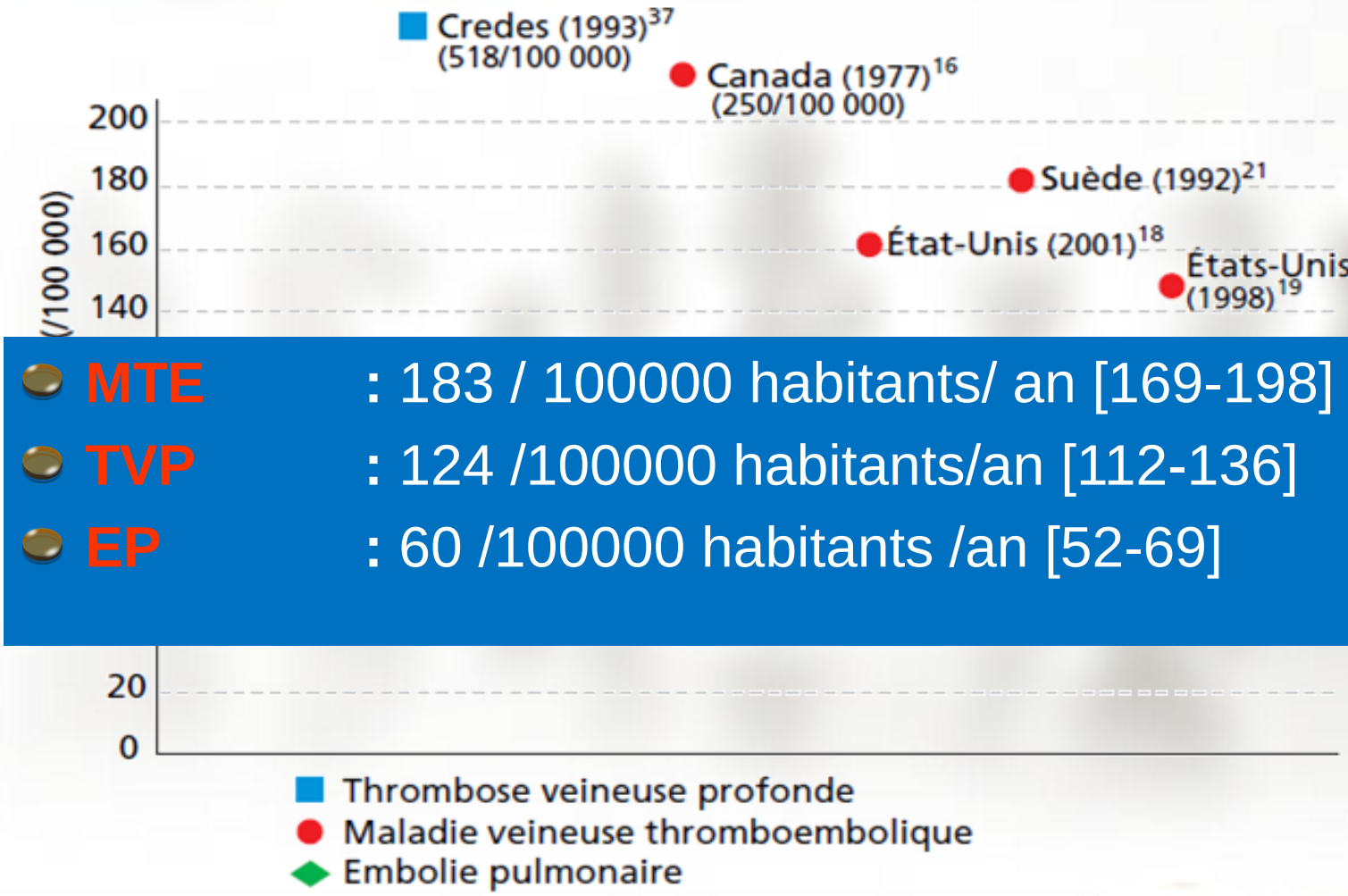
PRÉVENTION DE LA MALADIE THROMBOEMBOLIQUE VEINEUSE EN MILIEU MÉDICAL

Pr Souheil Elatrous

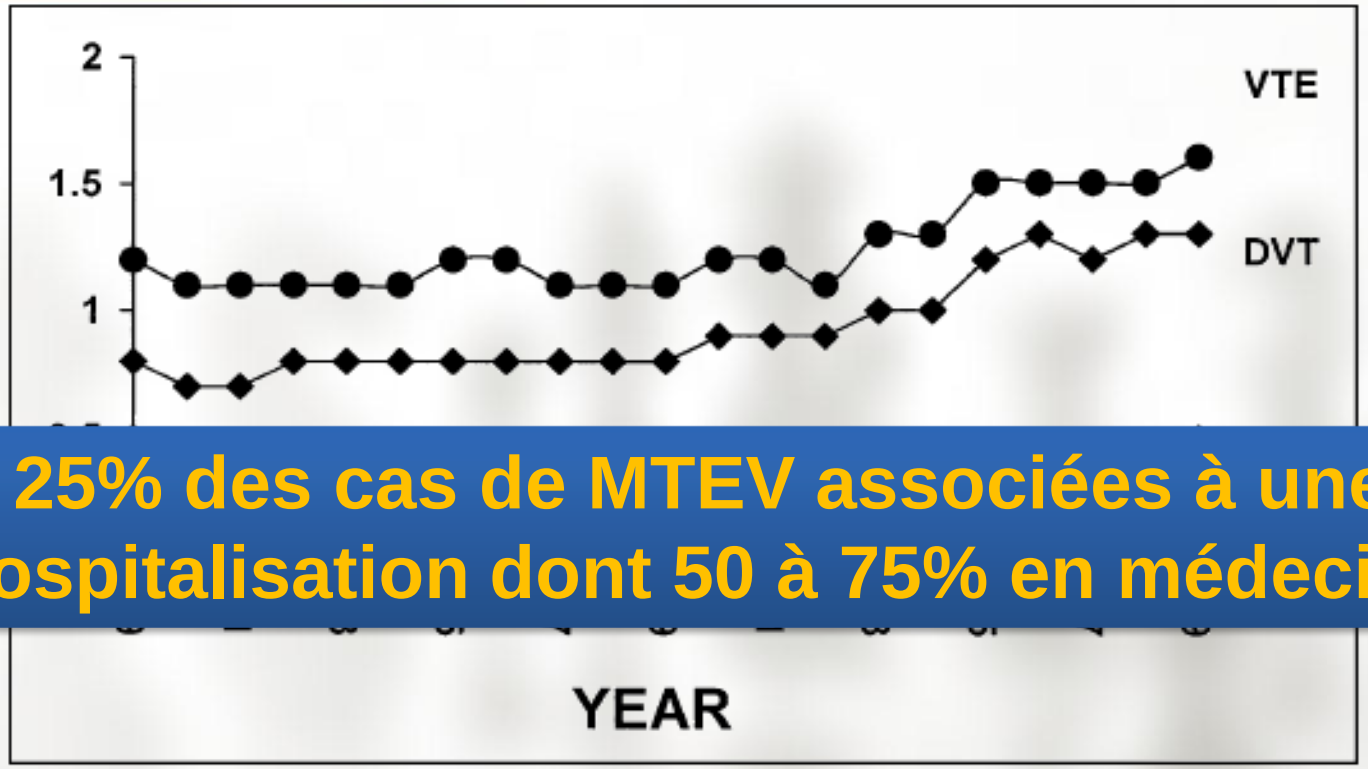


- **MTE** : 183 / 100000 habitants/ an [169-198]
- **TVP** : 124 /100000 habitants/an [112-136]
- **EP** : 60 /100000 habitants /an [52-69]




Trends in the Incidence of Pulmonary Embolism and Deep Venous Thrombosis in Hospitalized Patients

Paul D. Stein, MD, Afzal Beemath, MD, and Ronald E. Olson, PhD



25% des cas de MTEV associées à une hospitalisation dont 50 à 75% en médecine

FIGURE 1. Incidences of PE, DVT, and VTE in hospitalized adults from 1979 to 1999. The incidence of DVT increased (slope = 0.028%/year, r = 0.92, p <0.0005). The incidence of PE did not change. The incidence of VTE increased in parallel to the incidence of DVT.

Am J Cardiol 2005;95:1525–1526

Incidence

Groupe placebo

Etudes	Moyen diagnostic	TVP	TVP proximale	Embolie pulmonaire
MEDENOX	phlébographie	14.9	2	0.3
PREVENT	Echo	4.96	à	à
ARTEMIS	phlébographie	10.5	4.9	1.5

Incidence

- L'hospitalisation pour raison médicale aiguë augmente d'un facteur 8 le risque relatif de MTEV
- L'incidence des MTE asymptomatiques chez les patients hospitalisés pour une pathologie médicale aiguë varie 5 à 28 %.
- Peut à tout moment se révéler par un épisode brutal d'embolie pulmonaire




Fatal pulmonary embolism in hospitalised patients: a necropsy review

R Alikhan, F Peters, R Wilmott, A T Cohen

J Clin Pathol 2004;**57**:1254–1257. doi: 10.1136/jcp.2003.013581

Table 3 Necropsy rate and fatal pulmonary embolism 1966–2000

Year	Necropsy n (%)*	Fatal PE n (%)†
1966–1970	3167 (71%)	192 (6.1%)
1971–1975	3523 (53%)	187 (5.3%)
1976–1980	2660 (41%)	120 (4.5%)
1981–1985	2354 (35%)	54 (2.3%)
1986–1990	2963 (46%)	62 (2.1%)
1991–1995	3581 (48%)	139 (3.9%)
1996–2000	3252 (38%)	126 (3.9%)

EP fatale 2.1-6.1

Fatal pulmonary embolism in hospitalised patients: a necropsy review

R Alikhan, F Peters, R Wilmott, A T Cohen

J Clin Pathol 2004;**57**:1254–1257. doi: 10.1136/jcp.2003.013581

Table 2 Fatal pulmonary embolism and reason for hospitalisation (1991–2000)

Year	Surgical n (%)	Non-surgical n (%)	Total (n)
1991	7 (1.5)	17 (3.7)	24
1992	4 (0.8)	21 (4.2)	25
1993	3 (0.6)	29 (5.6)	32
1994	8 (1.6)	19 (3.7)	27
1995	10 (1.6)	21 (3.3)	31
1996	5 (0.8)	25 (3.9)	30
1997	5 (0.9)	22 (4.1)	27
1998	1 (0.2)	15 (3.2)	16
Total	51 (1.0)	214 (4.2)	265 (5.2)

n, cases of fatal pulmonary embolism; %, percentage of necropsies undertaken.

Fatal pulmonary embolism in hospitalised patients: a necropsy review

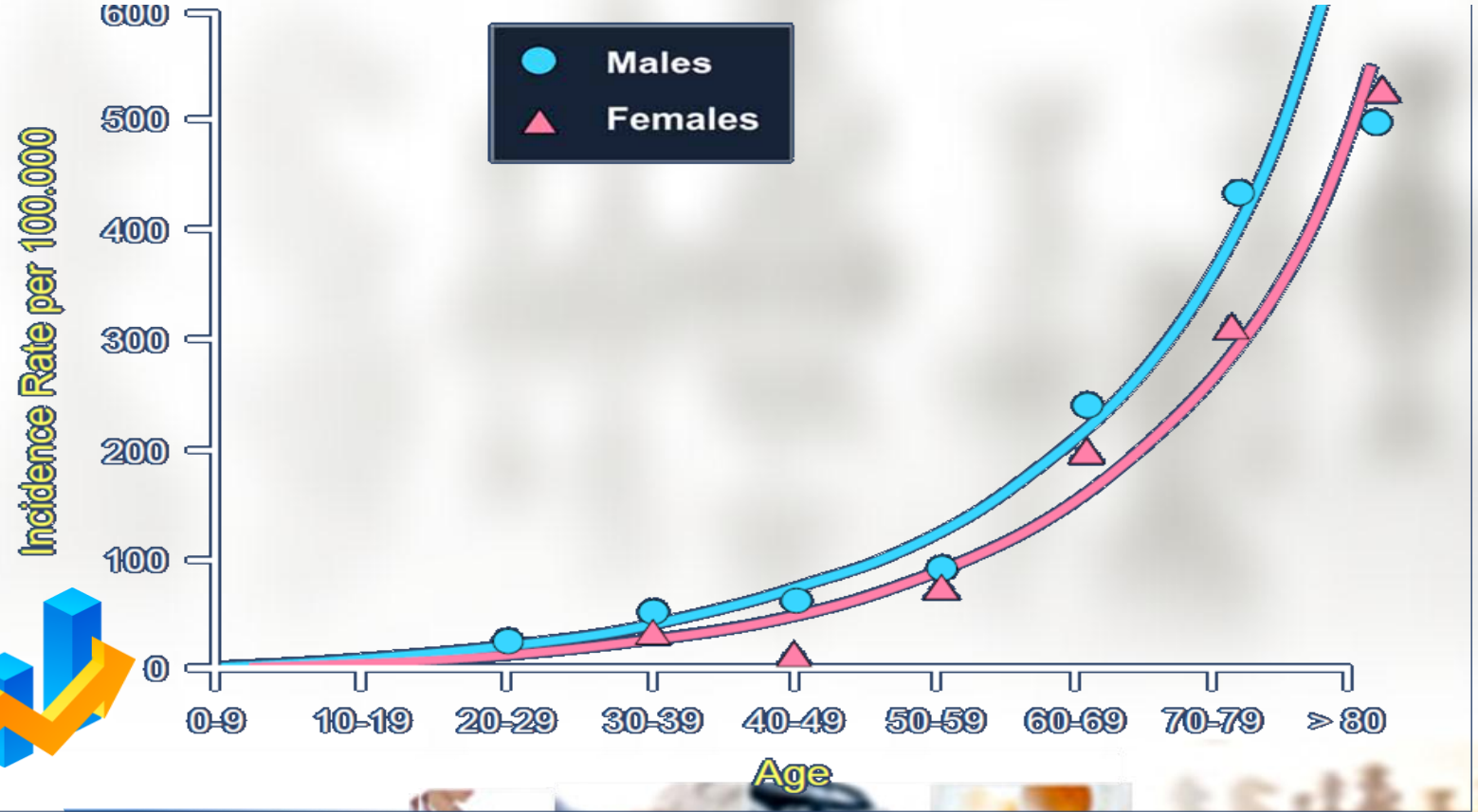
R Alikhan, F Peters, R Wilmott, A T Cohen

J Clin Pathol 2004;**57**:1254–1257. doi: 10.1136/jcp.2003.013581

Table 4 Fatal pulmonary embolism associated with defined medical conditions

Medical condition	Fatal PE (n)	Fatal PE (%)*
Myocardial infarction	3	2.7
Cerebrovascular accident	4	3.6
Chronic obstructive pulmonary disease	8	7.3
Heart failure	13	11.8
Cancer	24	20.9
Infection	26	23.6
Other condition	33	30.0
All defined medical conditions	110	100

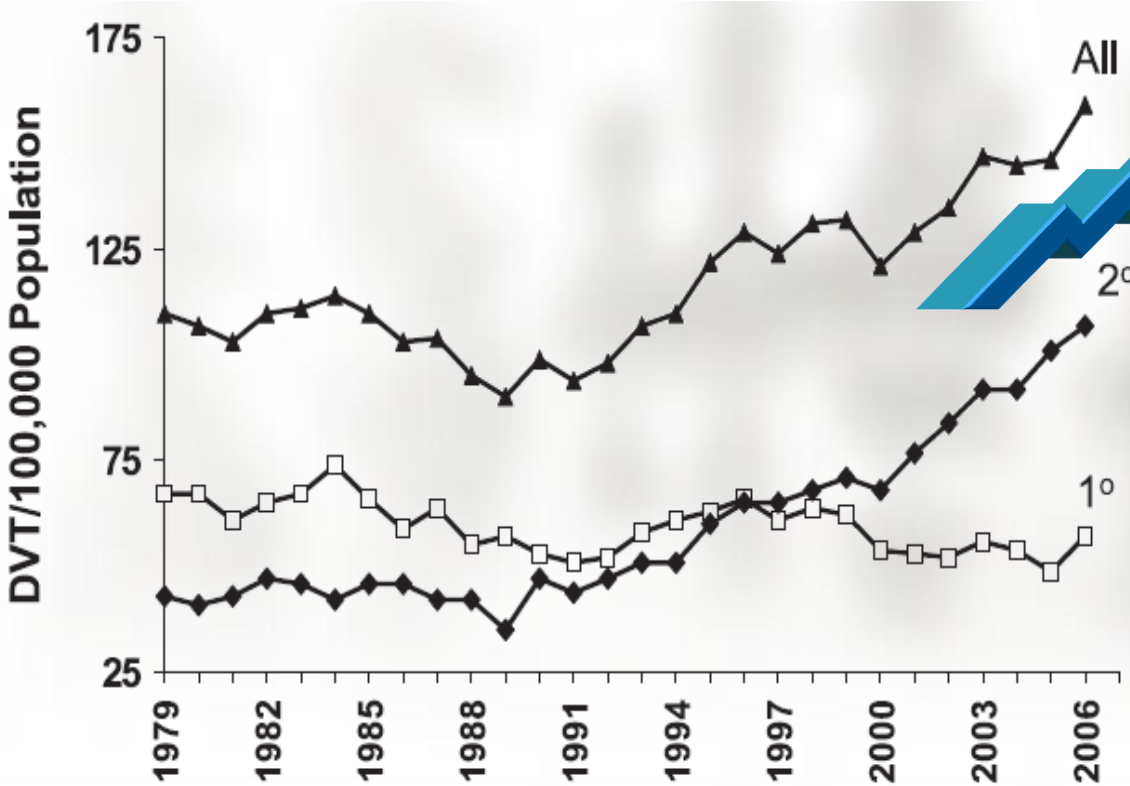
A Population-Based Perspective of the Hospital Incidence and Case-Fatality Rates of Deep Vein Thrombosis and Pulmonary Embolism



Arch Intern Med. 1991;151:933-938

Is the Campaign to Prevent VTE in Hospitalized Patients Working?

