMODAL DISTRIBUTION



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6

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Background



7

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Neonates



8





Neonates

INCIDENCE: 1.4 CASES PER 1,000 NICU ADMISSIONS

Amankwah EK, Atchison CM, Arlikar S, et al. Risk factors for hospital-sssociated venous thromboembolism in the neonatal intensive care unit . Thromb Res. 2014 Aug;134(2):305-9.

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90% IS CVC-RELATED

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NEONATES WILL BECOME ADULTS WITH ADULTS WITH CAVAL VEIN OR ILIACAL VEIN OCCLUSION

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NEONATES WILL BECOME ADULTS WITH ADULTS WITH CAVAL VEIN OR ILIACAL VEIN OCCLUSION

MEDICAL GUIDELINES



NEONATES WILL BECOME ADULTS WITH ADULTS WITH CAVAL VEIN OR ILIACAL VEIN OCCLUSION

MEDICAL GUIDELINES

RECURRENCE RISK

Teenagers







Risk factors

PROVOKED (90%)



Risk factors

Thromb...

Oral contrace...

Central venous catheter

Drug induced

Underlying diseases





DOAC AND LMWH PREFERRED **ANTICOAGULATION** (COMORBIDITIES)

EDOXABAN INSUFFICIENT DATA APIXABAN LIMITED DATA



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INITIAL THERAPY ALWAYS REQUIRES 5 DAYS OF LMWH

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INITIAL THERAPY ALWAYS REQUIRES 5 DAYS OF LMWH

GFR 130-140 $ML/MIN/1.73 M^{2}$

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Question





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ASH guidelines

CLINICAL GUIDELINES | NOVEMBER 28, 2023

American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing

Saskia Middeldorp, Robby Nieuwlaat, Lisa Baumann Kreuziger, Michiel Coppens, Damon Houghton, Andra H. James, Eddy Lang, Stephan Moll, Tarra Myers, Meha Bhatt, Chatree Chai-Adisaksopha, Luis E. Colunga-Lozano, Samer G. Karam, Yuan Zhang, Wojtek Wiercioch, Holger J. Schünemann, Alfonso Iorio



Blood Adv (2023) 7 (22): 7101-7138.

https://doi.org/10.1182/bloodadvances.2023010177

Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, et al.American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. Blood Adv. 2023 Nov 28;7(22):7101-7138.



Article history 🕑

ASH guidelines

Estimates used to calculate the effect of thrombophilia testing for patients with VTE

	Prevalence, median % (min-max)	RR for VTE recurrence, positive vs negative (95% CI)	Treatment effect for VTE recurrence, RR (95% CI)	Treatment effect major bleeding, RR (95% CI)
Any thrombophilia	38.0 (21.6-59.5)	1.65 (1.28-2.47)	0.15 (0.10-0.23)	2.17 (1.40-3.35)
FVL homozygous	1.5 (0.3-3.1)	2.10 (1.09-4.06)		
FVL heterozygous	17.5 (4.1-34.8)	1.36 (1.19-1.57)		
PGM	6.1 (1.4-16.3)	1.34 (1.05-1.71)		
Antithrombin (AT) deficiency	2.2 (0.2-8.7)	2.07 (1.50-2.87)		
Protein C (PC) deficiency	2.5 (0.7-8.6)	2.13 (1.26-3.59)		
Protein S (PS) deficiency	2.3 (0.7-7.3)	1.30 (0.87-1.94)		
AT, PC, or PS deficiency	7.0 (2.5-18.4)	1.62 (1.17-2.23)		
APLA	9.7 (1.9-19.4)	1.92 (0.99-3.72)		

24 Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, et al.American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. Blood Adv. 2023 Nov 28;7(22):7101-7138.



Thrombophilia



ISSUES V FIRST EDITION



CLINICAL TRIALS AND OBSERVATIONS | AUGUST 16, 2012

Inherited thrombophilia in children with venous thromboembolism and the familial risk of thromboembolism: an observational study

U Clinical Trials & Observations

Susanne Holzhauer, Neil A. Goldenberg, Ralf Junker, Christine Heller, Monika Stoll, Daniela Manner, Rolf Mesters, Anne Krümpel, Michael Stach, Ulrike Nowak-Göttl



Blood (2012) 120 (7): 1510-1515.



