2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

Todd Gensler MD

April 21, 2017

Thrombolysis for DVT—Everyone Should Get It

2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

Todd Gensler MD

April 21, 2017

Thrombolysis for DVT—Everyone with Acute Iliofemoral DVT and No Contraindication Should Get It


I use tPa for all of my DVT patients

OBJECTIVES

- Define post-thrombotic syndrome and its prevalence.
- Review the risk/incidence of bleeding both major and minor with thrombolysis.
- Definitively support the role of thrombolysis in iliofemoral DVT treatment.
  - Cochrane Database--1969-2011
  - CaVenT trial--2012
  - Attract trial—March 2017

DVT

- AFFECTS 2.5-5% OF GEN'L POPULATION AT SOME POINT IN THEIR LIFE
  - *Browse NL, Burnand KG, Lea Thomas M. Deep vein thrombosis: pathology, diagnosis and treatment. In: Browse NL, Burnand KG, Irvine AT, Wilson NM editor(s). Diseases of the veins. 2nd Edition. London: Edward Arnold, 1999:443-74*
  - *White RH. The epidemiology of venous thromboembolism. Circulation 2003;107(23):14-8.*
- ONLY 20% OF ILIOFEMORAL DVT CAN BE COMPLETELY RECANALIZED W/ AC ALONE

Iliofemoral venous thrombosis. Pathological considerations and surgical management

G. E. Mavor, J. M. D. Galloway

First published: January 1969 Full publicatio

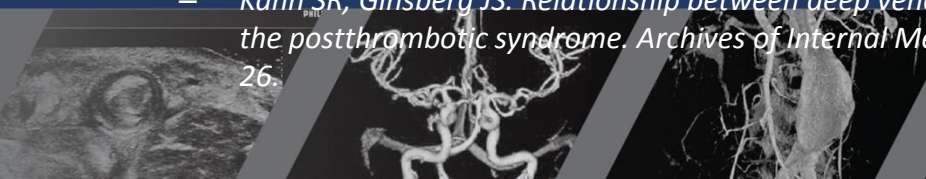
BJS

PTS

- **POST-THROMBOTIC SYNDROME AFFECTS UP TO 50% OF THOSE WHO HAVE HAD DVT-- some degree of pain, swelling, skin pigmentation or venous ulceration of the affected leg**
  - *Kahn SR. The post-thrombotic syndrome: progress and pitfalls. British Journal of Haematology 2006;134:357-65. [doi:10.1111/j.1365-2141.2006.06200.]*
  - *Schulman S, Lindmarker P, Holmström M, Lärfars G, Carlsson A, Nicol P, et al. Post-thrombotic syndrome, recurrence, and death 10 years after the first episode of venous thromboembolism treated with warfarin for 6 weeks or 6 months. Journal of Thrombosis and Haemostasis 2006;4(4):734-42*
- **USUALLY OCCURS W/IN 2 YRS**
  - *Brandjes DP, Buller HR, Heijboer H, Huisman MV, de Rijk M, Jagt H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. Lancet 1997;349(9054):759-62.*
  - *Kahn SR, Shrier I, Julian JA, Ducruet T, Arsenault L, Miron M, et al. Determinants and time course of the post thrombotic syndrome after acute deep venous thrombosis. Annals of Internal Medicine 2008;149:698-707.*
- **EVENTUAL VENOUS ULCERATION IN 6% DESPITE COMPRESSION**
  - *Johnson BF, Manzo RA, Bergelin RO, Strandness DE Jr. Relationship between changes in the deep venous system and the development of the postthrombotic syndrome after an acute episode of lower limb deep vein thrombosis: a one-to six-year follow-up. Journal of Vascular Surgery 1995;21(2):307-12.*
  - *Schulman S, Lindmarker P, Holmström M, Lärfars G, Carlsson A, Nicol P, et al. Post-thrombotic syndrome, recurrence, and death 10 years after the first episode of venous thromboembolism treated with warfarin for 6 weeks or 6 months. Journal of Thrombosis and Haemostasis 2006;4(4):734-42.*

VENOUS ULCERATION

- The prevalence of venous ulcers in the general population is around 1 in 1000
  - *Browse NL, Burnand KG, Lea Thomas M. Deep vein thrombosis: pathology, diagnosis and treatment. In: Browse NL, Burnand KG, Irvine AT, Wilson NM editor(s). Diseases of the veins. 2nd Edition. London: Edward Arnold, 1999:443-74.*
- Between 40% to 50% of patients with venous ulcers have evidence of post-thrombotic damage
  - *Kahn SR, Ginsberg JS. Relationship between deep venous thrombosis and the postthrombotic syndrome. Archives of Internal Medicine 2004;164:17–26.*



Villalta Scoring Scale

Five patient-related venous symptoms	Six clinician-rated signs
Pain	Pretibial edema
Cramps	Skin induration
Heaviness	Hyperpigmentation
Paraesthesia	Pain during calf compression
Pruritus	Venous ectasia
	Redness

Scoring — Each sign or symptom is rated as:

0 = None
1 = Mild
2 = Moderate
3 = Severe

Summed-up ratings = total score:

- <5 = no PTS
- 5-14 = mild/moderate PTS
- ≥15/venous ulcer = severe PTS

Enden T et al. *Lancet* 2012;379(9810):31-8.

HOW TO PREVENT PTS

- ANTICOAGULATION
- COMPRESSION THERAPY
- THROMBOLYSIS
  - PHARMA
  - MECHANICAL

VETO TRIAL

Acute DVT

Outcomes After Anticoagulation Alone

Determinants and Time Course of the Postthrombotic Syndrome after Acute Deep Venous Thrombosis

Susan R. Kahn, MD, MSc; Ian Shrier, MD, PhD; Jim A. Julian, MMath; Thierry Ducruet, MSc; Louise Arsenault, BA; Marie-José Miron, MD; Andre Roussin, MD; Sylvie Desmarais, MD; France Joyal, MD; Jeannine Kassis, MD; Susan Solymoss, MD; Louis Desjardins, MD*; Donna L. Lamping, PhD; Mira Johri, PhD; and Jeffrey S. Ginsberg, MD

Predictors of Post-Thrombotic Syndrome

- Common femoral or iliac vein thrombosis (OR 2.23 p<0.001)
- Post-thrombotic morbidity at 1 month (p<0.001)

Ann Int Med 2008; 149:698

SOX Trial

Elastic Compression Stockings vs Placebo Control

Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial

Susan R Kahn, Stan Shapiro, Philip S Wells, Marc A Rodger, Michael J Kovacs, David R Anderson, Vicky Tagalakis, Adrielle H Houweling, Thierry Ducruet, Christina Holcroft, Mira Johri, Susan Solymoss, Marie-José Miron, Erik Yeo, Reginald Smith, Sam Schulman, Jeannine Kassis, Clive Kearon, Isabelle Chagnon, Turnly Wong, Christine Demers, Rajendar Hanmiah, Scott Kaatz, Rita Selby, Suman Rathbun, Sylvie Desmarais, Lucie Opatrny, Thomas L Ortel, Jeffrey S Ginsberg, for the SOX trial investigators

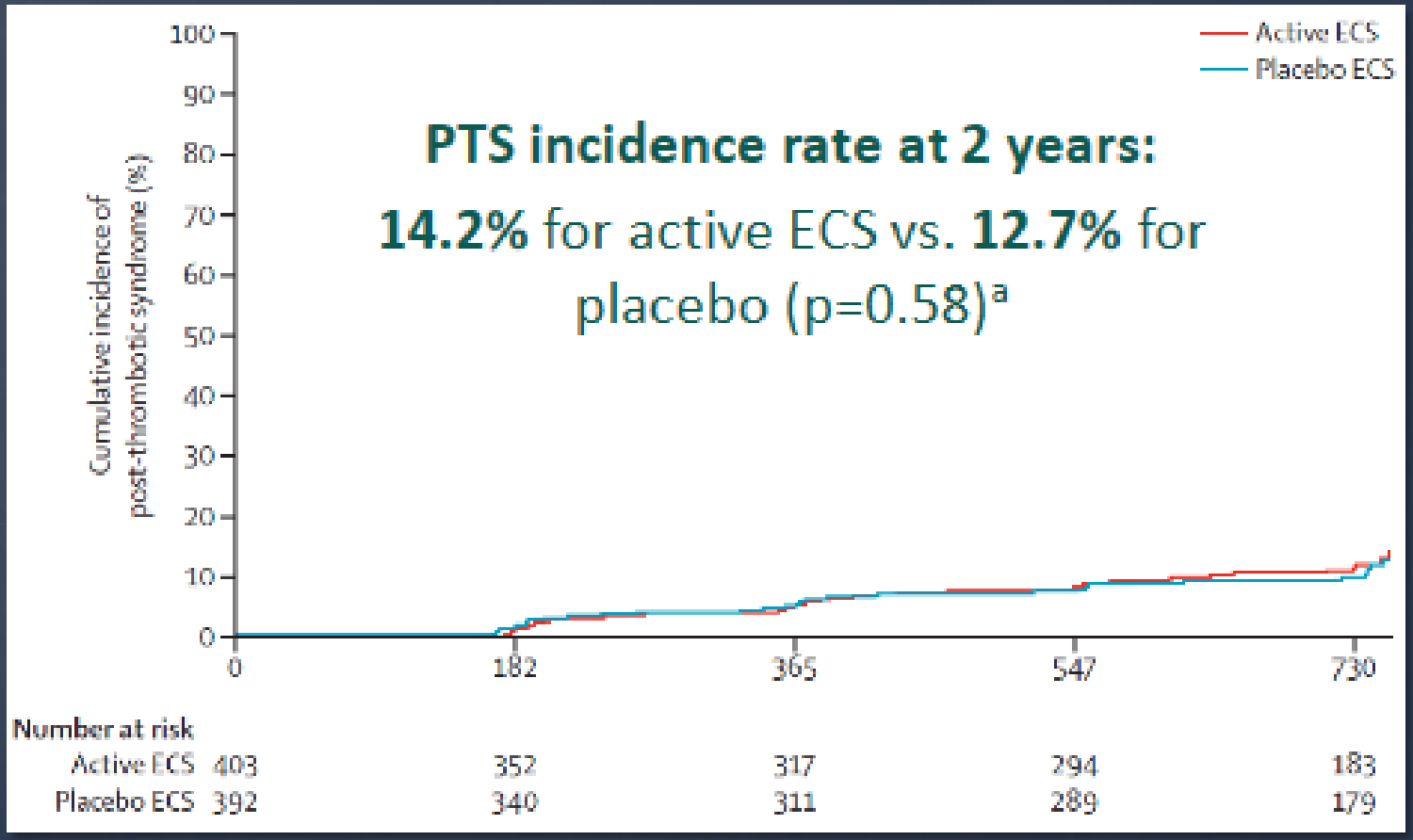
- **Objective:** To evaluate the effectiveness of elastic compression stockings (ECS), compared with placebo stockings to prevent post-thrombotic syndrome (PTS)
- **Design:** Multicenter, randomized, placebo-controlled trial of active (N=410) vs placebo (N=396) ECS
- **Key Inclusion Criteria:** First indicative, proximal DVT (with or without coexisting pulmonary embolism or distal DVT)
- **Primary Endpoint:** PTS diagnosed at 6 months or later using Ginsberg's criteria (ie, leg pain and swelling of ≥1 month)

Kahn SR, Shapiro S, Wells PS, et al SOX trial investigators. Lancet. 2014 Mar 8;383(9920):880-8

SOX Trial Results

Elastic Compression Stockings vs Placebo Control

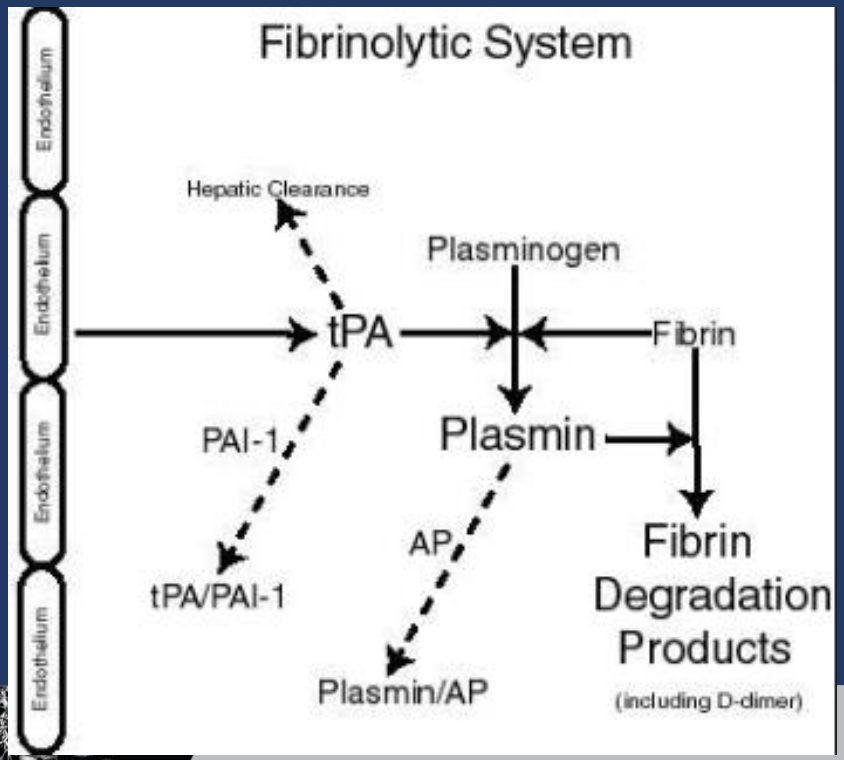
"ECS did not prevent PTS after a first proximal DVT"



Kahn SR, Shapiro S, Wells PS, et al SOX trial investigators. Lancet. 2014 Mar 8;383(9920):880-8

THROMBOLYSIS

- Drugs activate plasminogen
- Plasmin breaks links b/t fibrin molecules
- ROUTES OF ADMIN
  - peripheral vein
  - CDT
  - PCDT



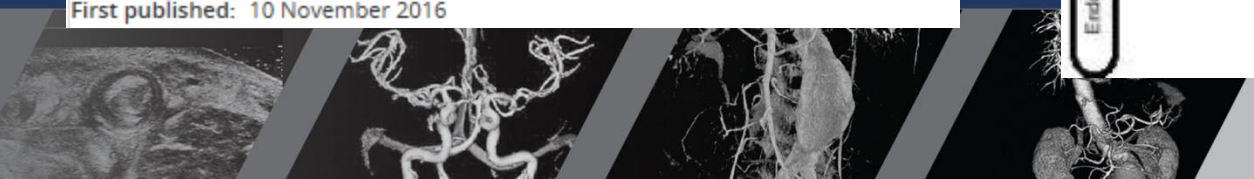
Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

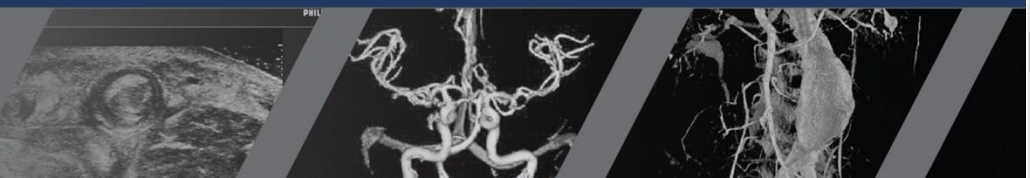
Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016



RATIONALE FOR THROMBOLYSIS—THE OPEN VEIN THEORY

- Dissolving the thrombus in the acute phase may reduce the risk of more permanent damage to the structure and function of the vein
- In particular venous valvular function, thus lowering the risk of post-thrombotic complications in the long term.