Paul D. Stein, MD, Master FCCP; Fadi Matta, MD; and James E. Dalen, MD, Master FCCP



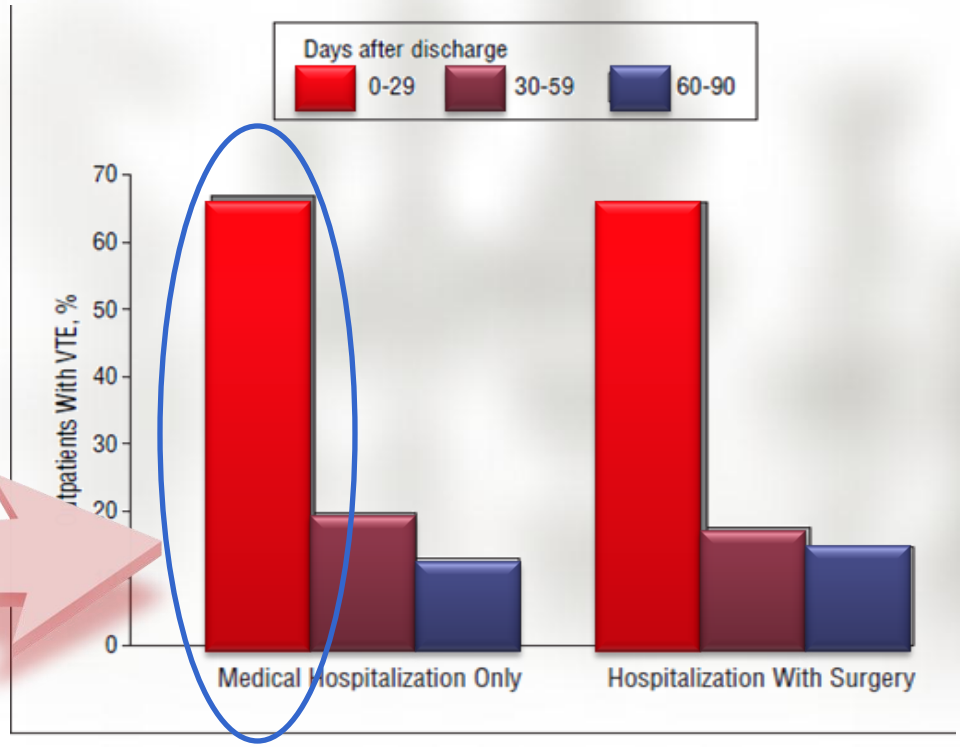
TVP x 3
1992-2006
EP X 2.5

CHEST 2011; 139(6):1317–1321

ORIGINAL INVESTIGATION

Venous Thromboembolism in the Outpatient Setting

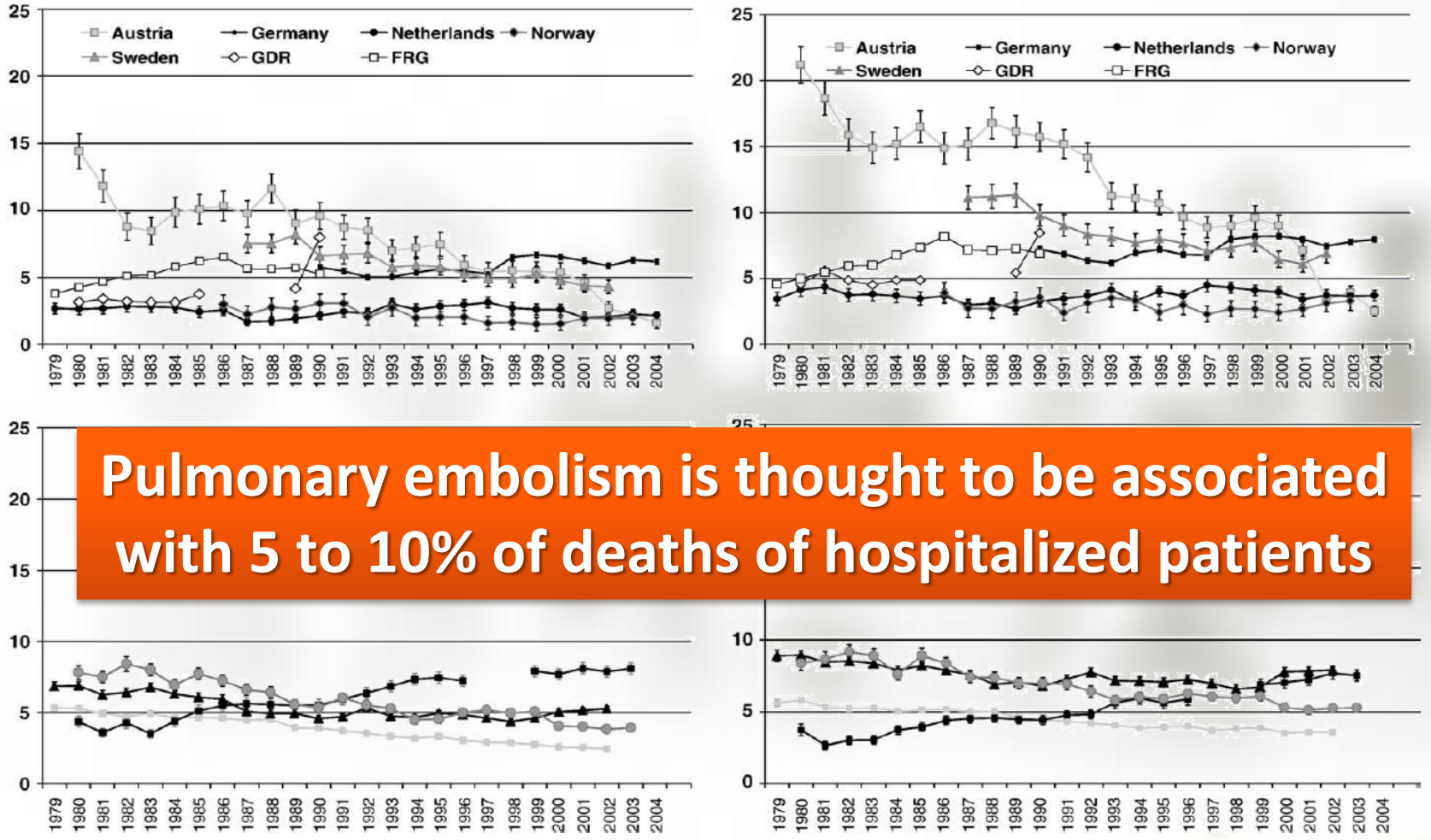
Frederick A. Spencer, MD; Darleen Lessard, MS; Cathy Emery, RN; George Reed, PhD; Robert J. Goldberg, PhD



Arch Intern Med. 2007;167(14):1471-1475

Trends in mortality of pulmonary embolism – an international comparison

Barbara Hoffmann [a,*], Christian R. Gross [b], Karl-Heinz Jöckel [a], Knut Kröger [c]



Pulmonary embolism is thought to be associated with 5 to 10% of deaths of hospitalized patients

Fig. 1. Sex-specific age-standardised pulmonary embolism mortality per 100,000 over time in different countries. Left panels show time trends for men, right panels for women.

Thrombosis Research 125 (2010) 303–308

La thrombo-prophylaxie est sous-utilisée en milieu médical

A Prospective Registry of 5,451 Patients With Ultrasound-Confirmed Deep Vein Thrombosis

Samuel Z. Goldhaber, MD, and Victor F. Tapson, MD, for the DVT FREE Steering Committee*

- 5,451 patients
- Echo Doppler = thrombose veineuse profonde
- Parmi les 2,726 patients qui ont développé leur TVP à l'hôpital, seulement 1,147 **(42%)** ont reçu une prophylaxie dans les 30 jours avant le diagnostic.

Am J Cardiol 2004;93:259–262

CHEST

Original Research

VENOUS THROMBOEMBOLISM

Venous Thromboembolism Prophylaxis in Acutely Ill Hospitalized Medical Patients*

Findings From the International Medical Prevention Registry on Venous Thromboembolism

12 pays et 52 hôpitaux
15156 patients

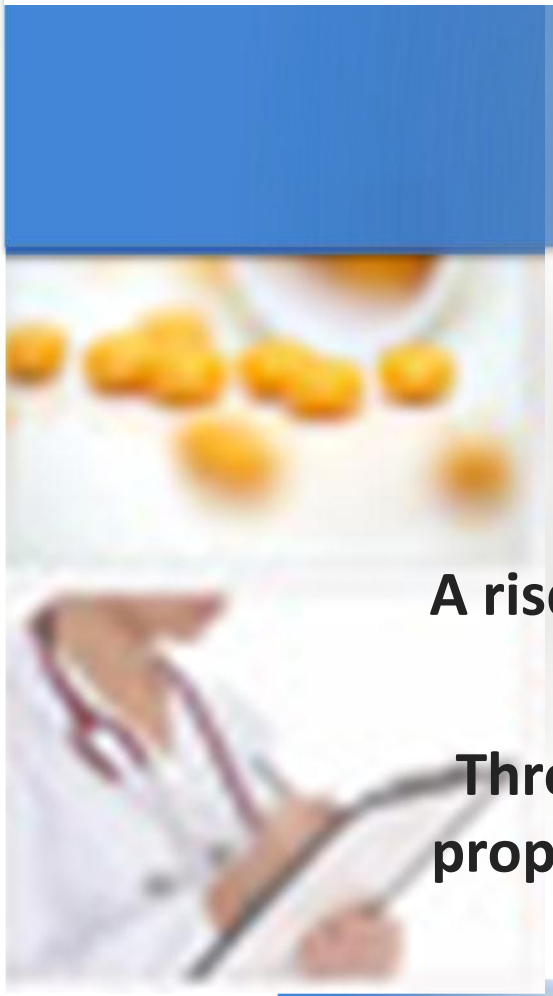
Table 2—*Use of VTE Prophylaxis in the Hospital**

Variables	United States	Other Participating Countries
Patients, Total No.	3,410	11,746
Patients receiving one or more types of VTE prophylaxis†	**54 %**	**49%**
LMWH (all doses)‡		
Once daily		
q12h	73/457 (16)	347/4,589 (8)
Other	4/457 (0.9)	11/4,589 (0.2)
UFH (all doses)‡	717/3,410 (21)	1,014/11,746 (9)
q12h	282/712 (40)	844/990 (85)
q8h	383/712 (54)	31/990 (3.1)
Other	47/712 (7)	115/990 (12)
Intermittent pneumatic compression	749/3,410 (22)	24/11,746 (0.2)
ES	94/3,410 (3)	794/11,746 (7)
Aspirin	97/3,410 (3)	165/11,746 (1)
Warfarin	77/3,410 (2)	73/11,746 (0.6)
Fondaparinux	11/3,410 (0.3)	5/11,746 (0.04)
Other	130/3,097 (4)	148/9,418 (2)

CHEST 2007; 132:936–945

Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study

*Alexander T Cohen, Victor F Tapson, Jean-Francois Bergmann, Samuel Z Goldhaber, Ajay K Kakkar, Bruno Deslandes, Wei Huang, Maksim Zayaruzny, Leigh Emery, Frederick A Anderson Jr, for the ENDORSE Investigators**

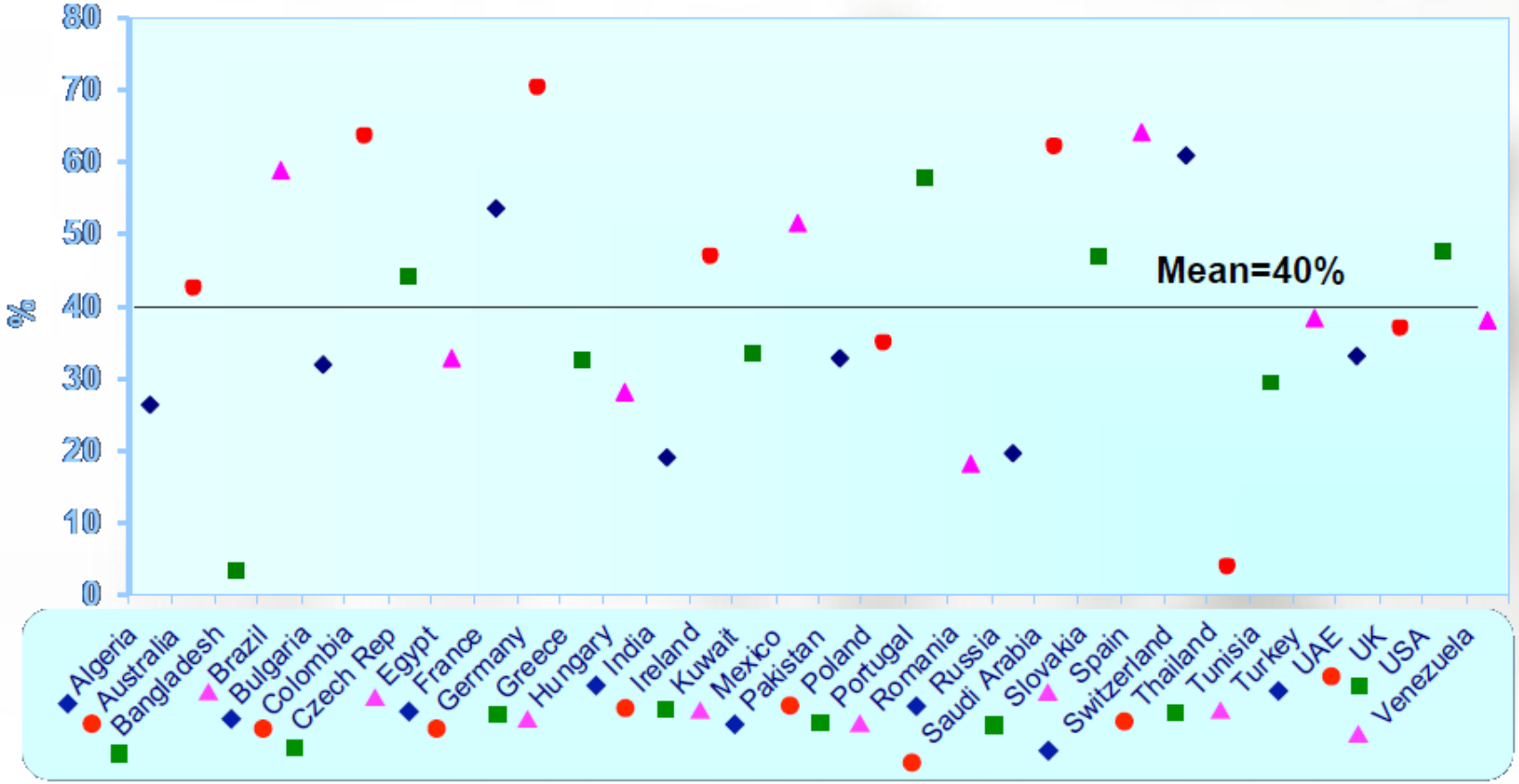


	chirurgicaux	Médicaux
	68183	
	30827 45%	37356 55%
A risque	19842 64.4%	15487 41.5%
Critères ACCP		
Thrombo-prophylaxie	11613 58.5%	6119 39.5%

Lancet 2008; 371: 387–94

Etude Endorse

Patients médicaux



Variability in the use of thromboprophylaxis and outcomes in critically ill medical patients

Krista L. Lentine, MD, MS,[a] Kara E. Flavin[b], Michael K. Gould, MD, MS[b,c]

275 patients

205 patients
75%

55 patients (20%)
pharmacologique

102 patients (38%)
mécanique

48 patients (18%)
mécanique et pharmacologique

The American Journal of Medicine (2005) 118, 1373-1380

Risque de MTE
en absence de prophylaxie

- Patients médicaux [1,2] : 10-26%
- AVC [3] : 11-75 %
- IDM [3] : 17-34%
- Insuffisance cardiaque [4] : 20-40%
- Réanimation médicale [1,5,6] : 25-42%

1-Cade Crir Care Med 1982; 10:448
2-Belch JJ et al Scott Med J 1981;26:115-7
3-Nicolaides et al. Int Angiol 1997 ; 16:3-38
4- Anderson et al Am Heart J 1950;39:697-702
5- Dekker et al Thromb Haemost 1991;65:1348
6- Hirst Dr et al JAMA 1995; 274:335-7

Facteurs de risque

- **Le risque de MTEV est souvent le résultat de la conjonction de 2 types de facteurs :**

- Des facteurs de risque **liés à la pathologie aiguë**

- Des facteurs de risque permanents **liés au patient** lui-même.




