Is the brain a new determinant of the risk of VTE in women?

Jean-Christophe Gris, M.D., Ph.D.,

Department of Haematology, University Hospital, Nîmes and University of Montpellier, France
I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation.

Meet the Hemostasis Experts X, Athens, October 8, 2026

Disclosures



- Grants:
  - Bayer Healthcare SAS, Sanofi SA, Stago
- Scientific Advisory Boards:
  - Sanofi SA, LFB, Novo Nordisk, Coagulant Therapeutics
- Speaker / speaker bureau member, supports:
  - Alexion Pharma France, Amgen, Astra-Zeneca, Bayer, Bristol-Myers-Squibb, Boehringer-Ingelheim, Daïchi-Sankyo, Fumouze diagnostics-Sofibel, Glaxo-Smith-Kline, Horiba ABX SAS, Laboratoire Français des Biotechnologies (LFB), Léo Pharma, Novo Nordisk, Oséus, Pfizer, Sanofi SA, Shire, Stago

Birth of a new horizon

FACTORS AFFECTING THE COAGULATION TIME OF BLOOD

IV. The Hastening of Coagulation in Pain and Emotional Excitement

By W. B. CANNON and W. L. MENDENHALL

[From the Laboratory of Physiology in the Harvard Medical School]

Received for publication March 30, 1914

IN the preceding paper of this series evidence was given to prove that stimulation of splanchnic nerves, with accompanying increase of adrenal secretion, results in more rapid clotting of blood. Recent experiments have shown that certain conditions — such as pain and emotional excitement — likely to arise in the natural life of organisms and known to be attended by nervous discharges over splanchnic courses, are also attended by increased secretion of adrenalin into the blood.[1] Does the adrenalin thus liberated have any effect on the rate of coagulation? The observations here recorded were made in order to obtain an answer to that question.

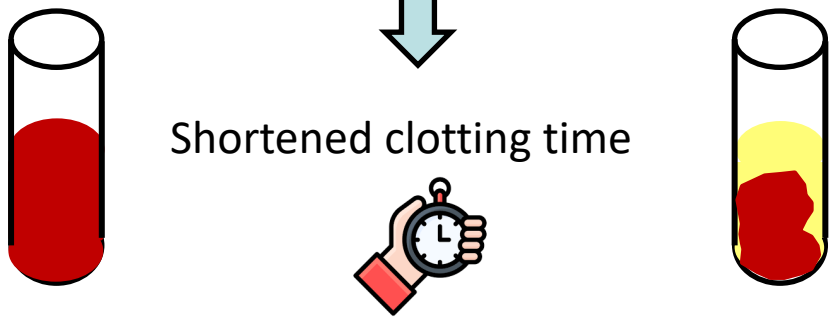
The effect of "painful" stimulation. — In experiments on the action of stimuli which in the unanaesthetized animal would cause pain, faradic stimulation of a large nerve trunk (the stump of the cut sciatic), and operation under light anaesthesia, were the methods used to affect the afferent nerves. Elliott found that repeated excitation of the sciatic nerve was especially efficient in exhausting the adrenal glands of their adrenalin content, and also that this reflex persisted after removal of the cerebral hemispheres.[2] It was to be expected, therefore, that with well-stored glands, sciatic stimulation, even in the decerebrate animal, would call forth an amount of adrenal secretion which would decidedly hasten clotting. The following case illustrates such a result:

[1] Cannon: This journal, 1914, xxxiii, p. 357.
[2] Elliott: Journal of physiology, 1912, xliv, pp. 406, 407.

Am J Physiol 1914; 34: 251-61



Emotionally aroused cats



« Adaptative for a healthy organism »

« Adaptative for a healthy organism » physiological paradigm:

Ensures survival by minimising blood loss due to injury in « fight or flight »situations…

Austin AW, Wissmann T, von Kanel R.
Stress and hemostasis: an update.
Sem Thromb Hemost 2013; 39:902-12

« Adaptative for a healthy organism » physiological paradigm:

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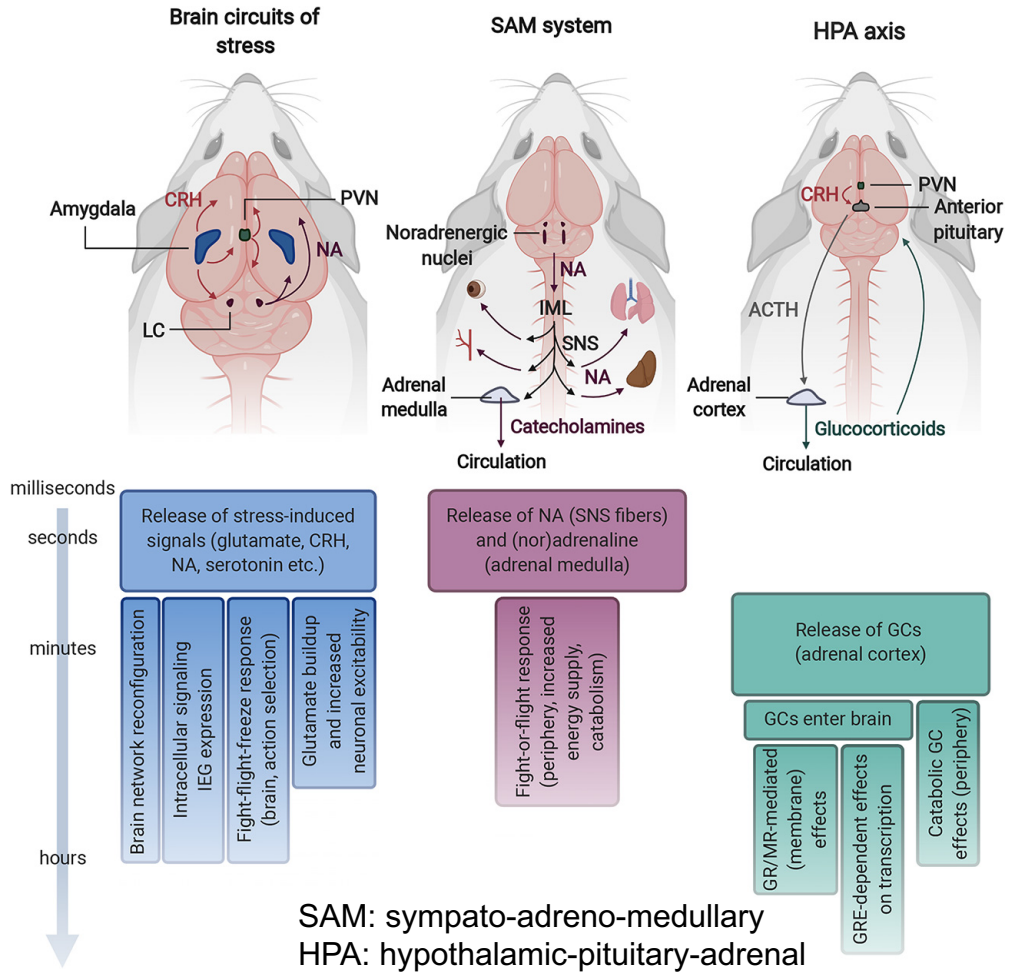
Stress and hemostasis: an update.
Sem Thromb Hemost 2013; 39:902-12

But blurs the line
between adaptative acute and maladaptive chronic stress reactions

Floriou-Servou A et al.
The acute stress response in the multiomic era.
Biol Psychiatry 2021; 89:1116-26.

« Successful stress coping
also requires the efficient termination of the stress response.
Maladaptive coping
- particularly in response to severe or repeated stressors-
can lead to allostatic (over)load,
causing wear and tear on tissues, exhaustion, and disease. »



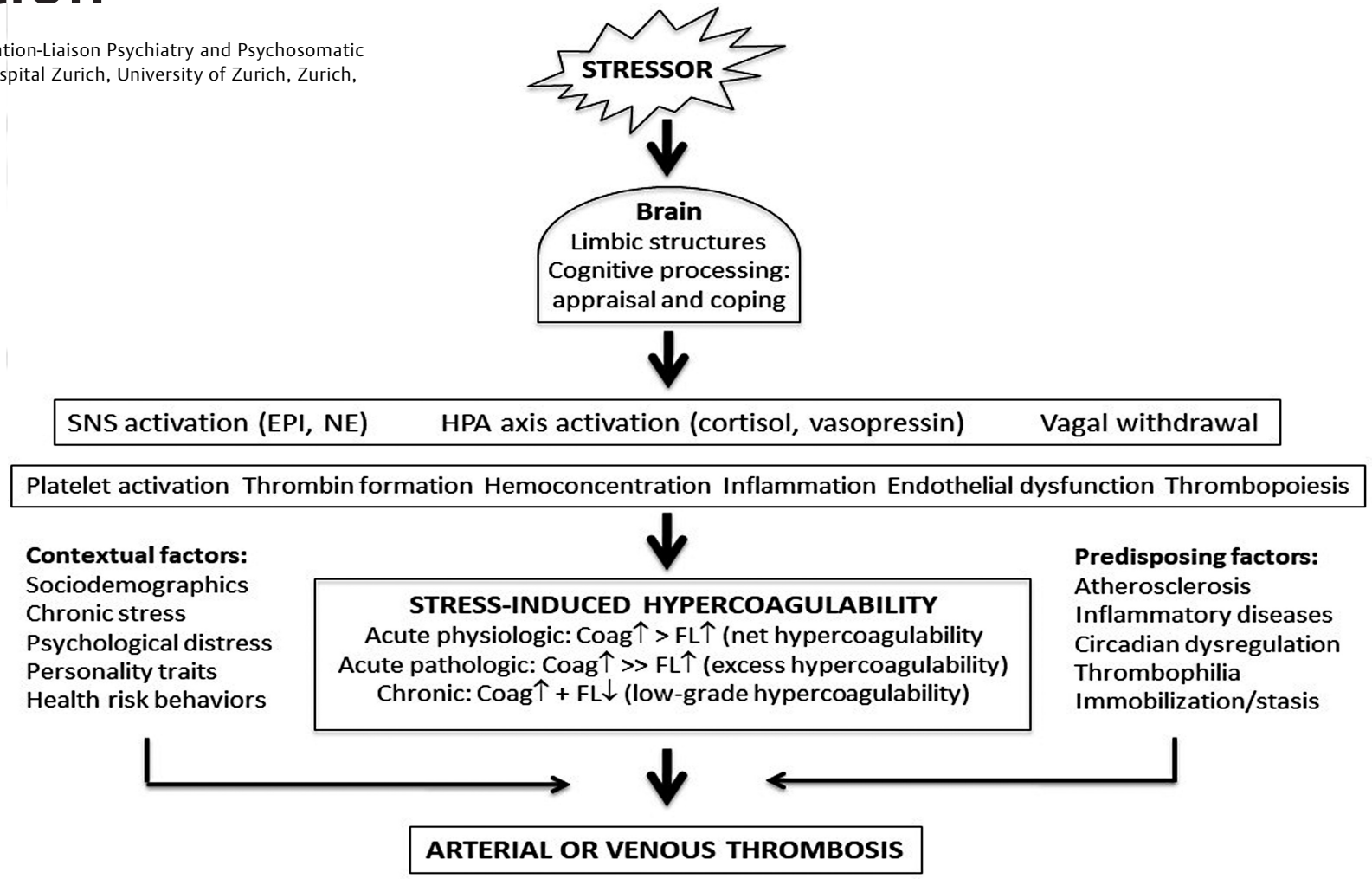
SAM: sympato-adreno-medullary
HPA: hypothalamic-pituitary-adrenal

Stress-Induced Hypercoagulability: Insights from Epidemiological and Mechanistic Studies, and Clinical Integration

Roland von Känel, MD[1]

Department of Consultation-Liaison Psychiatry and Psychosomatic Medicine, University Hospital Zurich, University of Zurich, Zurich, Switzerland

Semin Thromb Hemost 2025;51:381–400.