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

Thrombolysis for acute deep vein thrombosis

Cochrane Database of Systematic Reviews

Lorna Watson ✉, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

Editorial Group: Cochrane Vascular Group

- RANDOMIZED TRIALS ONLY
- ACUTE DVT, defined as onset of symptoms within seven days and confirmed by objective testing
- EXCLUSION--trials including participants with
  - chronic or recurrent venous thrombosis
  - treatment after a maximum of 21 days from the onset of symptoms

TRIAL DETAILS—no standardized protocols

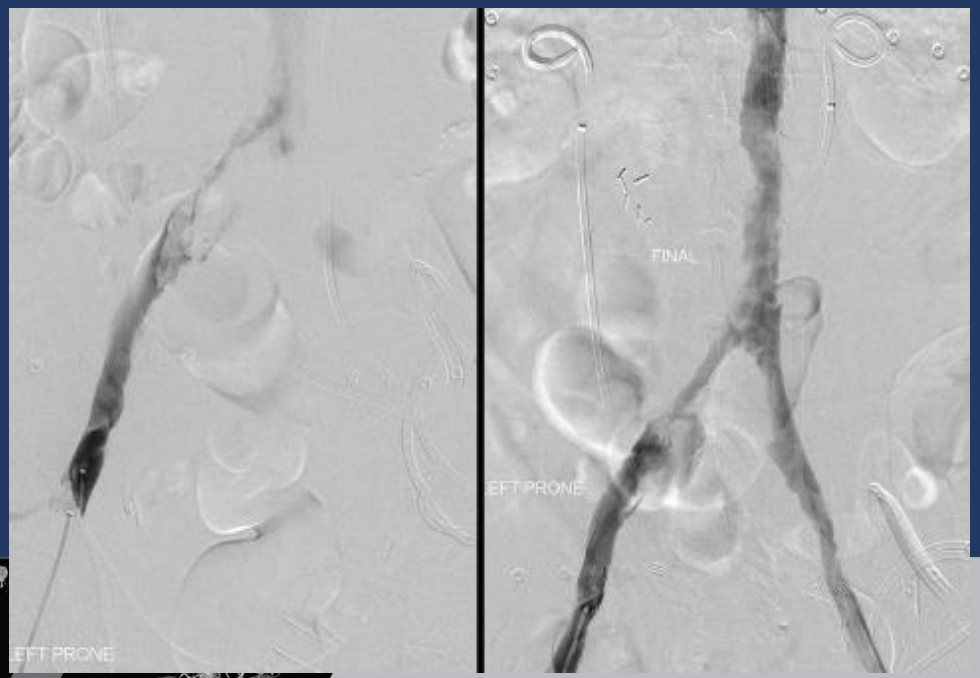
- 1969-2011
- The majority of trials assessed systemic thrombolysis, with streptokinase the most common agent used
- DOSAGES of thrombolytics varied
- Route of administration varied
- Heparinization varied
- Duration of anticoagulation after initial event varied
- 9 trials: <50pts
- 2 trials: >100pts (largest 250pts)

Contraindications for Lysis

- surgery or head trauma within the previous three months
- malignancy
- renal and hepatic dysfunction
- bleeding dysfunction

OUTCOME MEASURES

- EARLY--up to one month
- INTERMEDIATE--6 months to 5 yrs
- LATE-->5 yrs



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

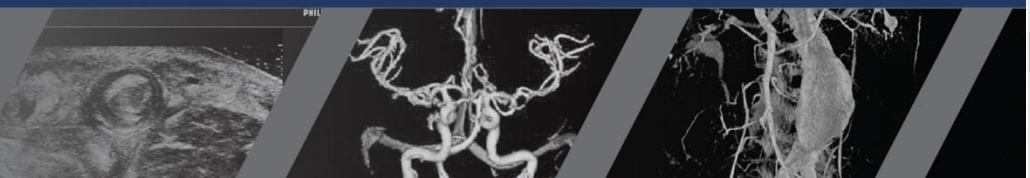
New search | Review | Intervention

Lorna Watson ✉, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

PRIMARY OUTCOMES

- Any improvement in venous patency
- Complete clot lysis
- Bleeding complications (defined as bleeding causing treatment to be stopped, requiring transfusion or surgery, or causing chronic or fatal sequelae)
- Stroke and in particular haemorrhagic stroke
- PTS
- Venous Ulcer
- Mortality



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

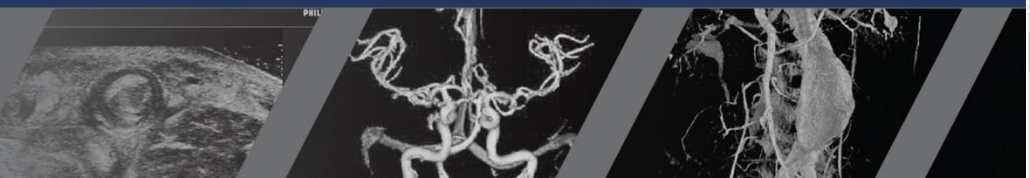
New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

SECONDARY OUTCOMES

- Recurrent DVT
- PE
- Venous function
    - assessed by duplex ultrasound or other objective means such as foot volumetry or ambulatory venous pressure measurements
- Quality of life (QoL)
- Cost



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

RESULTS-PTS


Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

- Pooling all types of thrombolysis, the results showed a reduction in the risk of PTS with use of thrombolysis by 34% at the intermediate time point (RR 0.66; NNTB 5) and a reduction in the risk of PTS of 42% at late follow-up (RR 0.58; NNTB 4).

- There was no difference in ulceration beyond six months; data were limited by small numbers and the short length of follow-up, as ulcers are more likely to occur later than a year or two after the DVT.

RESULTS--BLEEDING

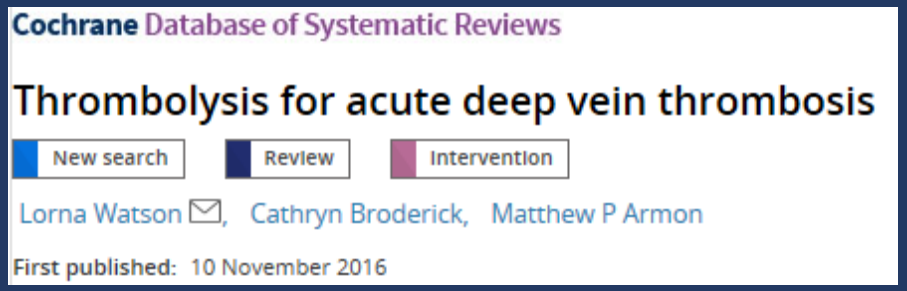
- Participants receiving thrombolysis were significantly more likely than control participants to experience a bleeding complication.

- 9% (62/662) of patients in the thrombolysis group experienced a bleeding complication compared to 4% (19/441) of patients in the standard anticoagulation group

- Most bleeding complications occurred in earlier studies

RESULTS--ICH

- Out of a total of 1103 participants 3 events occurred in the treatment group (a rate of 0.3%) and none in the control group. The pooled RR was 1.92 (95% CI 0.34 to 10.86) with wide uncertainty regarding the true effect


Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

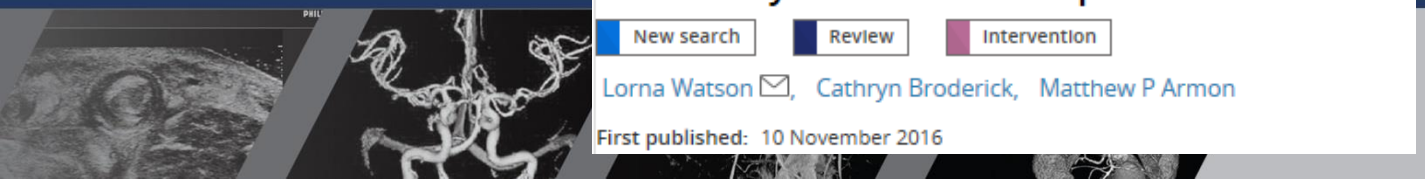
First published: 10 November 2016

RESULTS--ICH

- Three intracerebral bleeds occurred in these trials (Common 1976—streptokinase & P Vera; Goldhaber 1990—controlled HTN; Marder 1977—remote Hx of CVA). Adoption of current contra-indications may have prevented these events in more recent trials
- Two of the early deaths in the treatment groups may also have been prevented with the use of current contra-indications to thrombolysis: a participant with metastatic carcinoma (Common 1976), and a participant with recent surgery (Kakkar 1969).

RESULTS--MORTALITY

- A total of 5 (? 2 possibly preventable) events occurred in the treatment group and 7 in the control group out of a total 529 participants. The pooled RR was 0.76 (95% CI 0.31 to 1.89)



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

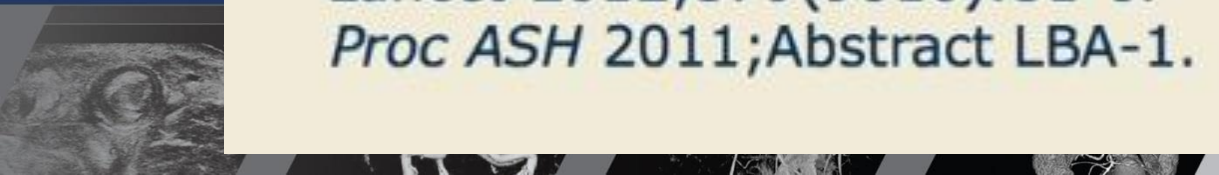
Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

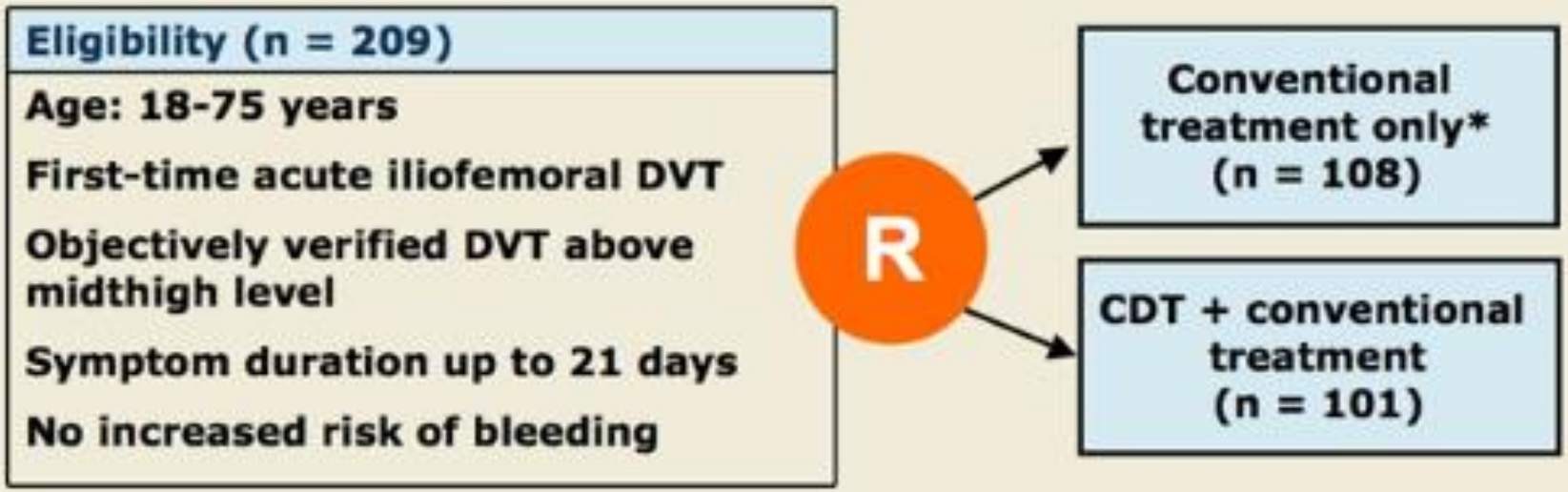
CaVenT Trial

Long-Term Outcome After Additional Catheter-Directed Thrombolysis versus Standard Treatment for Acute Iliofemoral Deep Vein Thrombosis (The CaVenT Study): A Randomised Controlled Trial

Enden T et al.
Lancet 2012;379(9810):31-8.
Proc ASH 2011;Abstract LBA-1.



CaVenT Trial: Study Design



* Initial low molecular weight heparin (LMWH) and warfarin followed by warfarin alone with target intensity international normalized ratio (INR) of 2.0-3.0

- Randomization was stratified for involvement of the pelvic veins.
- **Primary outcomes:**
  - Frequency of PTS at 24 months, assessed by the Villalta score
  - Iliofemoral patency after 6 months

Enden T et al. *Lancet* 2012;379(9810):31-8.

Villalta Scoring Scale

Five patient-related venous symptoms	Six clinician-rated signs
Pain	Pretibial edema
Cramps	Skin induration
Heaviness	Hyperpigmentation
Paraesthesia	Pain during calf compression
Pruritus	Venous ectasia
	Redness

Scoring — Each sign or symptom is rated as:

0 = None
1 = Mild
2 = Moderate
3 = Severe

Summed-up ratings = total score:

- <5 = no PTS
- 5-14 = mild/moderate PTS
- ≥15/venous ulcer = severe PTS

Enden T et al. *Lancet* 2012;379(9810):31-8.

Exclusion criteria

- Anticoagulant treatment before trial entry for more than the past 7 days
- Contraindications to thrombolytic treatment, including bleeding diathesis
- Indications for thrombolytic treatment—eg, phlegmasia caerulea dolens or isolated vena cava thrombosis
- Severe anaemia (haemoglobin <80 g/L)
- Thrombocytopenia (platelets $<80 \cdot 10^9$/L)
- Severe renal failure (estimated creatinine clearance <30 mL/min)
- Severe hypertension—ie, persistent systolic blood pressure higher than 160 mm Hg or diastolic blood pressure higher than 100 mm Hg
- Pregnancy or thrombosis within 7 days postpartum
- Less than 14 days postsurgery or post-trauma
- History of subarachnoid or intracerebral bleeding
- Disease with life expectancy less than 24 months
- Drug misuse or mental disease that could interfere with treatment and follow-up
- Former ipsilateral proximal deep vein thrombosis
- Malignant disease needing chemotherapy
- Any thrombolytic treatment within 7 days before trial inclusion

CaVenT t-PA dosing

- 20 mg alteplase at 0·01 mg/kg per h for maximum 96 h, and the maximum dose was 20 mg/24 h.
- Unfractionated heparin adjusted to keep activated partial thromboplastin time at 1·2–1·7 times higher than the upper normal limit.
- Additional antiplatelet treatment was not given

Outcomes: Additional CDT versus Standard Therapy

Outcome	Additional CDT (n = 90)		Standard therapy only (n = 99)		*p*-value
	n	% (95% CI)	n	% (95% CI)	
PTS after 6 mo	27	30.3 (21.8-40.5)	32	32.2 (23.9-42.1)	0.77
PTS after 24 mo	37	**41.1** (31.5-51.4)	55	**55.6** (45.7-65.0)	0.047
Iliofemoral patency after 6 mo*	58	**65.9** (55.5-75.0)	45	**47.4** (37.6-57.3)	0.012

* Five patients had inconclusive patency assessments, and 1 was lost to follow-up. At completion of 24 months of follow-up, 189 patients were available for analysis.

- PTS is defined as a Villalta score ≥5.
- *p*-values stated are from an unadjusted Chi-square test.
- Absolute risk reduction of long-term endpoint PTS at 24 months of follow-up in CDT versus standard therapy: 14.4% (95% CI 4-502).

NNT=7

Enden T et al. *Lancet* 2012;379(9810):31-8.

PTS After 24 Months in Patients with Iliofemoral Patency or Insufficient Recanalization After 6 Months

Outcome	Regained iliofemoral patency (n = 103)		Insufficient recanalization (n = 80)		*p*-value
	n	% (95% CI)	n	% (95% CI)	
PTS after 24 mo	38	**36.9** (28.2-46.5)	49	**61.3** (50.3-71.2)	0.001

- Absolute gain in short-term endpoint iliofemoral patency after 6 months in CDT versus standard therapy group: 18.5% (95% CI 4.2–31.8).
- Absolute risk reduction in the frequency of PTS after 24 months in patency versus insufficient recanalization: 24.4% (95% CI 9.8–37.6).

NNT--6

Enden T et al. *Lancet* 2012;379(9810):31-8.

Adverse Events (AEs)

AEs	Additional CDT (n = 101)	Standard treatment (n = 108)
Bleeding complications	20	0
Major bleeding complications	3	0
Clinically relevant bleeding complications	5	0
Deaths	0	NR
Pulmonary embolisms	0	NR
Cerebral hemorrhages	0	NR
Nonbleeding complications	4	NR
Recurrent VTE at 24 mo	10	18

NR = not reported

During follow-up, 28 patients had recurrent VTE and 11 had cancer; no significant difference between treatment groups ($p > 0.05$).

Enden T et al. *Lancet* 2012;379(9810):31-8.

20 Bleeding Complications

- MAJOR—3
  - ABDOMINAL WALL HEMATOMA--XFUSION
  - POPLITEAL FOSSA HEMATOMA REQUIRING FASCIOTOMY FOR COMPARTMENT SYNDROME
  - INGUINAL PUNCTURE SITE HEMATOMA
- CLINICALLY RELEVANT—5
- NO DEATHS
- NO CEREBRAL HEMORRHAGES

Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial

Ylva Haig, MD, Tone Enden, MD, Ole Grøtta, MD, Prof Nils-Einar Kløw, MD, Carl-Erik Slagsvold, MD, Waleed Ghanima, MD, Leiv Sandvik, MSc, Geir Hafsahl, MD, Prof Pål Andre Holme, MD, Lars Olaf Holmen, MD, Anne Mette Njaaastad, MD, Gunnar Sandbæk, MD, Prof Per Morten Sandset, MD on behalf of the CaVenT Study Group†

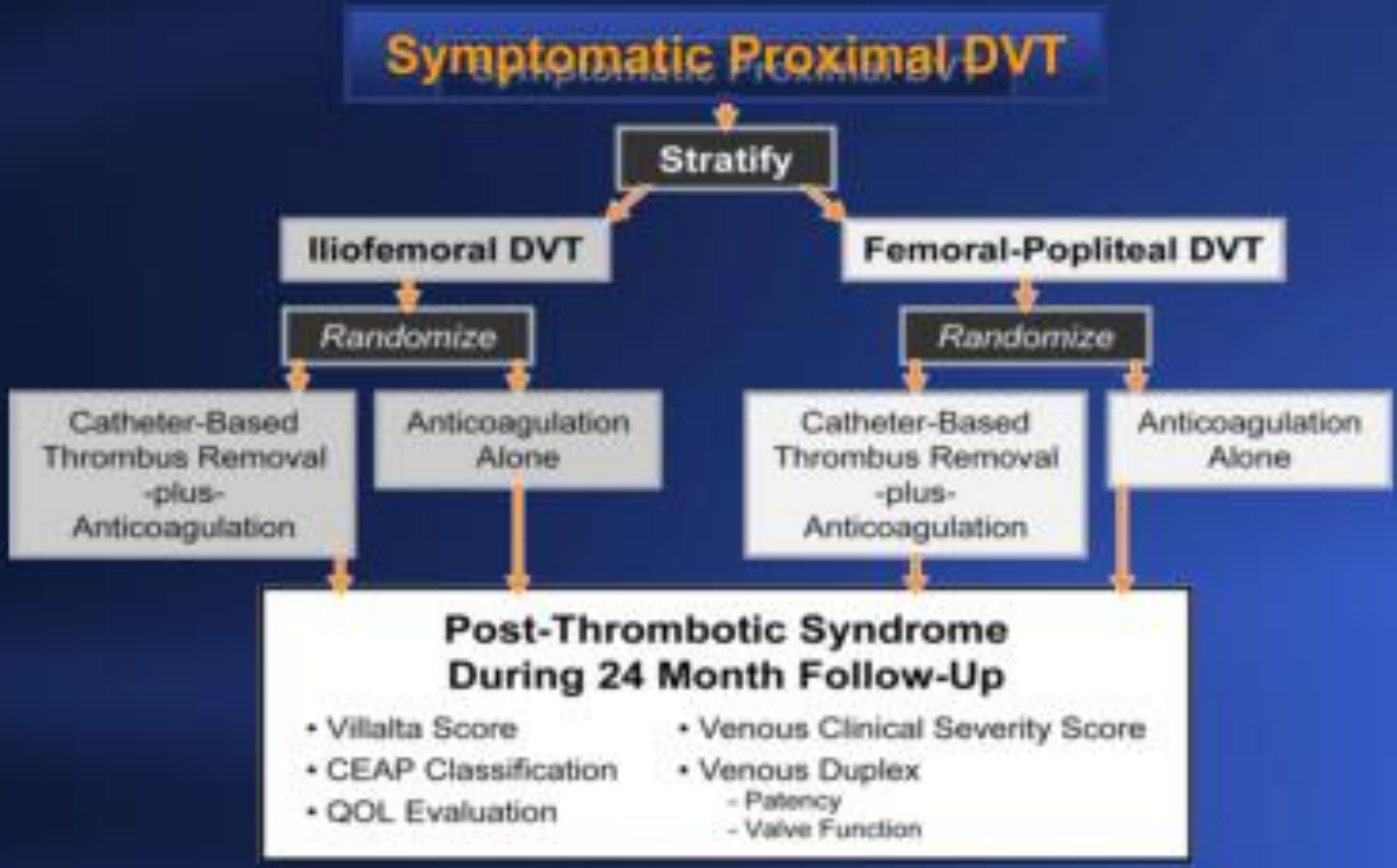
Volume 3, No. 2, e64–e71, February 2016

- 5 year follow-up--176 patients (84% of the 209 patients originally randomised)
- 87 (CDT) and 89 (control)
- 37 CDT pts (43%; 95% CI 33–53) developed PTS
- 63 Control pts (71%; 95% CI 61–79) (p<0·0001) developed PTS
- **Absolute risk reduction of 28% and NNT--4**

