SFTH
SOCIÉTÉ FRANÇAISE DE THROMBOSE ET D'HÉMOSTASE
CONGRÈS DE LA SOCIETE FRANÇAISE DE THROMBOSE ET D'HÉMOSTASE
30 SEPT. 02 OCT. 2026

Poids extrêmes : quelle molécule? Quelle posologie?

Isabelle Gouin-Thibault

Service d'Hématologie-Hémostase Biologique, CHU Pontchaillou

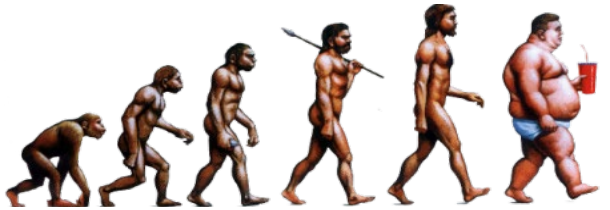
IRSET - Inserm UMR_S 1085, Université Rennes

GIHP
F-CRIN NETWORK INNOVTE INvestigation Network On Venous Thrombo-Embolism

Liens d’intérêt

- Leo-Pharma, Viatris

Obésité

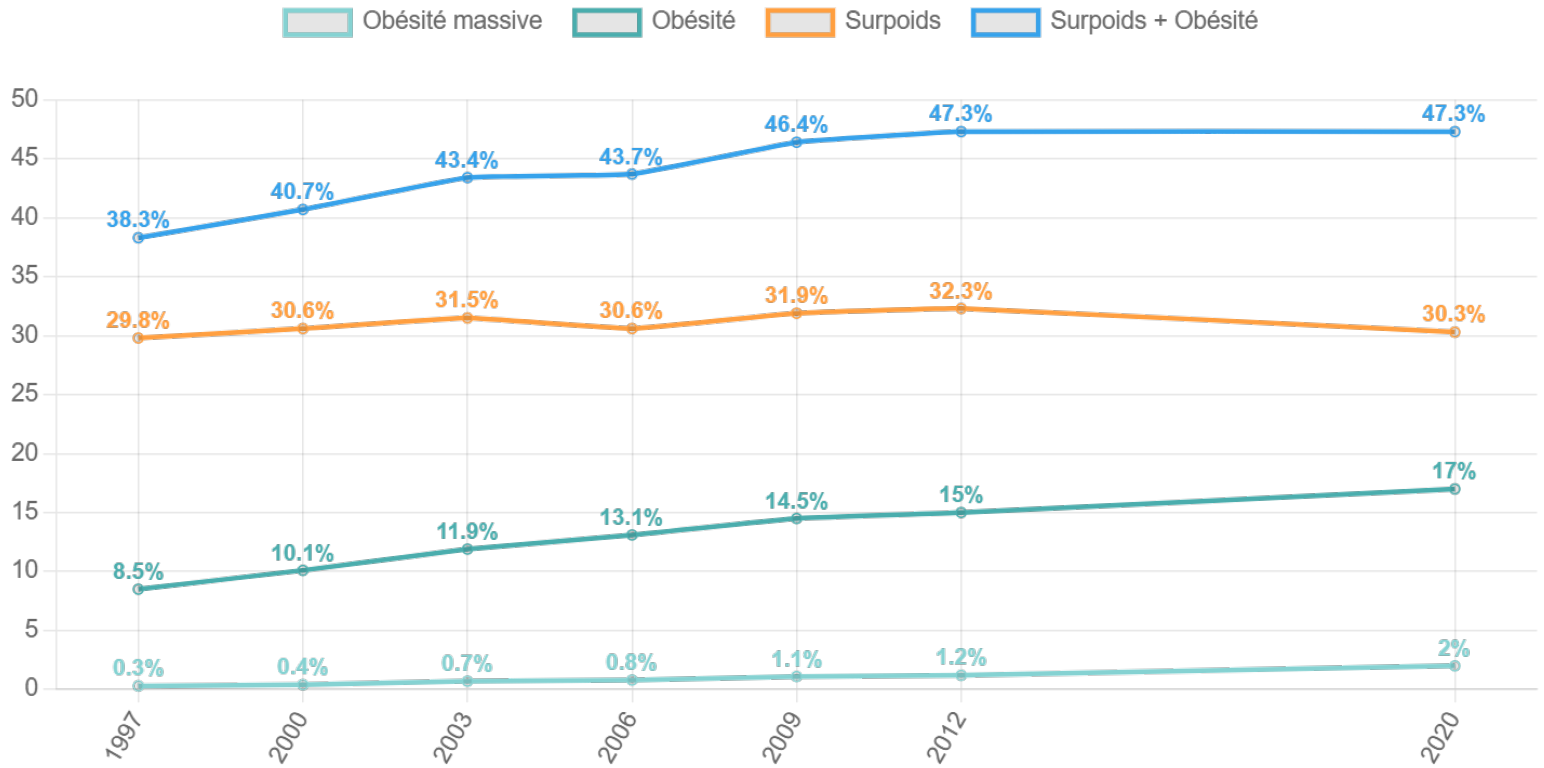


$$IMC = \frac{\text{poids (en kg)}}{\text{taille}^2 \text{ (en m}^2\text{)}}$$

Classification	
Maigreur	< 18,5
Normal	18,5 - 24,9
Surpoids	25,0 - 29,9
Obésité classe I	30,0 - 34,9
Obésité classe II	35,0 - 39,9
Obésité classe III	≥ 40,0

Prévalence mondiale de l'obésité *(WHO, 2022)* :
1 personne sur 8
Adultes : 890 millions

France



Ligue contre l'obésité

Obésité et risque thrombotique

- Facteur de risque d'évènements thromboemboliques veineux, de récidives, et d'évènements cardiovasculaires

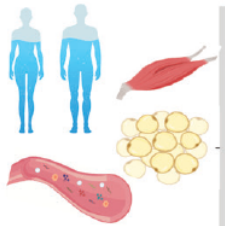
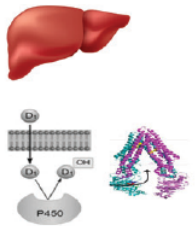
Table 1 Relative risks of pulmonary embolism and deep venous thrombosis according to age among obese and non-obese patients

	Pulmonary embolism		Deep venous thrombosis	
	Obese vs non-obese		Obese vs non-obese	
Age groups	Relative risk	(95% CI)	Relative risk	(95% CI)
<40 y	5.19	(5.11–5.28)	5.20	(5.15–5.25)
40–49 y	1.94	(1.91–1.97)	2.13	(2.11–2.15)
50–59 y	1.25	(1.23–1.27)	1.67	(1.65–1.68)
60–69 y	1.42	(1.40–1.44)	1.88	(1.87–1.90)
70–79 y	2.07	(2.04–2.10)	1.89	(1.87–1.91)
>80 y	3.15	(3.08–3.22)	2.16	(2.12–2.20)
All ages	2.18	(2.16–2.19)	2.50	(2.49–2.51)

CI = confidence interval.