SNS: sympathetic nervous system;
HPA: hypothalamic-pituitary-adrenal;
Coag: coagulation;
FL: fibrinolysis

PROSPECTIVE COHORT STUDIES: *associations between stress exposure and VTE (1)*

Stress exposure	Outcome	Ref	Effect size
Acute emotional stress: natural disaster; earthquaque	Incident DVT	Sahebi A, Disaster Med Public Health Prep 2023; 17:e304	9.1% (7.3%-10.8%)
Socio economic status position: Medium vs. Low household income	Incident VTE	Holst AG, Circulation 2010; 121:1896-1903	aRR: 0.80 (0.67-0.96)
Socio economic status position: High occupational class	Incident PE	Rosengren A, J Thromb Haemost 2008; 6:558-64	aRR: 0.57 (0.39-0.83)
Work stress: Long working hours, ≥ 55 hours per week.	Incident VTE Incident DVT	Kivimäki M, Epidemiology 2018;29:e42-e44	aHR: 1.50 (1.10-2.20) aHR: 1.70 (1.10-2.60)
Chronic psychologic stress: Persistent stress (previous 1-5 years)	Incident VTE Incident PE	Rosengren A, J Thromb Haemost 2008; 6:558-64	aHR: 1.80 (1.21-2.67) aHR: 1.66 (1.12-2.48)
Negative social interactions / personality traits: Bereavement (within 90 days after death of partner)	Incident PE	Carey IM, JAMA Intern Med 2014; 174:598-605	aIRR: 2.37 (1.18-4.75)

VTE: venous thromboembolism; DVT: deep vein thrombosis; PE: pulmonary embolism;

RR: relative risk; HR: hazard ratio; IRR: incidence rate ratio; SIR: standardised incidence rate; OR: odds ratio;
u: unadjusted; a: adjusted

PROSPECTIVE COHORT STUDIES: *associations between stress exposure and VTE (2)*

Psychological distress

Stress exposure	Outcome	Ref	Effect size
Psychological distress: depression (psychiatric diagnosis)	Incident VTE Incident PE	Kowal C, Psychosom Med 2020; 82:838-49	aOR: 1.29 (1.24-1.35) aOR: 1.29 (1.11-1.50)
Psychological distress: anxiety disorder	Incident VTE Incident PE	Kowal C, Psychosom Med 2020; 82:838-49	aOR: 1.14 (1.00-1.29) aOR: 1.49 (1.10-2.02)
Psychological distress: adjustment disorder	Incident VTE	Gradus JL, BMJ Open 2015; 5:e009343	uSIR: 1.90 (1.80-2.00)
Psychological distress: posttraumatic stress disorder	Incident VTE	Sumner JA, J Am Heart Assoc 2016; 5:e003197	aHR: 1.90 (1.43-2.54)
Psychological distress: depression	Recurrent VTE in a VTE population	Von Känel R, PLoS One 2015; 10:e0125858	aOR: 1.44 (1.02-2.06)

VTE: venous thromboembolism; DVT: deep vein thrombosis; PE: pulmonary embolism;

RR: relative risk; HR: hazard ratio; IRR: incidence rate ratio; SIR: standardised incidence rate; OR: odds ratio;
u: unadjusted; a: adjusted

HYPERCOAGULABILITY LABORATORY MARKERS in acute and chronic stress: *review*

Roland von Känel, Sem Thomb Hemost 2025; 31:381-400.

Acute psychological stress	FXII:C↑, FVIII:C↑, aPTT↓, FVII:C↑, PT↓, fibrinogen↑, TAT complex↑, D-dimer↑, t-PA activity↑, ECLT↓, VWF↑, platelet activation (P-selectin expression, β-thromboglobulin↑, platelet factor 4↑), platelet aggregation↑, antithrombin↑
Low socioeconomic status/position	Fibrinogen↑, FVII:C↑ FVII:Ag↑
Work stress	Fibrinogen↑, FVII:C↑, FVIII:C↑, PAI-1 antigen↑, PAI-1 activity↓, t-PA activity↓, VWF↑, platelet aggregation↑
Perceived chronic stress	aPTT↓, D-dimer↑, platelet activation
Caregiving stress	D-dimer↑, t-PA antigen↑
Bereavement	VWF antigen↑, FVIII:C↑, platelet aggregation↑
Anger proneness/hostility	Platelet activation↑, platelet aggregation↑
Depression	Fibrinogen↑, PAI-1 activity↑, D-dimer↑, platelet activity↑, mean platelet volume↑
Anxiety	Fibrinogen, PAI-1 antigen↑, α2-antiplasmin↑, D-dimer↑, platelet reactivity↑, mean platelet volume↑
Posttraumatic stress disorder	Soluble tissue factor↑, FVIII:C↑, VWF↑, platelet reactivity↑

No available behavioural interventional trial targeting haemostasis markers in stressed patients with VTE

(only scarse data
on patients with acute coronary syndrome
or coronary heart disease).



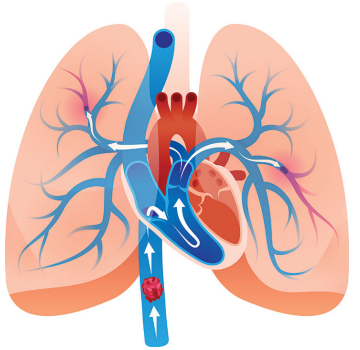


Is VTE in women a psychosomatic disease?

A revealing case report



- *A rather ordinary start:*
  - Valérie A., a 38-year-old woman
    - wanted to become a nun but eventually accepted a man's love...
  - No family history of VTE
  - Use of COCs during 15 years and 3 pregnancies
    - no thrombotic complications
  - First « COC triggered » proximal DVT / pulmonary embolism PE
    - 3 months of anticoagulant treatment, followed by discontinuation
  - Negative thrombophilia screening



- Inclusion in our female cohort
  - annual medical check-up: variable and sometimes elevated D-dimers

- *A surprising development:*
  - Six years later on: PE recurrence
    - no triggering risk factors; ?
      - but something subtle has changed in the global way she is…
    - long-term secondary thromboprophylaxis by VKA: warfarin®
      - regularly attended the anticoagulation clinic
      - bruises, but…
      - discussions and exchanges that are gradually becoming easier

- ***An unexpected confession***
  - Third husband: oyster farmer in the Thau lagoon, Sète, France





- *Chronic domestic violence*, both psychological and physical
- PE recurrence after an extremely violent row and a physical assault

First, extending the field of case reports…

Data mining on 10 years of striking evidences collected during thrombophilia screening

Moscow - Nîmes



Is intimate partner abuse underestimated as a precipitating factor for venous thromboembolism in women?

Jean-Christophe Gris[1,2,3,4] | Mariya Gennadevna Nikolaeva[5] | Jamilya Khizroeva[4] | Victoria Bitsadze[4] | Alexander Makatsariya[4] | Sylvie Ripart[6] | Antonia Perez-Martin[3,7]

J Thromb Haemost. 2023;21:3203–3206

…We therefore suspect that ***intimate partner abuse*** *could be* ***underestimated*** *as a contributing factor to* ***VTE*** *and deserves to be investigated and evaluated in depth...*

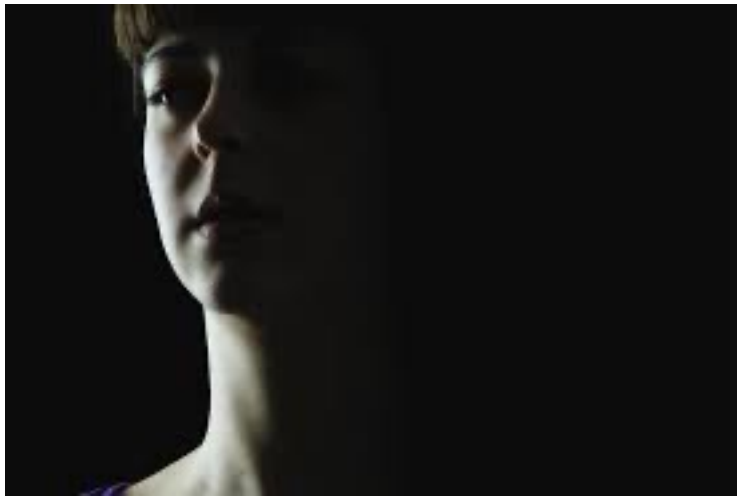
Cases of venous thromboembolism in women of childbearing age, associated with situations of obvious domestic violence.

Case	Country	Age, y	Event(s)	Risk factors	Domestic violence	Initial explanation
1	F	24	Proximal DVT, PE	Third-generation COCs, FVL-h	Beaten and caned by a drunken partner	Negative
2	F	31	Proximal DVT, PE	Early pregnancy (8 wks)	Marital rape, punching	Negative
3	F	21	Distal DVT	Morbid obesity	Hit by a baseball bat on the legs	Positive
4	F	37	Proximal DVT	PT-h	Multiple kicks on the lower limbs, addicted partner	Negative
5	F	34	PE	None	Prolonged private boxing session with gloves	Negative
6	R, Moscow	18	Distal DVT, PE	Second generation COCs	Beating and punched by a drunken partner	Negative
7	R, Moscow	29	Proximal DVT	FVL-H	Multiple kicks on the lower limbs, drunken partner	Negative
8	R, Moscow	23	PE	Obesity	Beaten and punched by a mentally ill partner	Negative
9	R, Moscow	34	Bilateral distal DVT	Second generation COCs	Prolonged immobilization with tight ropes	Positive
10	R, Moscow	37	Proximal DVT, PE	None	Marital rape, punching	Negative
11	R, Moscow	42	Proximal DVT	May-Turner syndrome	Rape at work, beating	Negative
12	R, Moscow	26	Distal DVT, PE	Third-generation COC	Violent assault by thieves at home, beatings	Positive
13	R, Moscow	22	Proximal DVT	FVL-h	Repeated canings by a drunken partner	Negative
14	R, Moscow	35	Distal DVT	None	Extremely violent sexual games, coercion, bondage	Negative
15	R, Moscow	35	Portal thrombosis	Crohn's disease	Attempted rape, punching	Negative
16	R, Barnaul	31	DVT, upper limb	Second generation COCs	Multiple slaps and punches	Positive
17	R, Barnaul	36	PE	None	Marital rape, punching	Negative
18	R, Barnaul	20	Proximal DVT	Obesity	Multiple kicks on the belly	Negative
19	R, Barnaul	27	Distal DVT, PE	None	Hit on the lower limb by an iron	Negative

COCs, combined oral contraceptives; DVT, deep venous thrombosis; F, France; FVL, factor V Leiden polymorphism; -h, heterozygous; -H, homozygous; PE, pulmonary embolism; PT, prothrombin 20210A polymorphisms; R, Russian Federation.

How to easily screen for intimate partner violence?

A widely, world-validated tool:
the
Woman Abuse Screening Tool*
« WAST » questionnaire



* Brown JB et al., Fam Med 1996; 28:422-8

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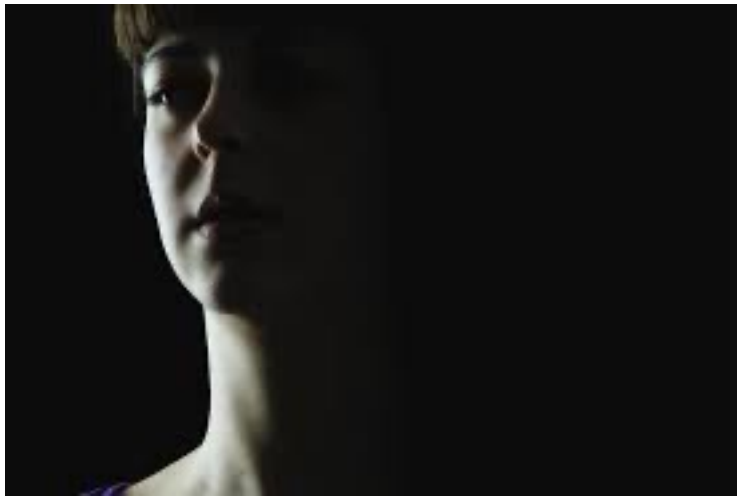


* Brown JB et al., Fam Med 1996; 28:422-8

THE WOMEN ABUSE SCREENING TOOL (*i.e.* "WAST"), *8 ITEMS.*

3 possible answers to each item, from 0 to 2 points; individual score: sum of the points.

Total score at least equal to 5 (≥ 5): positive intimate partner violence situation.

Item 1. In general, how would you describe your relationship?

A lot of tension (2 points) Some tension (1 point) No tension (no point)

Item 2. Do you and your partner work out arguments with:

Great difficulty (2 points) Some difficulty (1 point) No difficulty (no point)

Item 3. Do arguments ever result in your feeling down or bad about yourself?

Often (2 points) Sometimes (1 point) Never (no point)

Item 4. Do argument ever result in hitting, kicking, or pushing?

Often (2 points) Sometimes (1 point) Never (no point)

Item 5. Do you ever feel frightened by what your partner says or do?

Often (2 points) Sometimes (1 point) Never (no point)

Item 6. Has your partner ever abused you physically?

Often (2 points) Sometimes (1 point) Never (no point)

Item 7. Has your partner ever abused you emotionally?

Often (2 points) Sometimes (1 point) Never (no point)

Item 8. Has your partner ever abused you sexually?

Often (2 points) Sometimes (1 point) Never (no point)

Verbal/psychological violence

Physical violence

Sexual violence

WAST score > 4 (5 and more):
Positive Intimate Partner Violence **IPV** situation

Second, testing the reality in our daily practice…

What about the women we currently see, investigate, treat and follow as outpatients?

Outpatients' clinic for hematological investigations,
University Hospital CHU, Nîmes

300 female Patients
vs.
300 female Controls (hospital staff)

WAST questionnaire.