THE LANCET Haematology

The ATTRACT Trial

Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis



Study Population

- Symptomatic proximal DVT involving the iliac, common femoral, and/or femoral vein
  - stratify randomization by thrombus extent
  - actual: 60% with "iliofemoral" DVT
- EXCLUDE patients with:
  - Higher bleeding risk, CNS lesions
  - Acute limb threat or massive PE
  - Symptom duration > 2 weeks
  - Same-leg PTS or DVT < 2 yrs
  - Active cancer

Primary Measure

Villalta Scale

- The best-validated measure to diagnose incident PTS, evaluates 5 symptoms and 6 signs of PTS, highly sensitive to mild-moderate forms of PTS
- PTS = score $\geq$ 5 or presence of ulcer in index leg
- 692 patients provides 80% power to detect 1/3 reduction in PTS over 2 years, alpha 0.05, 2-tailed, assuming 10% loss to follow-up of randomized pts

Secondary Outcomes

PRESENT

- PTS Severity (Villalta Scale, VCSS, CEAP Clinical Class)
- QOL (SF-36, VEINES-QOL)
- Relief of pain (Likert scale) & swelling (limb circumference)
- Safety (bleeding, VTE, death) & costs (dollars per QALY)
- Mechanism (obstruction and reflux by ultrasound - VSDS)

ABSENT

- What biomarkers of clot amplification/resolution, inflammation, vascular injury can predict which patients are best-suited?
- What are the biological effects of catheters/devices upon vein wall & blood?
- Collaborative opportunity for valuable future studies

ATTRACT

- 692 patients with acute proximal deep vein thrombosis involving the femoral, common femoral, and/or iliac vein into the ATTRACT study at 56 centres
- Randomised 337 catheter-directed thrombolysis and 355 to anticoagulation alone
- AngioJet thrombectomy system (Boston Scientific); the Trellis-8 Peripheral Infusion System (Medtronic. This device is no longer on the market); or catheter-directed rt-PA infusion for up to 24 hours

ATTRACT

- Pharmacomechanical catheter-directed thrombolysis reduces early deep vein thrombosis symptoms and post-thrombotic syndrome severity
- Researchers also found that DVT patients who received both blood-thinning drugs and PCDT were 25 percent less likely (18 percent with PCDT vs. 24 percent without) to develop moderate-to-severe PTS

ATTRACT RESULTS

- The open vein hypothesis is likely relevant to post-thrombotic syndrome progression and there is a suggestion that targeting this therapy to patients with iliofemoral deep vein thrombosis based on the high risk of post-thrombotic syndrome [might be beneficial],” Vedantham added.

SUMMARY

- PTS occurs in at least 40% and up to 70% of patients after iliofemoral DVT w/ AC alone.
- Overall risk for any bleeding complication w/ lysis is 8-10% w/ ICH risk of 0-0.3%.
- Cochrane, CaVenT and Attract all support PCDT in patients w/ iliofemoral DVT and no contraindication.


VIRGINIA
LYSIS
GEORGETOWN UNIVERSITY


Sterile water f
injection
50 ml
to be used to
reconstitute
Actilyse®
50 mg
Actilyse®
50 mg
For i.v. infusion
HK-30511
Protect from light.
Store below 30°C
Boehringer
Ingelheim

THANK YOU


VIRGINIA
LYSIS
GEORGETOWN UNIVERSITY

- Data from subgroups and secondary analyses suggest that catheter-directed thrombolysis may have a benefit in patients who have acute iliofemoral deep vein thrombosis

Chest

Volume 149, Issue 2, February 2016, Pages 315–352

Evidence-Based Medicine

Antithrombotic Therapy for VTE Disease : CHEST Guideline and Expert Panel Report

Clive Kearon, MD, PhD[a], Elie A. Akl, MD, MPH, PhD[a, b], Joseph Ornelas, PhD[c], Allen Blaivas, DO, FCCP[d], David Jimenez, MD, PhD, FCCP[e], Henri Bounameaux, MD[f], Menno Huisman, MD, PhD[g],

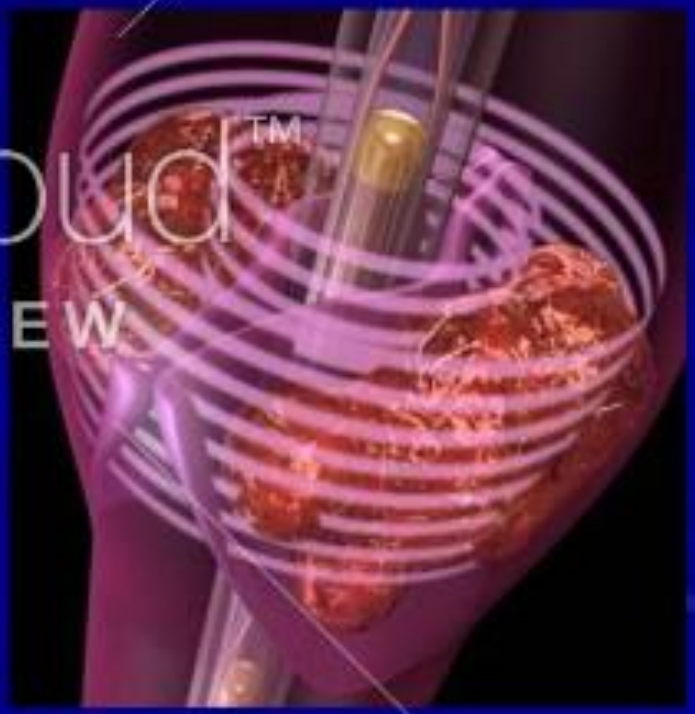
Show more

http://dx.doi.org/10.1016/j.chest.2015.11.026

Remarks: Patients who are most likely to benefit from CDT (see text), who attach a high value to prevention of PTS, and a lower value to the initial complexity, cost, and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone.

DUTCH-CAVA Study
NCT 00970619 (Netherlands)

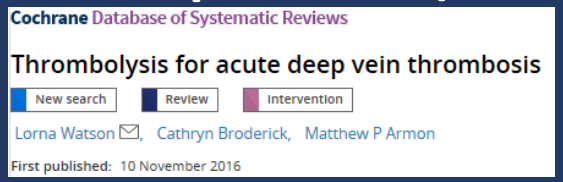
- 180 patients with first-episode iliofemoral DVT
- Randomized to AC vs. AC + US-Assisted CDT
- Primary Outcome – PTS at 1 year (also – QOL, recurrent VTE, reflux)



RESULTS--ULCERATION

3--treatment group VS 2--control group

342 participants (P = 0.87)


Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

RESULTS—COMPARISONS 2,3,4

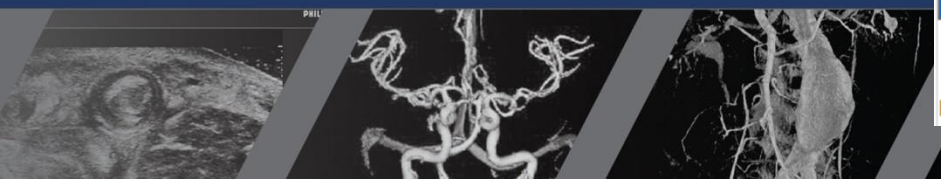
- Comparison 2 (SYSTEMIC VS CONTROL)
- Comparison 3 (LOCO-REG VS CONTROL)
- Comparison 4 (CDT VS CONTROL)

NO STATISTICAL DIFFERENCE

RESULTS--BLEEDING

- Most bleeding episodes and deaths occurred in the earlier studies.

- It is notable that no bleeding occurred in the Elsharawy 2003 study. This may have been due to strict exclusion criteria and the close radiological monitoring and dose titration depending upon clot lysis.



RESULTS--BLEEDING

- Participants receiving thrombolysis were significantly more likely than control participants to experience a bleeding complication.

- 9% (62/662) of patients in the thrombolysis group experienced a bleeding complication compared to 4% (19/441) of patients in the standard anticoagulation group (RR 2.23; 95% CI 1.41 to 3.52, P = 0.0006; moderate quality evidence; NNT of 17.)
- Most bleeding complications occurred in earlier studies

RESULTS--BLEEDING

- Participants receiving thrombolysis were significantly more likely than control participants to experience a bleeding complication.

- 9% (62/662) of patients in the thrombolysis group experienced a bleeding complication compared to 4% (19/441) of patients in the standard anticoagulation group (RR 2.23; 95% CI 1.41 to 3.52, P = 0.0006; moderate quality evidence; NNT of 17.)
- Most bleeding complications occurred in earlier studies

Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

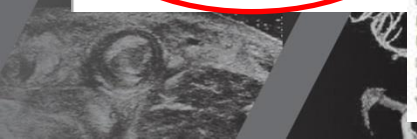
First published: 10 November 2016

Treatment with any thrombolysis for acute DVT

Patient or population: patients diagnosed with acute DVT
Setting: hospital
Intervention: any thrombolysis
Comparison: control anti-coagulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with control	Risk with any thrombolysis				
Complete clot lysis (intermediate, 6 months to under 5 years after treatment)	Study population 325 per 1000	793 per 1000 (455 to 1000)	RR 2.44 (1.4 to 4.27)	630 (7 RCTs)	⊕⊕⊕⊖ MODERATE [1]	78 (of 240) patients treated with standard anticoagulation had complete clot lysis compared to 198 (of 390) in the thrombolysis group
Bleeding (early, up to 1 month after treatment)	Study population 43 per 1000	96 per 1000 (61 to 152)	RR 2.23 (1.41 to 3.52)	1103 (17 RCTs)	⊕⊕⊕⊖ MODERATE [1]	Although 17 studies reported on bleeding, these were small studies
Post-thrombotic syndrome (intermediate, 6 months to under 5 years after treatment)	Study population 658 per 1000	434 per 1000 (348 to 533)	RR 0.66 (0.53 to 0.81)	306 (3 RCTs)	⊕⊕⊕⊖ MODERATE [1]	96 (of 146) patients treated with standard anticoagulation developed PTS compared to 72 (of 160) treated with thrombolysis
Post-thrombotic syndrome (late, 5 year follow-up after treatment)	Study population 673 per 1000	390 per 1000 (303 to 518)	RR 0.58 (0.45 to 0.77)	211 (2 RCTs)	⊕⊕⊕⊖ MODERATE [1]	72 (of 107) patients treated with standard anticoagulation developed PTS compared to 41 (of 104) treated with thrombolysis

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

Treatment with catheter directed thrombolysis for acute DVT

Patient or population: patients diagnosed with acute deep vein thrombosis
Setting: hospital
Intervention: catheter-directed thrombolysis
Comparison: control anti-coagulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with control	Risk with catheter directed thrombolysis				
Complete clot lysis (intermediate, 6 months to under 5 years after treatment)	Study population 58 (of 116) patients treated with standard anticoagulation had complete clot lysis compared to 81 (of 108) in the CDT group		RR 2.52 (0.52 to 12.17)	224 (2 RCTs)	⊕⊕⊕⊖ MODERATE [1]	
Bleeding (early, up to 1 month after treatment)	Study population Cannot define risk as no events reported in the standard anticoagulation group		RR 7.69 (0.40 to 146.90)	224 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2]	None (of 116) patients in the standard anticoagulation group had bleeding complications compared to 3 (of 108) in the CDT group.
Post-thrombotic syndrome (intermediate, 6 months to under 5 years after treatment)	Study population 556 per 1000	411 per 1000 (306 to 556)	RR 0.74 (0.55 to 1.00)	189 (1 RCT)	⊕⊕⊕⊖ MODERATE [3]	55 (of 99) patients in the standard anticoagulation group developed PTS compared to 37 (of 90) in the CDT group.
Post-thrombotic syndrome (late, 5 year follow-up after treatment)	Study population 708 per 1000	425 per 1000 (319 to 559)	RR 0.60 (0.45 to 0.79)	176 (1 RCT)	⊕⊕⊕⊖ MODERATE [3]	63 (of 89) patients in the standard anticoagulation group developed PTS compared to 37 (of 87) in the CDT group.

Emailed Kirk Freeman

- *DUTCH CAVA-trial. Ultrasound accelerated catheter-directed thrombolysis for primary iliofemoral deep vein thrombosis (IFDVT) compared to non-invasive conventional anticoagulant therapy alone: a Dutch randomized controlled multicenter clinical trial. https://clinicaltrials.gov/ct2/show/NCT00970619 (accessed 11 June 2015).*

INDICATIONS FOR EARLY THROMBUS REMOVAL

- **Patients meeting the following criteria:**
  - **(a) a first episode of acute iliofemoral deep venous thrombosis**
  - **(b) symptoms <14 days in duration**
  - **(c) a low risk of bleeding**
  - **(d) ambulatory with good functional capacity and an acceptable life expectancy (Grade 2C)**

Early thrombus removal strategies for acute deep venous thrombosis: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum

May 2012 Volume 55, Issue 5, Pages 1449–1462

Mark H. Meissner, MD, Peter Gloviczki, MD, Anthony J. Comerota, MD, Michael C. Dalsing, MD, Bo G. Eklof, MD, David L. Gillespie, MD, Joann M. Lohr, MD, Robert B. McLafferty, MD, M. Hassan Murad, MD, Frank Padberg, MD, Peter Pappas, MD, Joseph D. Raffetto, MD, Thomas W. Wakefield, MD

JVS

TECHNIQUES for EARLY THROMBUS REMOVAL

- **Strategy of pharmacomechanical thrombolysis be considered over CDT alone (Grade 2C)**

- **The use of mechanical devices alone, without the concurrent use of thrombolytic drugs, cannot be routinely recommended.**

Early thrombus removal strategies for acute deep venous thrombosis: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum

May 2012 Volume 55, Issue 5, Pages 1449–1462

Mark H. Meissner, MD, Peter Gloviczki, MD, Anthony J. Comerota, MD, Michael C. Dalsing, MD, Bo G. Eklof, MD, David L. Gillespie, MD, Joann M. Lohr, MD, Robert B. McLafferty, MD, M. Hassan Murad, MD, Frank Padberg, MD, Peter Pappas, MD, Joseph D. Raffetto, MD, Thomas W. Wakefield, MD

JVS

ARTICLES DOCUMENTING IMPROVED QOL

Treatment of acute iliofemoral DVT: a systematic review and meta-analysis

- Low-quality evidence suggests that surgical thrombectomy decreases the incidence of postthrombotic syndrome and venous reflux
- Catheter-directed pharmacologic thrombolysis decreases the incidence of postthrombotic syndrome and venous obstruction

Treatment of acute iliofemoral deep vein thrombosis

Edward T. Casey, DO, M. Hassan Murad, MD, MPH, Magaly Zumaeta-Garcia, MD, Mohamed B. Elamin, MBBS, Qian Shi, PhD, Patricia J. Erwin, MLS, Victor M. Montori, MD, MSc, Peter Gloviczki, MD, Mark Meissner, MD

May 2012 Volume 55, Issue 5, Pages 1463–1473

JVS

REVIEW

- **Catheter-directed thrombolysis for extensive iliofemoral deep vein thrombosis: review of literature and ongoing trials**
- **Aaron Liew Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, UK & James Douketis**
- **Pages 189-200 | Received 10 Sep 2015, Accepted 13 Nov 2015, Accepted author version posted online: 15 Nov 2015, Published online: 17 Dec 2015**

TORPEDO TRIAL

PEVI + AC vs AC alone

91 pts 92 pts

Recurrent VTE (mean f/u 30m)

4 (4.5%) of the 88 13 (16%) of the 81

PTS

6 (6.8%) 24 (29.6%)

Thrombus Obliteration by Rapid Percutaneous Endovenous Intervention in Deep Venous Occlusion (TORPEDO) Trial: Midterm Results