Stein, Am J Med. 2005 ; Ageno W, Circ 2008 ; Ihaddadene and Carrier, Expert Opin Drug Saf. 2016 ; Ageno W, RPTH 2026 ; Ageno W, Obesity Surgery 2026

Obésité et modifications pharmacocinétiques

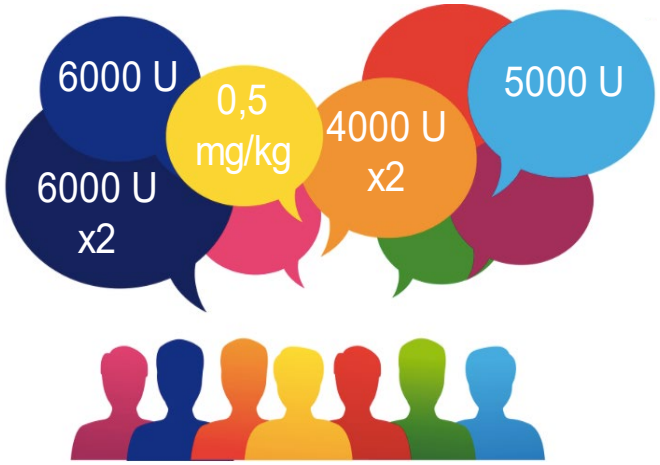
		Obesity (class ≥2)	GLP1R and GLP1R/GIP agonists
Absorption		↑gastric emptying time and pH, intestinal motility, gut wall permeability Gut dysbiosis ↓ Tmax ↑oral bioavailability if BMI >40 mg/m2 ↑subcutaneous adipose tissue, but ↓ local blood flow, thus slow transdermal absorption	↑ gastric emptying time and pH ↓small intestinal transit Possible ↑ Tmax and Cmax Possible ↑ AUC
Distribution		↓lean/fat body mass ratio and blood flow in fat tissue ↑ blood volume, cardiac output, splanchnic, hepatic, renal blood flow ↑ Vd and ↓ C_{max} for hydrophilic drugs, no change in half-life; ↑↑ Vd into fat tissue and half-life for lipophilic drugs; ↓ C_{max} Changes in Vd cannot be predicted only on lipophilicity ↑ acute phase proteins, α1 acid glycoprotein, free fatty acids, plasma lipids; ↓ free fraction of drugs (i.e. warfarin) ↑ carboxylesterase-1 in gastrointestinal adipose tissue	Indirect changes of Vd of lipophilic drugs and half-life of drugs that accumulate in the adipose tissue, in relation to body weight loss ↓ acute phase proteins that may indirectly affect drug biotransformation
Metabolism		↑liver size, hepatic blood flow and first-pass effect of drugs with high and moderate hepatic extraction If NAFLD/NASH: ↓hepatic blood flow, metabolizing enzymes and transporters, biliary clearance (bile stasis) ↓CYP3A4, 2C19, 2B6; ↑ UGT (phase II) activities No change or ↑ CYP1 A2, 2C9, 2D6 and 2E1 activities and P-gp ↓ Overall drug's biotransformation if NAFLD	No documented direct effect on CYP450s or phase II metabolising enzymes or drug transporters Possible indirect effects through reduced systemic inflammation
Excretion		↑ kidney size and renal blood flow and filtration at initial phases ↓ GFR (high intra-glomerular pressure and comorbidities) later. Uncertain impact on renal drug clearance Best formula describing renal function uncertain in severe obesity	Possible indirect effects through increased filtration rate

Pitocco D, ECR 2026

Obésité et anticoagulation : problématique

- **HNF et AVK** : suivi biologique
- **HBPM**
  - Dose préventive : fixe ou adaptée au poids ?
  - Dose thérapeutique : adaptée au poids ou limitée ?
- **Anticoagulants Oraux Directs**

  Dose fixe : risque de "sous-dosage “ ?



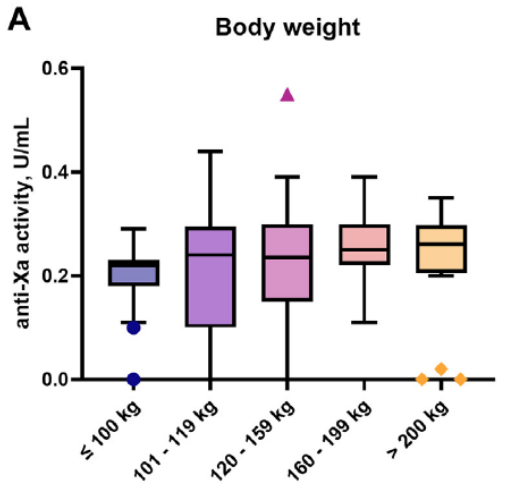
HBPM : thromboprophylaxie

- **Etudes basées sur activité anti-Xa**
- **Peu de données cliniques**

Doses majorées / adaptées au poids : pas de surdosage

- Patients médicaux, n=66
- > 50 UI/kg/j tinzaparin
- Cible anti-Xa au pic : 0,2 – 0,4 UI/mL

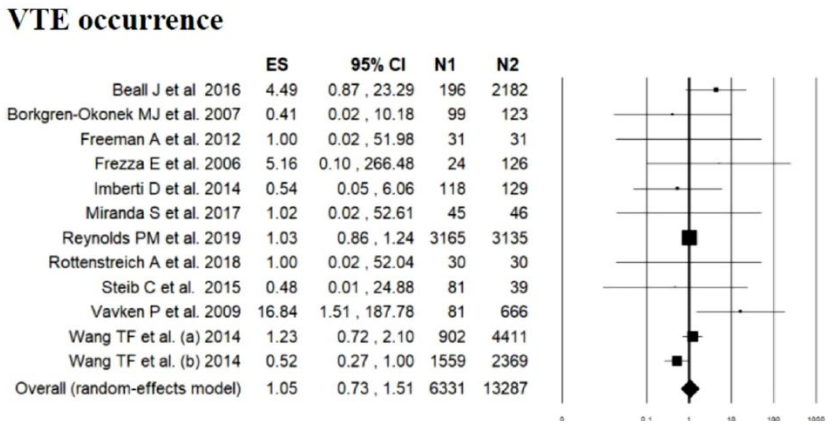
Weight (kg)	≤100	101-119	120-159	160-199	≥200
Dosage (IU)	4500	6000	8000	10,000	12,000
Patients (*n*, %)	18 (27.2)	11 (16.7)	20 (30.3)	6 (9.1)	11 (16.7)

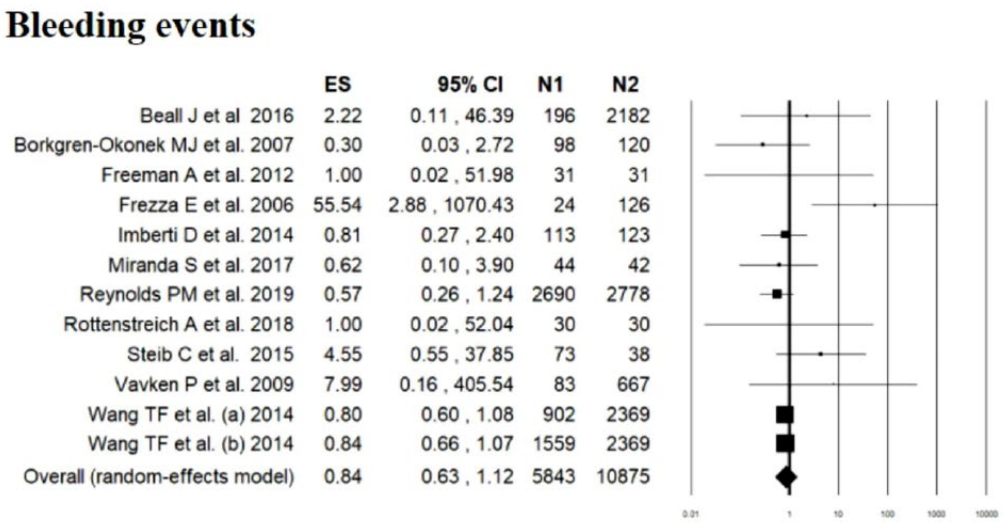


Rondina MT, Thromb res 2010 ; Freeman A, Am j Hematol 2012 ; Miranda S, Thromb Res 2017 ; Freeman AL, Exp Rev Cardiovasc Ther 2010 ; Patel JP, BJH 2011 ; Ihaddadene R, Exp Op Druf Saf 2017 ; He Z, Crit rev Onclol/Hematol 2017 ; Vandiver JW, J Thromb Thrombolysis 2016, War Phyo, J Pharm Tec 2025

Pfrepper C. RPTH 2023;7(2):100054.