High prevalence of intimate partner violence in outpatient women addressed for hematological investigations

Chloé Bourguignon , Jérémy Laurent, Géraldine Lissade-Lavigne , Mathias Chea , Jean-Christophe Gris

Minerva Med 2024 Sep 18.
doi: 10.23736/S0026-4806.24.09466-7.

Outpatients' clinic for hematological investigations, University Hospital CHU, Nîmes
300 female Patients *vs.* 300 female Controls (hospital staff).
WAST questionnaire.

WAST, total score: *categories*	**0-4**	**5-16**	**%**	
Patients	266	34	**11.5% (7.1%-15.9%)**	
Controls	297	3	1% (0%-2.4%)	*P < 0.0001*

Intimate partner violence "IPV" situation (WAST score ≥ 5):

13 of the 89 women coming for VTE-related investigations	13.0%	(6.4%-19.6%)
4 of the 18 women coming for bleeding-related investigations,	18.2%	(2.0%-34.3%)
17 of the 193 women coming for an abnormal blood cell count	8.5%	(4.6%-12.4%)

Third, studying intimate partner violence as a risk factor for VTE in women

The Abnormal Female Haemovascular Interface « AFHI » registry

Third, studying intimate partner violence as a risk factor for VTE in women

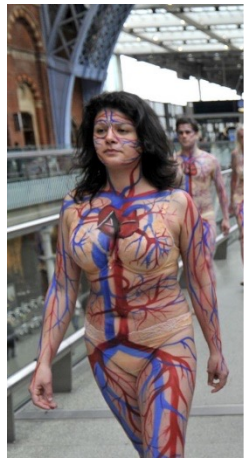
The Abnormal Female Haemovascular Interface « AFHI » registry

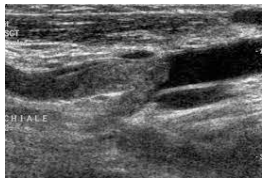




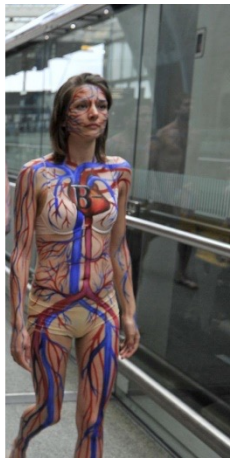
Nîmes University Hospital,
University of Montpellier,
UMR 1318 INSERM-INRIA-UM “IDESP”,
France

♀ 18-55 ans

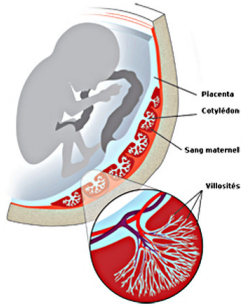




Haemovascular interface



Haemo-placental interface

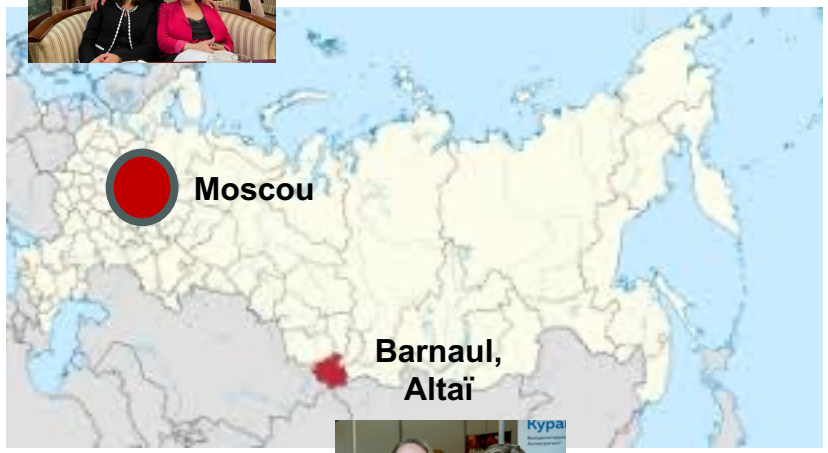


1st thrombosis
or/and
1st placenta-mediated disease,
January 1st, 2010-…
January 1st, 2026: N= 42.682

I.M. Sechenov First Moscow State Medical University, Moscow;
Russian Federation.









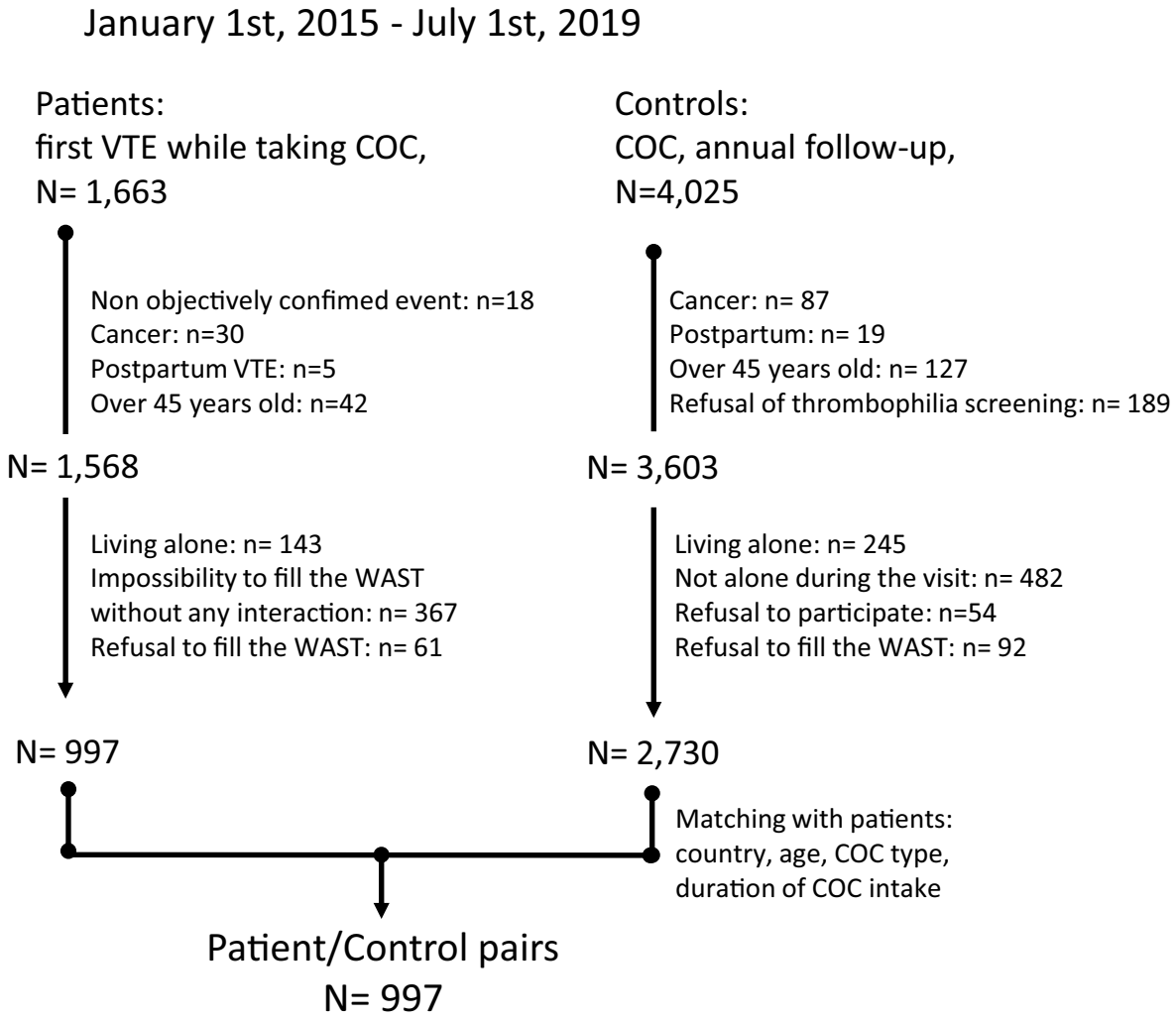
Altai State Medical University, Barnaul;
Russian Federation.

Women, first VTE event while taking combined oral contraceptives COCs

Matched 1:1 case-control study

Women, first VTE event while taking combined oral contraceptives COCs

Matched 1:1 case-control study



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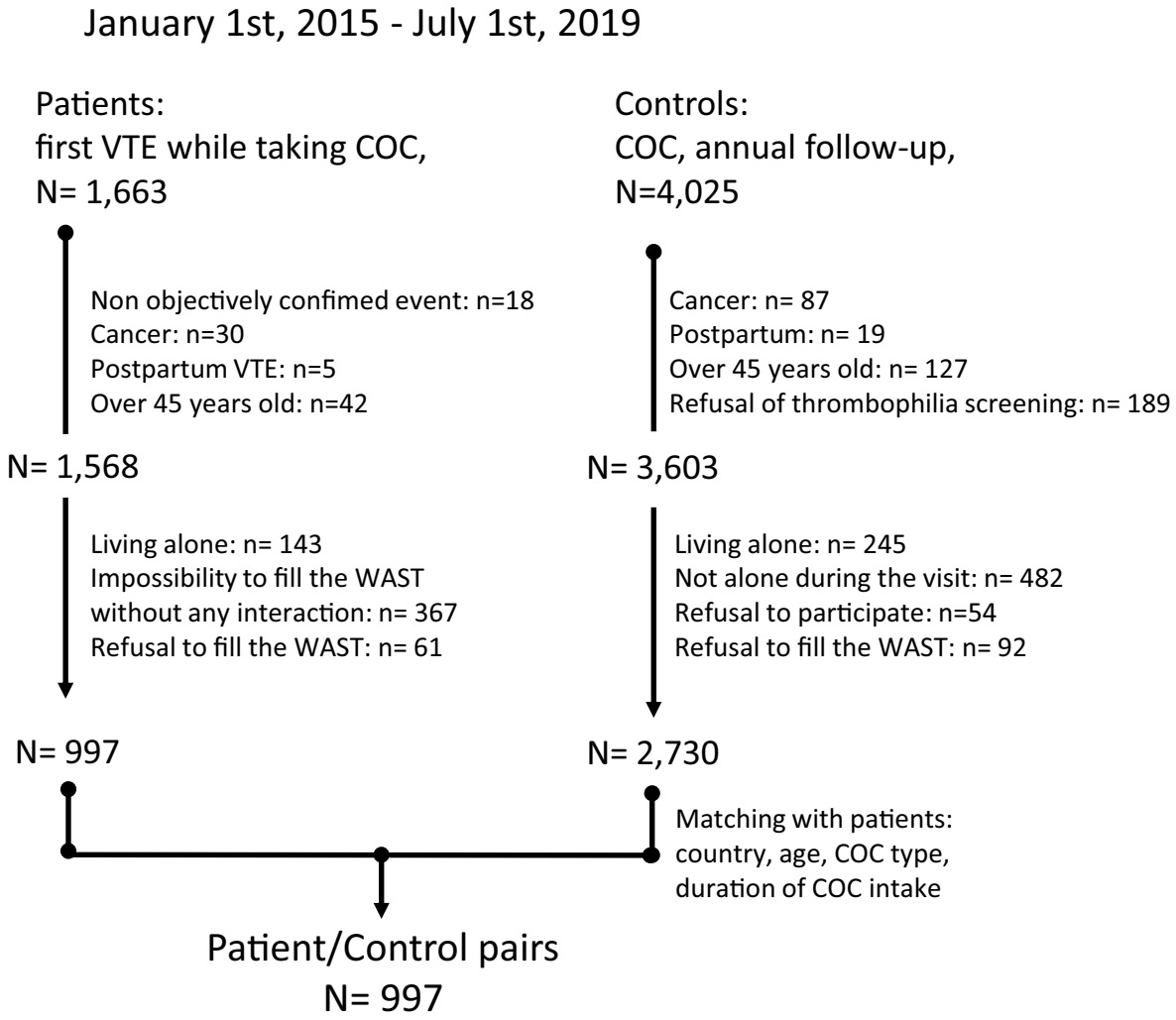
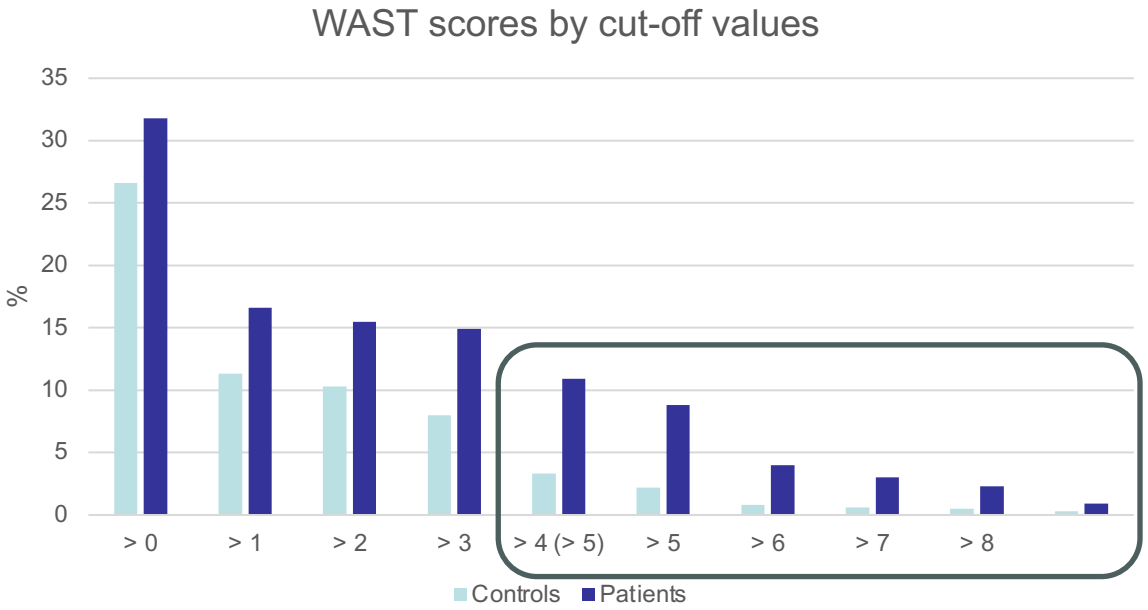


Characteristics of the 1994 women who were under study. Quantitative data are given as medians, [IQR], (range) and qualitative data as numbers (%).