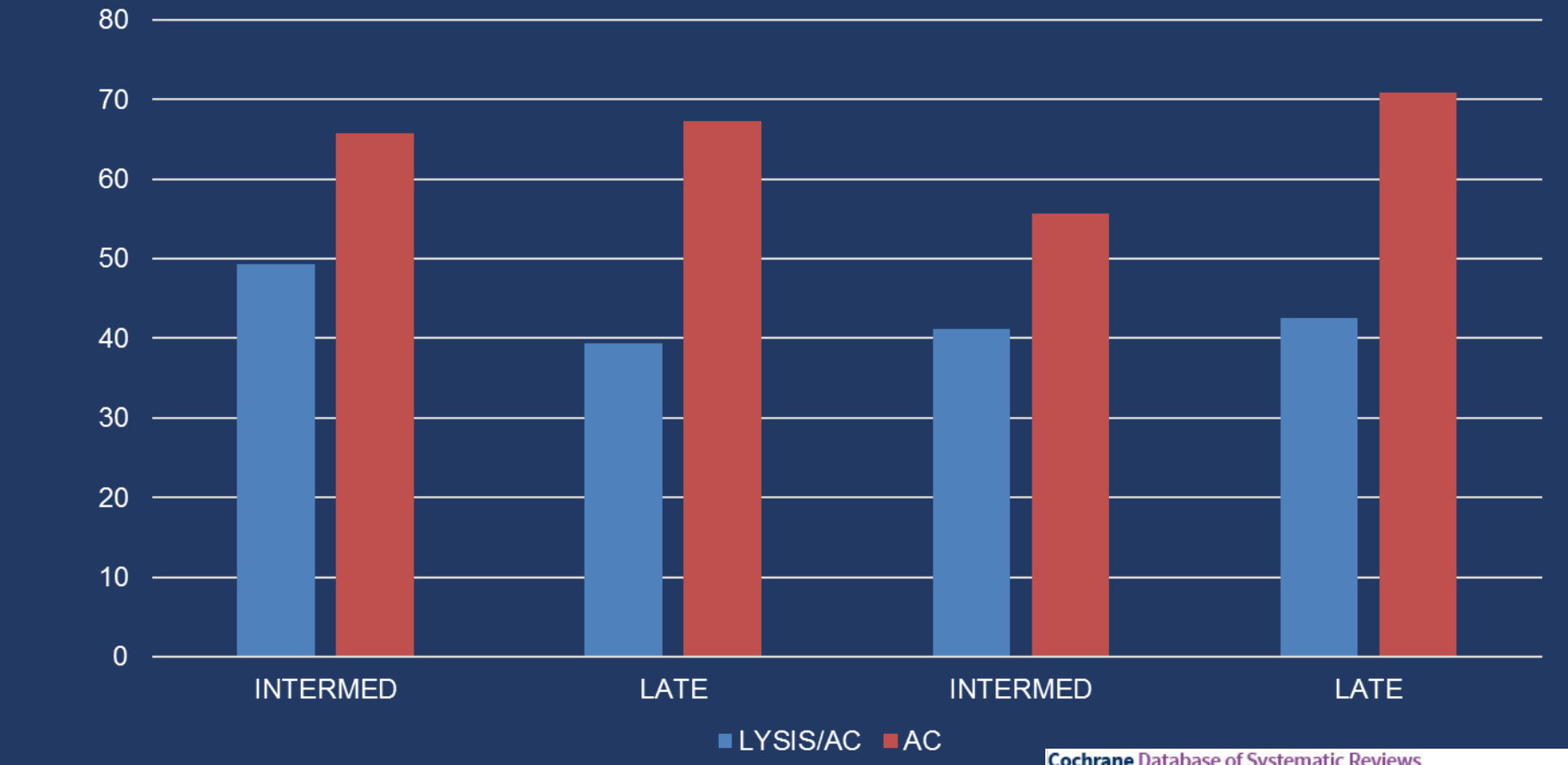
Vol 19, Issue 2, 2012

Mohsen Sharifi, MD , Curt Bay, PhD , Mahshid Mehdipour , Jalaladdin Sharifi, MD

Journal of Endovascular Therapy

PTS

ANY LYSIS vs CDT LYSIS



Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016

17 trials/1103 participants

Study	Potential levels of leg vein included
Arneson 1978	proximal to calf
Common 1976	not specified
Elliot 1979	proximal
Elsharawy 2002	femoral and iliofemoral
Enden 2011	pelvic, iliofemoral, femoral
Goldhaber 1990	popliteal or more proximal
Goldhaber 1996	proximal
Kakkar 1969	not specified
Kiil 1981	not specified
Marder 1977	calf up to iliac vein
Schulman 1986	calf vein thrombosis only
Schweizer 1998	not specified
Schweizer 2000	popliteal or more proximal
Tsapogas 1973	not specified
Turpie 1990	proximal
Ugurlu 2002	popliteal up to inferior vena cava
Verhaeghe 1989	popliteal or more proximal

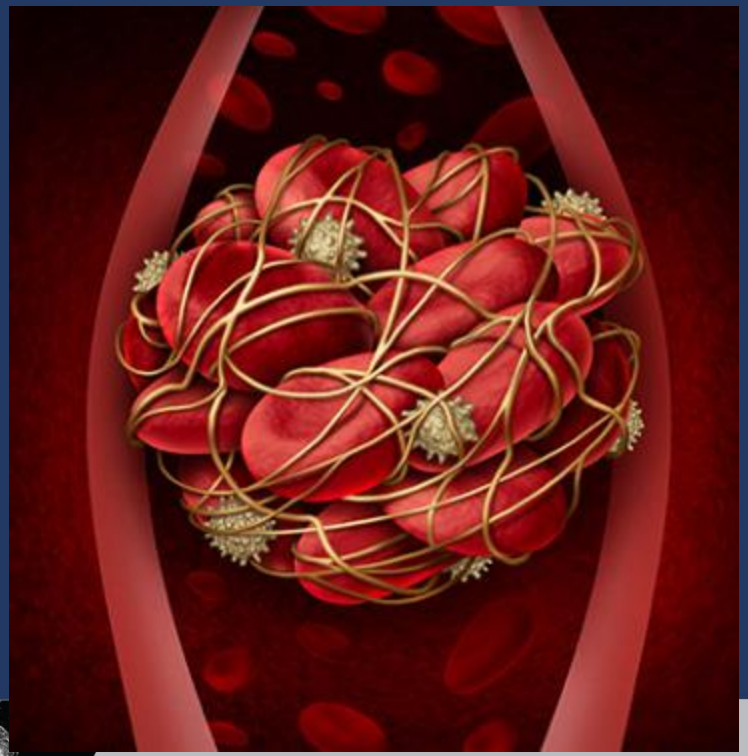
Cochrane Database of Systematic Reviews

Thrombolysis for acute deep vein thrombosis

New search | Review | Intervention

Lorna Watson ✉, Cathryn Broderick, Matthew P Armon

First published: 10 November 2016



The ATTRACT Trial

Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis

NIH Sponsored Trial

Registration No. - NCT00790335

http://clincialtrials.gov

The ATTRACT Trial

Almost 7 Years

Almost 700 Patients

Almost Done

…What Will We Find?

Anthony J. Comerota, MD, FACS, FACC
Director, Jobst Vascular Institute
Adjunct Professor of Surgery, University of Michigan

JOBST VASCULAR INSTITUTE
PROMEDICA

Figure 1. Acute femoropopliteal deep venous thrombosis before percutaneous endovenous intervention. Note the inflammatory appearance of the left lower extremity (A). Normalization of the limb 14 hours post percutaneous endovenous intervention (B).

CaVenT t-PA dosing

- 20 mg alteplase (Actilyse, Boehringer-Ingelheim, Ingelheim am Rhein, Germany) diluted in 500 mL 0·9% NaCl was given at 0·01 mg/kg per h for maximum 96 h, and the maximum dose was 20 mg/24 h. Unfractionated heparin was given simultaneously as a continuous intravenous infusion and the dose was adjusted to keep activated partial thromboplastin time (Cephotest, Axis-Shield, Oslo, Norway) at 1·2–1·7 times higher than the upper normal limit. Additional antiplatelet treatment was not given

NICE 2012

National Clinical Guideline Centre. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophiliatesting. Clinical Guideline.

Methods, evidence and recommendations.

Thrombolytic therapy

Deep vein thrombosis

1.2.6 Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:

- symptoms of less than 14 days' duration **and**
- good functional status **and**
- a life expectancy of 1 year or more **and**
- a low risk of bleeding. **[2012]**

Post Thrombotic Syndrome

Ambulatory Venous Pressures & Symptoms

- 28 mmHg – Asymptomatic
- 36 mmHg – Varicosities
- 41 mmHg – Edema
- 47 mmHg – Hyperpigmentation
- 60 mmHg – Ulceration

Greater pressure associated with worse PTS symptoms

Linder et al: J Vasc Surg 1986

PTS and QOL

- CDT pts 1999 to 2008
- 109 pts completed
  - Short form 36 health assessment survey (sf-36)
  - Venous Insufficiency Epidemiological and Economic Study (VEINES)
- Mean F/U 71 months
- 18 pts developed PTS (16.5%)
- Pts with patent deep veins and sufficient valves have higher QOL scores than patients with reflux and occluded veins

Postthrombotic syndrome and quality of life in patients with iliofemoral venous thrombosis treated with catheter-directed thrombolysis

December 2011 Volume 54, Issue 6, Supplement, Pages 18S–25S

Rikke Broholm, MD, PhD, Henrik Sillesen, MD, DMSc, Mogens Trab Damsgaard, MS, Maja Jørgensen, MD, Sven Just, MD, Leif Panduro Jensen, MD, Niels Bækgaard, MD

JVS

Fixed low-dose ultrasound-assisted catheter-directed thrombolysis followed by routine stenting of residual stenosis for acute ilio-femoral deep-vein thrombosis

Thrombosis and Haemostasis 111.6/2014

Rolf P. Engelberger[1]; Jennifer Fahrni[1]; Torsten Willenberg[1]; Frederic Baumann[1]; David Spirk[2]; Nicolas Diehm[1]; Dai-Do Do[1]; Iris Baumgartner[1]; Nils Kucher[1]

[1]Clinic for Angiology, Swiss Cardiovascular Center, Inselspital, University Hospital and University of Bern, Switzerland; [2]Institute of Pharmacology, University of Bern, Switzerland

- Prospective, non-randomized
- 87 pts w/ iliofemoral DVT (up to 28d)
- U/S asst'd CDT w/ fixed dose (20 mg tPA) for 15 h
- Routine stenting of residual venous stenosis
  - Residual luminal narrowing >50%
  - Static flow
  - Collateral flow at site of suspected stenosis

Thrombosis and Haemostasis
International Journal for Vascular Biology and Medicine

RESULTS

- At 15h—77% pts had thrombolysis success (<50% stenosis)
- Venous stents in 80% pts
- One major bleed—RP hematoma—4 U PRBCs
- Freedom from PTS at 1 yr—94% by Villalta score

Fixed low-dose ultrasound-assisted catheter-directed thrombolysis followed by routine stenting of residual stenosis for acute ilio-femoral deep-vein thrombosis

Rolf P. Engelberger[1]; Jennifer Fahrni[1]; Torsten Willenberg[1]; Frederic Baumann[1]; David Spirk[2]; Nicolas Diehm[1]; Dai-Do Do[1]; Iris Baumgartner[1]; Nils Kucher[1]

[1]Clinic for Angiology, Swiss Cardiovascular Center, Inselspital, University Hospital and University of Bern, Switzerland; [2]Institute of Pharmacology, University of Bern, Switzerland

Catheter-directed thrombolysis plus anticoagulation versus anticoagulation alone in the treatment of proximal deep vein thrombosis – a meta-analysis

Guo-Cheng Du[1,2*], Mao-Chun Zhang[3*], and Ji-Chun Zhao[1]

Vasa 2015; 44: 195–202

- 3 RCTs and 3 non-randomized trials
- Efficacy outcome—PTS—significant decline in CDT pts
- Safety outcome—Major Bleeding—significant increase in CDT pts

Vasa
European Journal of Vascular Medicine

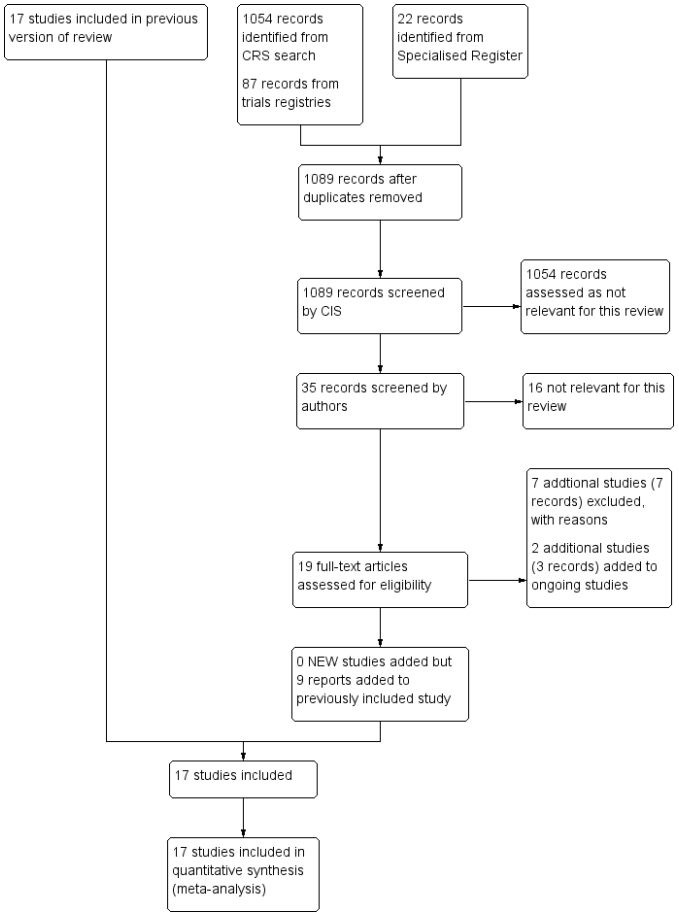
Study	Design	Region	Mean age (year)	Male (%)	Compared groups (no.)	Thrombolytic agent	Clinical outcomes	Duration of follow-up	Quality score
AbuRahma et al., 2001[23]	Prospective	USA	47	39	CDT + AA (18) vs. AA (33)	Urokinase, rtPA	Patency rate, long-term symptom resolusion, major complications	5 years	NOS: S4C2O3 = 9
Elsharawy et al., 2002[10]	RCT	Egypt	46	31	CDT + AA (18) vs. AA (17)	Streptokinase	Patency rate, venous function, major complications	6 months	Jadad: R2B2A1 = 5
Enden et al., 2009[13]	RCT, multicenter	Norway	52	62	CDT + AA (50) vs. AA (53)	Alteplase	Patency rate, venous function, major complications	6 months	Jadad: R2B2A1 = 5
Enden et al., 2012[6]	RCT, multicenter	Norway	52	63	CDT + AA (90) vs. AA (99)	Alteplase	Patency rate, major complications, PTS, recurrent DVT	2 years	Jadad: R2B2A1 = 5
Lee et al., 2013[24]	Retrospective	Taiwan	62	51	CDT + AA (27) vs. AA (26)	Urokinase	Patency rate, major complications, PTS, venous function, recurrent DVT	15 months	NOS: S4C2O3 = 9
Bashir et al., 2014[11]	Retrospective	USA	53	51	CDT + AA (3594) vs. AA (3594)	NA	Mortality, major complications	6 years	NOS: S4C2O3 = 9

CDT, catheter-directed thrombolysis; NA, not available; PTS, post-thrombotic syndrome; RCT, randomized controlled trial; Jadad score for RCTs: randomization (R0-2), blinding (B0-2) and attrition information (A0-1); Newcastle-Ottawa Scale (NOS) for cohort studies: selection (S0-4), comparability (C0-2), and outcome (O0-3).

PTS

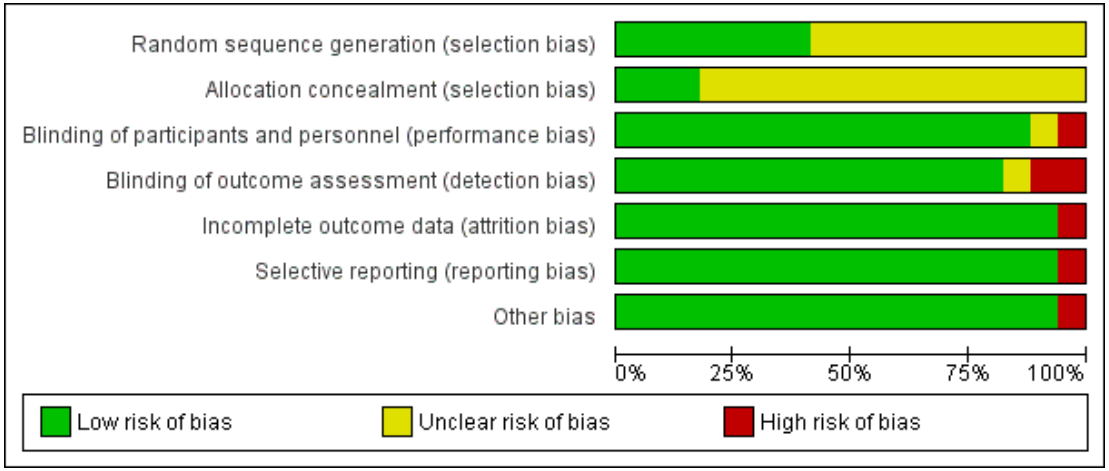
- LIFELONG
- INCREASED RISK FOR RECURRENCE
- RECURRENT DVT INCREASES RISK AND SEVERITY OF PTS 6X

Thrombolysis for acute deep vein thrombosis



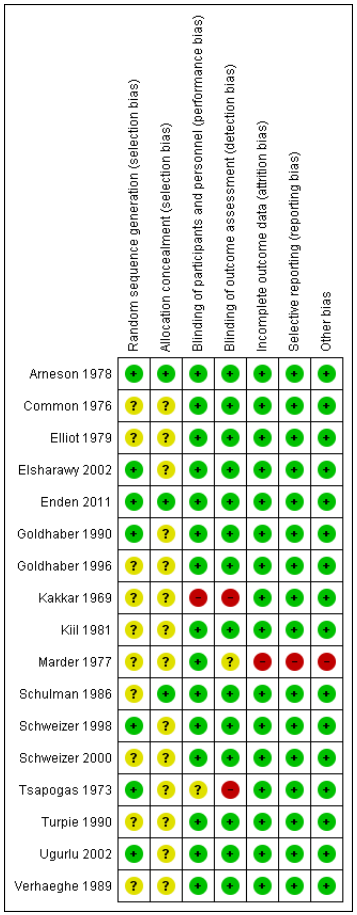
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-0001