Facteurs de risque

Risques liés à la pathologie aiguë

Facteurs majeurs

Paralysie récente d'un ou des 2 membres inférieurs
Post-infarctus du myocarde récent
Insuffisance cardiaque décompensée
Insuffisance respiratoire aigue

Facteurs mineurs

Cancer évolutif
Sepsis sévère
Syndrome nephrotique
MICI (évolutive)
Syndrome myéloprolifératif (évoutif)
Déshydratation sévère

Risques liés au malade

Facteurs majeurs

Antécédents TE documentés
Thrombophilie (déficits ATIII, PC,PS..)

Facteurs mineurs

Age >60 ans
Obésité (IMC > 30)
Insuffisance veineuse
Grossesse
Post-partum (1 mois)
Oestrogenothérapie à forte dose
Anticorps antiphospholipides
Insuffisance cardiaque non décompensée
Insuffisance respiratoire chronique

Chez un patient **alité, en milieu médical, une thromboprophylaxie est recommandée**

1- En présence d'un facteur majeur **Grade A**

2- En présence de 2 facteurs mineurs **Grade C**




RAMs (Risk Assessment Models)

Objectifs:

- Améliorer la prophylaxie en augmentant le rapport risque-bénéfice du traitement
- Améliorer le rapport coût-efficacité

Critères	Définition De l'↗ du risque
Score 3 : Cancer actif, ATDC TVP / EP, IdM, AVC ischémique avec paralysie d'un membre, infection chronique pulmonaire obstructive, thrombophilie **Score 2 :** insuffisance cardiaque congestive insuffisance rénal chronique / syndrome néphrotique, infection aiguë sévère, plâtre, alitement prolongé **Score 1 :** grossesse / postpartum, voyage récent longue durée, paralysie des membres inférieures, traitement par thalidomide, cathéter central, obésité, âge > 60 ans, tabac	**Score cumulatif > 4**

Lecumberri 2008, Thromb Haemost 100: 699-70

Score de Kucher

	Score utilisé
Cancer Antécédent Thrombo-embolique Hypercoagulabilité Thrombophilie	3
Intervention chirurgicale majeure	2
Age > 70 IMC > 29 Alitement non lié à une opération Contraception oestroprogestative Traitement substitutif de la ménopause	1

Le risque est considéré comme augmenté s'il atteint ou dépasse 4

Evaluation du risque

Risque Faible :
Patient ambulatoire sans facteur de risque, hospitalisation prévue pendant 48 heures, chirurgie ambulatoire ou mineure

Risque Intermédiaire :
Autres patients, insuffisance respiratoire, cardiaque, infection aiguë ou syndrome inflammatoire

Risque Elevé :
Arthroplastie membres inférieurs, fractures hanche, bassin ou extrémités inférieures, activité intrinsèque avec paralysie, multiple traumatismes.

Maynard G. A. et al, J Hospital Medicine 2010; 5 :10-18

Predictive and Associative Models to Identify Hospitalized Medical Patients at Risk for VTE

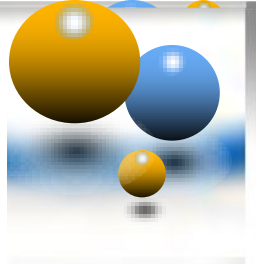


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Table 1—*Characteristics of Acutely Ill Hospitalized Medical Patients*

Characteristic	Patients (N = 15,156)
Women, %	50
Age, y	68 (52-79)
Weight (No. = 10,433), kg	69 (59-81)
Length of hospital stay, d	7 (5-13)
Immobile for ≥ 7 d, including days immediately prior to admission (No. = 15,125), %	19
Time immobile (No. = 1,169), d preadmission	3 (1-15)

Table 2—*Occurrence of VTE (N = 143)*[a]

Days After Hospital Admission	In-hospital VTE (n = 79)	Postdischarge VTE (n = 64)	All VTE (N = 143)
1-7	42 (53)	0	42 (29)
8-30	32 (41)	24 (38)	56 (39)
31-60	5 (6)	23 (36)	28 (20)
61-91	0	17 (27)	17 (12)

CHEST 2011; 140(3):706–714

Predictive and Associative Models to Identify Hospitalized Medical Patients at Risk for VTE

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Table 4—*Adjusted Cox Predictive Model for 3-Month VTE and Points Assigned to Each Independent Risk Factor*

VTE Risk Factor	HR (95% CI)	χ^2	*P* Value	Points
Previous VTE	5.0 (3.3-7.8)	53	< .001	3
Known thrombophilia	5.2 (1.3-21.5)	5.2	.02	3
Cancer	2.0 (1.3-3.1)	11	.001	1
Age > 60 y	1.8 (1.2-2.7)	8.5	.004	1

Score ≥ 2 → risque > 2% d'accident pendant les 2 mois suivant l'admission

Répartition des malades :

Score 0-1 : 77 %
Score 2 : 16 %
Score 3 : 9 %
Score > 4 : 7 %

CHEST 2011; 140(3):706–714

PRÉVENTION DE LA MALADIE
THROMBOEMBOLIQUE VEINEUSE
EN MILIEU MÉDICAL.

PRÉVENTION
EN MILIEU MÉDICAL

- PRÉVENTION DE LA MALADIE THROMBOEMBOLIQUE VEINEUSE EN MILIEU MÉDICAL.

Prévention en milieu médical

3 études

MEDENOX

PREVENT

ARTEMIS

A COMPARISON OF ENOXAPARIN WITH PLACEBO FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM IN ACUTELY ILL MEDICAL PATIENTS

MEYER MICHEL SAMAMA, M.D., ALEXANDER THOMAS COHEN, M.D., JEAN-YVES DARMON, M.D., LOUIS DESJARDINS, M.D., AMIRAM ELDOR, M.D., CHARLES JANBON, M.D., ALAIN LEIZOROVICZ, M.D., HÉLÈNE NGUYEN, PHARM.D., CARL-GUSTAV OLSSON, M.D., PH.D., ALEXANDER GRAHAM TURPIE, M.D., AND NADINE WEISSLINGER, M.D., FOR THE PROPHYLAXIS IN MEDICAL PATIENTS WITH ENOXAPARIN STUDY GROUP*

The NEW ENGLAND JOURNAL of MEDICINE

TABLE 3. INCIDENCE OF VENOUS THROMBOEMBOLIC EVENTS.

OUTCOME	PLACEBO	20 mg OF ENOXAPARIN	40 mg OF ENOXAPARIN
	number (percent)		
Primary outcome			
No. of patients evaluated	288	287	291
Venous thromboembolic events	43 (14.9)	43 (15.0)	16 (5.5)
Deep-vein thrombosis alone	40 (13.9)	42 (14.6)	16 (5.5)
Pulmonary embolism alone	2 (0.7)	0	0
Deep-vein thrombosis and pulmonary embolism	1 (0.3)	1 (0.3)	0
Proximal deep-vein thrombosis	14 (4.9)	13 (4.5)	5 (1.7)
Distal deep-vein thrombosis	27 (9.4)	30 (10.5)	11 (3.8)
Symptomatic deep-vein thrombosis	2 (0.7)	3 (1.0)	1 (0.3)
Death from pulmonary embolism	0	0	0
Secondary outcome			
No. of patients evaluated	263	263	272
Venous thromboembolic events	45 (17.1)	46 (17.5)	19 (7.0)
Deep-vein thrombosis alone	41 (15.6)	44 (16.7)	17 (6.2)
Pulmonary embolism alone	2 (0.8)	0	0
Deep-vein thrombosis and pulmonary embolism	1 (0.4)	1 (0.4)	0
Proximal deep-vein thrombosis*	17 (6.5)	14 (5.3)	6 (2.2)
Distal deep-vein thrombosis*	27 (10.3)	31 (11.8)	12 (4.4)
Symptomatic deep-vein thrombosis	4 (1.5)	6 (2.3)	3 (1.1)
Death from pulmonary embolism	1 (0.4)	1 (0.4)	2 (0.7)

TVP 14.9 vs 15 vs 5.5%

RR : 0.37

RRR : 0.63

RRA : 9.4%

NNT : 10

N Engl J Med 1999;341:793-800

A COMPARISON OF ENOXAPARIN WITH PLACEBO FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM IN ACUTELY ILL MEDICAL PATIENTS

MEYER MICHEL SAMAMA, M.D., ALEXANDER THOMAS COHEN, M.D., JEAN-YVES DARMON, M.D., LOUIS DESJARDINS, M.D., AMIRAM ELDOR, M.D., CHARLES JANBON, M.D., ALAIN LEIZOROVICZ, M.D., HÉLÈNE NGUYEN, PHARM.D., CARL-GUSTAV OLSSON, M.D., PH.D., ALEXANDER GRAHAM TURPIE, M.D., AND NADINE WEISSLINGER, M.D., FOR THE PROPHYLAXIS IN MEDICAL PATIENTS WITH ENOXAPARIN STUDY GROUP*

TABLE 5. INCIDENCE OF ADVERSE EVENTS.*

ADVERSE EVENT	PLACEBO	20 mg OF ENOXAPARIN	40 mg OF ENOXAPARIN
	number (percent)		
Treatment period (days 1–14)			
No. of patients evaluated	362	351	360
Death from any cause	16 (4.4)	15 (4.3)	12 (3.3)
Hemorrhage†	31 (8.6)	41 (11.7)	45 (12.6)
Major	4 (1.1)	1 (0.3)	6 (1.7)
Fatal	0	0	1 (0.3)
Minor	27 (7.5)	40 (11.4)	39 (10.8)
Local reaction at injection site (hematoma >5 cm in diameter)	0	4 (1.1)	5 (1.4)‡
Thrombocytopenia§	13 (3.6)	10 (2.8)	8 (2.2)
Severe thrombocytopenia¶	3 (0.8)	0	0
Study period (days 1–110)			
No. of patients evaluated	362	351	360
Death from any cause‖	50 (13.9)	51 (14.7)	41 (11.4)
Hemorrhage**	51 (14.3)	59 (17.2)	62 (17.4)
Major	7 (2.0)	4 (1.2)	12 (3.4)
Fatal	0	1 (0.3)	2 (0.6)
Minor	45 (12.6)	57 (16.6)	51 (14.4)
Thrombocytopenia††	17 (4.8)	11 (3.2)	10 (2.8)
Severe thrombocytopenia¶	3 (0.8)	0	0

Hémorragie : 8.6 vs 11.7 vs 12.6%

RRA : 4%

NNH : 25

Thrombopénie : 3.6 vs 2.8 vs 2.2 %

RRA : 1.4%

NNH : 71

N Engl J Med 1999;341:793-800

Randomized, Placebo-Controlled Trial of Dalteparin for the Prevention of Venous Thromboembolism in Acutely Ill Medical Patients

Alain Leizorovicz, MD; Alexander T. Cohen, MD; Alexander G.G. Turpie, MD; Carl-Gustav Olsson, MD; Paul T. Vaitkus, MD, MBA; Samuel Z. Goldhaber, MD; for the PREVENT Medical Thromboprophylaxis Study Group*

TABLE 2. Patient Characteristics at Baseline*

	Dalteparin (n=1848)	Placebo (n=1833)
Age, mean (SD), y	68.5 (11.1)	68.5 (11.7)
Sex, n (%)		
Male	884 (47.8)	888 (48.4)
Female	964 (52.2)	945 (51.6)
BMI, mean (SD), kg/m²	27.4 (5.9)	27.5 (6.0)
Primary diagnosis, n (%)		
Acute congestive heart failure (NYHA class III or IV)	965 (52.2)	940 (51.3)
Acute respiratory failure	561 (30.4)	560 (30.6)
Other acute conditions	749 (40.5)	781 (42.6)
Infectious disease	673 (36.4)	687 (37.5)
Rheumatologic disorder	200 (10.8)	198 (10.8)
Inflammatory bowel disease	10 (0.5)	8 (0.4)
Risk factors, n (%)		
Age ≥75 y	611 (33.1)	615 (33.6)
Cancer	85 (4.6)	105 (5.7)
Previous deep vein thrombosis or pulmonary embolism	62 (3.4)	80 (4.4)
Obesity	558 (30.2)	560 (30.6)
Varicose veins	487 (26.4)	530 (28.9)
Hormone therapy	33 (1.8)	30 (1.6)
Chronic heart failure	925 (50.1)	946 (51.6)
Myeloproliferative syndrome	5 (0.3)	9 (0.5)
Chronic respiratory failure	176 (9.5)	183 (10.0)

Circulation. 2004;110:874-879.)

TABLE 3. Venous Thromboembolic Events

	Dalteparin, n/N (%)	Placebo, n/N (%)	RR (95% CI)
Primary end point (day 21)			
Venous thromboembolism and sudden death	42/1518 (2.77)	73/1473 (4.96)	0.55 (0.38–0.80)
Sudden death	5/1829 (0.27)	3/1807 (0.17)	1.65 (···)
Pulmonary embolism, fatal	0/1829 (0.00)	2/1807 (0.11)	0.00 (···)
Pulmonary embolism, symptomatic	5/1759 (0.28)	4/1740 (0.23)	1.22 (···)
Deep vein thrombosis: distal, symptomatic	3/1759 (0.17)	4/1739 (0.23)	0.74 (···)
Deep vein thrombosis: proximal, symptomatic	2/1759 (0.11)	7/1739 (0.40)	0.28 (···)
Deep vein thrombosis: proximal, asymptomatic	27/1507 (1.79)	53/1453 (3.65)	0.48 (0.31–0.77)
Secondary end point at day 14			
All-cause mortality	8/1846 (0.43)	7/1831 (0.38)	1.13 (0.41–3.12)
Secondary end point at day 21			
Deep vein thrombosis: proximal and symptomatic distal	32/1508 (2.12)	64/1464 (4.37)	0.49 (0.32–0.74)
All-cause mortality	43/1829 (2.35)	42/1807 (2.32)	1.01 (0.66–1.54)
Secondary endpoint at day 90			
Symptomatic venous thromboembolism (all deep vein thrombosis and pulmonary embolism)	15/1615 (0.93)	21/1583 (1.33)	0.70 (0.36–1.35)
All symptomatic pulmonary embolism	5/1615 (0.31)	6/1583 (0.38)	0.82 (0.25–2.67)
All symptomatic deep vein thrombosis	10/1614 (0.62)	15/1579 (0.95)	0.65 (0.29–1.45)
All-cause mortality	107/1747 (6.12)	103/1715 (6.01)	1.02 (0.78–1.33)

RR : 0.56

RRR : 0.44

RRA : 2.19%

NNT : 46

TABLE 4. Adverse Events (Safety Population)

	Dalteparin, n (%)	Placebo, n (%)
Mortality		
Day 14	8 (0.43)	7 (0.38)
Day 21	43 (2.35)	42 (2.32)
Day 90	107 (6.12)	103 (6.01)
Hemorrhage		
Fatal, day 21	2 (0.11)	1 (0.05)
Major, day 14	8 (0.43)	0 (0.00)
Major, day 21	9 (0.49)	3 (0.16)
Minor, day 14	16 (0.87)	5 (0.27)
Minor, day 21	19 (1.03)	10 (0.55)
Thrombocytopenia		
Day 14	10 (0.54)	6 (0.33)
Day 21	10 (0.54)	8 (0.44)

Mortalité:
NNH : 2000
Saignement majeur ou fatal:
NNH : 256




Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial

35 centres 8 pays

Fondaparinux 2,5 mg, placebo

Critères d'inclusion

- **Age ≥ 60 ans**
- **Alitement attendu ≥ 4 jours**

Et

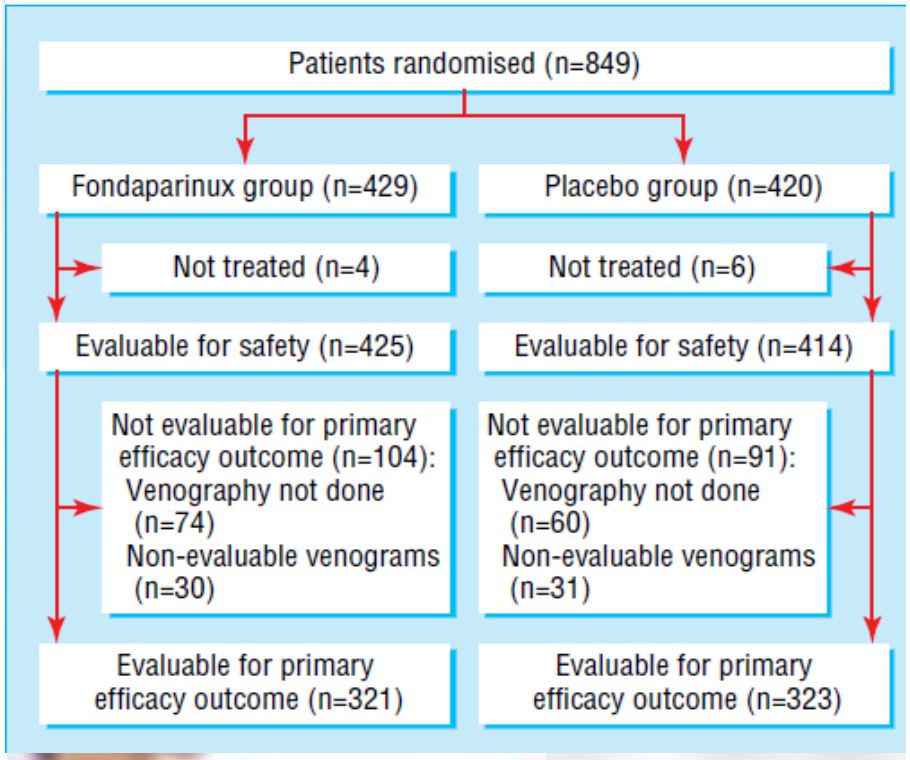
- **insuffisance cardiaque (III/IV NYHA) et/ou**
- **épisode aigu d'insuffisance respiratoire chronique, infection aiguë, et/ou épisode aigu d'une maladie inflammatoire**