Variable (missing values: n)	Controls	Cases	P
N	997	997	
Country of residence			
France	183 (18.4)	183 (18.4)	
Russia	814 (81.6)	814 (81.6)	
Age, years	29 [5.0] (18–42)	29 [5.0] (18–42)	
COC type			
Second generation	774 (77.6)	774 (77.6)	
Third generation	216 (21.7)	216 (21.7)	
Fourth generation	7 (0.7)	7 (0.7)	
Duration of COC intake, days	246 [152] (10–484)	243 [145] (57–464)	
BMI, kg.m-2	24.6 [5.85] (16.2–37.3)	25.3 [6.36] (15.2–38.4)	0.023
Systemic inflammatory disease (5)	25 (2.5)	53 (3.1)	0.0017
Active smoker	188 (18.9)	323 (32.4)	<0.0001
Varicose veins (7)	182 (18.3)	237 (23.8)	0.0030
Positive family history:			
of VTE, first degree relatives (7)	40 (4.0)	205 (20.6)	<0.0001
ABO blood group		0.0041	
O	498	433	
Non-O	499	564	
F5 rs6025, heterozygous (2)	57	220	<0.0001
F2 rs1799963, heterozygous (2)	23	49	0.0025
Antithrombin, protein C or S deficiency	7	31	0.0001
Persistently positive antiphospholipid antibodies	9	23	0.0191
FVIII > 1.5 kI.U.L-1	30	78	<0.0001
D-dimers, mg.L-1	178 [112] (60–615)	204 [143] (10–718)	<0.0001
COC-associated VTE event			
Distal DVT		652 (65.4)	
Proximal DVT		179 (18.0)	
Pulmonary embolism		166 (16.6)	
Additional risk factors for VTE			
Negative	518 (52.0)		
Positive *(more than one is possible)*		479 (48.0)	
Local trauma		59 (5.9)	
Cast immobilisation		145 (14.5)	
Recent surgery		89 (8.9)	
Prolonged bed rest		160 (16.0)	
Systemic infectious syndrome		103 (10.3)	
Systemic inflammatory flare-up		27 (2.7)	
Long-haul flight		24 (2.4)	

WAST score values, 0 to 16

WAST cut-off values	Controls: n (%)	Patients: n (%)	P
>0	265 (26.6)	317 (31.8)	0.0082
>1	113 (11.3)	165 (16.6)	0.0010
>2	103 (10.3)	155 (15.5)	0.0008
>3	80 (8.0)	149 (14.9)	<0.0001
>4 (*i.e.* ≥ 5, *positive WAST*)	33 (3.3)	109 (10.9)	<0.0001
>5	22 (2.2)	88 (8.8)	<0.0001
>6	8 (0.8)	40 (4.0)	<0.0001
>7	6 (0.6)	30 (3.0)	<0.0001
>8	5 (0.5)	23 (2.3)	0.0003
>9	3 (0.3)	9 (0.9)	0.1460



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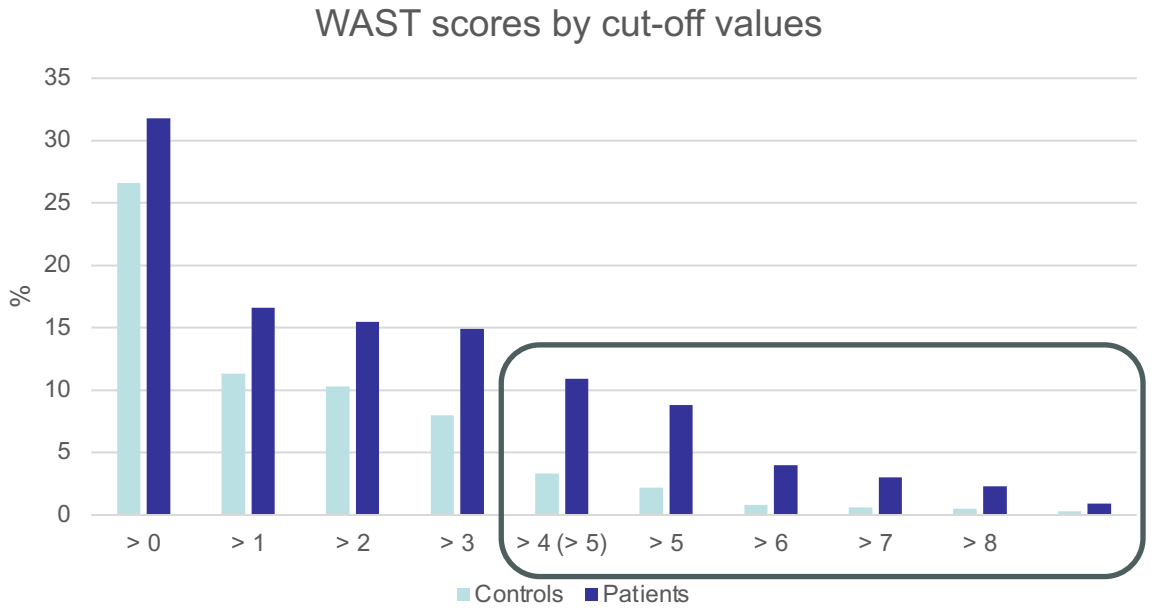

Univariate matched odds ratios (OR) for a first venous thromboembolic event in women taking combined oral contraceptives. $_{95\ \%}$CI: 95 % confidence interval.

Variable	OR, $_{95\ \%}$CI	P
Positive family history:		
of VTE, first degree relatives	6.193 (4.357–8.802)	<0.0001
Systemic inflammatory disease	2.183 (1.345–3.542)	0.0016
Active smoker	2.062 (1.677–2.536)	<0.0001
BMI, $kg.m^{-2}$	1.007 (0.987–1.028)	0.48
Varicose veins	1.396 (1.124–1.735)	0.0026
ABO blood group		
Non-O	Reference	
O	0.769 (0.645–0.918)	0.0036
F5 rs6025	4.669 (3.437–6.344)	<0.0001
F2 rs1799963	2.189 (1.323–3.621)	0.0023
Antithrombin, protein C or S deficiency	4.539 (1.989–10.357)	0.0003
Persistently positive antiphospholipid antibodies	2.592 (1.193–5.631)	0.0161
FVIII > 1.5 $kI.U.L^{-1}$	2.736 (1.778–4.208)	<0.0001
D-dimers, $mg.L^{-1}$	5.587 (2.777–11,24)	<0.0001
WAST score value ≥ 5	3.586 (2.404–5.349)	<0.0001

Multivariate matched odds ratio (aOR) for a first VTE event In women taking COCs.

Variable	aOR, 95 %CI	P
Positive family history:		
of VTE, first degree relatives	4.255 (2.915–6.211)	<0.0001
Systemic inflammatory disease	2.016 (1.185–3.430)	0.0097
Active smoker	2.023 (1.616–2.532)	<0.0001
O blood group	0.711 (0.585–0.863)	0.0006
F5 rs6025	3.506 (2.525–4.67)	<0.0001
F2 rs1799963	1.795 (1.039–3.101)	0.0360
Antithrombin, protein C or S deficiency	2.650 (1.091–6.436)	0.0266
Persistently positive antiphospholipid antibodies	3.210 (1.429–7.209)	0.0047
FVIII > 1.5 kI.U.L^{-1}	2.839 (1.788–4.508)	<0.0001
D-dimers, mg.L^{-1}	5.562 (2.606–11,872)	<0.0001
WAST score value $\geq$ 5	3.720 (2.438–5.677)	<0.0001

All results are adjusted on all the variables with a p value lower or equal to 0.15 after univariate analysis.
Only main effects with $p < 0.05$ are shown.

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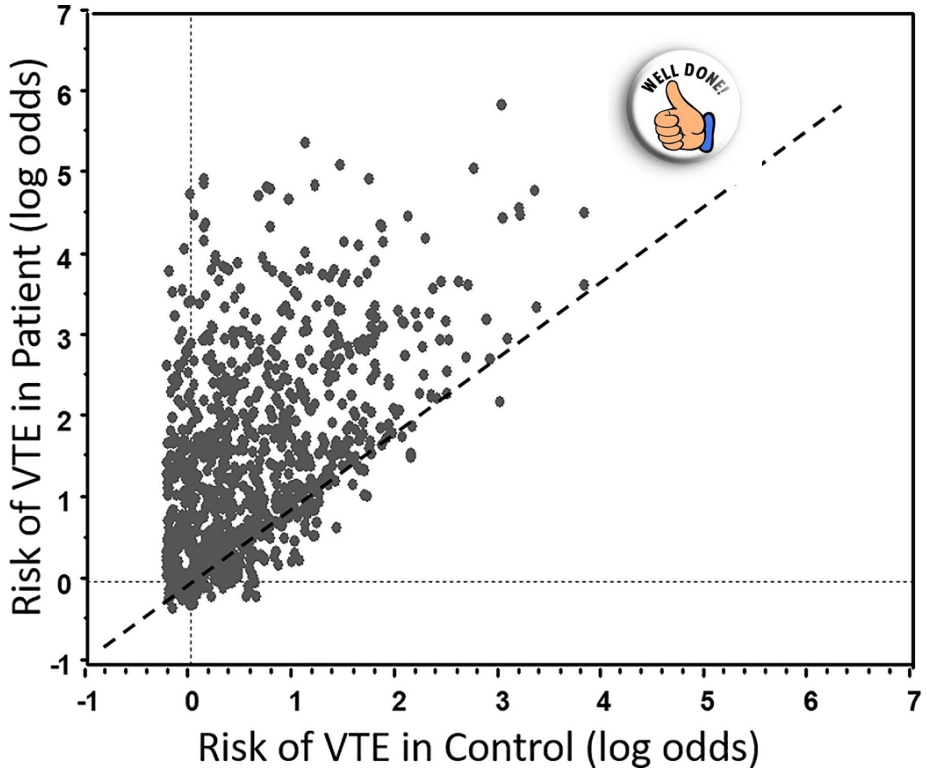
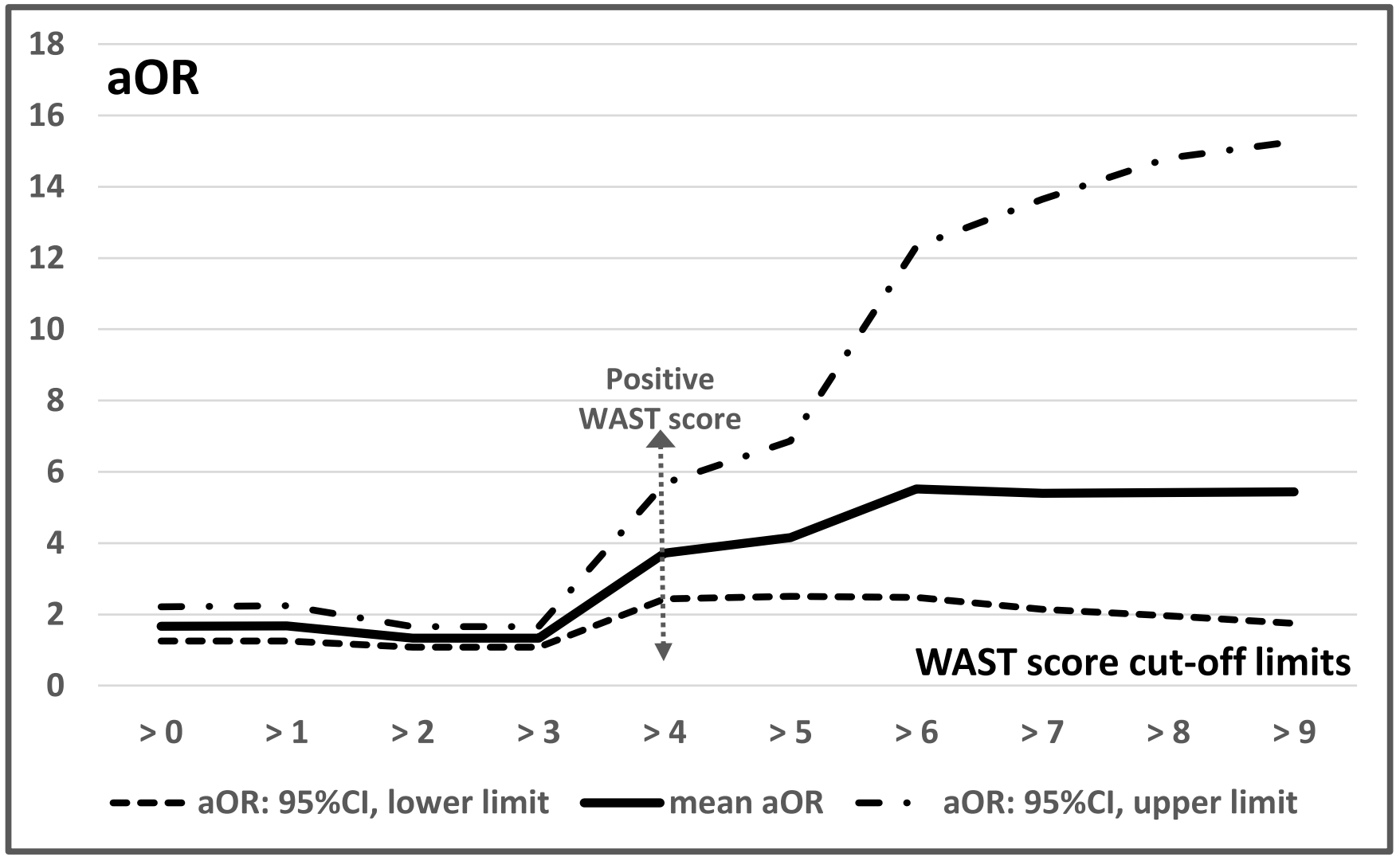