COLLECTIONS V ABSTRACTS V AUTHOF

Distribution of IT in relatives with and without VTE

ІТ	No VTE (n = 488), no. (%)	VTE (n = 47), no. (%)	VTE per IT status, no. (%)
No IT	373 (76.7)	14 (29.8)	14/387 (3.6)
Any IT	113 (23.3)	33 (70.2)	33/146 (22.6)
Type of IT			
FV G1691A	76	12	12/88 (13.6)
Single	74	7	7/81 (8.6)
+ FII G20210A	2	0	0
+ AT/PC/PS deficiency	0	5	5/5 (100.0)
FII G202010A	35	5	5/40 (12.5)
Single	32	5	5/37 (13.5)
+ FV G1691A	2	0	0
+ AT/PC/PS deficiency	1	0	0
AT/PC/PS deficiency	5	18	18/23 (78.2)
Single	4	13	13/17 (76.5)
+ FV G1691A	0	5	5/5 (100.0)
+ FII G20210A	1	0	0

IT indicates inherited thrombophilia; and VTE, venous thromboembolism.

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Question



> J Thromb Haemost. 2024 Jul;22(7):2081-2092. doi: 10.1016/j.jtha.2024.04.003. Review Epub 2024 Apr 19.

Evaluation, analysis, and reporting of medication adherence for clinical trials of anticoagulants in children: guidance from the ISTH SSC Subcommittee on Pediatric and Neonatal Thrombosis and Hemostasis

Meghan E McGrady¹, Vera Ignjatovic², Sophie Jones³, Aisha Bruce⁴, Neil A Goldenberg⁵, Mattia Rizzi⁶, Courtney D Thornburg⁷, Kevin E Todd⁸, Lori Luchtman-Jones⁹

Abstract

In response to growing recognition that nonadherence prevents children, adolescents, and young adults from achieving the therapeutic benefits of anticoagulant medication, the International Society on Thrombosis and Haemostasis Scientific and Standardization Committee Subcommittee on Pediatric and Neonatal Thrombosis and Hemostasis convened a working party on medication adherence. The

primary aim of this article was to synthesize recommendations from the larger adherence science literature to provide guidance regarding the classification, collection, and interpretation of anticoagulation adherence data. The secondary aim of this article was to evaluate the degree to which trials published from 2013 to 2023 adhered to these guidance recommendations. As less than half of all trials reported on adherence and none included all recommended elements, the proposed International Society on Thrombosis and Haemostasis Scientific and Standardization Committee guidance has the potential to enhance the rigor and reproducibility of pediatric anticoagulant research.



COGNITIVELY "COMPLETE" AT 25



FAST: FRONTOSTRIATAL REWARD CIRCUITS

SLOW: PREFRONTAL CORTEX



MEDICATION NON-ADHERENCE

NEGLECTING LIFESTYLE GUIDELINES

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BE PATIENT AND STATE IT

ASK HOW OFTEN THEY FORGET THEIR MEDICATION, NOT IF

REPEAT IMPORTANT INFORMATION

A FOLLOW-UP CALL CAN BE HELPFUL

















26/05/2025

Results of no transitioning care

Cerebral palsy: 25% discontinuity care

Lever transplantation: 10% more rejections

Schmidt A, J pediatric nursing 2020; Garcia-Rodriguez F, Pediatric Rheumatol 2022

Cystic fibrose: worse pulmonary function tests, weight loss

Diabetes: more ER/hospital admissions, HbA1C

Congenital heart disease: 50-75% drop out

IBD: 20-25% drop out

Impact on QoL and health

Impact on QoL & health

Reduced physical and psychosocial wellbeing

Increased risk of mortality and morbidity

Increase in disease symptoms

Increase in ER visits, hospital admissions and outpatient visits

26/05/2025

Schmidt A, J pediatric nursing 2020, Eros A, Inflamm Bowel Dis 2020

- **Behaviour & environment**
- Therapy (non)adherence
 - Lost to follow-up
- Less trust in new healthcare professional
 - Differences in healthcare systems
 - Parental overcautioness

what can be done?

Therapy (non)adherence

Lost to follow-up

Less trust in new healthcare professional

Differences in healthcare systems

Parental overcautioness

Disease understanding

Support of parents

Personalized approach

26/05/202



Strenghten selfmanagement and self-efficacy



Collaboration pediatric and adult healthcare team

Transitioning protocol

	Experim	ental	Co	ontrol
Study	Events	Total	Events	Total
Hospital admission	rates			
Cole 2015	13	44	17	28
Otto 2019	4	20	9	18
Fixed effect model		64		46
Heterogeneity: I ² = 0%	$\tau^2 = 0, \tau^2$	p = 0.9	3	

Odds R



		Experimental		Control	
26/05/2025	Study	Events	Total	Events	Total
	Drop-out (Adult clinic)				
	Cole 2015	2	44	7	28
	Jensen 2015	52	210	15	26
	Otto 2019	3	21	6	24
	Random effects model		275		78
	Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p = 0).45		