HBPM : thromboprophylaxie





Méta-analyse : dose ajustée / dose fixe

IMC ≥ 30 kg/m² → pas de bénéfice

Ceccato D. Eur J Int Med 2021

Venous thromboembolic (VTE) events in the cohort stratified by BMI and Prophylaxis.

Population	Prophylaxis	VTE	No VTE	VTE (%)	OR	95% CI	p Value
BMI < 40 kg/m² (N = 5313)	Standard	68	4343	1.54	ref.		
	High-dose	17	885	1.88	1.23	0.72-2.10	0.46
BMI ≥ 40 kg/m² (N = 3928)	Standard	35	2334	1.48	ref.		
	High-dose	12	1547	0.77	0.52	0.27-1.00	0.05

Bleeding events in the cohort stratified by BMI and prophylaxis.

Population	Prophylaxis	Bleeding	No Bleeding	Bleeding (%)	OR	95% CI	p Value
BMI < 40 kg/m² (N = 5313)	Standard	376	4035	8.52	ref.		
	High-dose	62	840	6.87	0.79	0.60-1.05	0.10
BMI ≥ 40 kg/m² (N = 3928)	Standard	200	2169	8.44	ref.		
	High-dose	112	1447	7.18	0.84	0.66-1.07	0.15

IMC ≥40 kg/m² :

énoxaparine 4000 UI/12h *vs* 4000 UI/24h

plus efficace et tolérance équivalente

Wang CC, et al. Thromb Hemost 2015 ;113(1):185-92.

HBPM thromboprophylaxie : propositions



- **Pas d'ajustement** des posologies d'HBPM ou de fondaparinux pour un IMC compris **entre 30 et 39 kg/m²**
- **Ajustement** des posologies pour un **IMC > 40 kg/m²**
  - **Enoxaparine : 4000 UI x 2 / jour ou 6000 UI x 1 / jour**
  - **Daltéparine : 5000 UI x 2 / j**
  - **Tinzaparine : 50 UI / kg x 1 / j**
  - **Fondaparinux : 5 mg x 1 / jour**

SFMV
Société Française de Médecine Vasculaire

GIHP Groupe d'intérêt en hémostase péri-opératoire

RFE 2026 ; RCP tinzaparine ; Miranda S. Thromb Res2017

HBPM traitement : dose adaptée au poids ou limitée ?

- Peu d'études cliniques
- Etudes pharmacologiques , mesure anti-Xa
  - Enoxaparine : **≤144 kg, BMI≤48 kg/m^2 ,** 1,5 mg/kg/j
  - Dalteparine : **≤ 190 kg, BMI≤58 kg/m^2 ,** 100 UI/kgx2
  - Tinzaparine : **100-222 kg, BMI 36-75kg/m^2**, 175 UI/kg

Pas de différences entre obèses et non obèses

Sanderink GJ, CPT 2002; Matisse investigators Blood 2002 et NEJM 2003 ; Bazinet A, Thromb Res 2005; Hainer JW, Thromb Hemost 2002 ; Wilson SJ, Hemostasis 2001 ; Smith J, Am J Health Syst Pharm 2003 ; Barrett JS, CPT 2001 ; Al-Yassen E, JTH 2005 ; Barba R, JTH 2005 ; Ihaddadene R, Expert Opin. Drug Saf 2016 ; Maclachlan KH, Semin Thromb Hemos 2019 ; Abildgaard A, Sem Thromb Hemost 2020 ; Mirza R, Blood Advances 2020, Pfrepper C, Thromb Research 2022

HBPM : traitement dose adatée au poids ou limitée ?

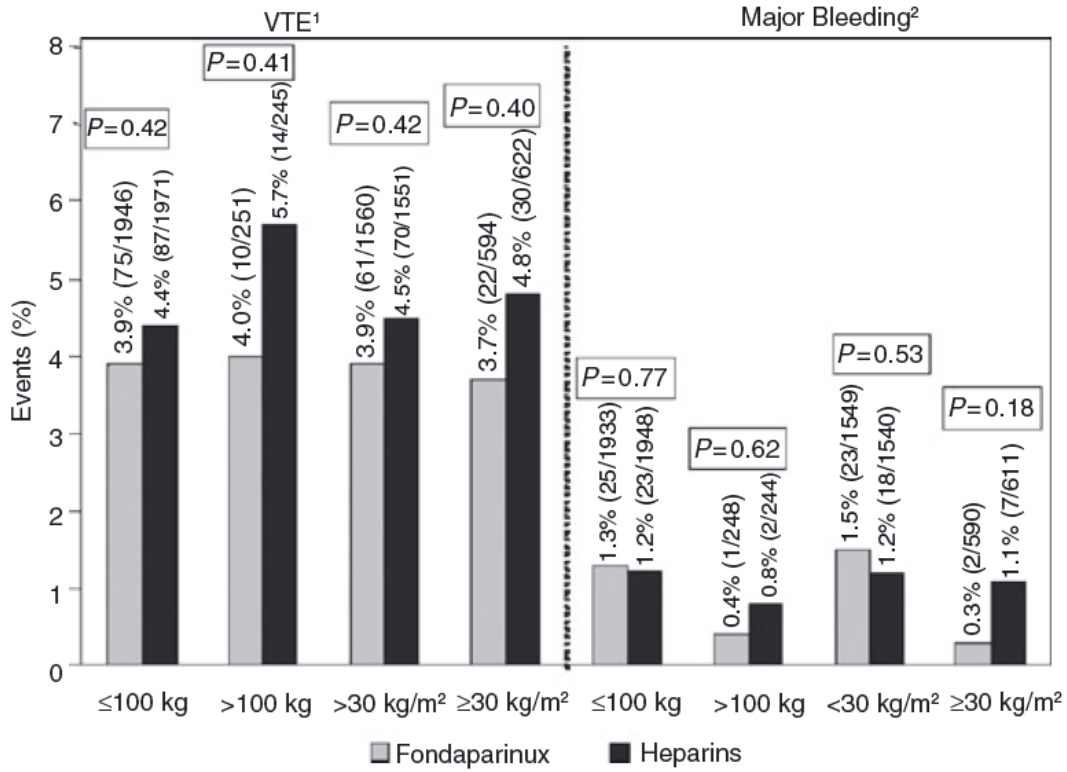
Registre RIETE **Pts > 100 kg**	**HBPM limitée** ‡ n=454 dose max 18 000 UI/j	**HBPM non limitée** n=2392
âge	**57** ± 16	**55** ± 13
poids kg / IMC kg/m^2	**107** ± 9 / **36** ± 5	**111** ± 13 / **38** ± 6
• Enoxaparine	**28** %	**91** %
• Tinzaparine	**55** %	**3** %

	HBPM capée **N = 454**	**HBPM non capée** **N = 2392**	**RR** **(IC95%)**
Récidive MTEV n (%/an)	2 (10.9 %/an)	6 (6.43 %/an)	1.69 (0.24 – 8.67)
Hgie majeure n (%/an)	0	24 (25.7 %/an)	-
Récidive + Hgie maj n (%/an)	2 (11.0 %/an)	30 (32.3 %/an)	0.34 (0.05 – 1.46

Mirza R, Blood Advances 2020

Fondaparinux

- **Fondaparinux: > 100kg (11%), 10 mg**
  - Matisse trials PE *vs* HNF : poids maximal 176 kg
  - Matisse VTE *vs* énoxaparine : poids maximal 159 kg



Davidson BL. J Thromb Haemost 2007;5:1191-4 ; Matisse investigators Blood 2002 et NEJM 2003

Fondaparinux / énoxaparine



Résultats observés sous enoxaparine

Dose énoxaparine : 1 mg / kg / 12 h sans limite de poids

	< 100 kg	**> 100 kg**
n (%)	1971 (89 %)	245 (11 %)
poids (médiane, rang)	76 (33 → 100)	**111** (100 → 217)
dose quotidienne (mg)	152 (60 → 200)	**220** (206 → 344)
Récidives MTEV	4.4 %	5.7 %
Hgie majeure	1.2 %	0.8 %

Diapo P. Mismetti

Davidson BL. J Thromb Haemost 2007

JMV—Journal de Médecine Vasculaire 49 (2024) 170—175

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



RECOMMENDATIONS

Unresolved questions on venous thromboembolic disease. Venous thromboembolism (VTE) management in obese patients. Consensus statement of the French Society of Vascular Medicine (SFMV)

Sébastien Miranda[a,*], Marjolaine Talbot[b], Isabelle Gouin-Thibault[c], Benjamin Espinasse[d,e], Guillaume Mahe[b], on behalf the SFMV

HBPM / fondaparinux



Table 1 Suggested doses of anticoagulant in adult patient with BMI > 30.