Critère principal d'évaluation de l'efficacité (à J 15)

- **TVP proximales et distales dépistées par phlébographie,**
- **ETEV symptomatiques confirmés,**
- **EP fatales**

Cohen et al BMJ 2006

Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial



Primary efficacy outcome	Fondaparinux group	Placebo group
Venous thromboembolic events:		
Any	18	29
Proximal deep vein thrombosis	5	7
Distal deep vein thrombosis	13	22
Symptomatic deep vein thrombosis	0	0
Non-fatal pulmonary embolism	0	0
Fatal pulmonary embolism	0	5
Total No (%)	18/321 (5.6)	34/323 (10.5)
No (%) of any symptomatic venous thrombembolism up to day 32:		
Symptomatic deep vein thrombosis	0	0
Non-fatal pulmonary embolism	1	4
Fatal pulmonary embolism	3	7
Total No (%)	4/429 (1)	11/420 (3)

RR : 0.53
RRR : 0.47
RRA : 4.9%
NNT : 20

Cohen et al BMJ 2006

Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial

Table 3 Bleeding complications during study treatment of older (≥60 years) medical patients randomised to the anticoagulant fondaparinux or placebo

Bleeding complication	Fondaparinux group (n=425)	Placebo group (n=414)
Major bleeding:		
Fatal	0	0
Requiring surgical intervention	0	0
In a critical location	0	0
Overt bleeding plus a decrease in haemoglobin concentration ≥20 g/L (<48 hours) or transfusion of ≥2 units	1	1
Total No (%)	1 (0.2)	1 (0.2)
Minor bleeding	11 (2.6)	4 (1.0)

Table 4 Mortality up to day 32 in older (≥60 years) medical patients randomised to the anticoagulant fondaparinux or placebo

Variable	Fondaparinux group (n=425)	Placebo group (n=414)
Death from any cause:		
Fatal pulmonary embolism	3	7
Fatal bleeding*	2	1
Other causes	9	17
Total No (%)	14 (3)	25 (6)




Efficacité de la Thrombo prophylaxie

Etude	Thromboprophylaxie	Patients avec ATV (%)	RRR	RRA	NNT
MEDENOX[1] p<0.001	Placebo	14.9[a]	63%	9.4 %	10
	Enoxaparin 4000 IU	5.5			
PREVENT[2] p=0.0015	Placebo	5.0[a]	45%	2.19 %	46
	Dalteparin	2.8			
ARTEMIS[3] p=0.029	Placebo	10.5[b]	47%	4.9 %	20
	Fondaparinux	5.6			

A ATV à J 14; b ATV à J 15

1 Samama MM *et al. N Engl J Med 1999;341:793–800*
2 Leizorovicz A *et al. Circulation 2004;110:874–9*
3 Cohen AT *et al. BMJ 2006*

Meta-analysis: Anticoagulant Prophylaxis to Prevent Symptomatic Venous Thromboembolism in Hospitalized Medical Patients

Figure 2. Any pulmonary embolism during anticoagulant prophylaxis.

Study, Year (Reference)	Prophylaxis, *n/n*	Control, *n/n*	RR (Fixed) (95% CI)	RR (Fixed) (95% CI)
Belch et al., 1981 (38)	0/50	2/50		0.20 (0.01 to 4.06)
Dahan et al., 1986 (41)	1/132	3/131		0.33 (0.03 to 3.14)
Gardlund et al., 1996 (35)	3/5776	12/5917		0.26 (0.07 to 0.91)
Samama et al., 1999 (33)	0/291	3/288		0.14 (0.01 to 2.73)
Leizorovic et al., 2004 (23)	5/1759	4/1740		1.24 (0.33 to 4.60)
Mahé et al., 2005 (22)	10/1230	17/1244		0.59 (0.27 to 1.29)
Cohen et al., 2006 (42)	0/429	5/420		0.09 (0.00 to 1.60)
Lederle et al., 2006 (43)	1/140	3/140		0.33 (0.04 to 3.17)
Total (95% CI)				0.43 (0.26 to 0.71)

Figure 3. Fatal pulmonary embolism during anticoagulant prophylaxis.

Study, Year (Reference)	Prophylaxis, *n/n*	Placebo, *n/n*	RR (Fixed) (95% CI)	RR (Fixed) (95% CI)
Dahan et al., 1986 (41)*	1/132	3/131		0.33 (0.03 to 3.14)
Gardlund et al., 1996 (35)	3/5776	12/5917		0.26 (0.07 to 0.91)
Leizorovic et al., 2004 (23)	0/1829	2/1807		0.20 (0.01 to 4.11)
Total (95% CI)				0.38 (0.21 to 0.69)
Total events	14	39		

0.001 0.01 0.1 1 10 100 1000

Favors Treatment Favors Placebo

Meta-analysis: Anticoagulant Prophylaxis to Prevent Symptomatic Venous Thromboembolism in Hospitalized Medical Patients

Figure 4. Symptomatic deep venous thrombosis during anticoagulant prophylaxis.

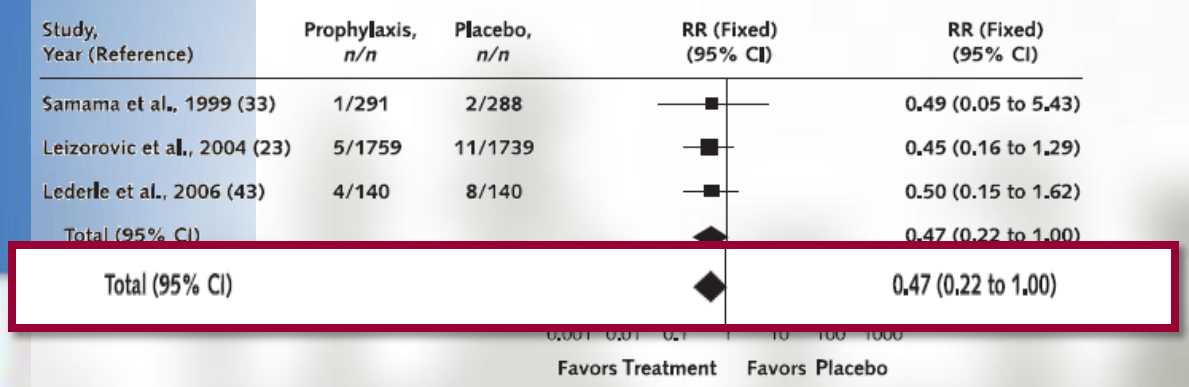
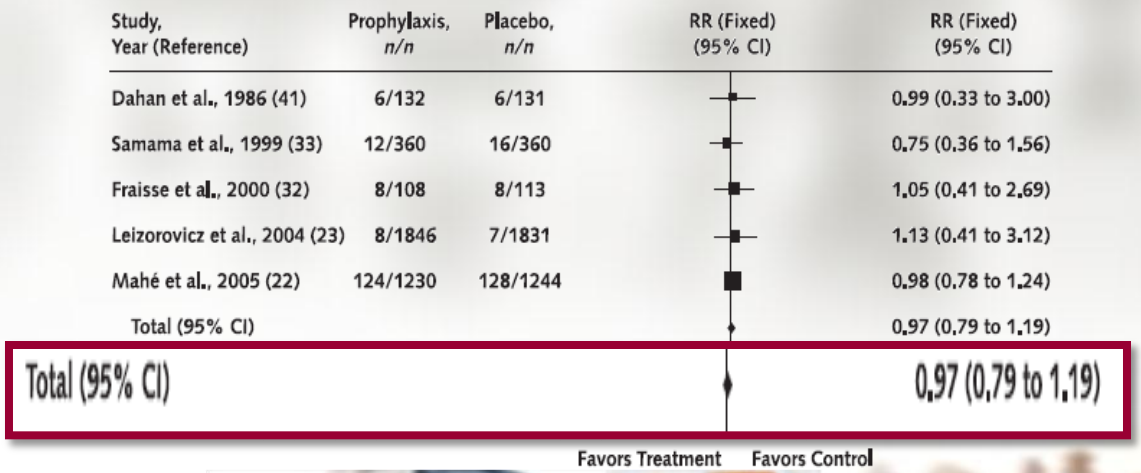


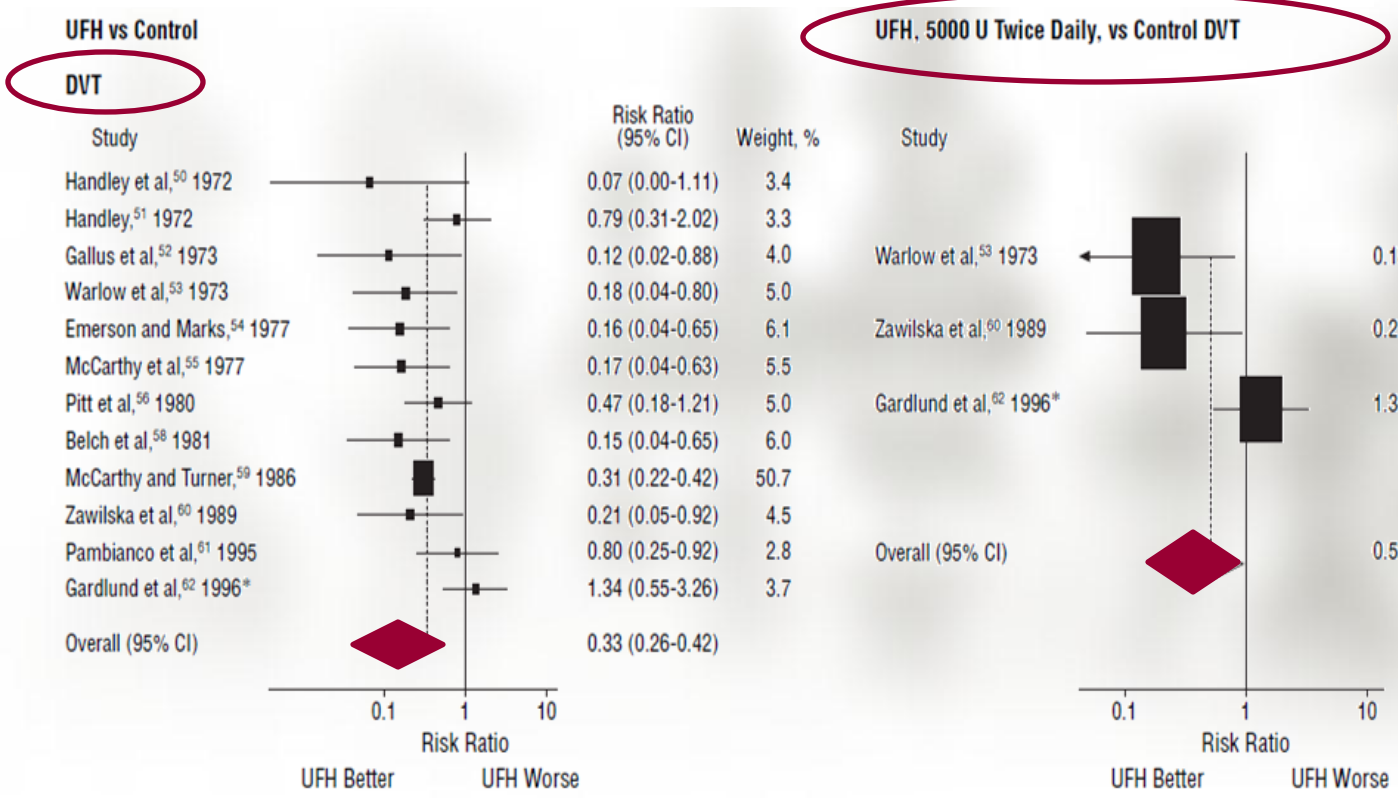
Figure 5. All-cause mortality during anticoagulant prophylaxis.



Pharmacological Venous Thromboembolism Prophylaxis in Hospitalized Medical Patients

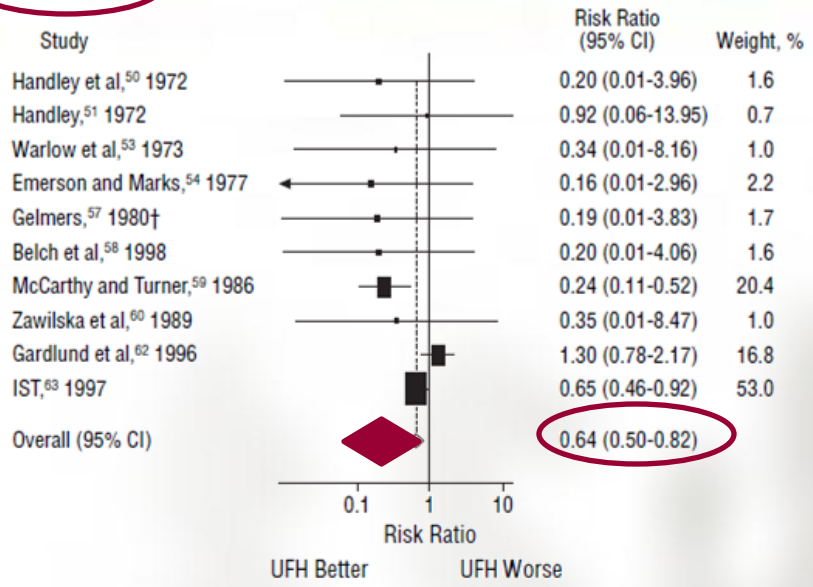
A Meta-analysis of Randomized Controlled Trials

Lironne Wein; Sara Wein; Steven Joseph Haas, BPharm, BPharmSci(Hons), MSHPA; James Shaw, MBBS, PhD, FRACP; Henry Krum, MBBS, PhD, FRACP

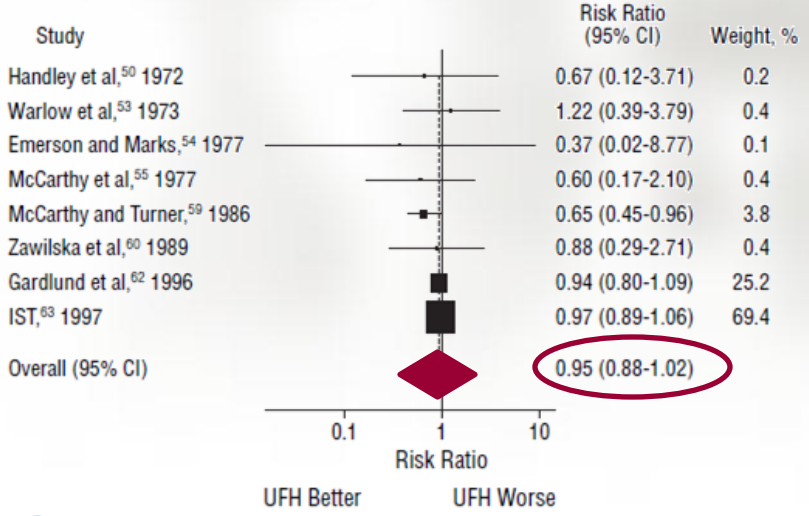


Arch Intern Med. 2007;167(14):1476-1486

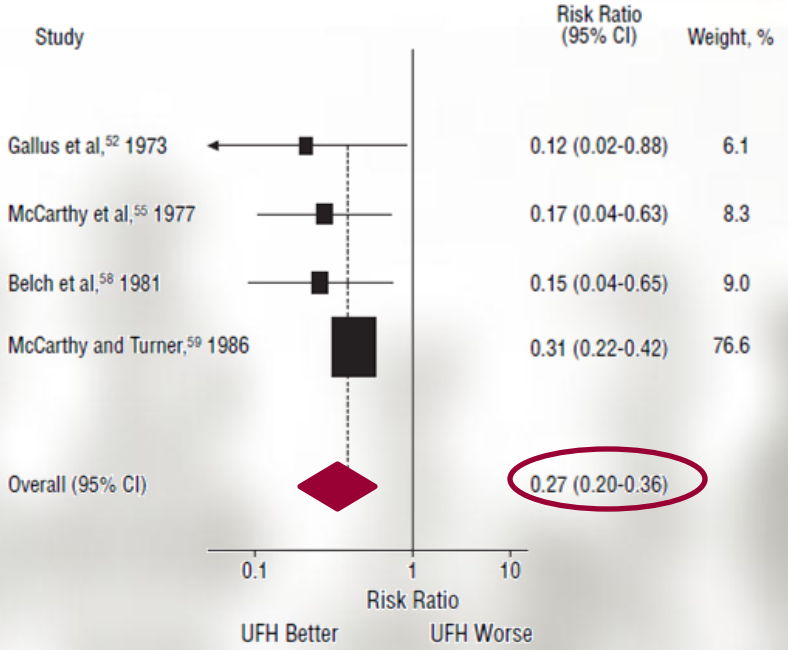
PE



Mortality



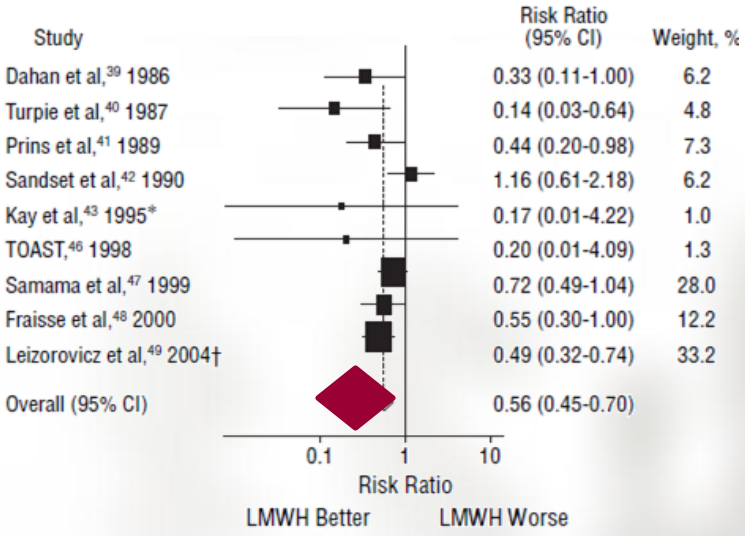
UFH, 5000 U 3 Times Daily, vs Control DVT