Predicted probability of VTE
(logarithm of odds from the multivariate model)
in pairs of Cases and Controls



Sensitivity analysis of the WAST score as a risk factor for VTE in women taking COCs.

Matched odds ratios were adjusted for a positive family history of VTE, systemic inflammatory disease, active smoking, arterial hypertension, O blood group, *F5* rs6025 - *F2* rs1799963 polymorphisms, AT protein C or S deficiency, persistant aPL Abs, FVIII > 1.5 $kU.L^{-1}$ and D-dimers.

Multivariate models constructed based on WAST score results, *by type of violence:*

items 3, 5, 7:	**verbal/psychological violence**	(observed values: 0, 1, 2, 3, 4, 5)
items 4, 6:	**physical violence**	(observed values: 0, 1, 2)
item 8:	**sexual violence**	(observed values: 0, 1)

Type / level of violence	aOR* (95% C.I.)	P
Verbal/psychological, ≥2	**2.41 (1.13-5.15)**	**0.023**
Physical, > 0	1.54 (0.61-3.86)	0.36
Sexual, >0	1.56 (0.53-4.57)	0.42

* Matched odds ratios: adjusted for a positive family history of VTE, systemic inflammatory disease, active smoking, arterial hypertension, O blood group, *F5* rs6025 - *F2* rs1799963 polymorphisms, AT protein C or S deficiency, persistant aPL Abs, FVIII > 1.5 $kU.L^{-1}$ and D-dimers.

Intimate partner violence as a risk factor for venous thromboembolism in women on combined oral contraceptives: An international matched case-control study

Mathias Chéa [a], Chloé Bourguignon [a,b], Sylvie Bouvier [a,b,c], Eva Nouvellon [a,b], Jeremy Laurent [a,d], Antonia Perez-Martin [b,d], Eve Mousty [e], Sylvie Ripart [e], Mariya Gennadevna Nikolaeva [f], Jamilya Khizroeva [g], Victoria Bitsadze [g], Alexander Makatsariya [g], Jean-Christophe Gris [a,b,c,g,h,*]

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[e] *Department of Gynaecology and Obstetrics, CHU Nîmes, Univ Montpellier, Nîmes, France*
[f] *Department of Obstetrics and Gynaecology, Altai State Medical University, Barnaul, Russia*
[g] *Department of Obstetrics, Gynaecology and Perinatal Medicine, I.M. Sechenov First Moscow State Medical University, Moscow, Russia*
[h] *FCRIN_INNOVTE network, France*

Eur J Intern Med 2024 Apr;122:47-53.
doi: 10.1016/j.ejim.2023.12.016.

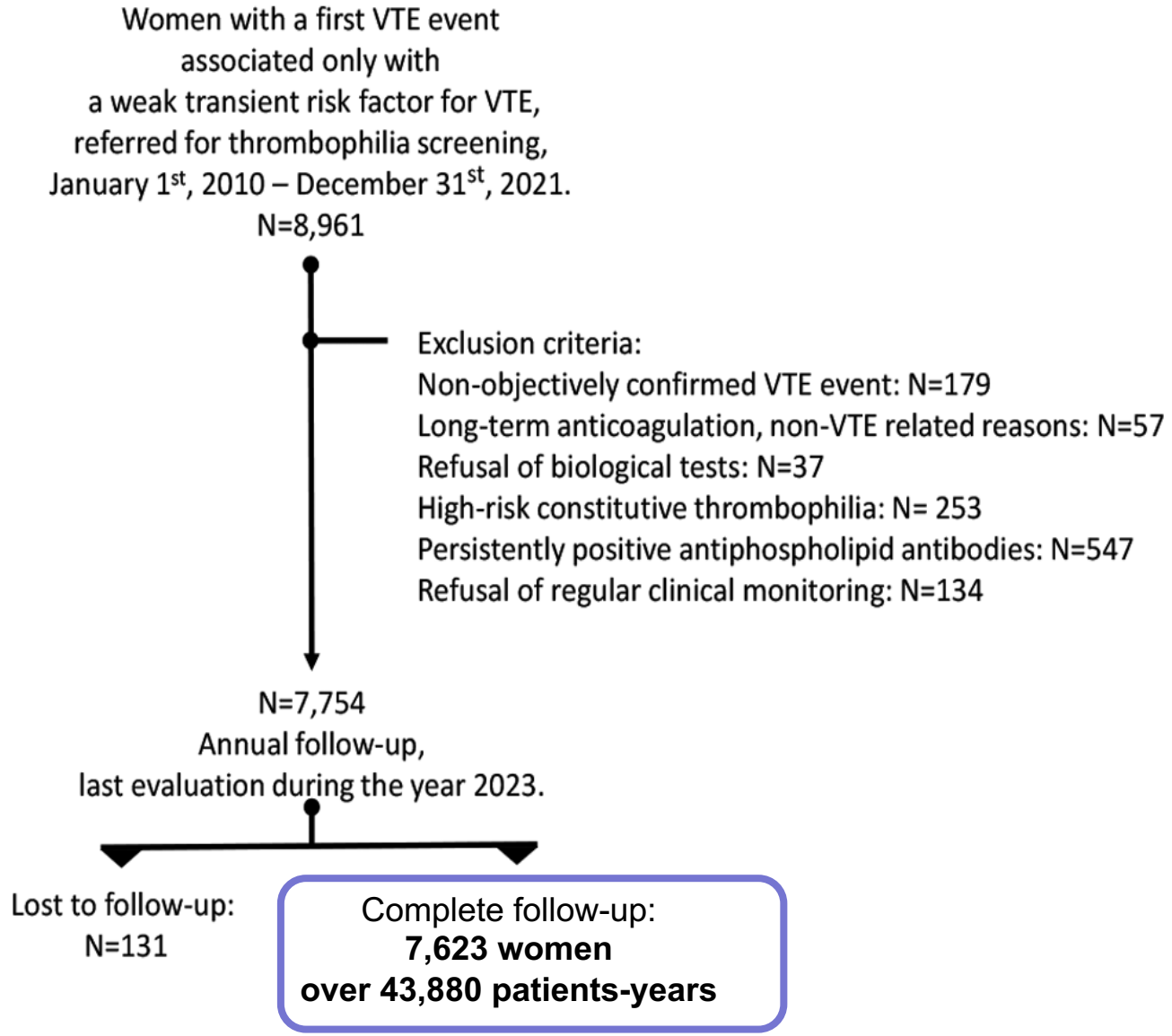


Women, *first VTE event* associated with / provoked by any ***weak transient clinical risk factor***

COCs
Pregnancy / puerperium
Minor trauma or fracture
Surgery lasting less than 30 minutes
Infection
Brief immobility

Women, *first VTE event* associated with / provoked by any ***weak transient clinical risk factor***

COCs	45.4%
Pregnancy / puerperium	4.8%
Minor trauma or fracture	15.9%
Surgery lasting less than 30 minutes	11.5%
Infection	8.1%
Brief immobility	14.2%



Are stress levels *and* intimate partner violence associated with *a first VTE recurrence?*

In case of any first suspicion of VTE recurrence during follow-up and *before* any objective test for diagnosis:

Screening for intimate partner violence IPV:
WAST questionnaire and score

In case of any first suspicion of VTE recurrence during follow-up and *before* any objective test for diagnosis:

Screening for intimate partner violence IPV:
WAST questionnaire and score

Perceived Stress Scale PSS, 10 item version:
PSS-10 questionnaire and score

PSS-10

Item 1. In the last month, how often have you been upset because of something that happened unexpectedly?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Item 2. In the last month, how often have you felt that you were unable to control the important things in your life?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Item 3. In the last month, how often have you felt nervous or "stressed"?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Item 4. In the last month, how often have you felt confident about your ability to handle your personal problems?
Never(4) Almost never(3) Sometimes(2) Fairly often(1) Very often(0)

Item 5. In the last month, how often have you felt that things were going your way?
Never(4) Almost never(3) Sometimes(2) Fairly often(1) Very often(0)

Item 6. In the last month, how often have you found that you could not cope with all the things that you had to do?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Item 7. In the last month, how often have you been able to control irritations in your life?
Never(4) Almost never(3) Sometimes(2) Fairly often(1) Very often(0)

Item 8. In the last month, how often have you felt that you were on top of things?
Never(4) Almost never(3) Sometimes(2) Fairly often(1) Very often(0)

Item 9. In the last month, how often have you been angered because of things that happened that were outside of your control?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Item 10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?
Never(0) Almost never(1) Sometimes(2) Fairly often(3) Very often(4)

Final individual score: *sum of the points between brackets;*

low stress: 0-13
moderate stress: 14-26;
high perceived stress: 27-40.



N=7,623
Median follow-up 5.3 [5.6] (0.22-12.7) years
43,880 patients-years
Suspicion of first VTE recurrence: N=4,772
positive recurrence: N=1,316
distal DVTs: N=485
proximal DVTs: N=530
PEs: N=301
Annualised recurrence rate:
2.99 (2.84-1.16) for 100 patients.years

Variable [missing value: *n*]	All	VTE recurrence		*P*
		Negative	Positive	
		(*n* = 3,456)	(*n* = 1,316)	
PSS self-questionnaire				
• Total score	15 [10] (1–40)	14 [9] (1–36)	19 [13] (2–40)	<0.0001
• By categories				<0.0001
– 0–13: low stress	2,108 (44.2)	1,680	428 (20.3)	
– 14–26: moderate stress	2,388 (50.0)	1,696	692 (29.0)	
– 27–40: high perceived stress	276 (5.8)	80	196 (71.0)	
WAST self-questionnaire [12]				
• Total score	0 [1] (0–11)	0 [1] (0–11)	0 [1] (0–11)	0.0219
• Score ≥ 5 (positive IPV)				<0.0001
– No	4,404 (92.3)	3,230	1,174 (26.7)	
– Yes	368 (7.7)	226	142 (38.6)	
• Score by values				0.0005
– 0	3,399 (71.3)	2,494	905 (26.6)	
– 1	688 (14.5)	496	192 (27.9)	
– 2	48 (1.0)	33	15 (30.6)	
– 3	61 (1.3)	53	8 (13.1)	
– 4	196 (4.2)	142	54 (27.6)	
– 5	74 (1.6)	46	28 (37.8)	
– 6	171 (3.6)	106	65 (38.0)	
– 7	31 (0.6)	18	13 (41.9)	
– 8	25 (0.5)	16	9 (36.0)	
– 9	46 (1.0)	28	18 (39.1)	
– 11	21 (0.4)	12	9 (42.9)	

Results of the total scores
obtained from the completion of the PSS-10 and WAST questionnaires
by the 4,772 patients
at the time of suspected recurrence of VTE:
Overall; then according to the final diagnosis.