VTE treatment	Type	Suggested dose	Notes
	Fondaparinux	10 mg once daily	
	Enoxaparin	100 IU/kg q12 h	Uncapped
	Tinzaparin	175 IU/kg once daily	Uncapped
	Dalteparin	200 IU/kg once daily first month 150 IU/kg once daily after first month	Uncapped

Miranda S, JMV 2024

Consensus on the Management of the Clinical Challenges of Venous Thromboembolism in Special Situations

Thromb Haemost 2025;125:944–959.

Cristina Marzo[1] Teresa Solanich[2] Dolors Tassies[3] Elena Pina[4] Maite Antonio Rebollo[5] Enrique Gallardo[6,7] Sonia Serradell[8] Marta Merino[9] Marina Carrasco[10] Albert Tugues[11]

Taking all the above into account, the use of a **dose of LMWH adjusted to the weight** of the patient **without establishing a maximum limit** is recommended for the treatment of VTE in obese patients with **weight greater than 100 kg** (**Grade III, B recommandation**)

A. Parenteral (LMWH and heparinoids)	
	Posology
Enoxaparin	1 mg/kg/12 h or 1.5 mg/kg/day
Tinzaparin	175 IU/kg/day
Bemiparin	115 IU/kg/day
Dalteparin	100 IU/kg/12 h or 200 IU/kg/day
Fondaparinux	<50 kg: 5 mg/24 h, 50–100 kg: 7.5 mg/24h, >100 kg: 10 mg/24 h

Patients avec risque hémorragique élevé

	Gestion péri-procédurale des AVK et post-procédurale des AOD en cas de poids corporel ≥100 kg * #	Grade	Accord
11.1	Chez un patient de poids corporel ≥100 kg nécessitant un relais péri-procédural des anticoagulants oraux, il est proposé d'utiliser les HBPM à doses curatives sans surveillance biologique en 1ère intention et de n'utiliser l'HNF qu'en 2ème intention.	2+	Fort
11.2	Chez un patient de poids corporel ≥100 kg ayant un relais péri-procédural par HBPM, les experts suggèrent de ne pas augmenter les posologies curatives des HBPM au-delà de celles recommandées pour 100 kg de poids corporel pour réduire le risque hémorragique, soit par exemple 18 000 UI x 1/j pour la tinzaparine, la daltéparine et la nadroparine et 10 000 UI x 2/j pour l'enoxaparine.	Avis d'experts	Fort

Propositions INNOVTE

- It is **proposed**, to use a **weight-based dose** of Low Molecular Weight Heparins (LMWH) using **actual body weight** for treatment of acute phase of VTE treatment
- In patients weighing **more than 150 kg**, the **experts suggest** to **cap** the dose **at 150 kg**
- In case of a **high bleeding risk**, the experts suggest **to cap** the dose at a **body weight of 100 kg**

NON VALIDEES

Mesure de l'activité anti-Xa



- **But** : **dépister une accumulation**
- **Pas d'index thérapeutique**
- **Indications** : complications hémorragiques , patients à risque d'accumulation (insuffisants rénaux sévères / sujets âgés / poids extrêmes….)

Seuil "d'accumulation / surdosage "
anti-Xa au pic (UI/mL)

	2 injections / j	1 Injection / j
Daltéparine	**1**	**/**
Enoxaparine	**1,5**	**nd**
Nadroparine	**nd**	**1,8**
Tinzaparine	**/**	**1,5**

Boneu B. STV 2003 ; Gouin-Thibault I, Encycl Med Chir, AKOS, 2013

Anticoagulants oraux directs

- Pas d'étude spécifique
- MTEV, FA : registres, analyses post-hoc, études de cohortes rétrospectives, meta-analyses : comparaisons rivaroxaban, apixaban et AVK ou comparaison entre les différents niveaux obésité

Efficacité et sécurité d'apixaban et rivaroxaban
dans les différents groupes de poids ou par rapport aux AVK

Kubitza J, J Clin Pharmacol 2007 ; Upreti VV, Br J Clin Pharmacol 2013 ; Arachchillage D, Thromb Res 2016 ; Di Nisio M. TH 2016 ; Piran S, RPTH 2018 ; Boonyawat K, JTH 2017 , Tittl L, Int J Cardiol 2017; Kido K, Ann Pharmaco 2019 ; Peterson ED Am Heart J 2019, Kushnir M, Lancet Hematol 2019 ; Doucette K, Advances in Hematology 2020 ; Coons JC, Pharmacotherapy 2020, Aloi KG, J Pharm Practice 2020, Park DY BMC 2023; Rosovsky RP, Am J Med 2023; Talerico R TH Open 2024 ; Shi J, Medicine 2026 ; Peterson ED, Am Heart J 2019; Salh QM, Cureus 2023, Elad B, Am J Cardiol 2023, Elfar S, BMC 2024

AOD et MTEV

Systematic Review and Meta-Analysis

Medicine

OPEN

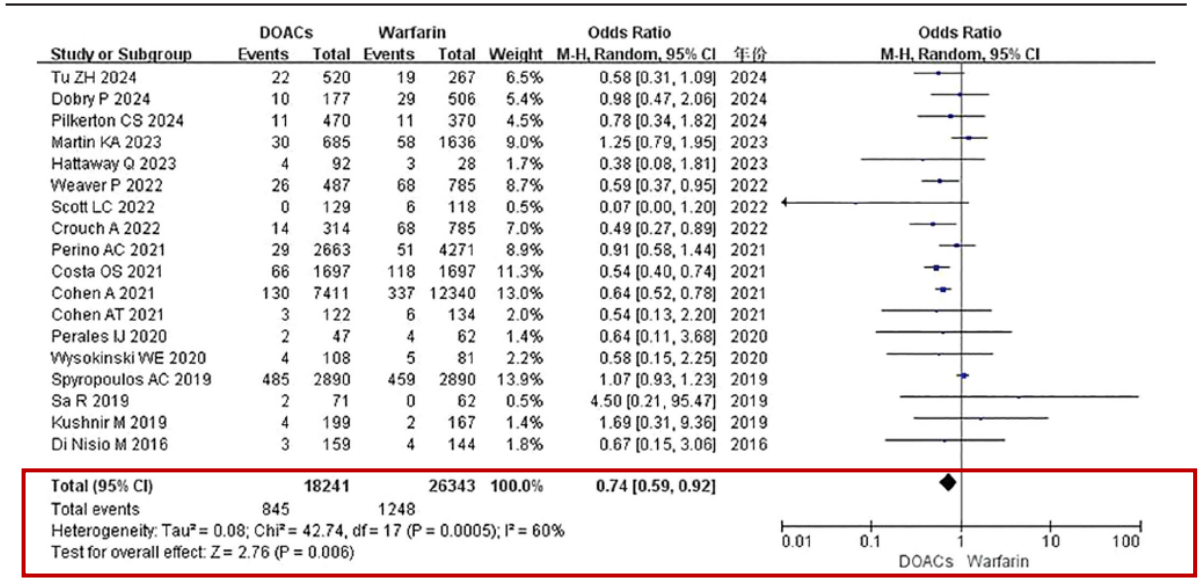
Safety and efficacy of direct acting oral anticoagulants in the treatment of patients with morbid obesity with venous thromboembolism