Arch Intern Med. 2007;167(14):1476-1486

LMWH vs Control

DVT



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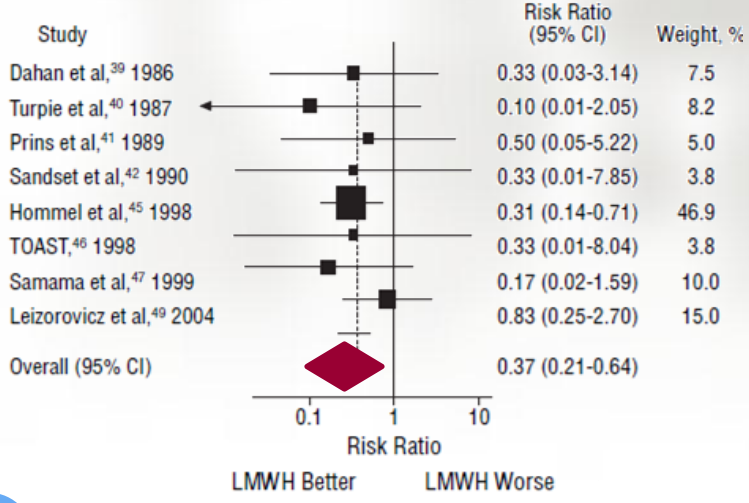
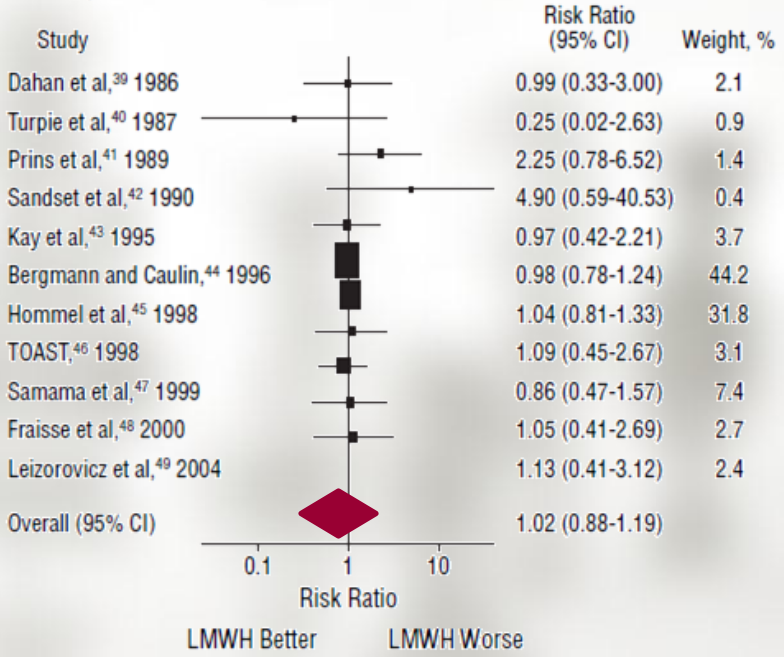


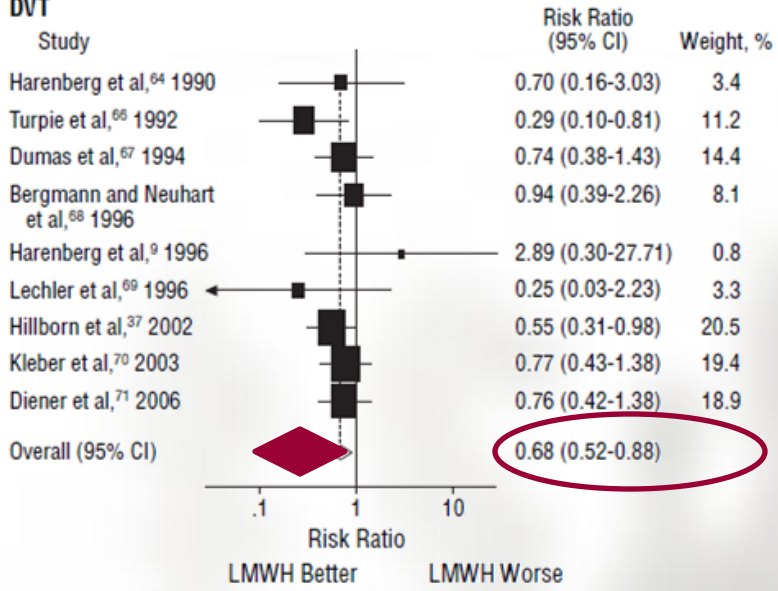
Mortality



Arch Intern Med. 2007;167(14):1476-1486

LMWH vs UFH

DVT



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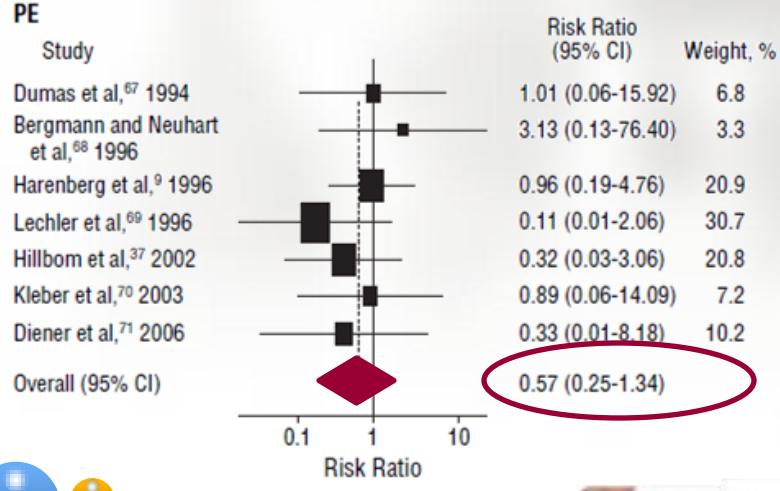
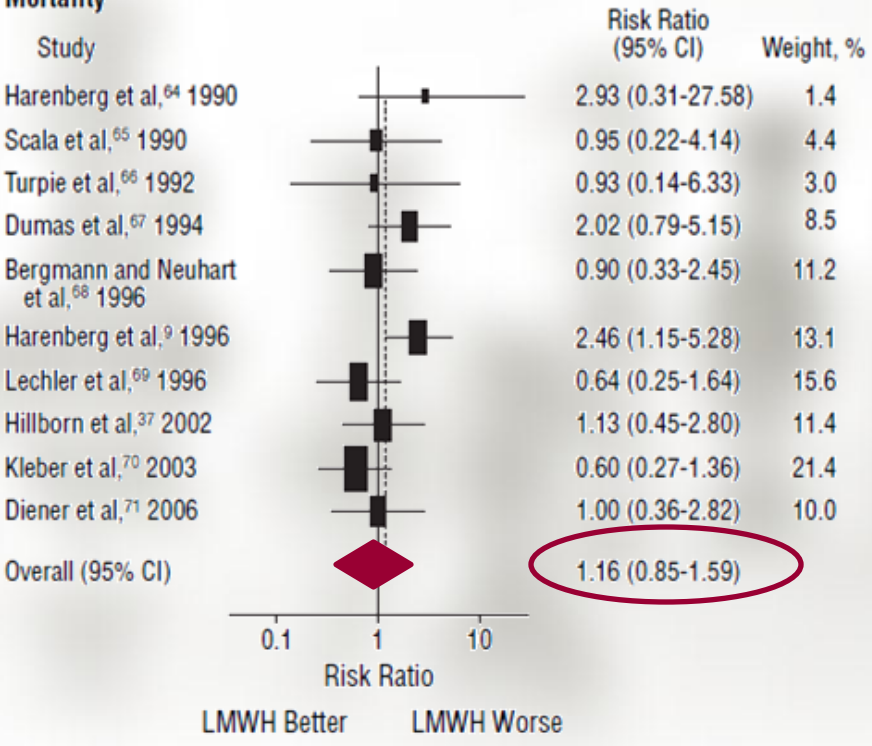


Mortality



Arch Intern Med. 2007;167(14):1476-1486

PRÉVENTION DE LA MALADIE
THROMBOEMBOLIQUE VEINEUSE
EN MILIEU MÉDICAL.

EN RÉANIMATION

Venous Thromboembolic Disease: An Observational Study in Medical-Surgical Intensive Care Unit Patients

Deborah Cook, John Attia, Bruce Weaver, Ellen McDonald, Maureen Meade, and Mark Crowther

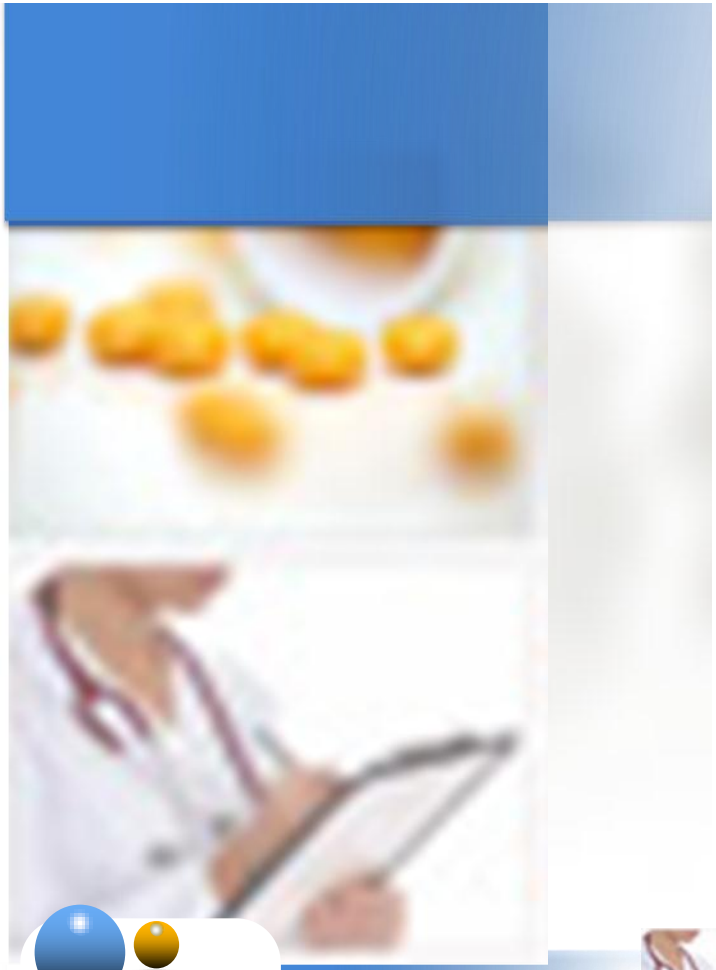


Table 2. ICU-Acquired Risk Factors For ICU-Acquired Venous Thromboembolism

Potential Risk Factor	Odds Ratio (95% CI)	*P* Value
Mechanical ventilation	1.56 (0.23–10.45)	.64
Immobility	2.14 (0.11–40.87)	.61
Femoral venous catheter	2.24 (0.41–12.20)	.35
Platelet count >450 × 10^9/L	0.99 (0.05–19.7)	.99
Sedative infusion	1.52 (0.28–8.16)	.63
Paralytic drug	4.81 (0.85–27.35)	.08
Emergency surgery in ICU	1.03 (0.19–5.50)	.97
VTE prophylaxis with heparin	0.08 (0.0–1.41)	.05
Aspirin	0.42 (0.08–2.29)	.31
TED stockings	0.63 (0.12–3.37)	.59
Central venous catheter heparin	1.05 (0.15–7.07)	.96
Warfarin	0.07 (0.01–0.49)	.01
Intravenous heparin	0.04 (0.01–0.25)	<.01

Journal of Critical Care, Vol 15, No 4, 2000: 127-132

Deep vein thrombosis during prolonged mechanical ventilation despite prophylaxis

Emad H. Ibrahim, MD; Manuel Iregui, MD; Donna Prentice, RN; Glenda Sherman, RN; Marin H. Kollef, MD; William Shannon, PhD

Table 2. Process of medical care

Process of Care	Deep Vein Thrombosis Present (n = 26)	Deep Vein Thrombosis Absent (n = 84)	*p* Value
Chemical paralysis, no. (%)	4 (15.4)	8 (9.5)	.473
Chemical paralysis days[a]	1.0 ± 0.0[b]	1.8 ± 1.0[b]	.240
Central venous catheter, no. (%)	17 (65.4)	68 (81.0)	.098
Central venous catheter days[c]	26.9 ± 22.2[b]	14.5 ± 12.1[b]	.024
Central venous catheter site, no. (%)			
Internal jugular	5 (29.4)	18 (26.5)	.807
Subclavian	9 (52.9)	32 (47.0)	.664
Femoral	3 (17.7)	18 (26.5)	.545
Hemodialysis, no. (%)	5 (19.2)	13 (15.5)	.651
	26 (1.00)	84 (1.00)	>.999

Crit Care Med 2002; 30:771–774

Deep venous thrombosis in medical-surgical critically ill patients: Prevalence, incidence, and risk factors

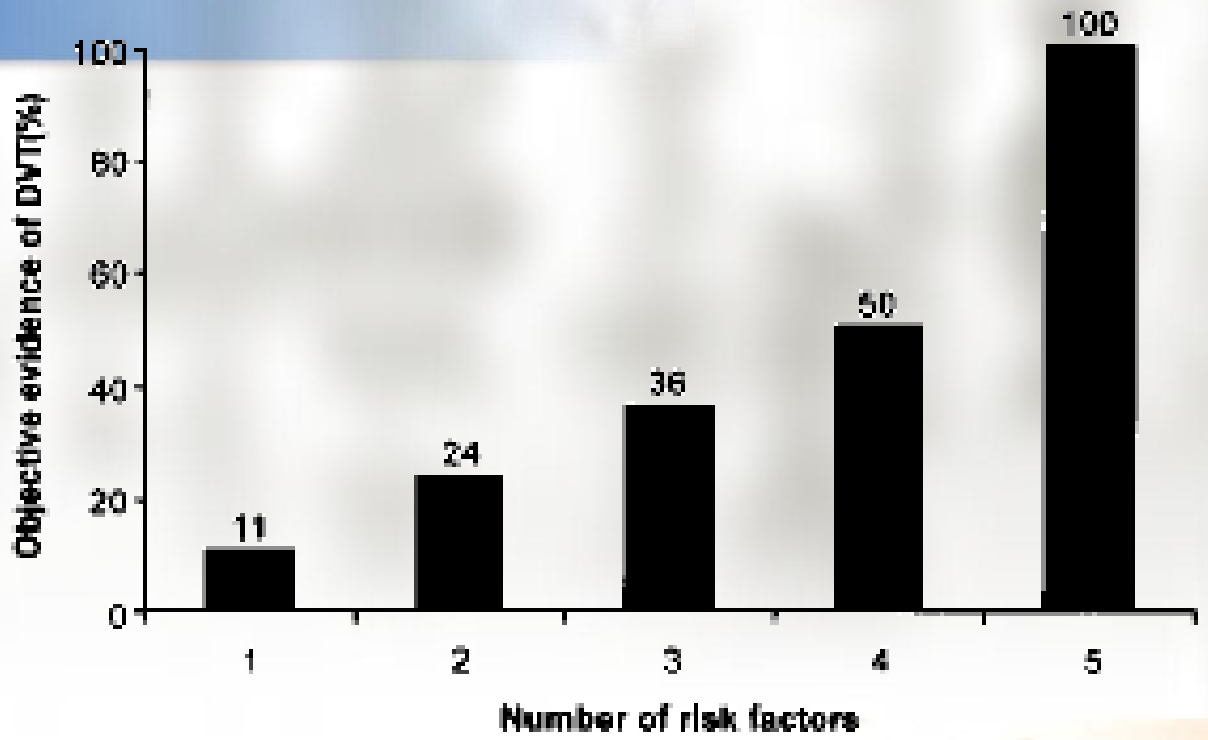
Deborah Cook, MD; Mark Crowther, MD; Maureen Meade, MD; Christian Rabbat; Lauren Griffith, MSc; David Schiff, MD; William Geerts, MD; Gordon Guyatt, MD