Risk factors for a positive VTE diagnosis in the 4,772 women included in the VTE_WEAK cohort who declared a suspicion of VTE recurrence during follow-up

	Univariate analysis			Multivariate analysis					
				Model 1 ($P < 0.0001$)			Model 2 ($P < 0.0001$)		
	cOR	95% CI	P	aOR	95% CI	P	aOR	95% CI	*P*
PSS self-questionnaire									
• Total score	1.107	1.097–1.118	<0.0001[a]	1.109	1.098–1.120	<0.0001			
• By category			<0.0001[a]						
– 0–13: low stress, reference	1								
– 14–26: moderate stress	1.602	1.395–1.839	<0.0001[a]				1.627	1.412–1.874	<0.0001
– 27–40: high perceived stress	9.617	7.262–12.736	<0.0001[a]				10.02	7.516–13.35	<0.0001
WAST self-questionnaire									
• Total score	1.065	1.033–1.099	<0.0001[a]	1.080	1.045–1.117	<0.0001			
• Score ≥ 5 (positive IPV)	1.729	1.387–2.155	<0.0001[a]				1.941	1.536–2.474	<0.0001

Adjusted on:

place of living, transient weak clinical risk factors associated with first VTE event, new superimposed risk factor for VTE, transient thromboprophylaxis, varicose veins at suspicion, family history of VTE at suspicion, diabetes mellitus at suspicion, non-O blood group, Factor XI levels

Association between the PSS-10 and WAST scores *and the type of VTE recurrence.*

	aOR[a]	95% CI	*P*
Distal DVT			
• PSS (moderate stress)	1.603	1.298–1.978	<0.0001
• PSS (high perceived stress)	10.11	7.084–14.43	<0.0001
• WAST ≥ 5 (positive IPV)	1.876	1.363–2.582	0.0001
Proximal DVT			
• PSS (moderate stress)	1.633	1.334–1.998	<0.0001
• PSS (high perceived stress)	9.643	6.796–13.68	<0.0001
• WAST ≥ 5 (positive IPV)	1.769	1.293–2.422	0.0004
PE			
• PSS (moderate stress)	1.638	1.262–2.126	<0.0001
• PSS (high perceived stress)	9.332	6.110–14.25	<0.0001
• WAST ≥ 5 (positive IPV)	1.781	1.200–2.644	0.0042

Adjusted on:

place of living, transient weak clinical risk factors associated with first VTE event, new superimposed risk factor for VTE, transient thromboprophylaxis, varicose veins at suspicion, family history of VTE at suspicion, diabetes mellitus at suspicion, non-O blood group, Factor XI levels,

Venous Thromboembolism at Low Risk of Recurrence in Young Women: Stress and Violence Associated with Recurrence. *An International Case-Control Study*

Victoria Bitsadze[1] Mariya Gennadevna Nikolaeva[2] Ève Mousty[3] Jamilya Khizroeva[1] Jérémy Laurent[4] Sylvie Ripart[3] Ekaterina Kudryavtseva[1] Lorris Le Collen[4] Anastasia Shatilina[1] Salim Allal[4] Elizaveta Lyadnova[1] Mathieu Fortier[5] Sylvie Bouvier[5,6,7] Mathias Chea[5,6,7] Marina Sabirovna Zainulina[8] Antonia Perez-Martin[4] Alexander Makatsariya[1] Jean-Christophe Gris[1,5,6,7,9]

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[6] UMR 1318 INSERM-Université de Montpellier IDESP, Montpellier University, France
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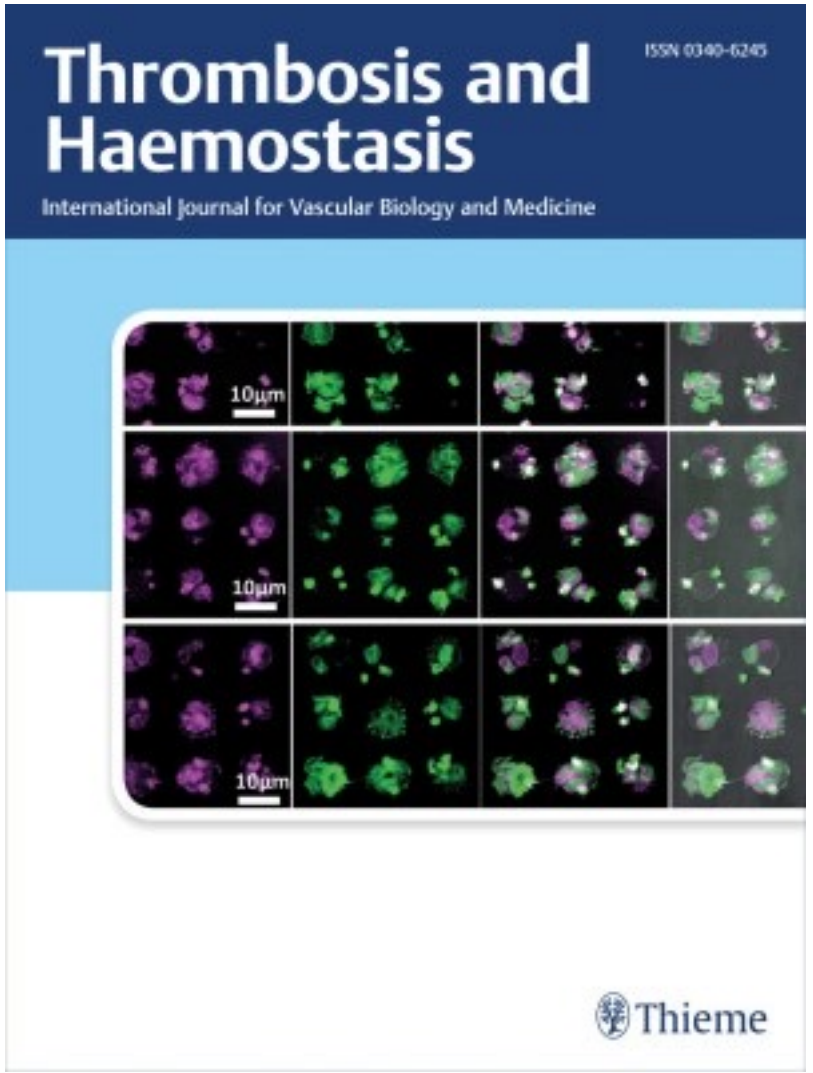
[9] FCRIN_INNOVTE network, France

Thromb Haemost

Thromb Haemost 2025 Jul;125(7):643-656.
doi: 10.1055/a-2484-0923.

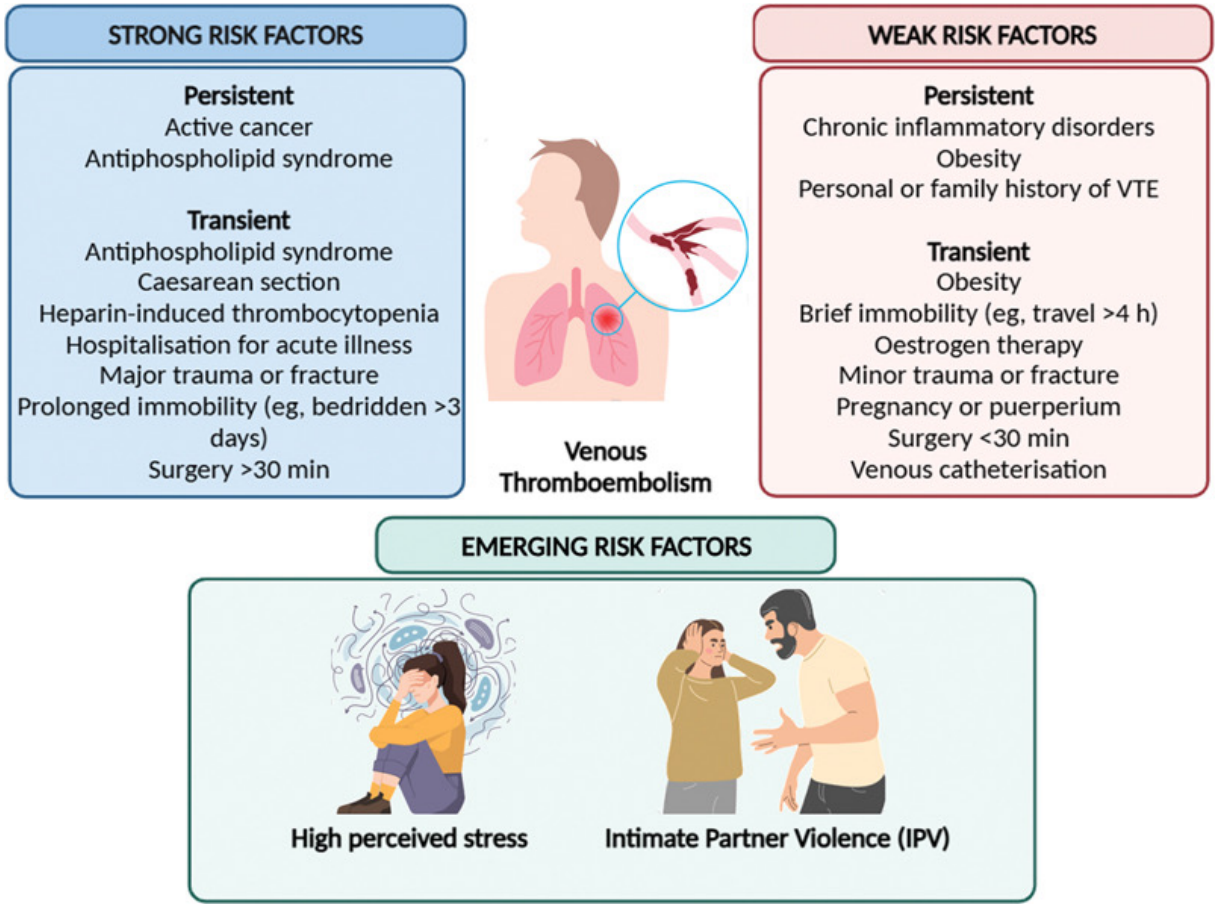


COMMENT ON THIS POST:

Soler-Espejo E, Roldán V, Marín F.

Stress, Partner Violence, and Coagulopathy: Unmasking **New Triggers** for Venous Thromboembolism.

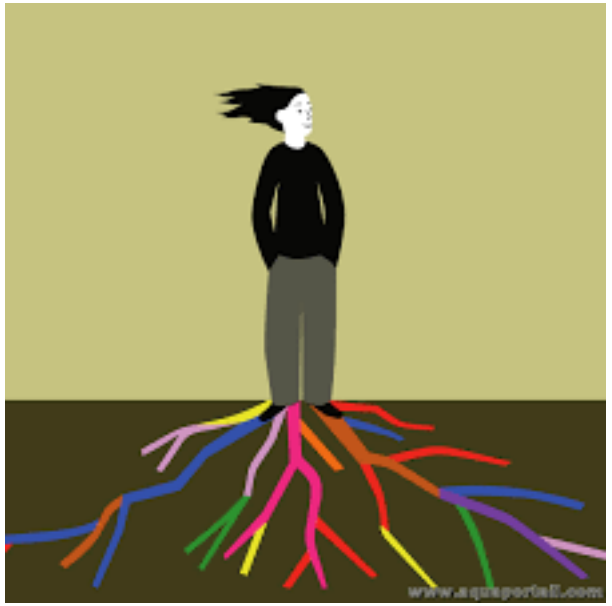
Thromb Haemost 2025 Jul;125(7):657-659. doi: 10.1055/a-2520-8725.





Yet unpublished data…

Resilience



What defines a resilient person?
Resilience is the ability to move through and grow from difficult times.
It's a skill you develop over time from the lessons and experiences you absorb as you grow up and face challenges.

Resilience is frequently used interchangeably with adaptability and coping.
Four main types of resilience have to be cultivated in order to support ourselves during difficult times:
physical resilience, mental resilience, emotional resilience and social resilience.

The seven characteristics of resilience are
competence, confidence, connection, character, contribution, coping and control.

Does resilience state after a first VTE event in women impacts of the risk of VTE recurrence?



The Brief Resilient Coping Scale "BRCS".

How to assess an individual's level of resilience

Consider how well the following statements describe your behaviour and actions on a scale from 1 (*i.e. "does not describe me at all"*) to 5 (i.e. *"describes me very well")*.