A meta-analysis

Jinping Shi, BS[a], Yan Zhang, MS[a], Yajuan Tang, MS[a,*], Liping Wang, MS[a], Han Xiao, BS[a]

- Obésité morbide : ≥ 120 kg ou IMC ≥ 40 kg/m^2
- 44 672 patients
- 20 études

Récidives MTEV

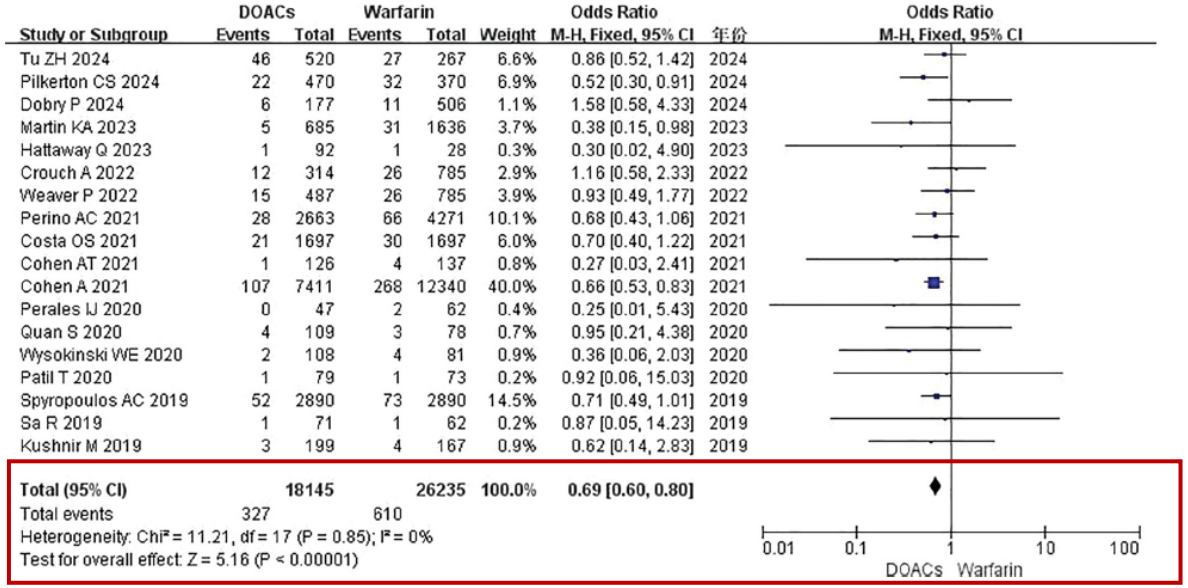


Study or Subgroup	DOACs Events	DOACs Total	Warfarin Events	Warfarin Total	Weight	Odds Ratio M-H, Random, 95% CI	年份
Tu ZH 2024	22	520	19	267	6.5%	0.58 [0.31, 1.09]	2024
Dobry P 2024	10	177	29	506	5.4%	0.98 [0.47, 2.06]	2024
Pilkerton CS 2024	11	470	11	370	4.5%	0.78 [0.34, 1.82]	2024
Martin KA 2023	30	685	58	1636	9.0%	1.25 [0.79, 1.95]	2023
Hattaway Q 2023	4	92	3	28	1.7%	0.38 [0.08, 1.81]	2023
Weaver P 2022	26	487	68	785	8.7%	0.59 [0.37, 0.95]	2022
Scott LC 2022	0	129	6	118	0.5%	0.07 [0.00, 1.20]	2022
Crouch A 2022	14	314	68	785	7.0%	0.49 [0.27, 0.89]	2022
Perino AC 2021	29	2663	51	4271	8.9%	0.91 [0.58, 1.44]	2021
Costa OS 2021	66	1697	118	1697	11.3%	0.54 [0.40, 0.74]	2021
Cohen A 2021	130	7411	337	12340	13.0%	0.64 [0.52, 0.78]	2021
Cohen AT 2021	3	122	6	134	2.0%	0.54 [0.13, 2.20]	2021
Perales IJ 2020	2	47	4	62	1.4%	0.64 [0.11, 3.68]	2020
Wysokinski WE 2020	4	108	5	81	2.2%	0.58 [0.15, 2.25]	2020
Spyropoulos AC 2019	485	2890	459	2890	13.9%	1.07 [0.93, 1.23]	2019
Sa R 2019	2	71	0	62	0.5%	4.50 [0.21, 95.47]	2019
Kushnir M 2019	4	199	2	167	1.4%	1.69 [0.31, 9.36]	2019
Di Nisio M 2016	3	159	4	144	1.8%	0.67 [0.15, 3.06]	2016
Total (95% CI)		**18241**		**26343**	**100.0%**	**0.74 [0.59, 0.92]**	
Total events	845		1248				

Heterogeneity: Tau² = 0.08; Chi² = 42.74, df = 17 (P = 0.0005); I² = 60%
Test for overall effect: Z = 2.76 (P = 0.006)

Figure 1. Forest plot for the recurrence rates of venous thromboembolism among morbidly obese patients administered DOACs versus warfarin. CI = confidence interval, DOAC = direct acting oral anticoagulant.

Saignements majeurs



Study or Subgroup	DOACs Events	DOACs Total	Warfarin Events	Warfarin Total	Weight	Odds Ratio M-H, Fixed, 95% CI	年份
Tu ZH 2024	46	520	27	267	6.6%	0.86 [0.52, 1.42]	2024
Pilkerton CS 2024	22	470	32	370	6.9%	0.52 [0.30, 0.91]	2024
Dobry P 2024	6	177	11	506	1.1%	1.58 [0.58, 4.33]	2024
Martin KA 2023	5	685	31	1636	3.7%	0.38 [0.15, 0.98]	2023
Hattaway Q 2023	1	92	1	28	0.3%	0.30 [0.02, 4.90]	2023
Crouch A 2022	12	314	26	785	2.9%	1.16 [0.58, 2.33]	2022
Weaver P 2022	15	487	26	785	3.9%	0.93 [0.49, 1.77]	2022
Perino AC 2021	28	2663	66	4271	10.1%	0.68 [0.43, 1.06]	2021
Costa OS 2021	21	1697	30	1697	6.0%	0.70 [0.40, 1.22]	2021
Cohen AT 2021	1	126	4	137	0.8%	0.27 [0.03, 2.41]	2021
Cohen A 2021	107	7411	268	12340	40.0%	0.66 [0.53, 0.83]	2021
Perales IJ 2020	0	47	2	62	0.4%	0.25 [0.01, 5.43]	2020
Quan S 2020	4	109	3	78	0.7%	0.95 [0.21, 4.38]	2020
Wysokinski WE 2020	2	108	4	81	0.9%	0.36 [0.06, 2.03]	2020
Patil T 2020	1	79	1	73	0.2%	0.92 [0.06, 15.03]	2020
Spyropoulos AC 2019	52	2890	73	2890	14.5%	0.71 [0.49, 1.01]	2019
Sa R 2019	1	71	1	62	0.2%	0.87 [0.05, 14.23]	2019
Kushnir M 2019	3	199	4	167	0.9%	0.62 [0.14, 2.83]	2019
Total (95% CI)		**18145**		**26235**	**100.0%**	**0.69 [0.60, 0.80]**	
Total events	327		610				

Heterogeneity: Chi² = 11.21, df = 17 (P = 0.85); I² = 0%
Test for overall effect: Z = 5.16 (P < 0.00001)

Figure 3. Forest plot for the rates of major bleeding events among morbidly obese patients administered DOACs versus warfarin. CI = confidence interval, DOAC = direct acting oral anticoagulant.