Thrombolysis for acute deep vein thrombosis



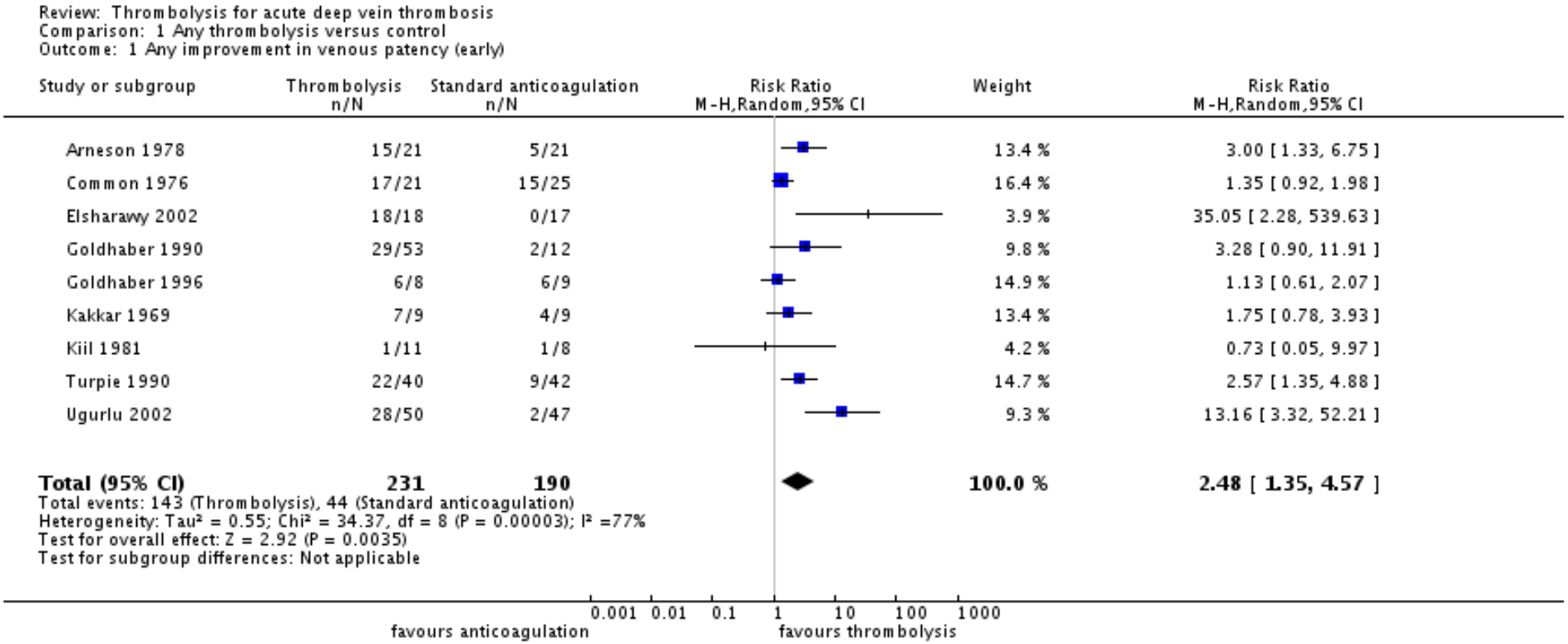
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-0002

Thrombolysis for acute deep vein thrombosis



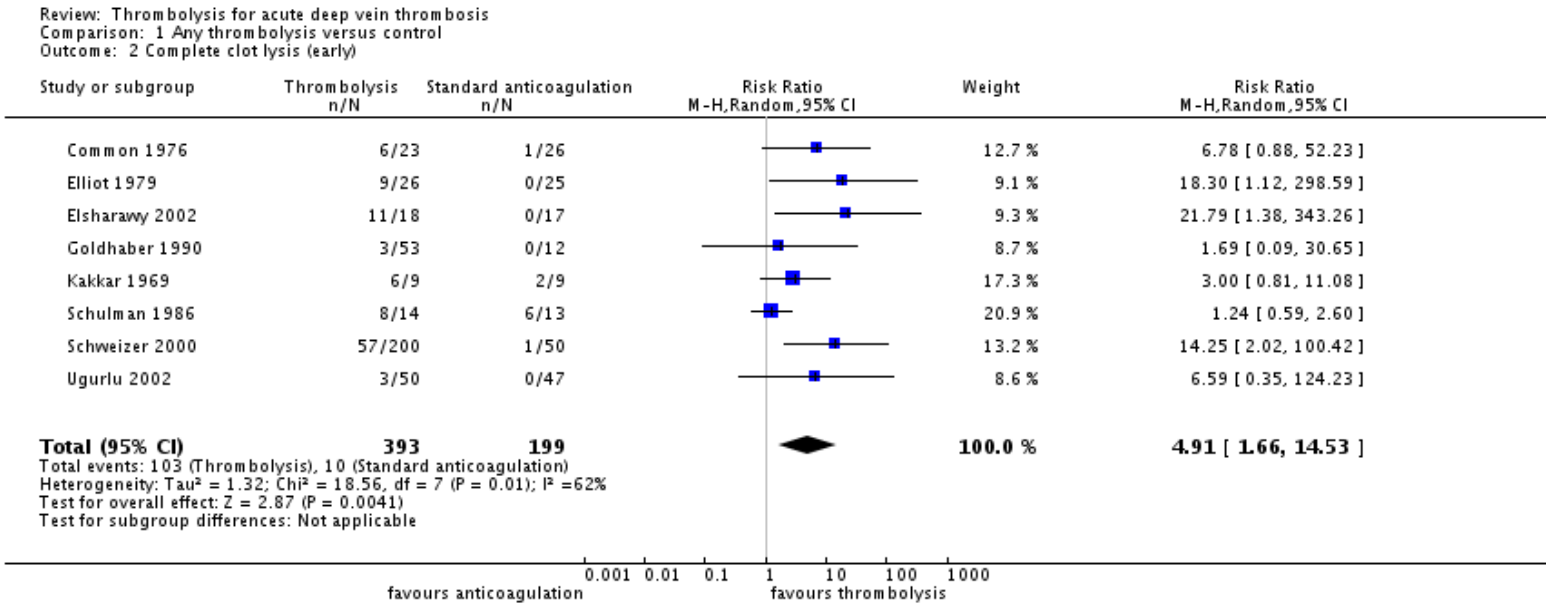
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-0003

Thrombolysis for acute deep vein thrombosis



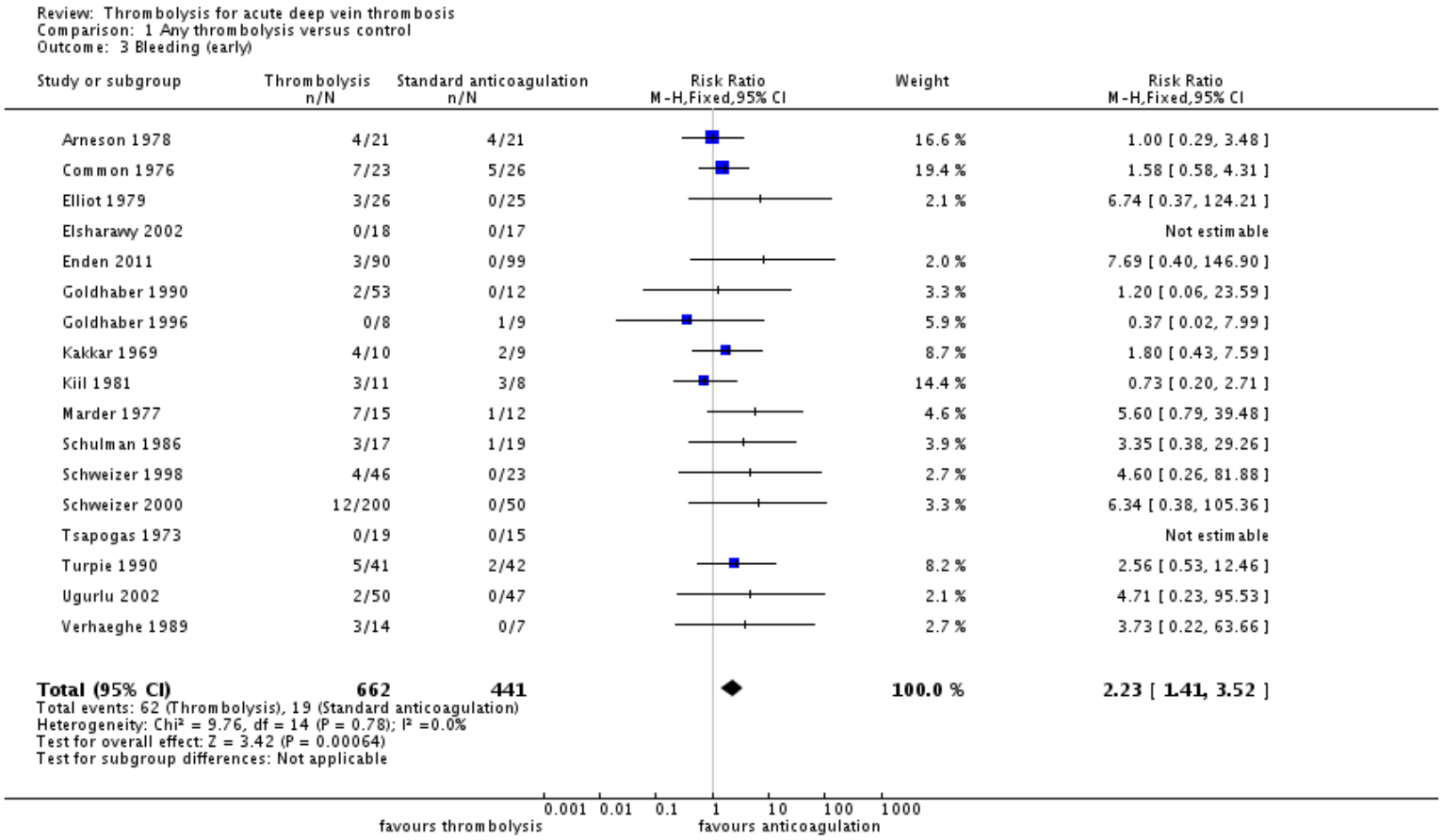
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00101

Thrombolysis for acute deep vein thrombosis



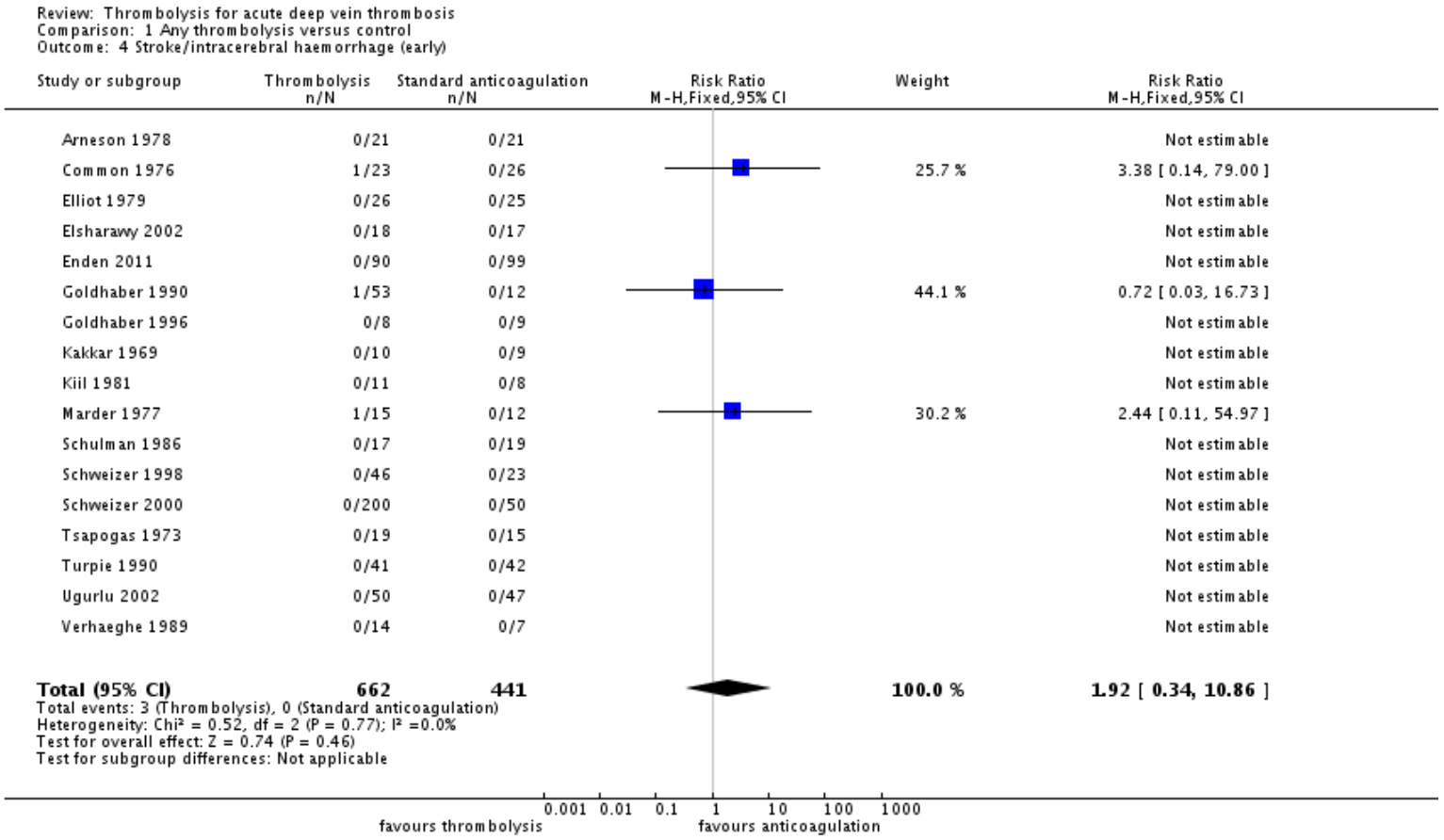
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00102

Thrombolysis for acute deep vein thrombosis



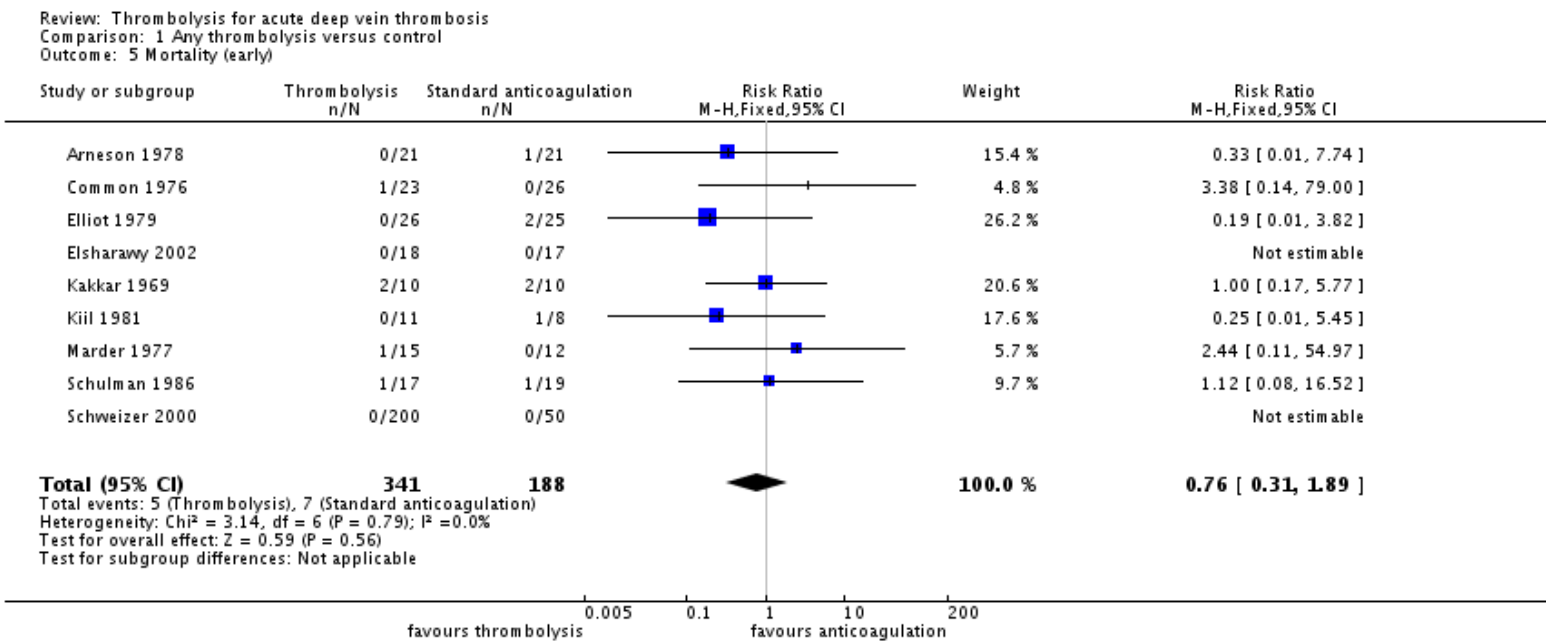
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00103