Table 2. Risk factors for intensive care unit-acquired lower extremity deep venous thrombosis

Risk Factor	Incident DVT	No DVT	Univariate Hazard Ratio (95% CI)	*p* Value	Multivariate Hazard Ratio (95% CI)	*p* Value
Personal or family history of VTE	7 (28.0)	13 (6.0)	3.7 (1.4–9.3)	.007	4.0 (1.5–10.3)	.004
Thrombophilic disorder	3 (12.0)	6 (2.8)	3.8 (1.1–12.8)	.03	—	
Chronic hemodialysis	4 (16.0)	13 (6.0)	3.3 (1.1–9.9)	.03	3.7 (1.2–11.1)	.02
Femoral central venous catheter	14 (56.0)	83 (38.4)	2.0 (0.9, 4.6)	.09	—	
Operation	8 (32.0)	38 (17.6)	2.9 (1.1–7.8)	.04	—	
Platelet transfusion	6 (24.0)	23 (10.6)	3.1 (1.2–7.9)	.02	3.2 (1.2–8.4)	.02
Vasopressor administration	9 (36.0)	43 (19.9)	3.0 (1.2–7.4)	.02	2.8 (1.1–7.2)	.03

Crit Care Med 2005 Vol. 33, No. 7

FDR et probabilité de TVP



AMERICAN COLLEGE OF CHEST PHYSICIANS

clinical investigations in critical care

Utilization of Venous Thromboembolism Prophylaxis in a Medical-Surgical ICU*

Richard P. Ryskamp, MD; and Steven J. Trottier, MD

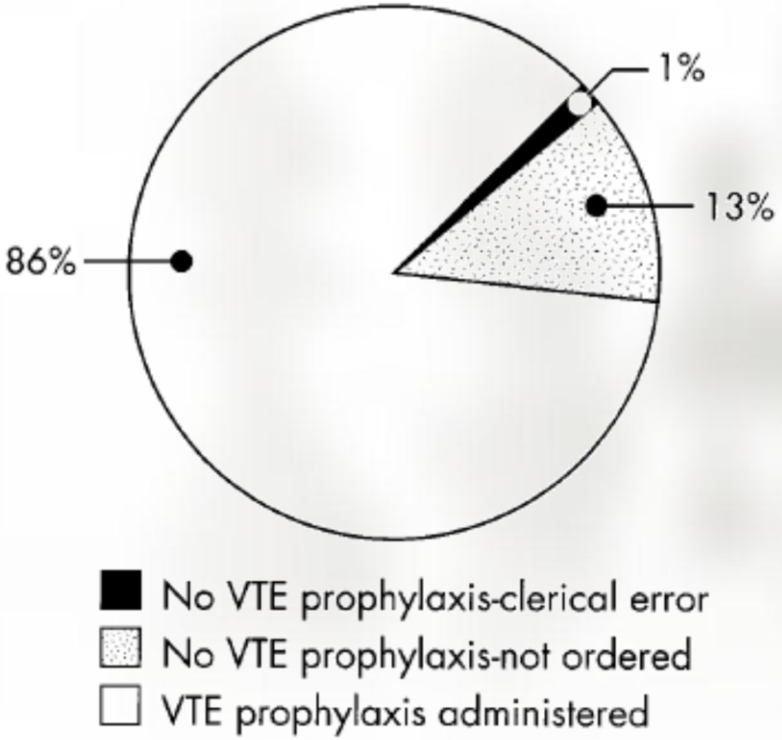


Table 1—*Methods of VTE Prophylaxis*

Method	No. of Patients	% of Study Patients
Pneumatic compression stockings	120	57
Low-dose subcutaneous heparin	55	26
IV heparin	11	5
Warfarin	5	2
Dextran	3	1
Inferior vena cava filter	7	3
None	30	14

CHEST 1998; 113:162-64

Prevention of Venous Thromboembolism in Critically Ill Medical Patients: A Franco-Canadian Cross-sectional Study

Jean Claude Lacherade, Deborah Cook, Daren Heyland, Carla Chrusch, Laurent Brochard, and Christian Brun-Buisson, for the French and Canadian ICU Directors Groups

Table 2. Heparin and Mechanical VTE Prophylaxis in French and Canadian ICUs

	France, n	%	Canada, n	%	*P* Value
Number of ICUs	113		29		—
Number of patients	875		347		—
Heparin prophylaxis	570	65.1	212	61.1	.24
UFH	54	6.2	187	53.9	<.0001
LWMH	514	58.7	25	7.2	<.0001
Not specified	2	0.2	0	0.0	—
No heparin prophylaxis	157	17.9	99	28.5	.02
Hemorrhage	57	6.5	37	10.7	.1
Severe coagulopathy	44	5.0	25	7.2	.85
No perceived indication	52	5.9	19	5.5	<.001
Other	4	0.5	18*	5.2	—
ICUs use of heparin prophylaxis					
UFH alone	6	5.4	17	58.6	<.0001
LWMH alone	94	83.2	0	—	<.0001
UFH and LWMH	13	11.3	12	41.3	<.01
Mechanical Prophylaxis	89	12.2	91	29.3	<.0001
Antiembolic stockings	89	12.2	61	19.6	.002
Pneumatic compression devices	0	0.0	42	13.5	<.0001
Therapeutic anticoagulation	148	16.9	36	10.4	.005

Journal of Critical Care, Vol 18, No 4 , 2003: 228-237

Nadroparin in the Prevention of Deep Vein Thrombosis in Acute Decompensated COPD

FRANÇOIS FRAISSE, LAURENT HOLZAPFEL, JEAN-MICHEL COULAUD, GERALD SIMONNEAU, BERNARD BEDOCK, MARC FEISSEL, PATRICK HERBECQ, REGINALD PORDES, JEAN-FRANÇOIS POUSSEL, LOUIS ROUX
and The Association of Non-University Affiliated Intensive Care Specialist Physicians of France

Patients were randomized to receive either nadroparin (Fraxiparine; Sanofi-Winthrop, Gentilly, France) or matching placebo by subcutaneous injection once daily. Taking previous clinical experience with nadroparin in high-risk surgical patients (8) into consideration, dosage was based on patients' body weight (3,800 AXa IU, i.e., 0.4 ml for 45 to 70 kg; 5,700 AXa, i.e., 0.6 ml for 71 to 110 kg). Nadroparin was supplied as a concentrated solution of 9,500 AXa IU/ml in disposable, prefilled syringes. Placebo 0.9% physiological saline was supplied in an identical manner.

RR : 0.54

RRR : 0.46

RRA : 12.7%

NNT : 7.8

PRIMARY EFFICACY CRITERION
(DVT DIAGNOSED BY VENOGRAPHY)

	Nadoparin (*n* = 84)	Placebo (*n* = 85)	p Value
DVT			
Present, n (%)	13 (15.5)	24 (28.2)	0.045
Absent, n (%)	71 (84.5)	61 (71.8)	0.045
Localizations			
Proximal, n*	3	7	1.00
Distal only, n	10	17	> 0.05
Segmental localization			
Subpopliteal, n	11	23	
Popliteal, n	1	5	
Superficial femoral, n	1	4	
Deep femoral, n	2	2	
External iliac, n	0†	1	
Common iliac, n	0†	0†	
Inferior vena cava, n	0†	0†	

Nadroparin in the Prevention of Deep Vein Thrombosis in Acute Decompensated COPD

FRANÇOIS FRAISSE, LAURENT HOLZAPFEL, JEAN-MICHEL COULAUD, GERALD SIMONNEAU, BERNARD BEDOCK, MARC FEISSEL, PATRICK HERBECQ, REGINALD PORDES, JEAN-FRANÇOIS POUSSEL, LOUIS ROUX
and The Association of Non-University Affiliated Intensive Care Specialist Physicians of France

Tout événement indésirable

NNH: 14

Pour événements graves:

NNH: 20

CLINICAL SAFETY: ADVERSE EVENTS*

	Nadroparin (*n* = 108)	Placebo (*n* = 113)	p Value
Total adverse events			
Patients, n (%)	50 (46.3)	45 (39.8)	0.33
Adverse events of which, n	84	79	
Hemorrhage	25	18	0.18
Major hemorrhage	6	3	0.28
Minor bleeding	19	15	
Thrombocytopenia	10	7	0.39
Serious adverse events†			
Patients, n (%)	27 (25)	22 (19.5)	0.32
Adverse events of which, n	34	28	
Hemorrhage	6	3	
Thrombocytopenia	3	2	
Adverse events resulting in early permanent discontinuation of therapy			
Patients, (%)	13 (12)	10 (8.8)	0.44
Adverse events of which, n	18	11	
Hemorrhage, n	5	2	0.41
Thrombocytopenia, n	7	3	0.40
Serious adverse events (considered to be related to treatment by the Committee on Critical events), n	7	3	
Hemorrhage, n	5	2	
Thrombocytopenia, n	1	1	

Dalteparin versus Unfractionated Heparin in Critically Ill Patients

The PROTECT Investigators for the Canadian Critical Care Trials Group and the Australian and New Zealand Intensive Care Society Clinical Trials Group

	Dalteparine 1873	HNF 1873	HR	IC 95%	p
TVP	5.1	5.8	0.92	0.68-1.23	0.57
EP	1.3	2.3	0.52	0.3-0.88	<0.01
Saignement majeur	5.5	5.6	1.1	0.84-1.21	0.96
Saignement mineur	13	13.2	0.47	0.16-1.35	0.16
Mortalité	15.2	16.2	0.97	0.82-1.15	0.71

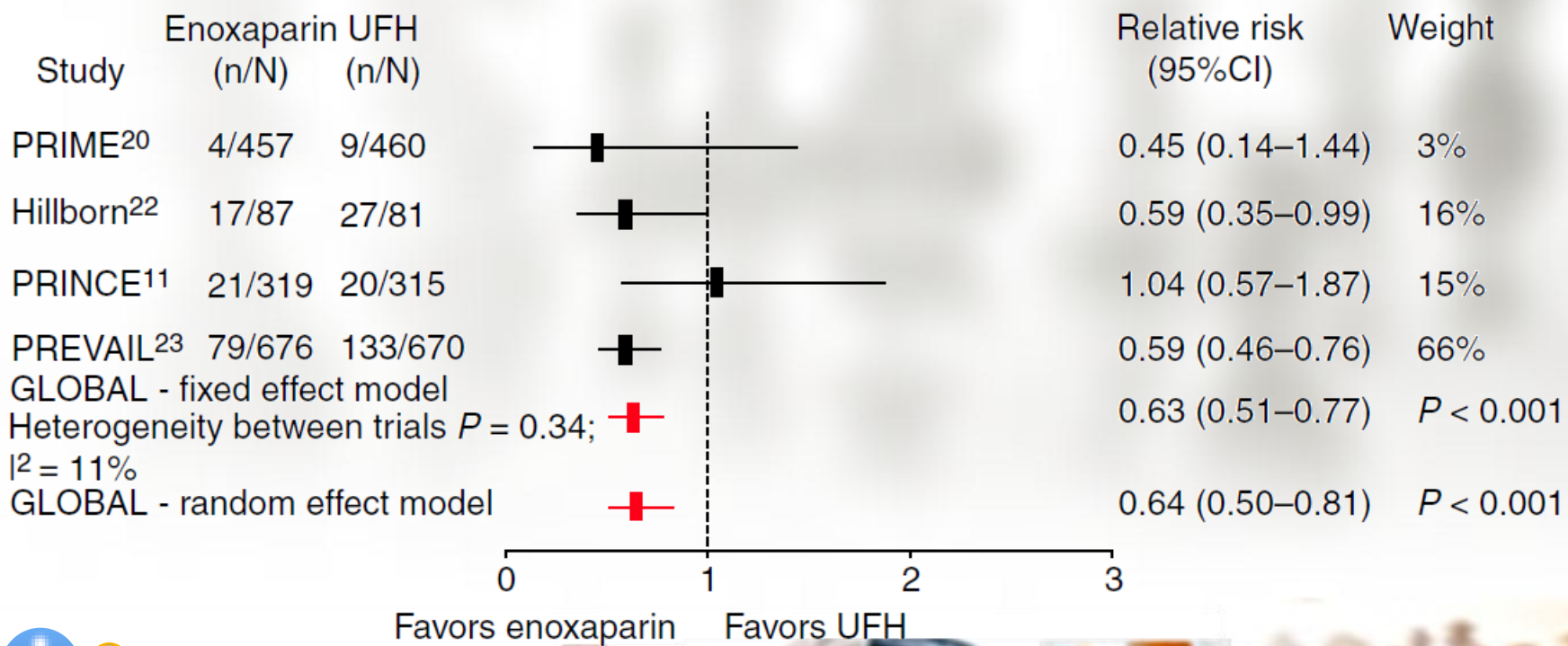
N Engl J Med 2011;364:1305-14.

HBPM vs HNF

Individual patient data meta-analysis of enoxaparin vs. unfractionated heparin for venous thromboembolism prevention in medical patients

S. LAPORTE,*† J. LIOTIER,‡ L. BERTOLETTI,*§ F.-X. KLEBER,¶ G. F. PINEO,** C. CHAPELLE,††
N. MOULIN§ and P. MISMETTI*†§

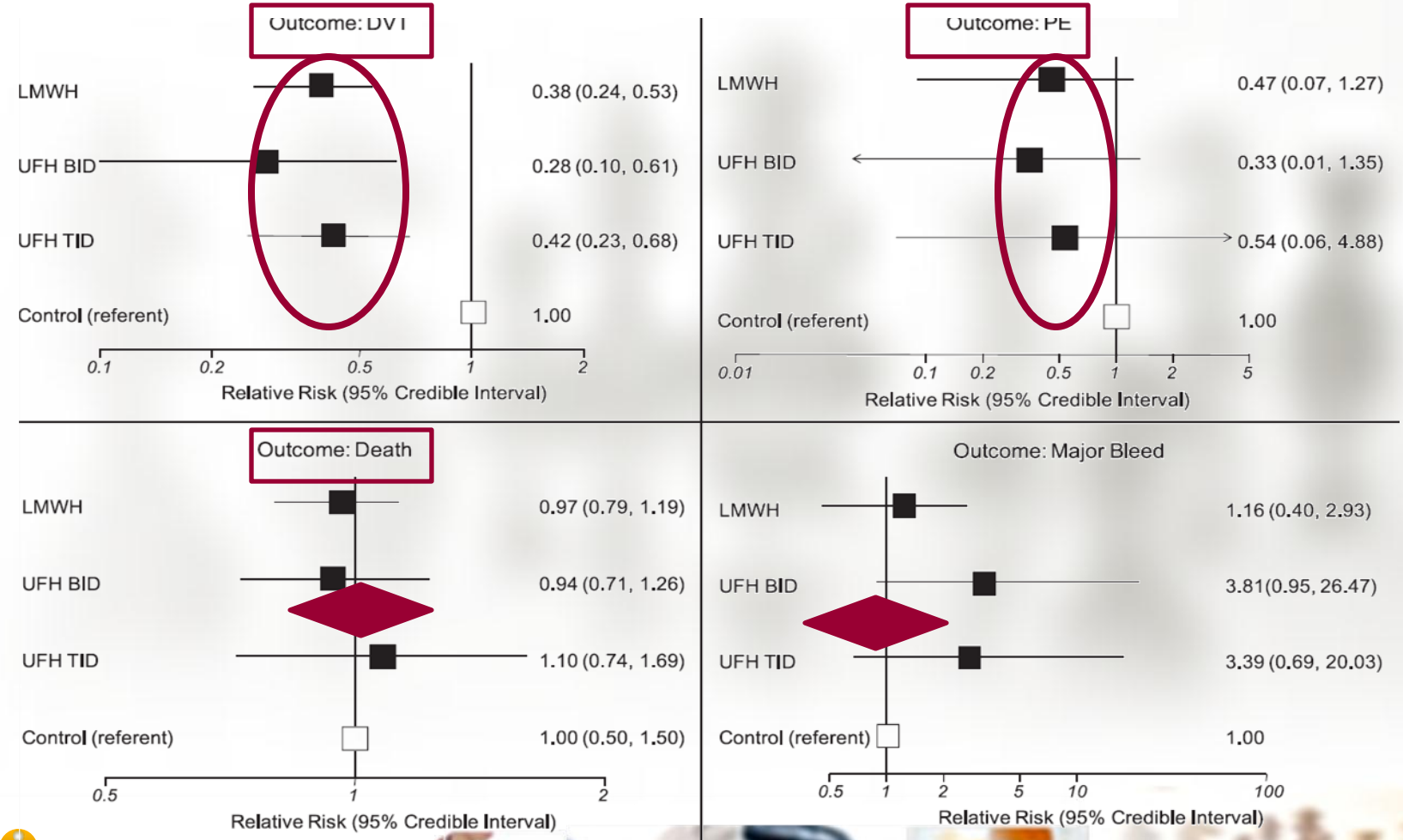
A



J Thromb Haemost 2011; 9: 464–72.