Subgroup analysis results.

Subgroup analysis	Study	Total study population	OR	95% CI	*P*
Recurrent VTE events with standard doses of DOACs vs warfarin	4[20,22,25,34]	2930	0.56	0.39–0.78	<.05
Major bleeding events of with standard doses of DOACs vs warfarin	5[20,22,25,27,29]	2873	0.95	0.61–1.47	.81
Recurrent VTE events of rivaroxaban vs warfarin	7[19,20,24,28,31,33,34]	11,247	0.71	0.47–1.09	.12
Major bleeding events of rivaroxaban vs warfarin	6[19,20,24,28,31,33]	10,944	0.73	0.55–0.95	<.05
Recurrent VTE events of apixaban vs warfarin	5[19,22,25,26,33]	21,398	0.62	0.51–0.75	<.05
Major bleeding events of apixaban vs warfarin	5[19,22,25,26,33]	21,405	0.67	0.55–0.83	<.05

CI = confidence interval, DOACs = direct acting oral anticoagulants, OR = odds ratio, VTE = venous thromboembolism.

Shi J, Medicine 2026

Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism:
Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation
K A. Martin et al, 2021

journal of thrombosis and haemostasis

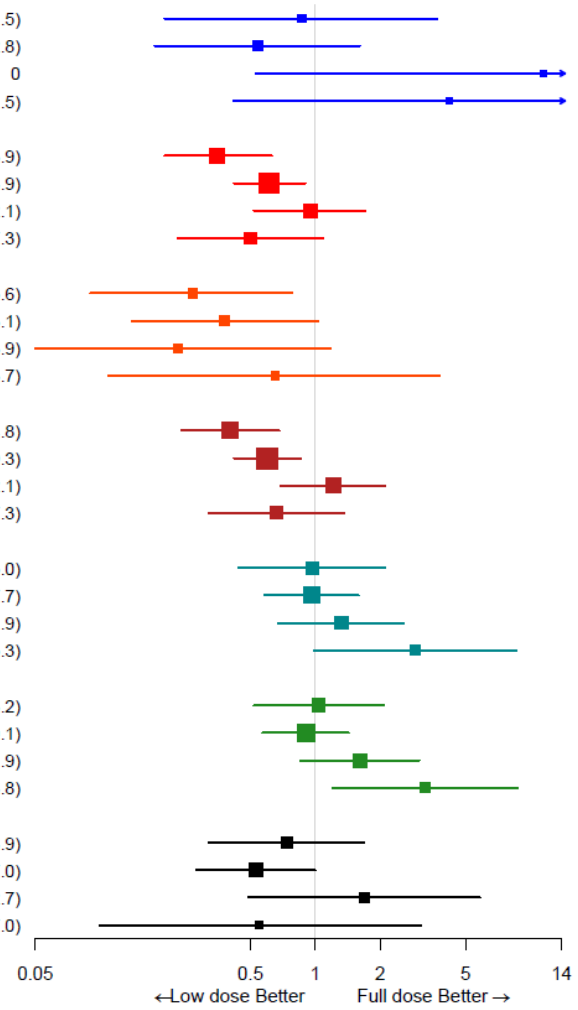
2021

Pour le **traitement de la MTEV,** il est suggéré d'utiliser la dose standard de **rivaroxaban ou d'apixaban quelque soit l'IMC ou le poids**. Il existe moins de données pour apixaban que pour rivaroxaban. Les AVK, HBPM ou le fondaparinux sont aussi des options.

Nous suggérons de **ne pas mesurer** régulièrement la **concentration** au pic ou en résiduelle **de l'AOD** du fait de données insuffisantes permettant de modifier la prise en charge.

AOD dose réduite ?

	Reduced dose N	Reduced dose n (5-y cum)	Full dose N	Full dose n (5-y cum)
Recurrent VTE				
BMI < 25	376	5 (2.6)	370	4 (1.5)
BMI 25-30	575	5 (0.9)	599	10 (2.8)
BMI 30-35	278	6 (3.8)	282	0
BMI ≥ 35	150	3 (2.9)	134	1 (1.5)
Relevant bleeding				
BMI < 25	376	18 (8.2)	370	40 (13.9)
BMI 25-30	575	44 (11.3)	599	70 (16.9)
BMI 30-35	278	22 (9.4)	282	24 (12.1)
BMI ≥ 35	150	12 (9.4)	134	20 (17.3)
Major bleeding				
BMI < 25	376	5 (2.8)	370	14 (5.6)
BMI 25-30	575	6 (2.6)	599	13 (3.1)
BMI 30-35	278	2 (0.8)	282	7 (3.9)
BMI ≥ 35	150	2 (1.4)	134	4 (3.7)
Net clinical benefit				
BMI < 25	376	22 (10.3)	370	43 (14.8)
BMI 25-30	575	48 (12.0)	599	79 (19.3)
BMI 30-35	278	28 (13.3)	282	24 (12.1)
BMI ≥ 35	150	15 (12.3)	134	20 (17.3)
Arterial event				
BMI < 25	376	14 (4.6)	370	13 (5.0)
BMI 25-30	575	30 (7.1)	599	32 (7.7)
BMI 30-35	278	19 (9.2)	282	17 (11.9)
BMI ≥ 35	150	14 (13.3)	134	6 (5.3)
Recurrent VTE or arterial event				
BMI < 25	376	19 (7.2)	370	16 (6.2)
BMI 25-30	575	35 (8.0)	599	41 (10.1)
BMI 30-35	278	24 (12.5)	282	17 (11.9)
BMI ≥ 35	150	17 (16.3)	134	7 (6.8)
All-cause death				
BMI < 25	376	10 (6.6)	370	17 (6.9)
BMI 25-30	575	15 (3.9)	599	28 (7.0)
BMI 30-35	278	7 (3.3)	282	5 (2.7)
BMI ≥ 35	150	3 (3.3)	134	4 (7.0)



RENOVE / obésité

Perte du bénéfice de la dose réduite en cas d'obésité ?