Thrombolysis for acute deep vein thrombosis



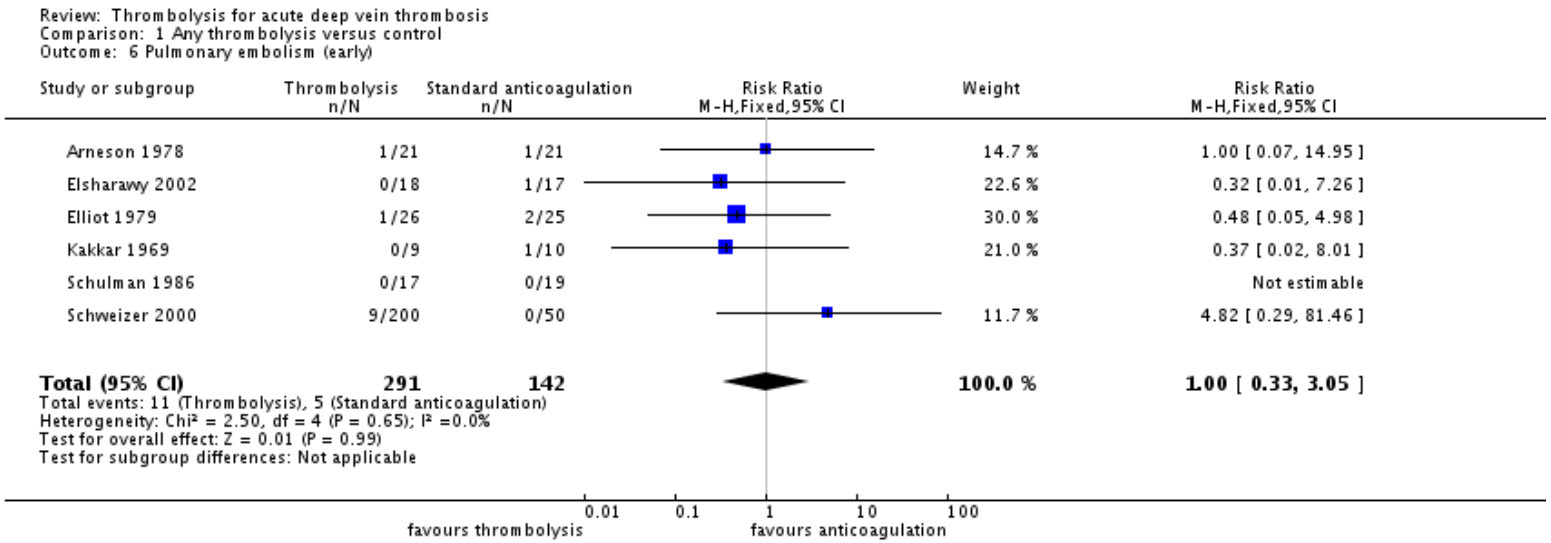
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00104

Thrombolysis for acute deep vein thrombosis



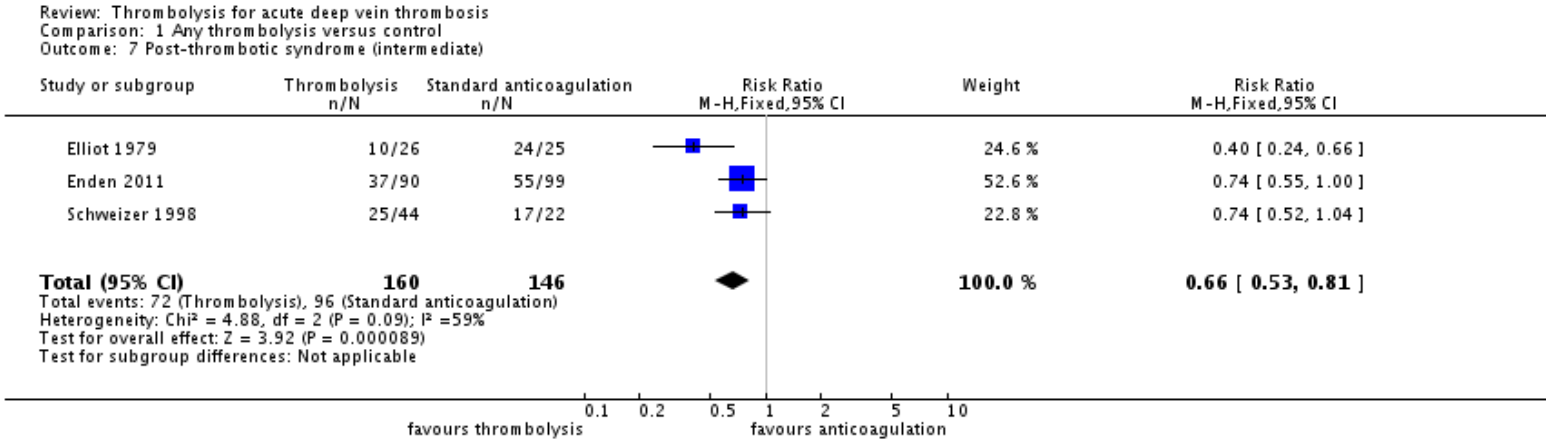
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00105

Thrombolysis for acute deep vein thrombosis



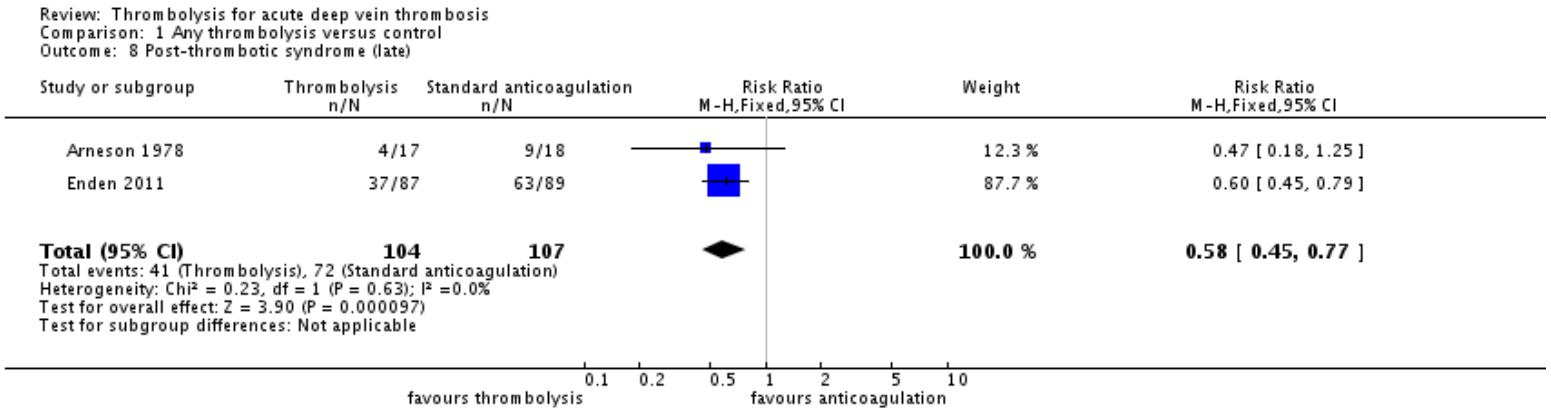
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00106

Thrombolysis for acute deep vein thrombosis



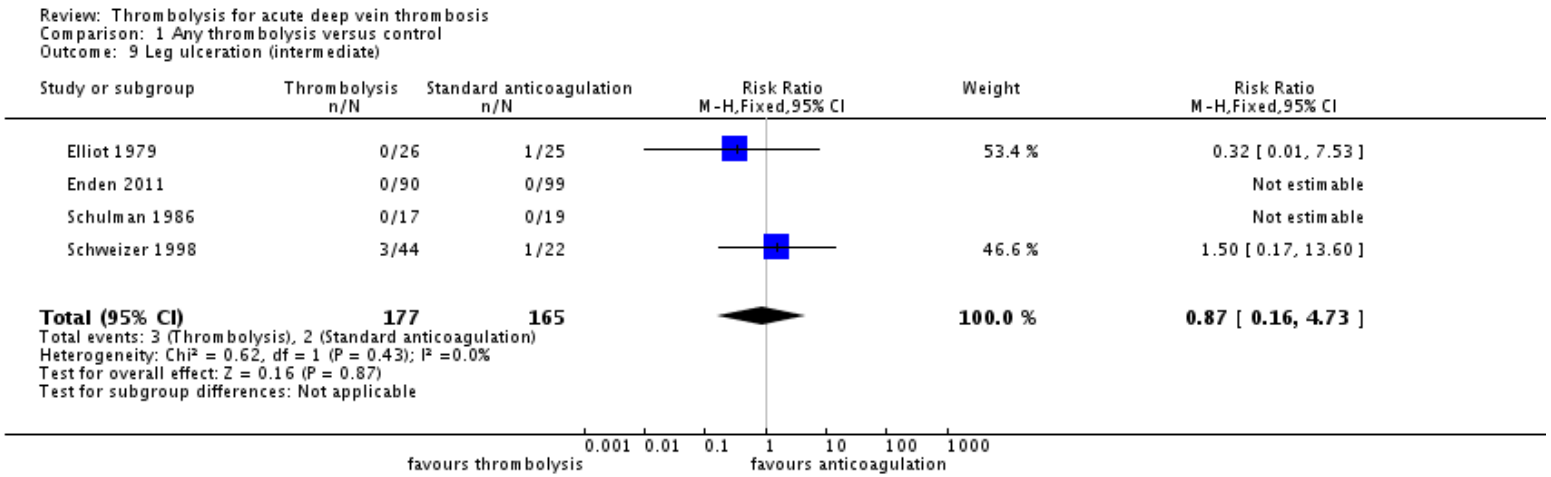
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00107

Thrombolysis for acute deep vein thrombosis



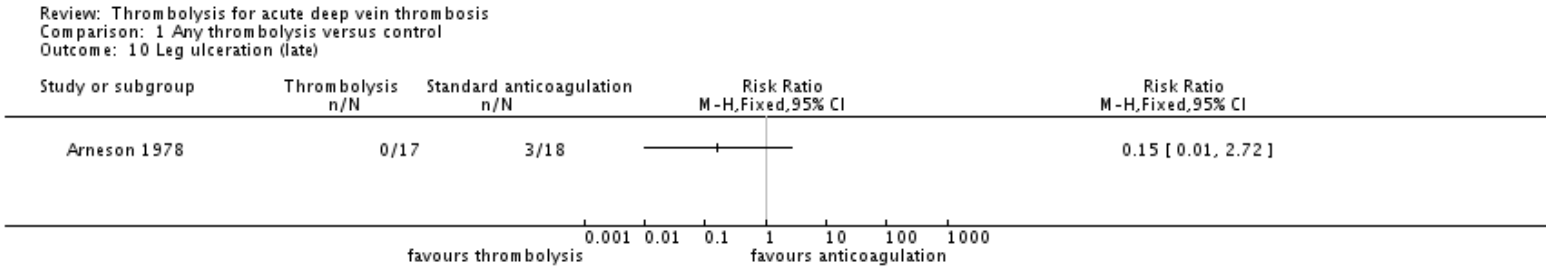
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00108

Thrombolysis for acute deep vein thrombosis



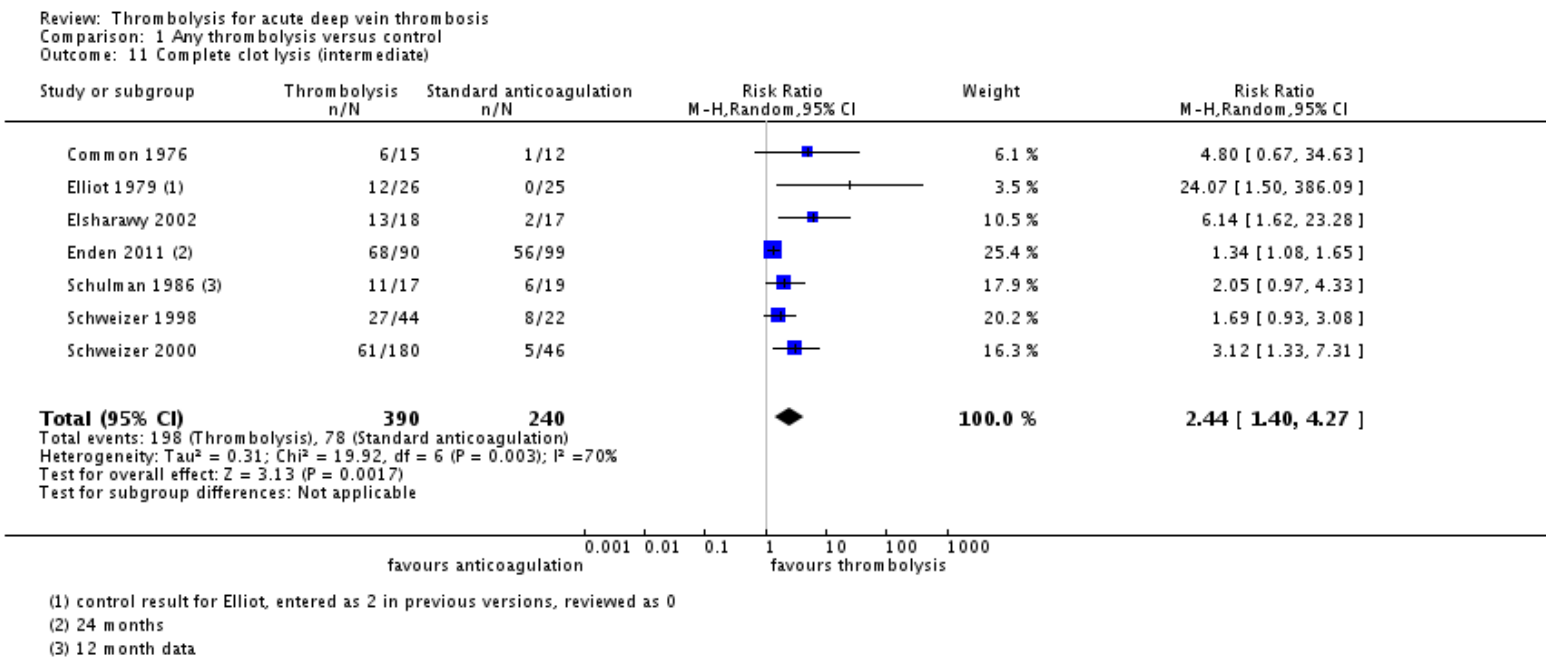
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00109

Thrombolysis for acute deep vein thrombosis



Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00110

Thrombolysis for acute deep vein thrombosis



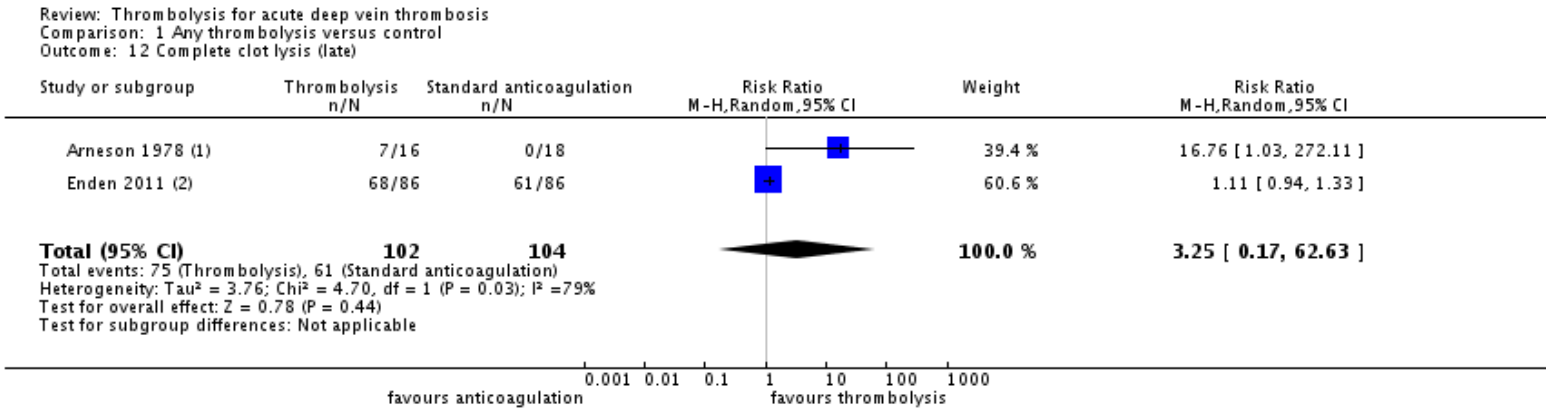
(1) control result for Elliot, entered as 2 in previous versions, reviewed as 0

(2) 24 months

(3) 12 month data

Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00111

Thrombolysis for acute deep vein thrombosis

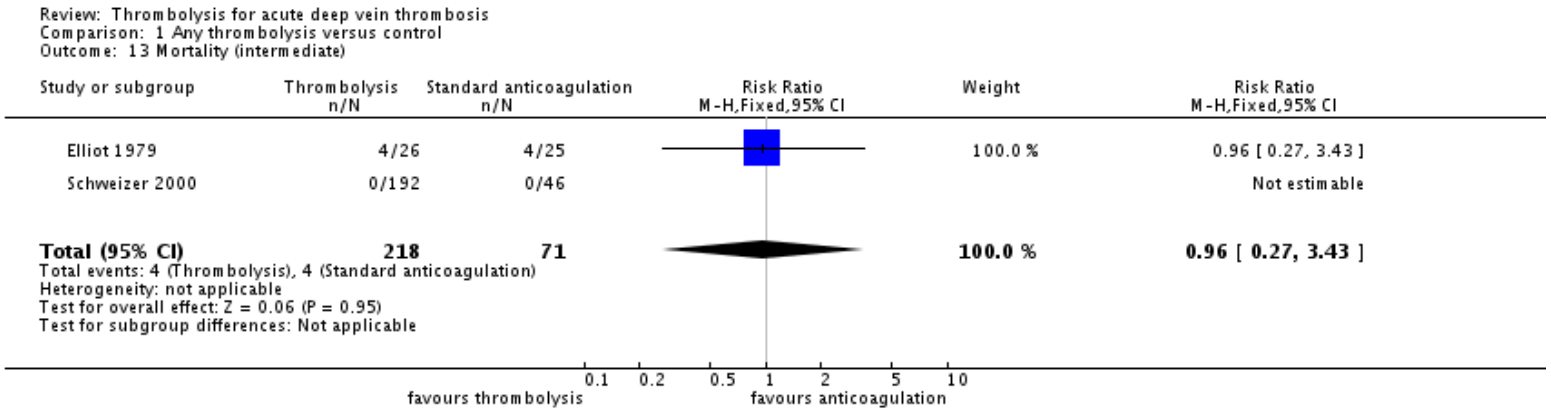


(1) mean follow up 6.5 years

(2) Four patients had inconclusive results and not reported.