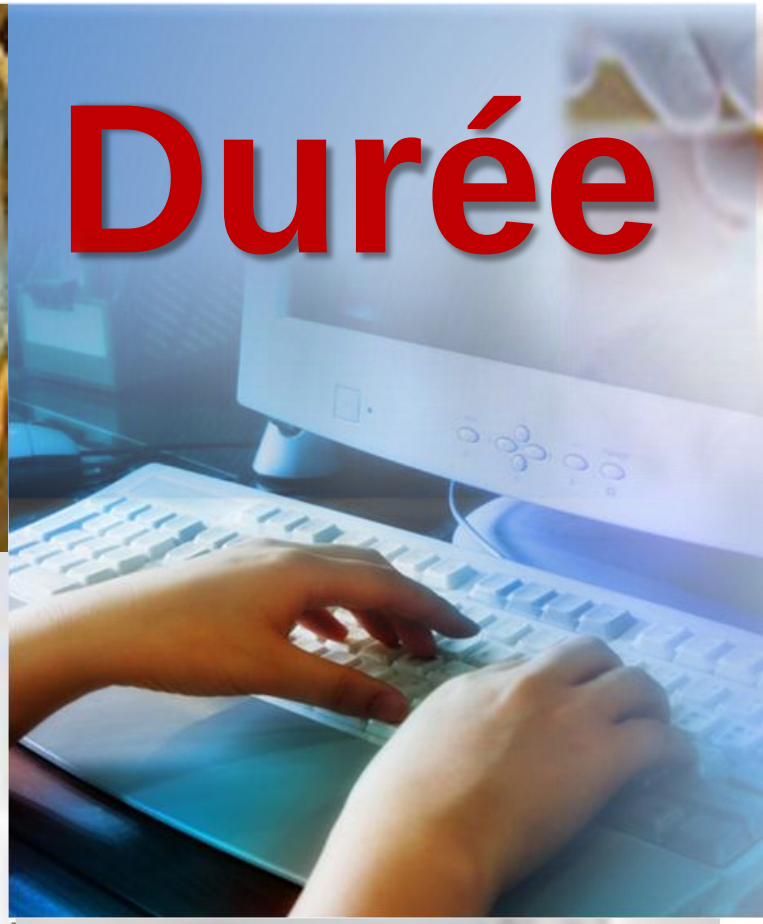
Dosing Frequency of Unfractionated Heparin Thromboprophylaxis

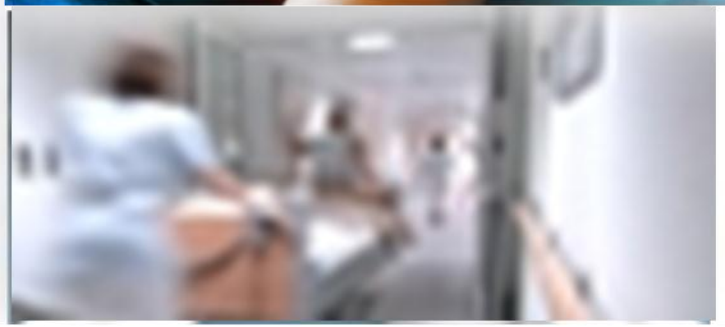
A Meta-analysis



CHEST 2011; 140(2):374–381

Durée





Durée

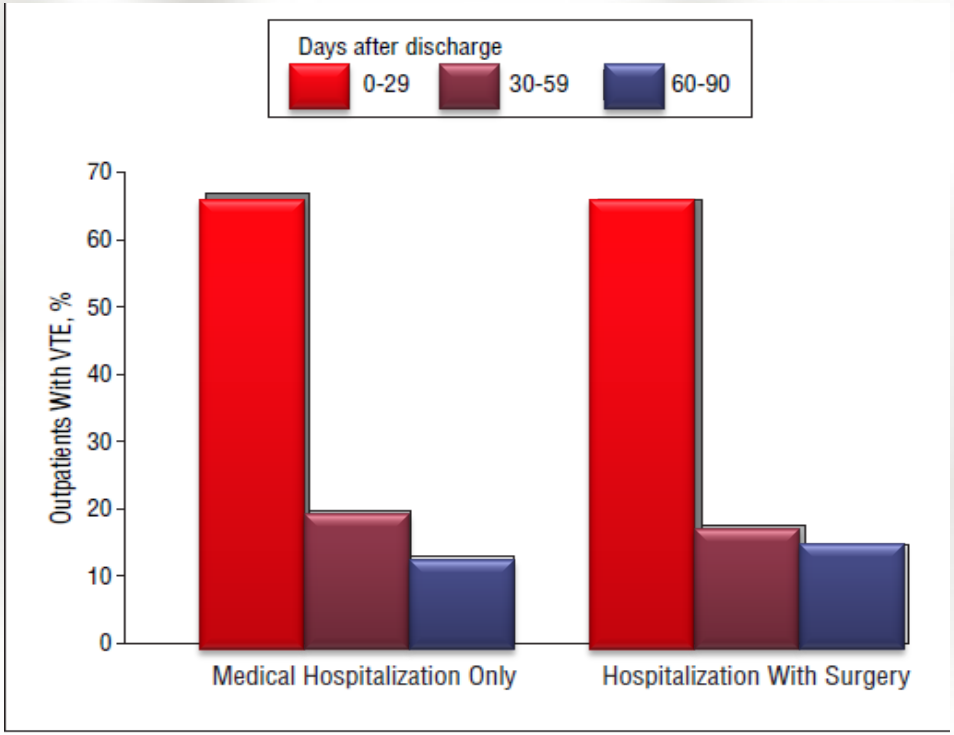
- MEDENOX , PREVENT , ARTEMIS 14 jours
- Durée de séjour en réanimation ≈ 8 jours
- 16.7 % uniquement prennent une durée appropriée

Venous Thromboembolism in the Outpatient Setting

Frederick A. Spencer, MD; Darleen Lessard, MS; Cathy Emery, RN; George Reed, PhD; Robert J. Goldberg, PhD

Table 1. Demographic and Clinical Characteristics of Patients According to Setting of VTE (Outpatient vs Inpatient)[a]

Characteristic	Outpatient (n = 1399)	Inpatient (n = 498)	*P* Value
Demographic Factors			
Age, mean, y	63.3	67.4	<.001
Age, y			
<55	33.0	21.2	<.001
55-64	13.9	17.2	
65-74	18.7	18.8	
≥75	34.5	42.8	
Female	56.2	51.9	.09
BMI[b]			
<25.0	31.5	37.9	.11
25.0-29.9	32.4	29.6	
≥30.0	36.1	32.5	
Medical History			
Recent prior hospitalization (without surgery)[c]	18.9	23.7	<.001
Recent surgery (without hospitalization)[c]	5.2	19.1	<.001
Recent prior hospitalization and surgery[c]	17.9	20.9	<.001
Recent malignant neoplasm[c]	29.0	32.3	.17
Recent infection[c]	18.6	46.8	<.001
Recent central venous catheter[c]	10.4	41.0	<.001
Previous DVT	17.4	8.6	.001
Previous PE	6.0	2.9	<.05
Previous DVT or PE	19.9	10.2	<.001
Recent intensive care unit discharge[c]	8.7	38.2	<.001
Recent hormonal therapy[c]	8.0	3.0	<.001
Recent fracture[c]	7.3	18.7	<.001
Recent chemotherapy[c]	7.7	8.0	.82
Recent heart failure[c]	4.2	16.5	<.001
Recent cardiac procedures[c]	2.9	7.8	<.001



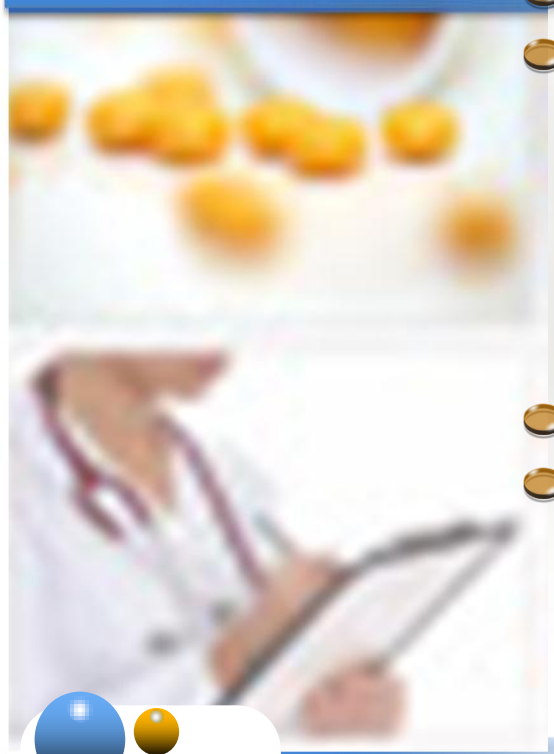
Arch Intern Med. 2007;167(14):1471-1475

ARTICLE | Annals of Internal Medicine

Extended-Duration Venous Thromboembolism Prophylaxis in Acutely Ill Medical Patients With Recently Reduced Mobility

A Randomized Trial

- ERC
- 370 sites dans 20 pays (Amérique, Europe et Asie)
- Inclusion :
  - ≥ 40 ans
  - Mobilité réduite
    - Niveau 1 repos au lit ou sédentarité
    - Niveau 2 repos au lit plus toilette sur place
      - Amendement : âge >75 ans, ATCD MTE, Cancer
- Enoxaparine 40 mg 28±4 j vs 10±4 j
- Critères de jugement :
  - TVP → J28
  - Saignement 48 h après dernière injection



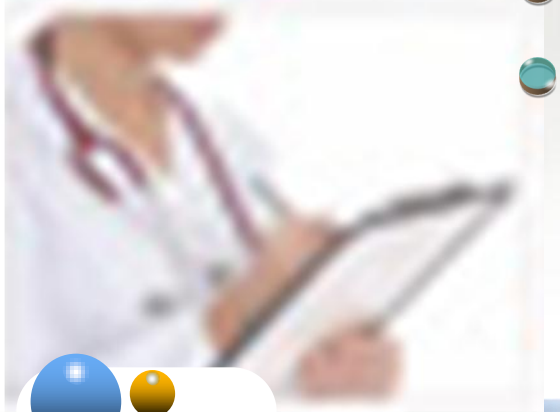
Ann Intern Med. 2010;153:8-18.

ARTICLE | Annals of Internal Medicine

Extended-Duration Venous Thromboembolism Prophylaxis in Acutely Ill Medical Patients With Recently Reduced Mobility

A Randomized Trial

- Réduction de l'incidence des TVP / placebo
  - 2.5% vs. 4%; RRA en faveur de l'enoxaparine, 1.53% [95.8% CI, 2.54% to 0.52%]).
- Augmentation du saignement majeur
  - (0.8% vs. 0.3%; RRA en faveur placebo, 0.51% [95% CI, 0.12% to 0.89%]).
- **NNT = 65 NNH = 196**
- **Femme , âge > 75 ans, niveau 1 de mobilité**



Ann Intern Med. 2010;153:8-18.

Prophylaxie non pharmacologique

Bas de contention ou contention élastique graduée

- Méta analyse
- 7 études contention élastique graduée isolé
  - 1027 patients
  - 15% vs 29%
  - OR 0.36 IC95% 0.26-0.49
- 9 études avec d'autres moyens
  - 1184 patients
  - 3% vs 14%
  - OR : 0.22 IC 95% 0.15-0.34

Amarigiri SV. Cochrane Library 2001




En pratique,

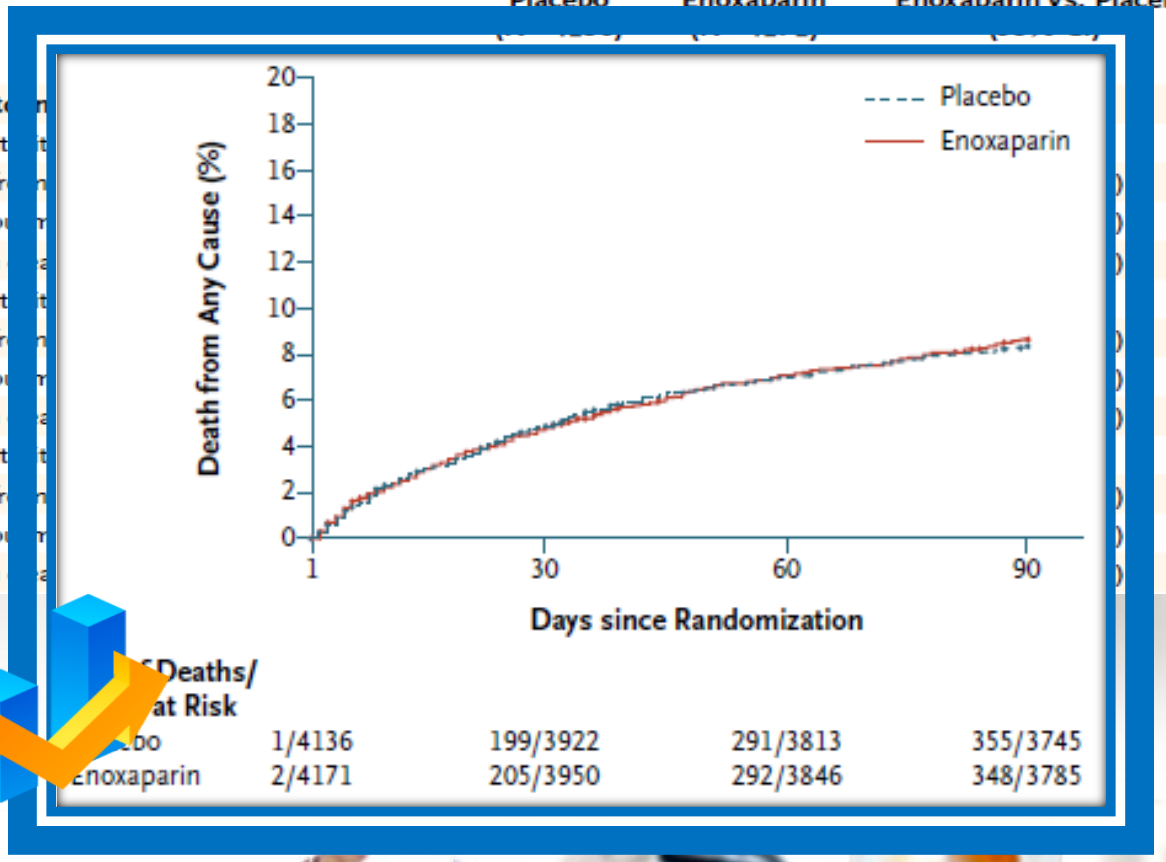
- seule pour un risque thromboembolique modéré en se substituant à l'héparinothérapie (HNF ou HBPM),
- en présence d'une contre-indication au traitement anticoagulant. Méta analyse

Amarigiri SV. Cochrane Library 2001

Low-Molecular-Weight Heparin and Mortality in Acutely Ill Medical Patients

Table 2. Efficacy Outcomes and the Characteristics and Primary Causes of Death.*

Variable	Placebo	Enoxaparin	Risk Ratio for Enoxaparin vs. Placebo	P Value†
Efficacy outcomes				
14-day mortality				
Death from any cause				0.95
Cardiopulmonary				0.56
Sudden death				0.29
30-day mortality				
Death from any cause				0.83
Cardiopulmonary				0.77
Sudden death				0.97
90-day mortality				
Death from any cause				0.71
Cardiopulmonary				0.82
Sudden death				0.77



	Deaths/ at Risk			
Placebo	1/4136	199/3922	291/3813	355/3745
Enoxaparin	2/4171	205/3950	292/3846	348/3785

N Engl J Med 2011;365:2463-72.

Compression pneumatique intermittente

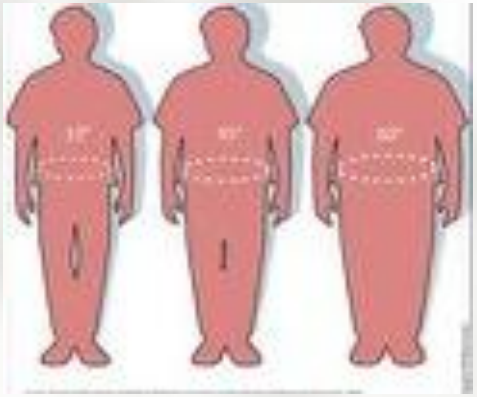
- **Les indications:**
  - des patients comateux (neurochirurgie ou traumatologie),
  - patient compliant et vigile, + contre indication des anticoagulants.
- Ramos R, et al. (Chest 1996;109:82 – 5) : dans une étude ayant inclus 2551 patients comparant l'association de la compression mécanique et HNF à l'héparine seule.
  - Les auteurs ont montré une **supériorité de l'association** avec une incidence de l'embolie pulmonaire de **1.5% VS 4% (P <0.001)**

Amarigiri SV. Cochrane Library 2001

PRÉVENTION DE LA MALADIE THROMBOEMBOLIQUE VEINEUSE EN MILIEU MÉDICAL.