Couturaud F. Lancet 2025
Sevestre MA. Soumis

AOD et FA

Meta-analyses, populations importantes de patients obéses / obésité sévères

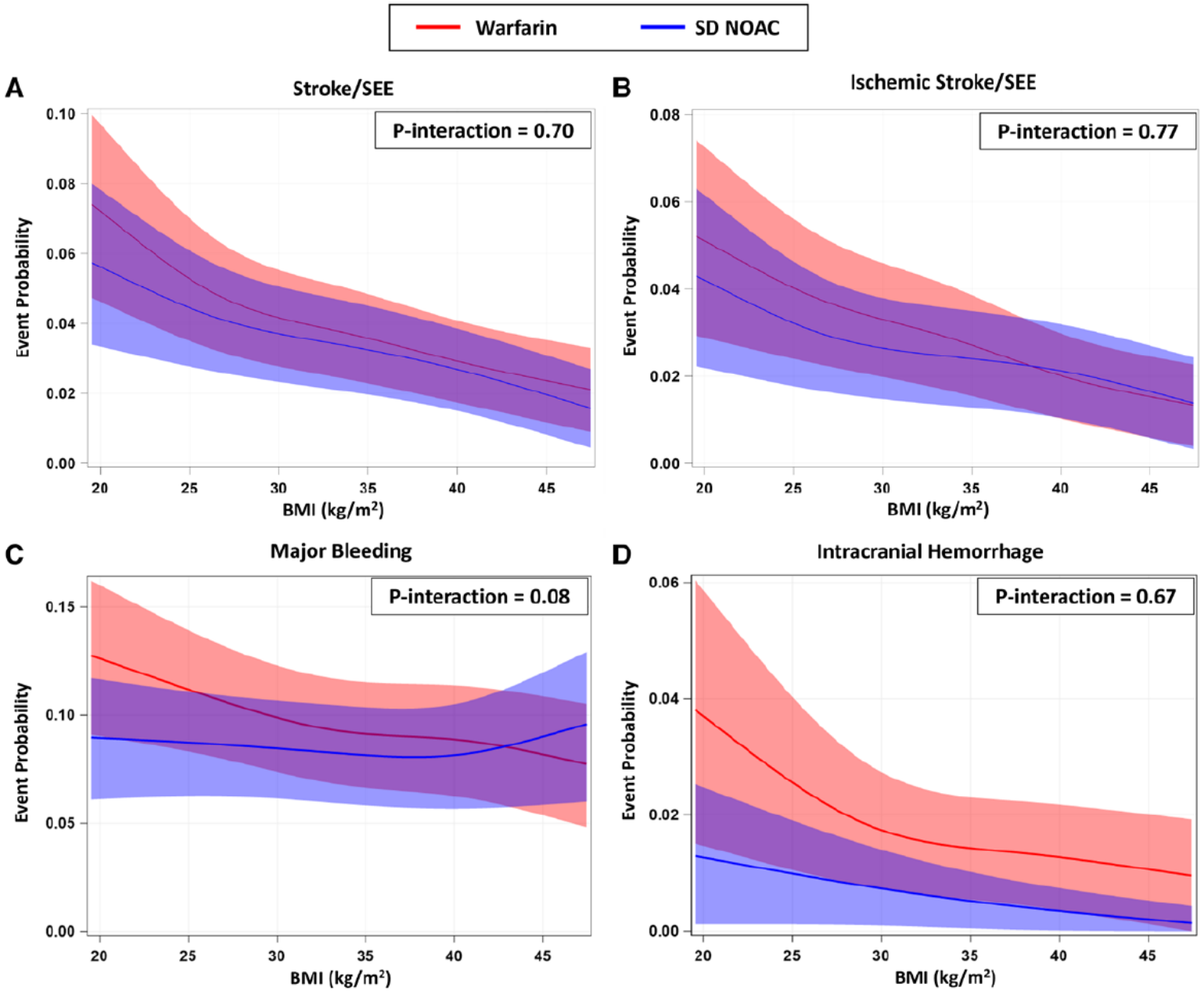
→ Efficacité et sécurité des AOD dans ces populations

Peterson ED, Am Heart J 2019; Salh QM, Cureus 2023, Elad B, Am J Cardiol 2023, Elfar S, BMC 2024

Efficacy and Safety of Non–Vitamin-K Antagonist Oral Anticoagulants Versus Warfarin Across the Spectrum of Body Mass Index and Body Weight: An Individual Patient Data Meta-Analysis of Four Randomized Clinical Trials of 58 464 Patients With Atrial Fibrillation

Siddharth M. Patel, MD, MPH; Eugene Braunwald, MD; Jan Steffel, MD; Giuseppe Boriani, MD, PhD; Michael G. Palazzolo, MS; Elliott M. Antman, MD; Erin A. Bohula, MD, DPhil; Anthony P. Carnicelli, MD; Stuart J. Connolly, MD; John Eikelboom, MBBS, MSc; Baris Gencer, MD, MPH; Christopher B. Granger, MD; David A. Morrow, MD, MPH; Manesh R. Patel, MD; Lars Wallentin, MD, PhD; Christian T. Ruff, MD, MPH; Robert P. Giugliano, MD, SM; on behalf of the COMBINE AF (A Collaboration Between Multiple Institutions to Better Investigate Non-Vitamin K Antagonist Oral Anticoagulant Use in Atrial Fibrillation) Investigators

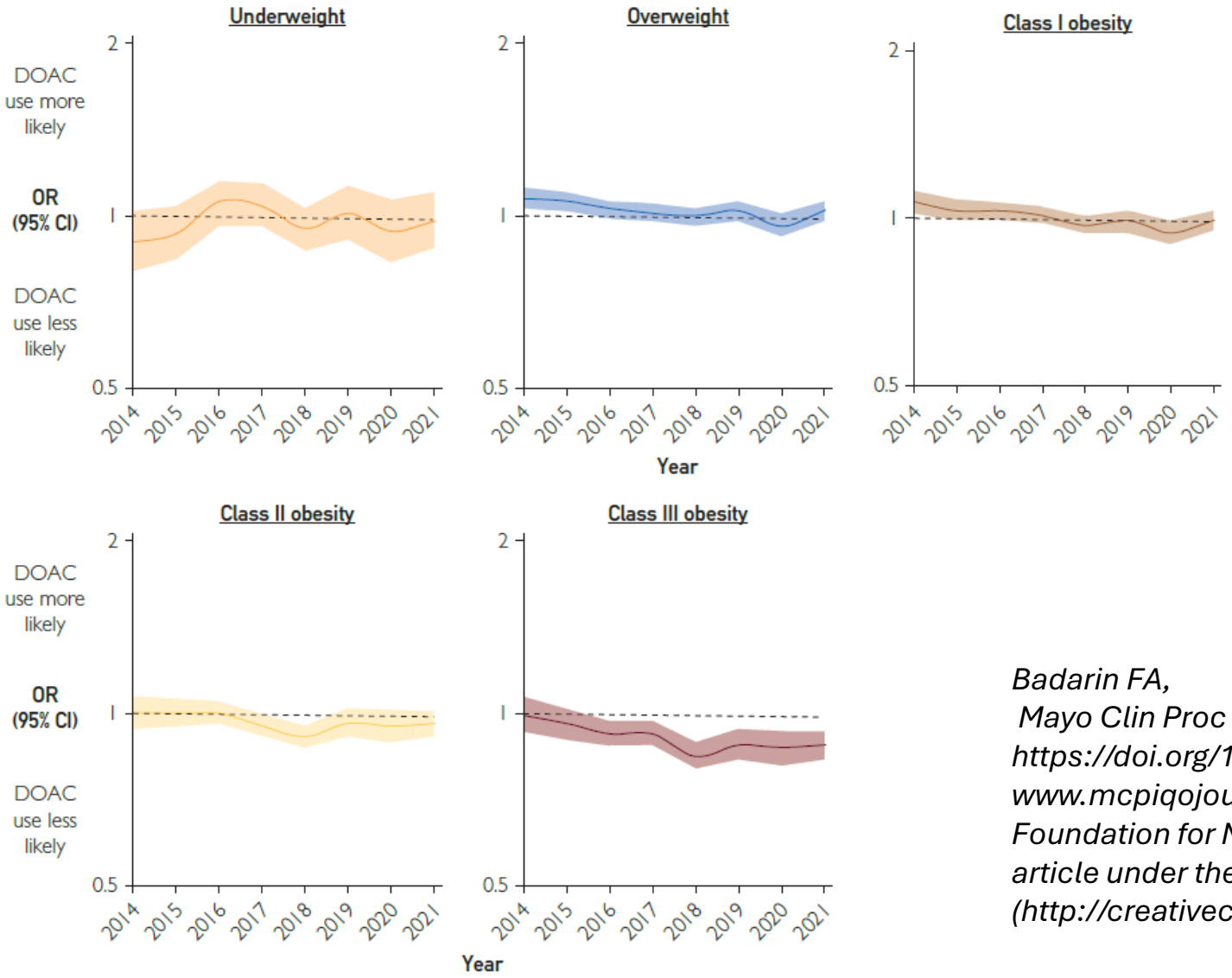
Circulation. 2024;149:00–00. DOI: 10.1161/CIRCULATIONAHA.123.066279



- N=58464
- AVC, embolies sytémiques : diminution avec augmentation du BMI
- Hémorragies majeures : perte du bénéfice des DOAC pour BMI les plus élevés ?