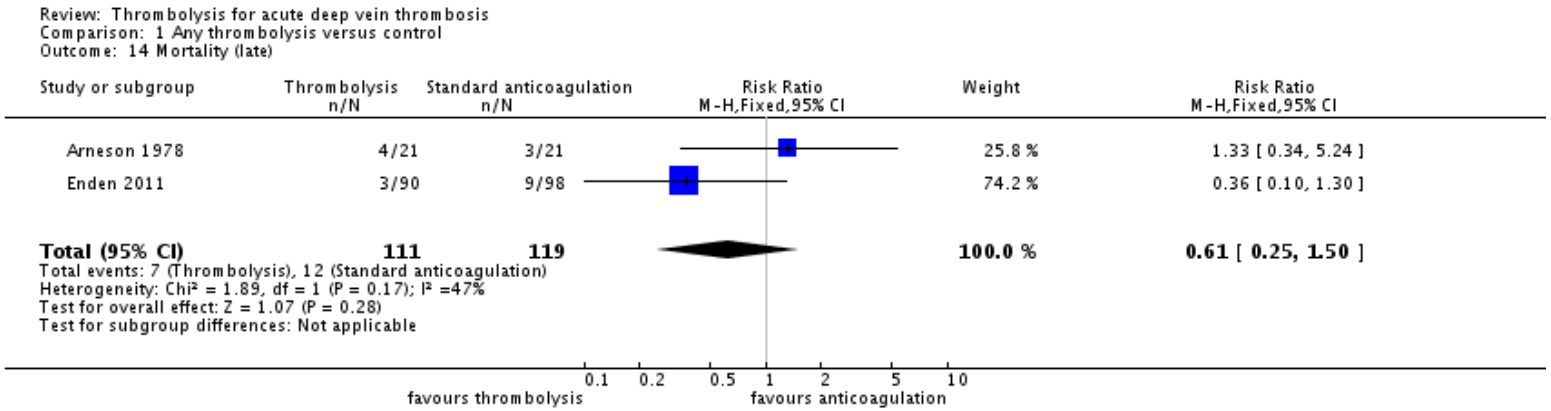
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00112

Thrombolysis for acute deep vein thrombosis



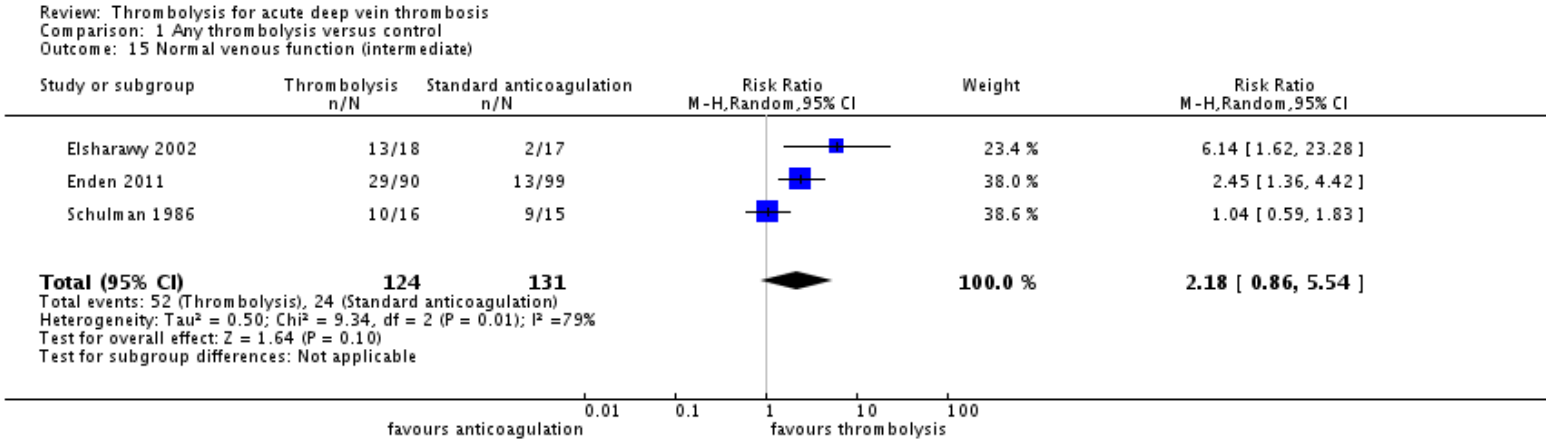
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00113

Thrombolysis for acute deep vein thrombosis



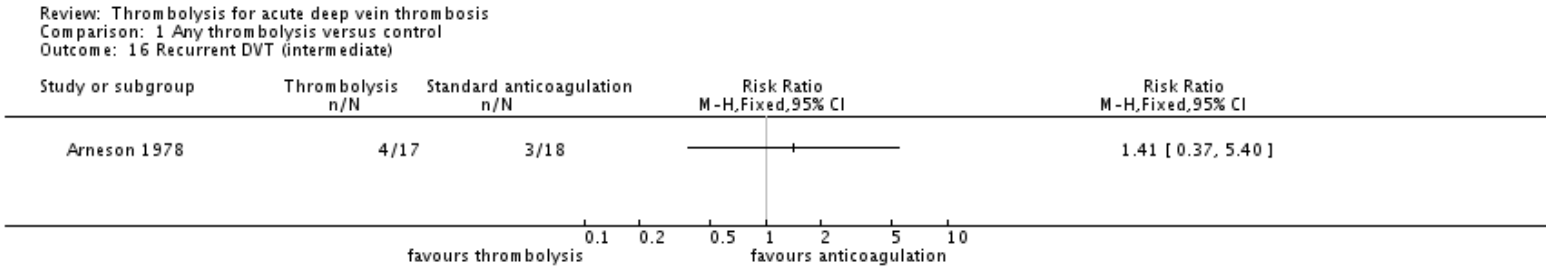
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00114

Thrombolysis for acute deep vein thrombosis



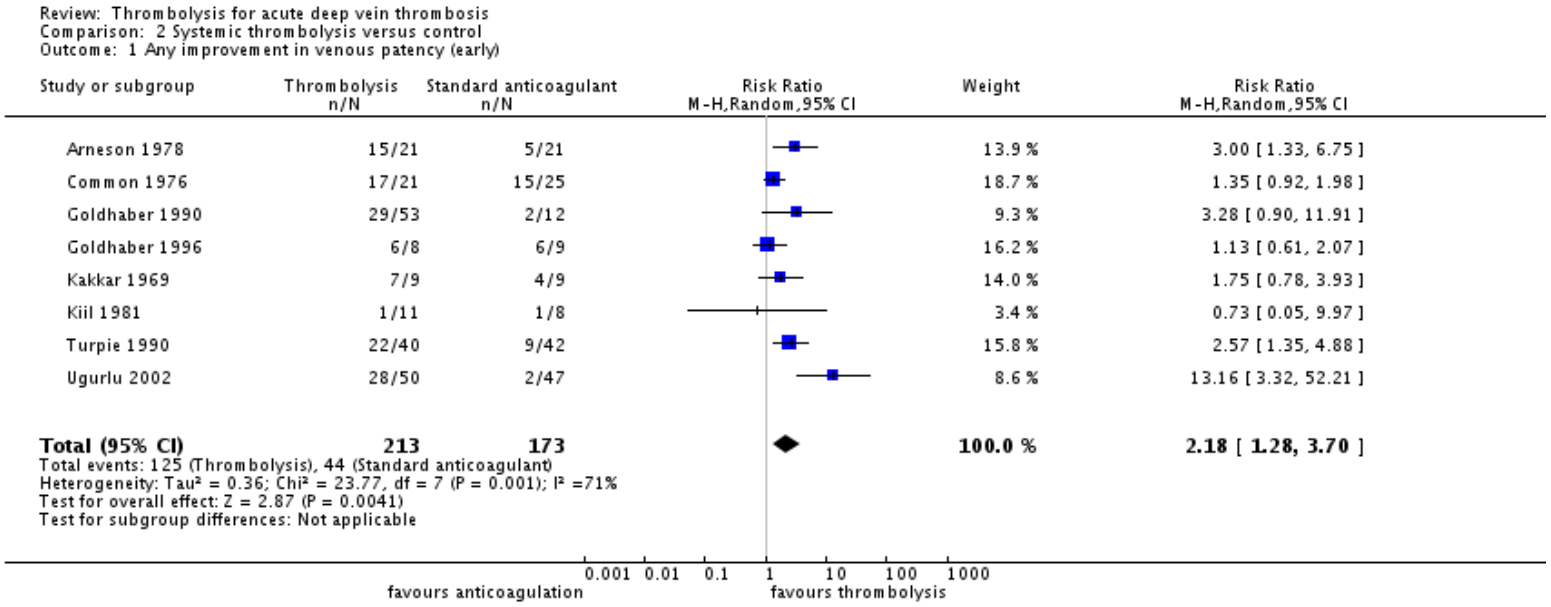
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00115

Thrombolysis for acute deep vein thrombosis



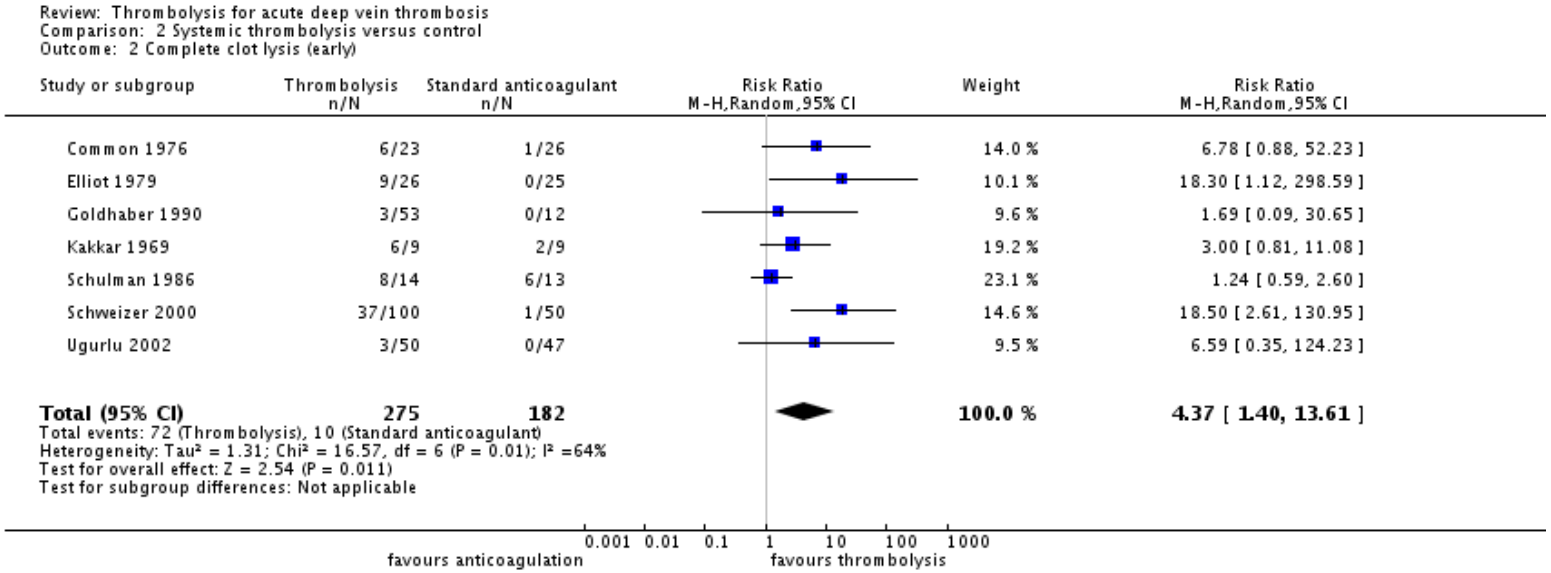
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00116

Thrombolysis for acute deep vein thrombosis



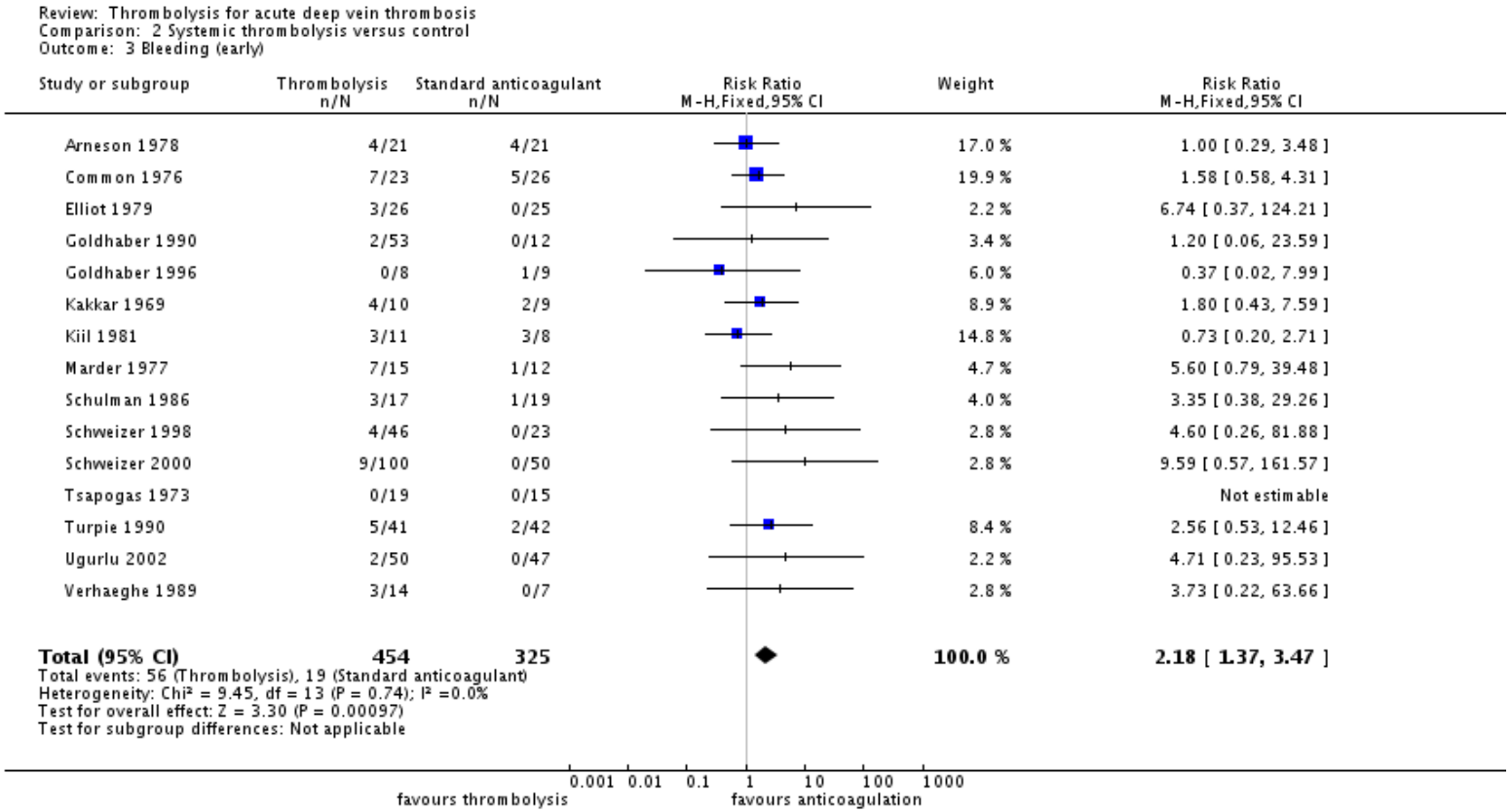
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00201

Thrombolysis for acute deep vein thrombosis



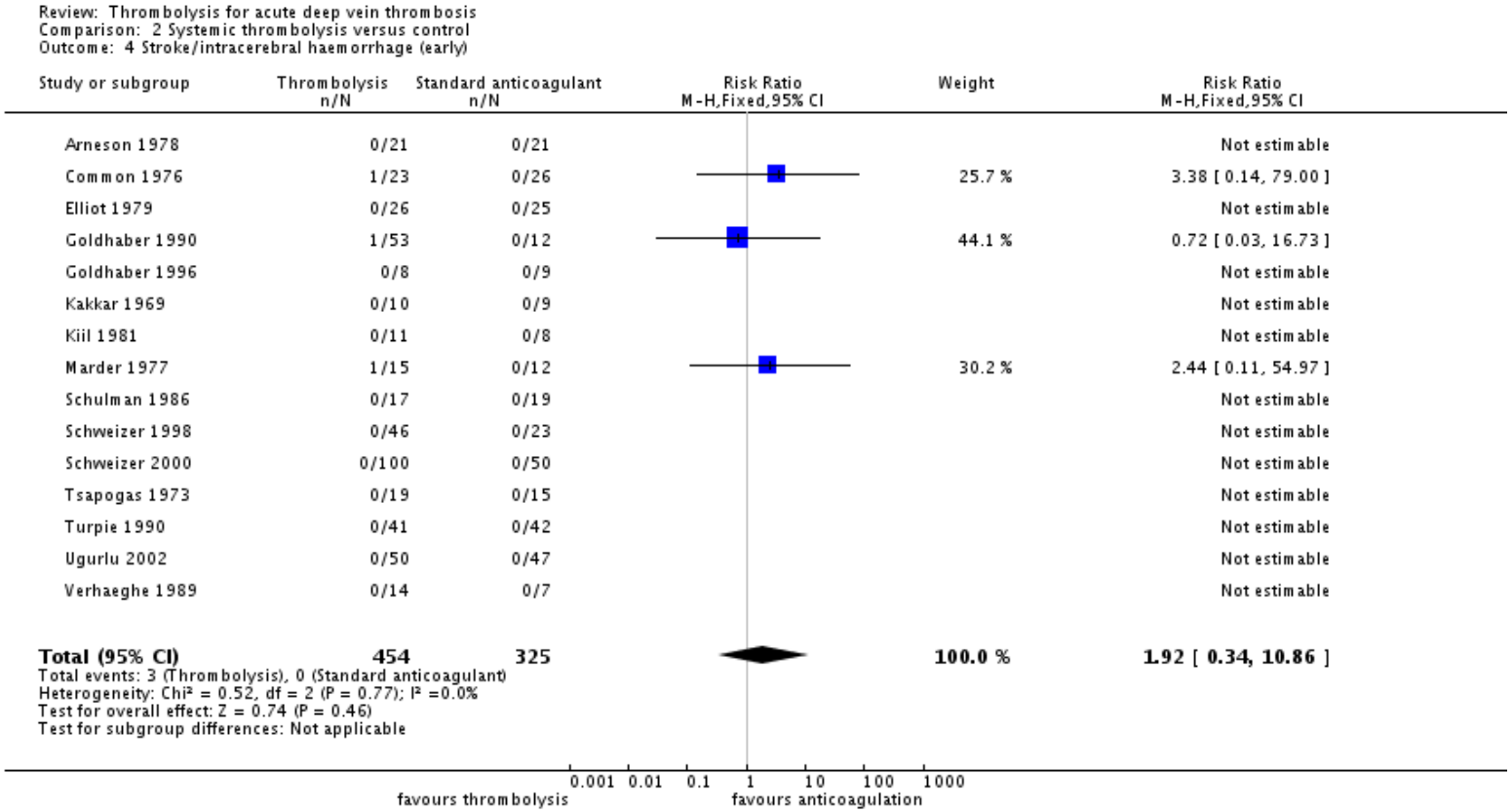
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00202