PROPHYLAXIE
&
PATIENTS OBÈSES
INSUFFISANCE RÉNALE

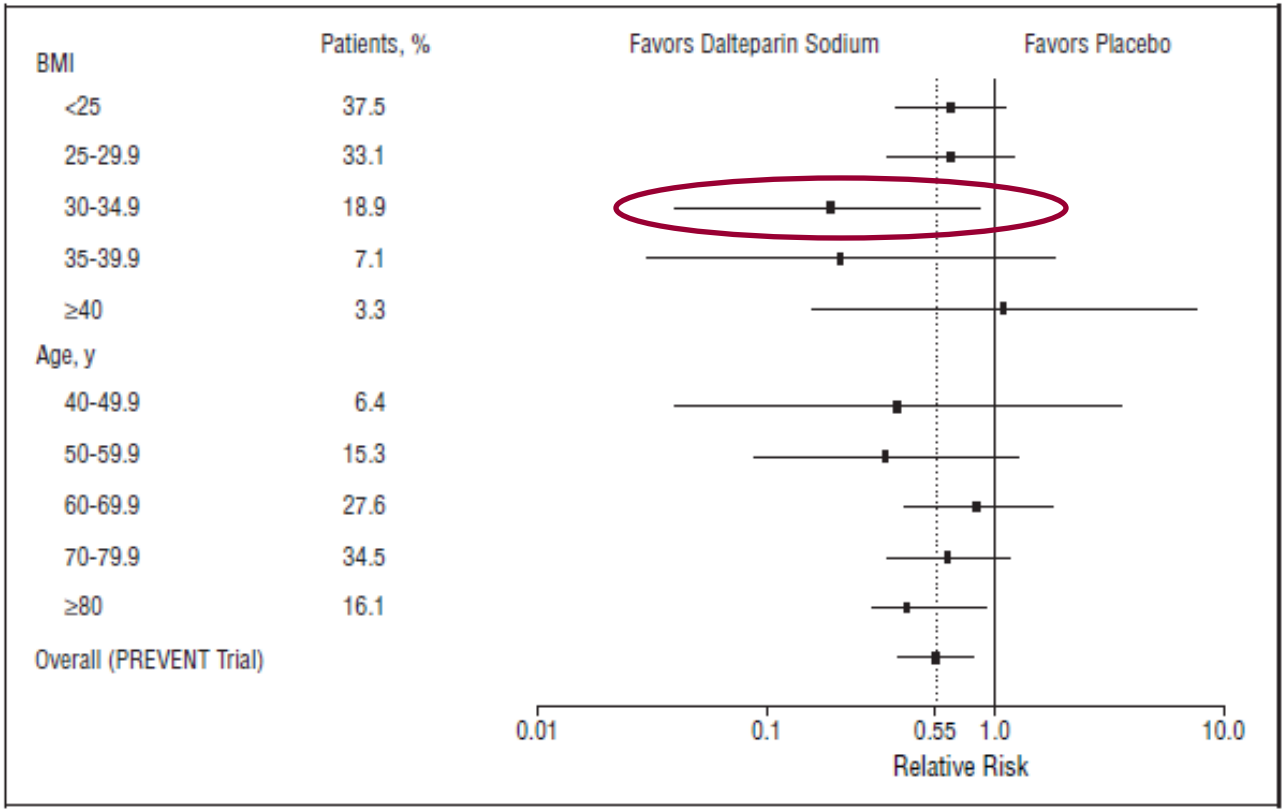
Sujets obeses



CLINICAL OBSERVATION

Efficacy and Safety of Fixed Low-Dose Dalteparin in Preventing Venous Thromboembolism Among Obese or Elderly Hospitalized Patients

A Subgroup Analysis of the PREVENT Trial



Arch Intern Med. 2005;165:341-345

Table 2. Components of the Primary End Point, According to Body Mass Index and Age*

End Point Component	Obese (n = 1118)	Nonobese (n = 2563)	Age <75 y (n = 2455)	Age ≥75 y (n = 1226)
Sudden death	4/1107 (0.36)	4/2529 (0.16)	5/2422 (0.21)	3/1214 (0.25)
PE: fatal	0/1107	2/2529 (0.08)	2/2422 (0.08)	0/1214
PE: symptomatic	3/1080 (0.28)	8/2419 (0.33)	4/2351 (0.17)	7/1148† (0.61)
DVT: distal, symptomatic	3/1080 (0.28)	4/2418 (0.17)	3/2350 (0.13)	4/1148 (0.35)
DVT: proximal, symptomatic	23/922 (2.49)	66/2070 (3.19)	45/2038 (2.21)	44/954‡ (4.61)
DVT: proximal, asymptomatic	22/917 (2.40)	58/2043 (2.84)	39/2019 (1.93)	41/941§ (4.36)

Table 3. Adverse Events According to the Presence or Absence of Obesity

	Nonobese			Obese		
Adverse Event	Dalteparin Sodium (n = 1290)	Placebo (n = 1273)	*P* Value	Dalteparin Sodium (n = 558)	Placebo (n = 560)	*P* Value
Mortality, %						
Day 21	5.5	6.0	.54	4.6	2.7	.14
Day 90	14.3	13.7	.94	9.9	8.6	.36
Hemorrhage, %						
Major day 21	1.6	0.3	.07	0	0.7	>.99
Minor day 21	2.5	1.8	.31	1.4	0.7	.22
Thrombocytopenia, %						
Day 21	1.5	1.0	.79	0.9	0.9	>.99



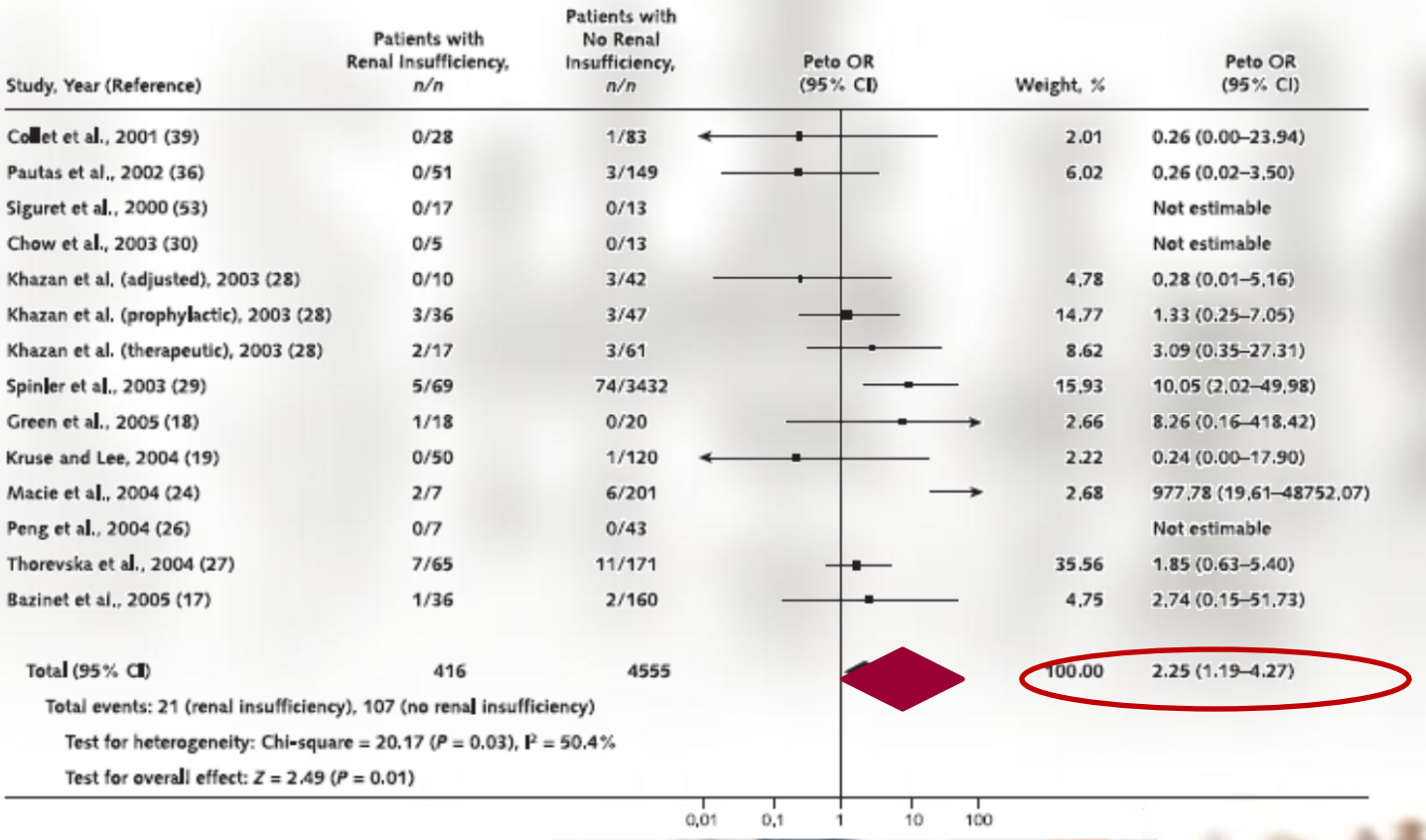

Insuffisance rénale

Annals of Internal Medicine | REVIEW

Meta-Analysis: Low-Molecular-Weight Heparin and Bleeding in Patients with Severe Renal Insufficiency

Wendy Lim, MD, BSc; Francesco Dentali, MD; John W. Eikelboom, MBBS; and Mark A. Crowther, MD, MSc

Figure 2. Peto odds ratio (*OR*) of major bleeding events in patients with severe renal insufficiency (creatinine clearance ≤30 mL/min) compared with patients without renal insufficiency (creatinine clearance >30 mL/min).



Ann Intern Med. 2006;144:673-684.

Figure 3. Peto odds ratio (OR) of major bleeding events with enoxaparin in patients with severe renal insufficiency (creatinine clearance ≤30 mL/min) compared with patients without renal insufficiency (creatinine clearance >30 mL/min).

Study, Year (Reference)	Patients with Renal Insufficiency, *n/n*	Patients with No Renal Insufficiency, *n/n*	Peto OR (95% CI)	Weight, %	Peto OR (95% CI)
All enoxaparin					
Collet et al., 2001 (39)	0/28	1/83		2.14	0.26 (0.00–23.94)
Chow et al., 2003 (30)	0/5	0/13			Not estimable
Khazan et al. (adjusted), 2003 (28)	0/10	3/42		5.08	0.28 (0.01–5.16)
Khazan et al. (prophylactic), 2003 (28)	3/36	3/47		15.71	1.33 (0.25–7.05)
Khazan et al. (therapeutic), 2003 (28)	2/17	3/61		9.17	3.09 (0.35–27.31)
Spinler et al., 2003 (29)	5/69	74/3432		16.95	10.05 (2.02–49.98)
Green et al., 2005 (18)	1/18	0/20		2.83	8.26 (0.16–418.42)
Kruse and Lee, 2004 (19)	0/50	1/120		2.36	0.24 (0.00–17.90)
Macie et al., 2004 (24)	2/7	6/201		2.85	977.78 (19.61–48752.07)
Peng et al., 2004 (26)	0/7	0/43			Not estimable
Thorevska et al., 2004 (27)	7/65	11/171		37.84	1.85 (0.63–5.40)
Bazinet et al., 2005 (17)	1/36	2/160		5.06	2.74 (0.15–51.73)
Subtotal (95% CI)	348	4393		100.00	2.59 (1.34–5.01)

Total events: 21 (renal insufficiency), 104 (no renal insufficiency)

Test for heterogeneity: Chi-square = 17.35 ($P = 0.04$), $I^2 = 48.1\%$

0.01 0.1 1 10 100

Favors Reduction in Bleeding Favors Increase in Bleeding

Ann Intern Med. 2006;144:673-684.

Prophylaxis Against Deep Vein Thrombosis in Critically Ill Patients With Severe Renal Insufficiency With the Low-Molecular-Weight Heparin Dalteparin

An Assessment of Safety and Pharmacodynamics: The DIRECT Study

- Etude multicentrique
- Dalteparine 5000/j
- Patients en I rénale cl créat ≤ 30 ml/min
- Bio accumulation : Anti-Xa > 0.4 (mesuré 2 X /sem)
- 138 patients (cl créat 18.9±6.5 ml/min
- Durée TTT : 7(4-12)

Arch Intern Med. 2008;168(16):1805-1812

Table 2. Trough Anti-Xa Levels According to the Duration of Dalteparin Treatment

Variable	Study Day (From Date of Study Enrollment) of Trough Anti-Xa Measurements				
	1-3	4-6	7-9	10-12	>12
Proportion of all trough anti-Xa levels ≥0.10 IU/mL, No./total No. (%)	13/67 (19.4)	26/149 (17.4)	19/55 (34.6)	11/63 (17.5)	24/93 (25.8)
Proportion of patients with at least 1 trough anti-Xa level ≥0.10 IU/mL, No./total No. (%)	13/63 (20.6)	25/103 (24.3)	19/54 (35.2)	11/48 (22.9)	16/37 (43.2)
Trough anti-Xa levels ≥0.10 IU/mL, median (IQR)	0.10 (0.10-0.13)	0.10 (0.10-0.14)	0.10 (0.10-0.13)	0.10 (0.10-0.12)	0.11 (0.10-0.13)

Table 3. Serial Anti-Xa Levels at 0, 1, 2, 4, 8, 12, 20, and 24 Hours After a Targeted 3, 10, and 17 Days of Dalteparin Treatment[a]

Hours After Dalteparin Administration	Median (IQR) Anti-Factor Xa Levels		
	After 3 Days of Dalteparin Prophylaxis (n=102)	After 10 Days of Dalteparin Prophylaxis (n=46)	After 17 Days of Dalteparin Prophylaxis (n=15)
0 (Before treatment)	<0.06 (<0.06-<0.06)	<0.06 (<0.06-<0.06)	<0.06 (<0.06-0.08)
1	0.16 (0.10-0.26)	0.20 (0.11-0.29)	0.23 (0.19-0.25)
2	0.28 (0.19-0.40)	0.29 (0.18-0.39)	0.32 (0.25-0.38)
4	0.29 (0.20-0.42)	0.35 (0.24-0.43)	0.34 (0.27-0.45)
8	0.19 (0.11-0.30)	0.23 (0.09-0.31)	0.17 (0.10-0.27)
12	0.09 (<0.06-0.15)	0.11 (<0.06-0.18)	0.10 (<0.06-0.29)
20	<0.06 (<0.06-0.06)	<0.06 (<0.06-0.06)	<0.06 (<0.06-0.11)
24	<0.06 (<0.06-<0.06)	<0.06 (<0.06-<0.06)	<0.06 (<0.06-0.06)

Prophylaxis Against Deep Vein Thrombosis in Critically Ill Patients With Severe Renal Insufficiency With the Low-Molecular-Weight Heparin Dalteparin

An Assessment of Safety and Pharmacodynamics: The DIRECT Study

- **TVP**
  - 7 patients (5.1%; 95% CI, 2.5%-10.2%)
  - Asymptomatique
  - 6 ont un KT fémoral
  - 0 EP
- **Saignement**
  - 10 patients (1.4%; 95% CI, 0.4%- 5.1%)
- **Clairance créatinine**
  - début 18.9 (6.4)
  - fin 28.4 (17.3)

Arch Intern Med. 2008;168(16):1805-1812

Executive Summary : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

- **1- Patients médicaux a risque de thrombose élevé**

  → thromboprophylaxie **Grade 1B**

  – HBPM (préférence du patient, compliance , facilité d'administration)

  – Faible dose HNF 2 X /j ou 3 x / j

  – Fondaparinux

- **Patients médicaux à faible risque:**

  – Prophylaxie pharmacologique ou mécanique **Grade 1B**

- **Patients médicaux + saignement ou haut risque de saignement**

  – Pas de prophylaxie **Grade 1B**

Chest 2012;141;7S-47S

Executive Summary : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

- **Patients médicaux + haut risque de thrombose + saignement ou haut risque de saignement** **Grade 2C**
  - Moyens mécaniques
  - Risque de saignement diminue et risque de thrombose persiste → moyen pharmacologique **Grade 2B**

- **Durée :** pas de prolongation en dehors de la période d'immobilisation et séjour hospitalier **Grade 2B**

Chest 2012;141;7S-47S

CHEST ONLINE

Executive Summary : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

- **Réanimation**
  - Pas de recherche systématique de TVP — **Grade 2C**
  - HBPM ou faible dose HNF — **Grade 2C**
  - Si saignement ou risque de saignement
    - Moyens mécaniques — **Grade 2C**
    - Si risque de saignement diminue
      → HBPM ou LDUH — **Grade 2C**

Chest 2012;141;7S-47S