Patel SM, Circulation 2024

AOD, poids extrêmes



- Registre PINNACLE, FA
- N = 950 644

Badarin FA,
Mayo Clin Proc Inn Qual Out n June 2026;10(3):100692 n
https://doi.org/10.1016/j.mayocpiqo.2025.100692
www.mcpiqojournal.org n ª 2026. Published by Elsevier Inc on behalf of Mayo Foundation for Medical Education and Research. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Anticoagulants et insuffisance pondérale

		IMC (kg/m²)
Insuffisance pondérale	Légère	17-18,49
	Modérée	16-16,99
	Sévère	< 16
Corpulence normale		**18,5-24,99**

- HBPM ou AOD, pas ou très peu de données : risque de surdosage ?
- HBPM si poids < 50 kg / IMC < 18, 5 kg/m²
  - Dose diminuée, surveillance clinique +++ : enoxaparine 2000 U / 3000 U, daltéparine 2500 U ???
  - Tinzaparine prophylaxie : 50 U/ Kg

RCP
Yam L, Pharmacotherapy 2019
Sebaaly J, Ann Pharmacother 2018

AOD et insuffisance pondérale

Table 3. Summary of Studies of DOAC Use for VTE Treatment in Underweight Patients

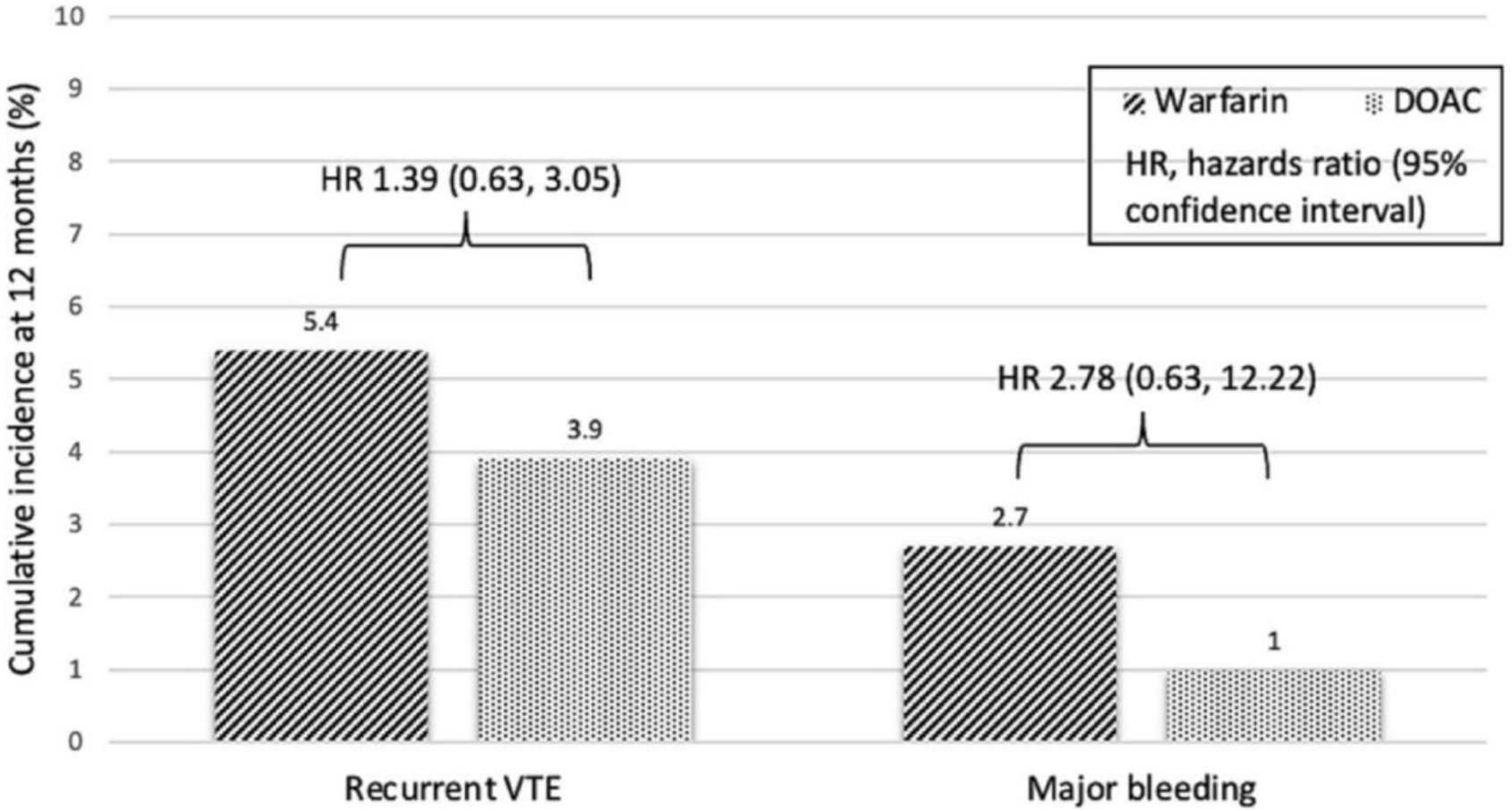
Reference	Study Design	Weight Categories	No. (% of Total)	Intervention	Results
Studies of Dabigatran					
Schulman et al[1] (2009)[a]	Randomized, double-blind, noninferiority	<50 kg	18 (0.7)	Dabigatran vs VKA	• Findings in underweight population: no VTE events occurred in either group
Schulman et al[24] (2014)[a]	Randomized, double-blind, noninferiority	<50 kg	57 (2.2)	Dabigatran vs VKA	• Findings in underweight population: 1 VTE event in warfarin group
Schulman et al[25] (2013)[a]	Double-blind, randomized	<50 kg	10 (0.7)	Dabigatran vs VKA	• Findings in underweight population: no VTE events recorded in either group
Study of Rivaroxaban					
Prins et al[27] (2013)	Pooled analysis of data from EINSTEIN-DVT and EINSTEIN-PE trials	≤50 kg	107 (7)	Rivaroxaban vs LMWH plus VKA	• Findings in fragile patients: lower rate of major bleeding with rivaroxaban (1.3% vs 4.5%; HR, 0.27 [95% CI, 0.13-0.54])
Study of Apixaban					
Agnelli et al[7] (2013)[a]	Randomized, double-blind, prospective	≤60 kg	225 (9)	Apixaban vs LMWH plus VKA	• Findings in underweight population: in patients with weight ≤60 kg, apixaban noninferior to VKA for acute VTE treatment (rate of recurrent VTE, 2.7 % vs 4.3%; $P = 0.43$)

Abbreviations: CI, confidence interval; DOAC, direct-acting oral coagulant; HR, hazard ratio; LMWH, low-molecular-weight heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.
[a]Study was underpowered to detect a difference in patients at weight extremes.

Covert K, Am J Health-Syst Pharm 2020

AOD / AVK et IMC < 18 kg/m^2 ou poids < 50 kg

Multicenter retrospective study, VTE
Warfarin, n=521
DOAC, n=205 (apixaban 32%, rivaroxaban 64%)



Martin K, Thromb Res 2023

AOD et insuffisance pondérale

Traitement de la MTEV

Drug	Final message
Rivaroxaban	Limited data
Apixaban	Safety and efficacy may be comparable to LMWH/VKAs
Dabigatran	Limited data

FA

Rivaroxaban	Limited data
Apixaban	Safety and efficacy may be comparable to VKAs
Dabigatran	Limited data on efficacy, but increased risk of bleeding

Talerico R, THOpen 2024