Final BRCS *score values: from 4 to 20.*

Items	**1**	**2**	**3**	**4**	**5**
1- I look for creative ways to alter difficult situations.					
2- Regardless of what happens to me, I believe I can control my reaction to it.					
3- I believe I can grow in positive ways by dealing with difficult situations.					
4- I actively look for ways to replace the losses I encounter in life.					

Categories of resilience:

low resilience (score < 13)
medium resilience (score 13–16)
high resilience (score 17–20)

Hahad O et al.
J Psychosom Res 2025 May;192:112116.
doi: 10.1016/j.jpsychores.2025.112116.

Sinclair VG, Wallston KA. The Development and Psychometric Evaluation of the Brief Resilient Coping Scale. Assessment 2004;11:94–101. doi: 10.1177/1073191103258144

The Connor-Davidson resilience Scale 10 "CD-RISC 10".

How to assess an individual's level of resilience

Consider how well the following statements describe your behaviour and actions on a scale from 0 (*i.e. "not true at all"*) to 4 (i.e. *"True nearly all the time")*.

Final CD-RISC 10 score values: from 0 to 40.

Items	Not true at all 0	Rarely true 1	Sometimes true 2	Often true 3	True nearly all the time 4
1- I am able to adapt when changes occur					
2- I can deal with whatever comes my way					
3- I try to see the humorous side of things when I am faced with problems					
4- Having to cope with stress can make me stronger					
5- I tend to bounce back after illness, injury or other hardships					
6- I believe I can achieve my goals, even if there are obstacles					
7- Under pressure, I stay focused and think clearly					
8- I am not easily discouraged by failure					
9- I think of myself as a strong person when dealing with life's challenges and difficulties					
10- I am able to handle unpleasant and painful feelings like sadness, fear and anger					

Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003;18(2):76-82. doi: 10.1002/da.10113.

TO MAKE IT SHORT:

3,894 young women included into the AFHI registry,

first VTE triggered by COCs (90.4%) *or* pregnancy / puerperium (9.6%).

Investigated as outpatients one month after the end of anticoagulation

characteristics

thrombophilia screening,…

BRCS and CD RISC-10 scores

Follow-up;

cumulative exposure time: 26,825 patient-years

769 VTE recurrences

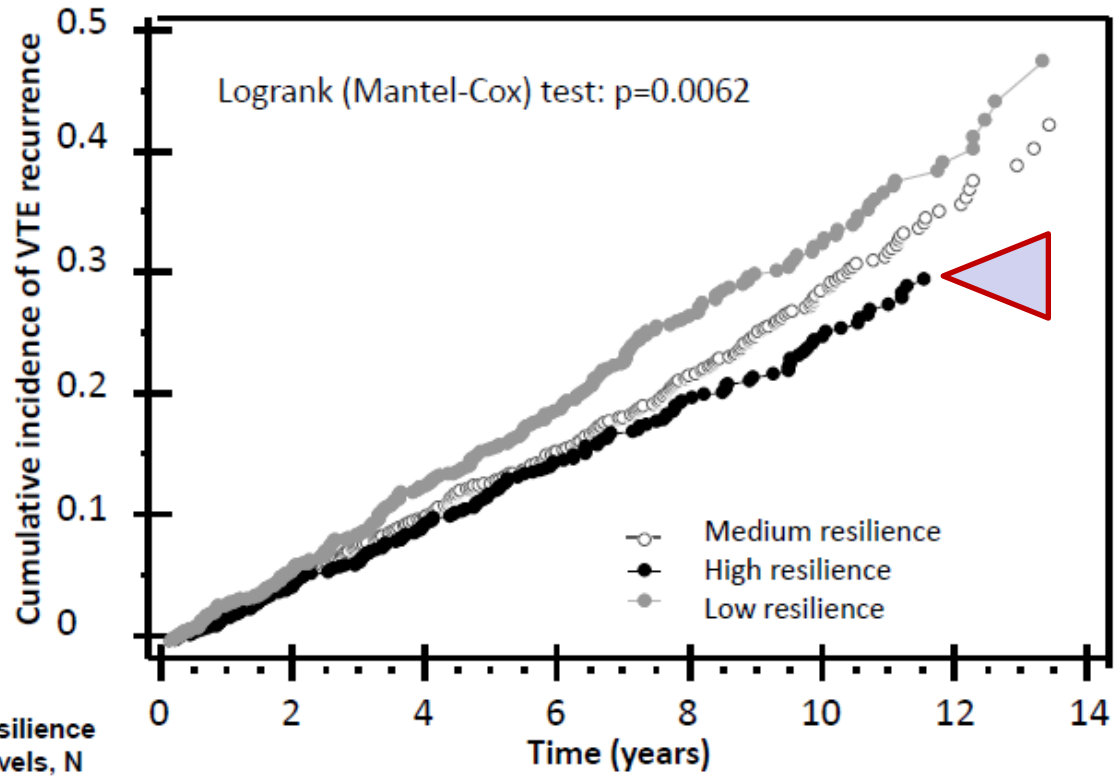
overall incidence of recurrence: 2.87 per 100 patient-years ($_{95\%}$ C.I.: 2.67–3.07).

Aim of the study:

to investigate the association between individually perceived psychological resilience with a recurrence of VTE in absence of chronic antithrombotic prophylaxis

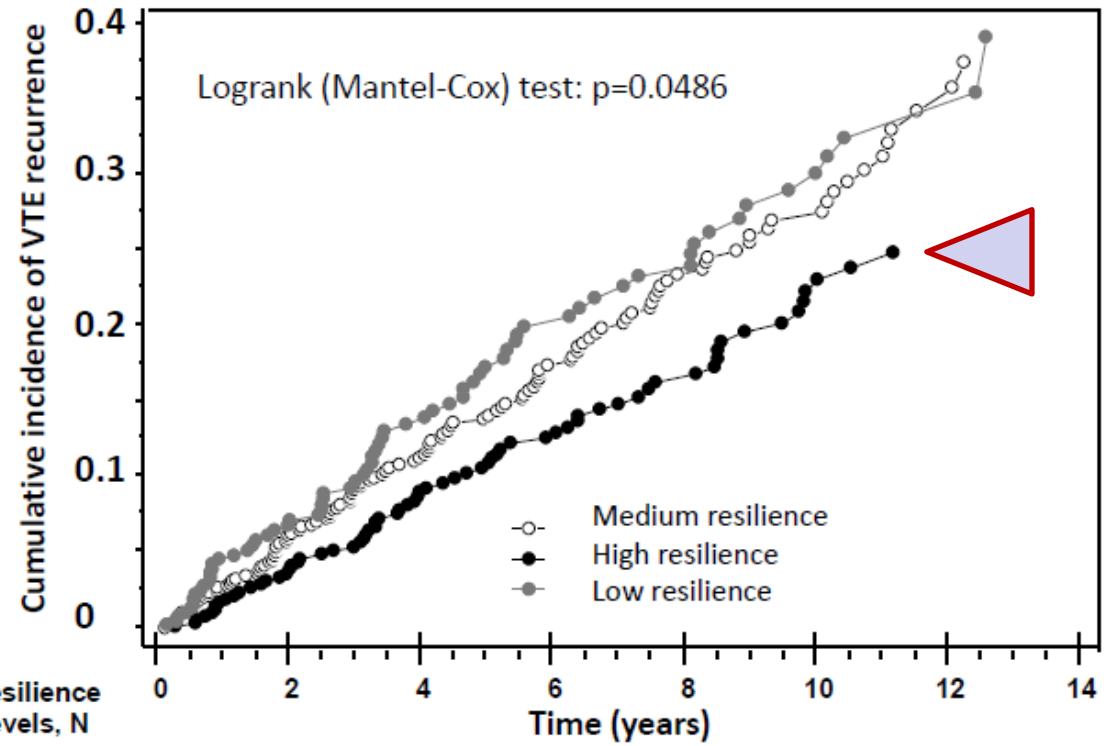
Kaplan-Meier estimates of the cumulative incidence of VTE recurrence according to baseline resilience levels (Brief resilient Comping Scale « BRCS » categories)

All initial VTE events



Resilience levels, N							
Low	1,128	972	778	592	436	280	113
Medium	1,755	1,539	1,25	989	751	466	172
High	1,011	898	738	580	439	296	119

Sensitivity analysis: initial proximal DVT or PE



Resilience levels, N							
Low	353	293	225	166	140	89	51
Medium	629	548	445	344	261	163	63
High	446	400	338	272	187	134	55

Predictors for VTE recurrence at univariate analysis, all women

Characteristic	VTE Recurrence (N = 769)	No VTE Recurrence (N=3,125)	HR	95% CI	P-value
Psychometrics					
Resilience Score (BRCS)					
Continuous			0.97	0.96 – 0.99	0.0005
Categories					0.0064
Low resilience	248	880	1 (Ref)	-	-
Medium resilience	345	1410	0.86	0.73 – 1.01	0.060
High resilience	176	835	0.73	0.60 – 0.89	0.002
CD-RISC 10					
Continuous			0.99	0.98 – 0.99	0.0006

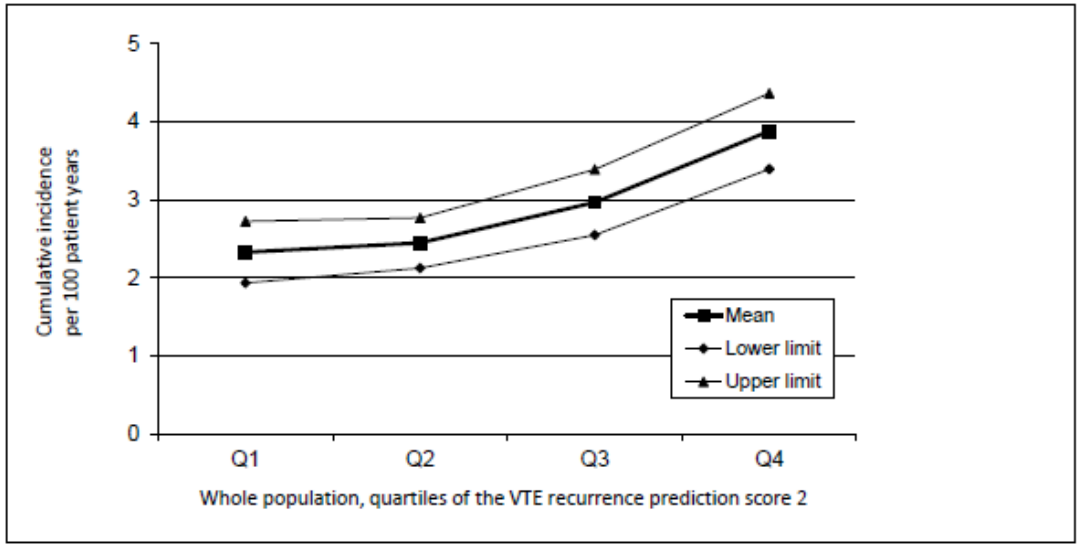
Predictive variables for recurrent VTE	Wald χ^2	Adjusted HR*	95% CI	p value
MODEL 3: Full Categorical Model				<0,0001
Resilience Score (BRCS)	8.93	-	-	0.0115
Low		1		
Medium resilience	3.29	0.859	0.729 – 1.012	0.0699
High resilience	8.76	0.747	0.615 – 0.906	0.0031
BMI Categories	9.65	-	-	0.0468
Normal		1		
Overweight	0.01	1.010	0.837 – 1.221	0.9139
Obesity Class I	1.17	1.110	0.919 – 1.340	0.2801
Obesity Class II	7.18	1.474	1.110 – 1.958	0.0074
Underweight	1.66	0.474	0.152 – 1.478	0.1981
D-Dimers (≥ P85)	6.35	1.270	1.055 – 1.530	0.0118
PTT Ratio (< P10)	9.75	1.407	1.136 – 1.744	0.0018

*All HR values in this model are adjusted on initial VTE phenotype, diabetes mellitus, factor IX ≥ 80th percentile, factor XI ≥ 80th percentile, factor II ≥ 95th percentile and thrombogenic polymorphisms.