Garcia-Rodriguez F, Pediatric Rheumatol 2022

latio	OR	95%-CI		
	0.27	[0.10;	0.74]	
	0.25	[0.06;	1.05]	
	0.26	[0.12;	0.60]	

lds Ratio	OR	95	%-C
-	0.16	[0.04;	0.66
	0.20	[0.08;	0.49
	0.52	[0.12;	2.21
	0.23	[0.12;	0.46

Multidisciplinary Teamwork

Pediatric healthcare team

TRANSITION COORDINATOR



- Guide parents in changing roles
 - Introduce adult specialist
 - Inform about differences in healthcare systems

Prepare adolescent to leave pediatric healthcare system Moment of transfer from pediatric to adult healthcare

- Warm (live/online) handover
- Written transfer

PROM's and PREM's

Patient and family



Consultations; topics to discuss



Long term

Treatment of PE in women

Counsel women with prior hormonal contraception-associated PE who discontinue anticoagulant therapy to receive thromboprophylaxis in the antepartum and postpartum period of

Management of bleeding risk

Re-assess bleeding risk on a regular basis, e.g. with a validated prediction scheme, take appropriate action in case of new modifiable risk factors or a drastic transition between bleeding risk classes.

Sport, lifestyle & travel

Counsel PE patients who discontinued stockings or prophylactic dosed anticoagulation during long-haul air

Sport, lifestyle & travel

Support PE patients in maintaining a healthy lifestyle including adequate

Cardiovascular risk factors

Limit period of overlapping antiplatelet /anticoagulant therapy in patients with PE and acute cardiovascular disease. After stopping antiplatelet therapy, patients continue oral anticoagulation

Klok F, eur heart journal 2022

A Management of bleeding risk

Rule out absolute contra-indications to anticoagulant treatment, identify optimal anticoagulant strategy, avoid unnecessary interventions.

Adherence! (How often do you forget your medication?) Alcohol, drugs



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Treatment of PE in women

Counsel women with prior hormonal contraception-associated PE who discontinue anticoagulant therapy to receive thromboprophylaxis in the antepartum and postpartum period of a future pregnancy.

Heavy menstrual bleeding pregnancy(wish)



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Heavy menstrual bleeding pregnancy(wish)



Sport, lifestyle & travel

Support PE patients in maintaining a healthy lifestyle including adequate physical activity.

Be active (not just gaming); Sports is good (but no (kick)boxing) Stop smoking school and profession





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Sport, lifestyle & travel

Support PE patients in maintaining a healthy lifestyle including adequate physical activity.



Post-PE syndrome

Consider psychological support for patients with incomplete functional recovery due to anxiety or depression. Be active (not just gaming); Sports is good (but no (kick)boxing) Stop smoking school and profession

Anxiety? Depression? Psychological support, physio, rehabilitation





Management of bleeding risk

Rule out absolute contra-indications to anticoagulant treatment, identify optimal anticoagulant strategy, avoid unnecessary interventions.

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Post-PE syndrome

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Genetic & acquired thrombophilia

Do not routinely screen for genetic thrombophilia.

Be active (not just gaming); Sports is good (but no (kick)boxing) Stop smoking school and profession

Anxiety? Depression? Psychological support, physio, rehabilitation

Thrombophilia screening? Vascular abnormalities?





- Young women with estrogen related thrombosis (with and without) anticoagulants!)
- Patients with severe thrombophilia
- Patients with indefinite anticoagulation
- Patients with thrombosis due to rheumatic disease (SLE)
- Patients with abdominal thrombosis ('rare site thrombosis')



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Sophia – Erasmus – way (what we do):

- Heleen van Ommen (pediatric hematology) contacts me
- First appointment preferably just before 18th year in adult out patient clinic

ne dult out patient clinic

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Sophia – Erasmus – way (what we do):

- Heleen van Ommen (pediatric hematology) contacts me
- First appointment preferably just before 18th year in adult out patient clinic
- at first consultation
 - Get acquinted, social context
 - Adherence! 'how often do you forget medication?'
 - Alcohol and drugs
 - Contact details (patient and not parent) and when to contact me
- at consultations thereafter
 - Anxiety, depression
 - Work, future, sports

To conclude

- Children are not small adults
- Young adults need special attention and are in between pediatric and adult 'protocols'
 - -Adherence!
 - -Sport, leisure time
 - -Anxiety
- -Women's health; heavy menstrual bleeding, pregnancy (wish) 26/05/2025
 - Have a transitioning protocol in your hospital
 - -'Warm' handover
 - Consistent treatment/care from pediatrician to adult-specialist