Multivariable models, *all women*

Predictive variables for recurrent VTE	Wald χ^2	HR	95% CI	p value
Score 2: -(0,292xBRCS:High 1/0) - (0.152x BRCS:Medium 1/0) + (0,388xBMI:Obesity class II 1/0) + (0,239xD-dimers: ≥ P85 1/0) + (0.342xPTTratio: < 10th percentile 1/0). Values: -0.152 [0.152] (-0.292, 0.969).	36.34	2.706	1.958-3.741	<0.0001

Derived predictive score



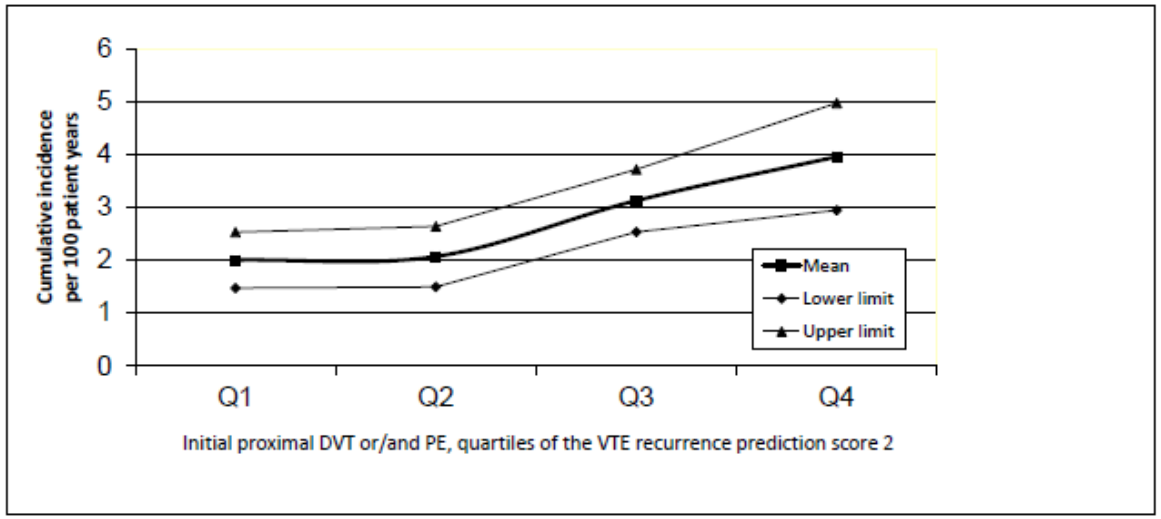
Multivariable models, *proximal DVT or/and PE*

Predictive variables for recurrent VTE	Wald χ^2	Adjusted HR*	95% CI	p value
MODEL 2	24.13			0.0011
Resilience, BRCS categories	5.77			0.0163
Low *or* medium		1		
High	5.77	0.714	0.542-0.940	0.0163
D-dimers $\geq$ 85th percentile	4.53	1.395	1.027-1.895	0.0332
ABO blood group: non-O	3.89	1.290	1.002-1.661	0.0486

* All HR values in this model are adjusted on BMI categories, FIX $\geq$ 95th percentile.

Predictive variables for recurrent VTE	Wald χ^2	HR	95% CI	p value
Score 2: - (0.337 BRCS High vs. others: High 1/0) + (0.333 DD-dimers: >=P85 1/0) + (0.255 ABO blood group: non-O 1/0). Values: 0 [0.337] (-0.337, 1.028).	19.73	2.746	1.756-4.289	<0.0001

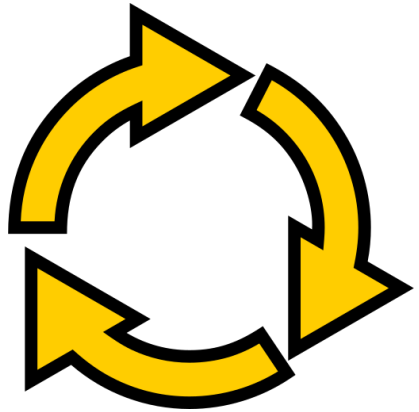
Derived predictive score



Summary of new inputs

International, multicenter, retrospective, observational study on prospectively collected data focused on non-anticoagulated women with a first episode of VTE associated with a weak transient clinical risk factor and no high-risk thrombophilia:

Women taking COCs:
intimate partner violence
is a risk factor
for a first
VTE event.



Women with a first VTE event triggered by a weak transient clinical risk factor suspected for first VTE recurrence:
intimate partner violence
and the
perceived stress level
are predictors
of recurrence.

Women with a first VTE event triggered by COCs use or pregnancy / puerperium:
high resilience level
protects from VTE recurrence.

Summary of new inputs

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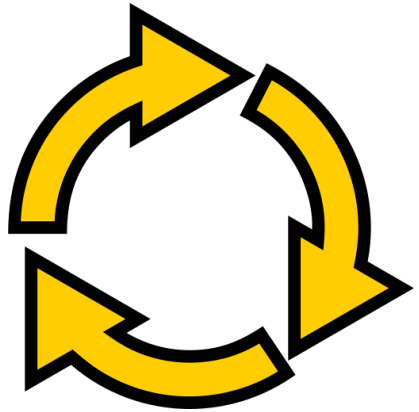

Women with a first VTE event triggered by a weak transient clinical risk factor suspected for first VTE recurrence:
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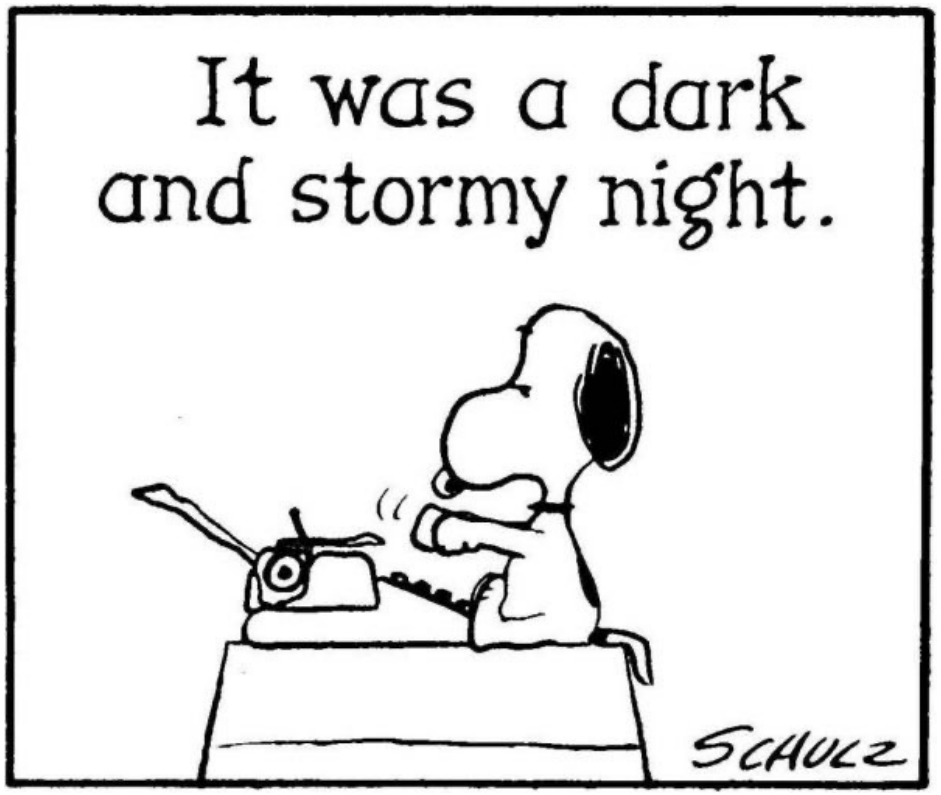
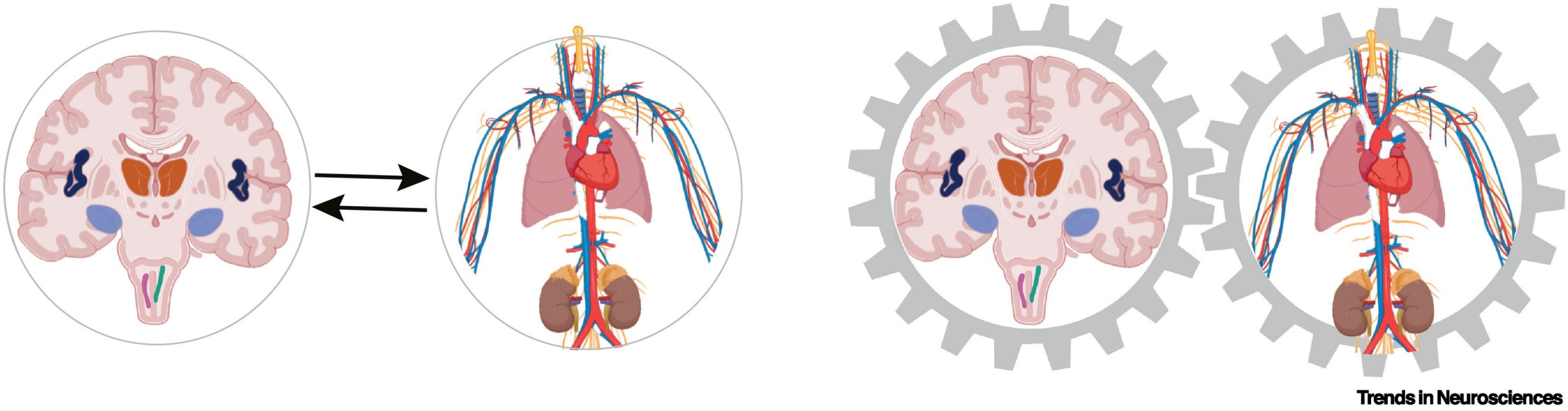
high resilience level
protects from VTE recurrence.

BUT:
Retrospective…
No laboratory marker of stress
Limited to the less severe VTE phenotypes
No interventional study
…

Conclusion

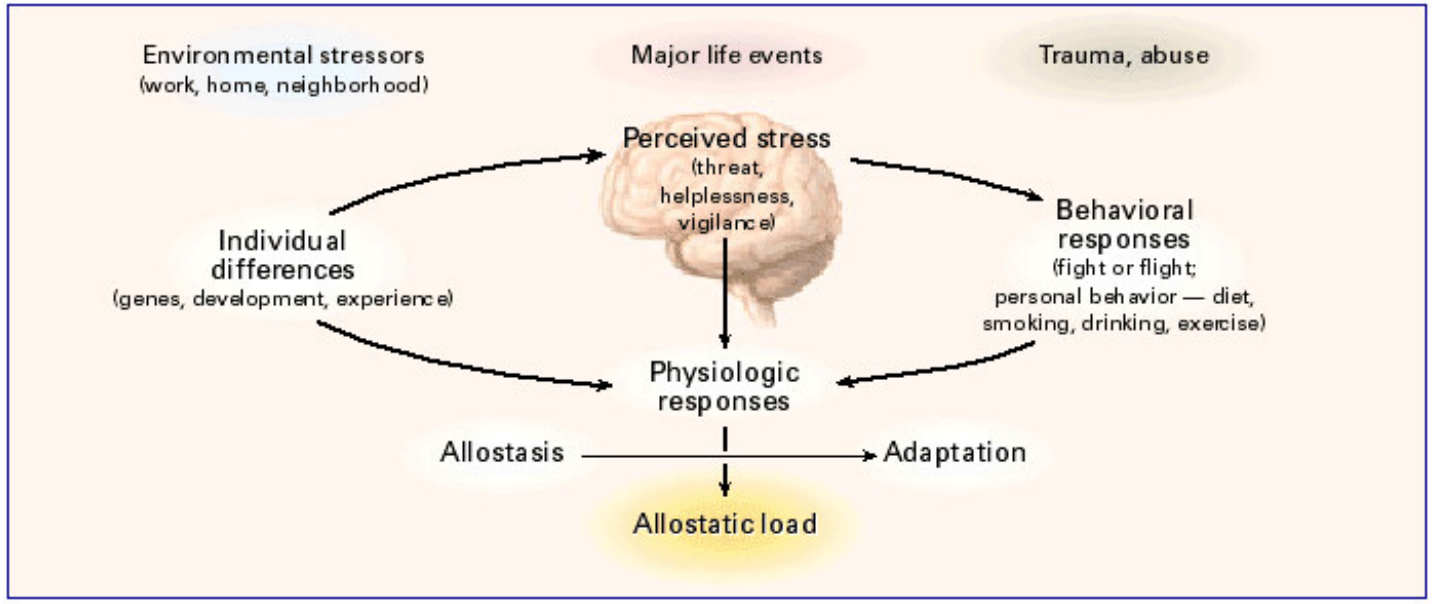


- A growing body of preliminary data suggests that VTE in young women has a contributing and prognostic component of a psychosomatic nature
  - *The brain is undoubtedly an organ that interacts with the body… and vice versa*



Trends in Neurosciences

- These data could support the so-called concept of *« stress-induced (thrombogenic) hypercoagulability »*
- Is it time, when it comes to VTE, to view individuals as a whole with a permeable blood-brain barrier? What are the medical promises of a global approach?



To be continued…

University of Montpellier

Σας ευχαριστούμε πολύ για την υπομονή σας



Sechenov University, Moscow

University Hospital of Nîmes

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- UMR UA11 INSERM
- Gynaecology Obstetrics
- Oncology

The NOHA network



- Intensive Care Unit
- Vascular Medicine
- Internal Medicine
- Clinical Research Unit