Thrombolysis for acute deep vein thrombosis



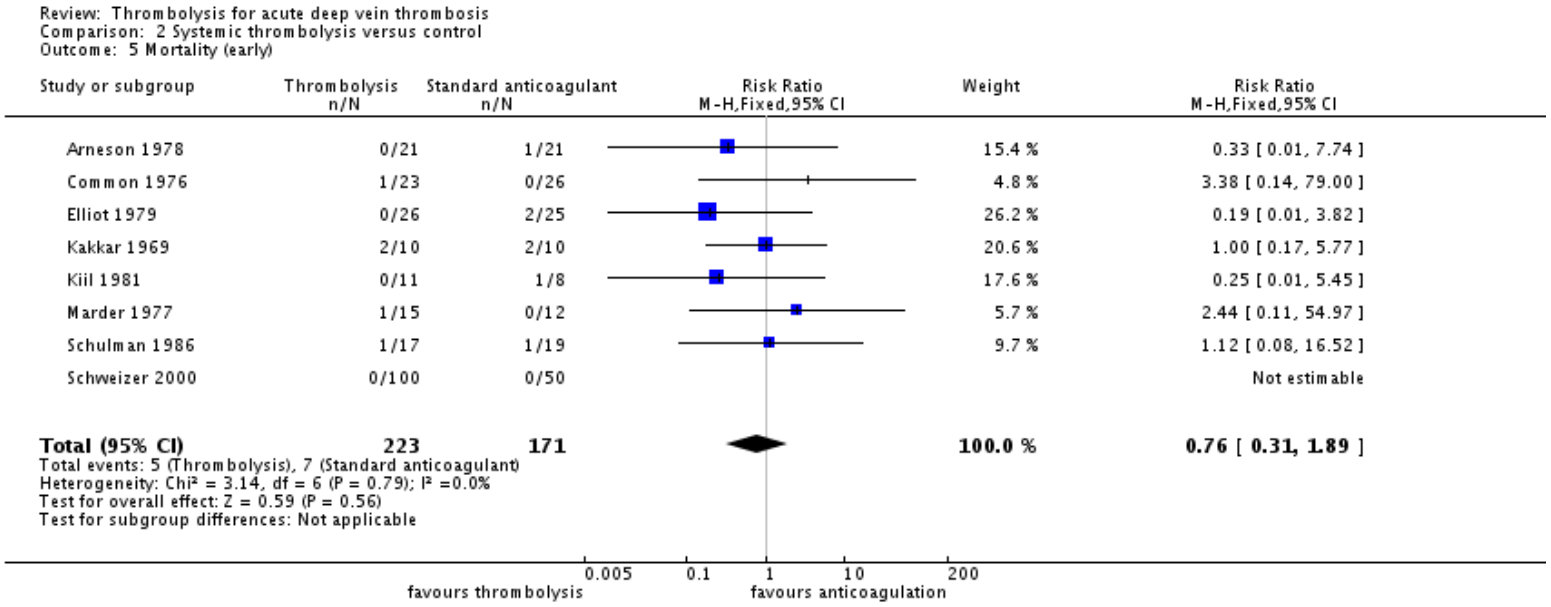
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00203

Thrombolysis for acute deep vein thrombosis



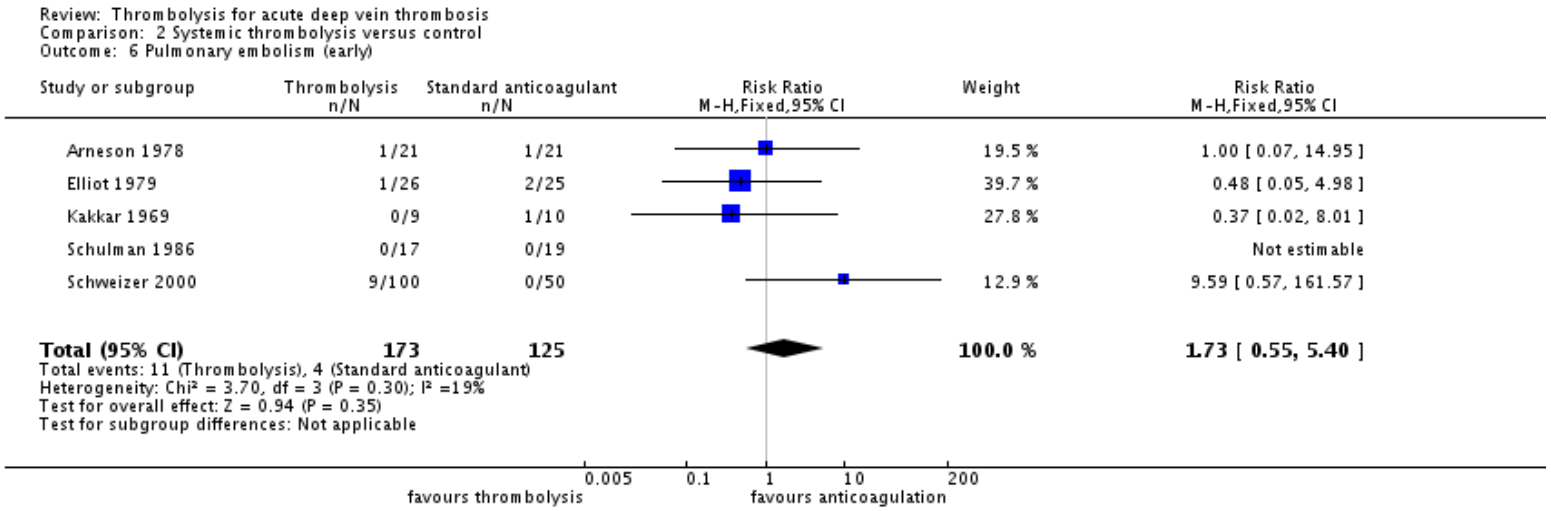
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00204

Thrombolysis for acute deep vein thrombosis



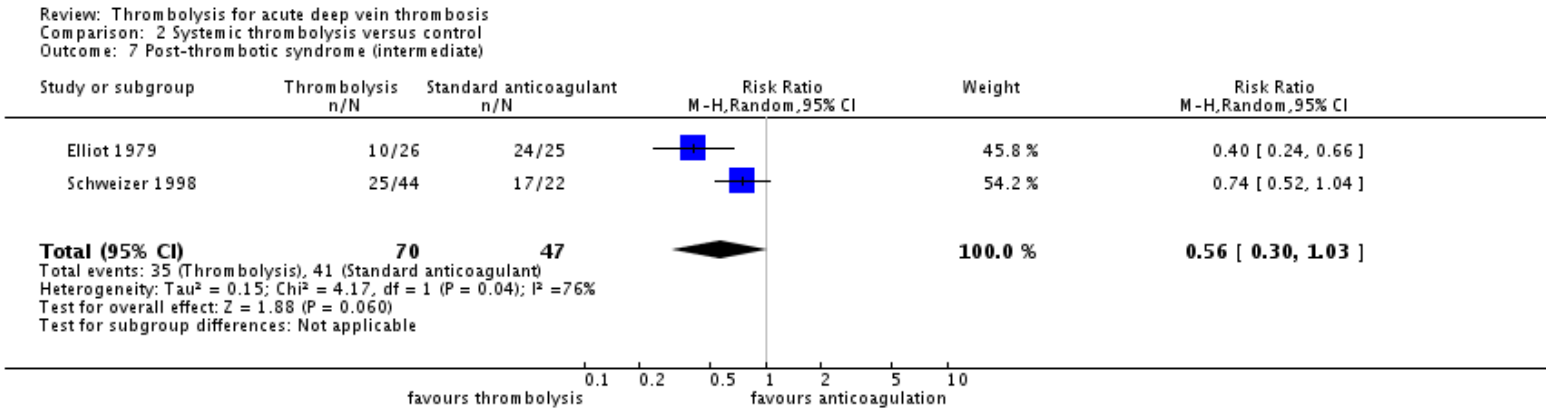
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00205

Thrombolysis for acute deep vein thrombosis



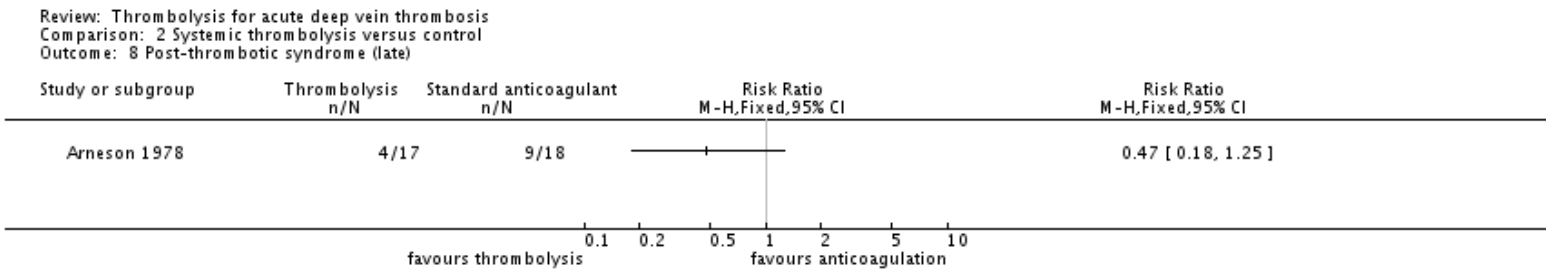
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00206

Thrombolysis for acute deep vein thrombosis



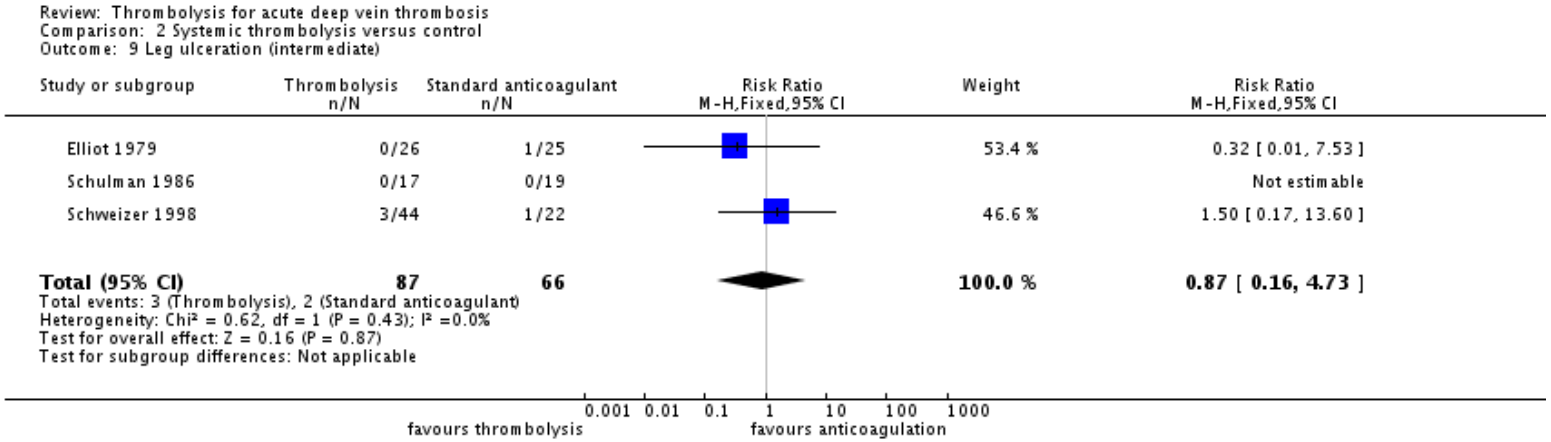
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00207

Thrombolysis for acute deep vein thrombosis



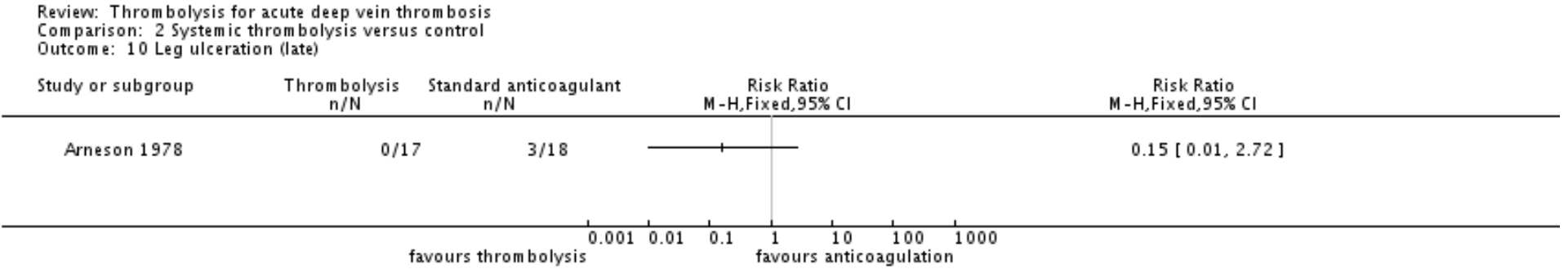
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00208

Thrombolysis for acute deep vein thrombosis



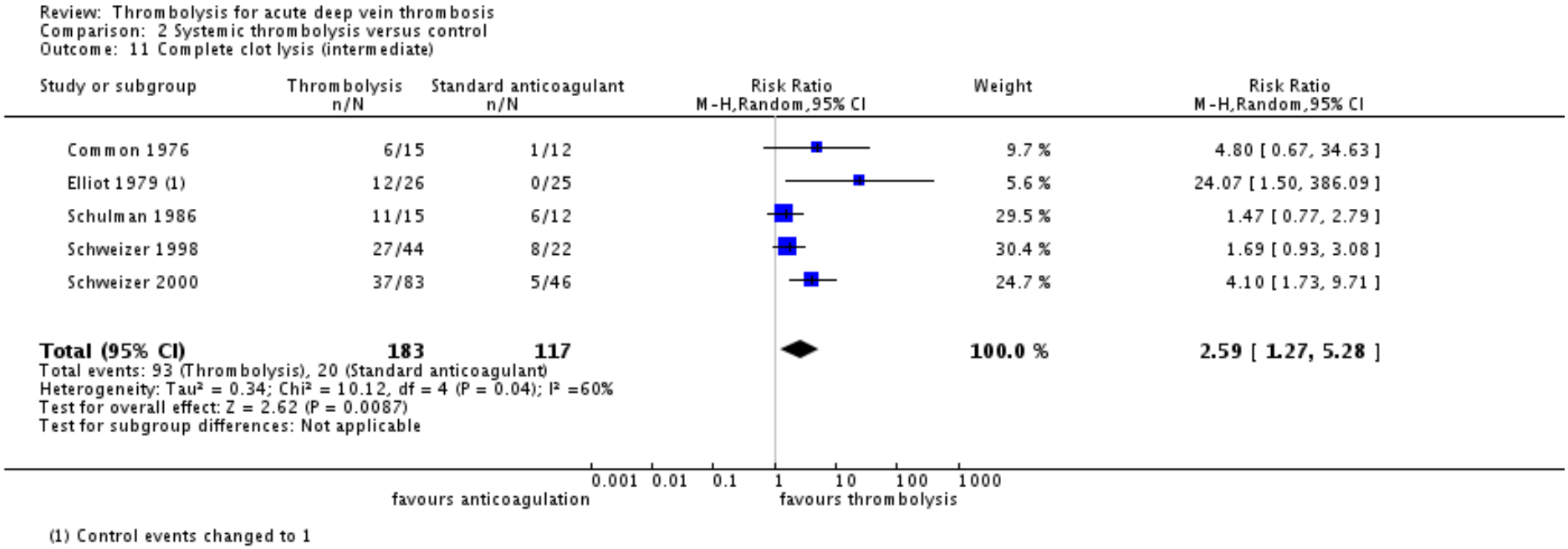
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00209

Thrombolysis for acute deep vein thrombosis



Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00210

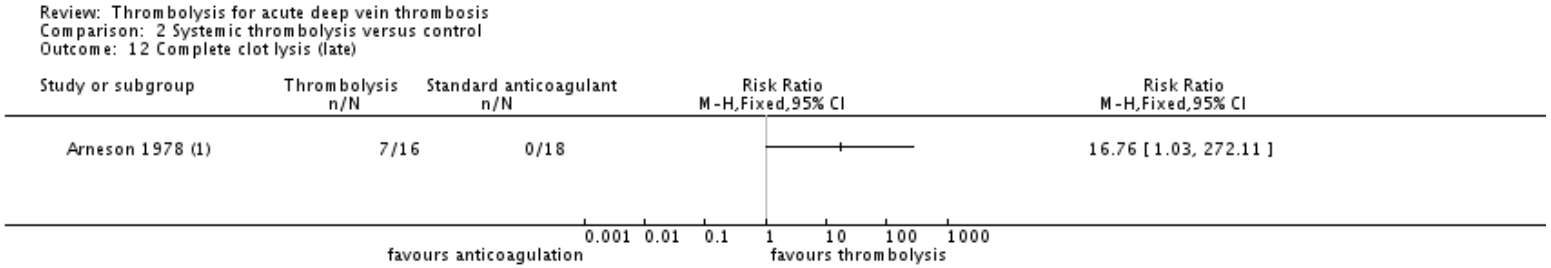
Thrombolysis for acute deep vein thrombosis



(1) Control events changed to 1

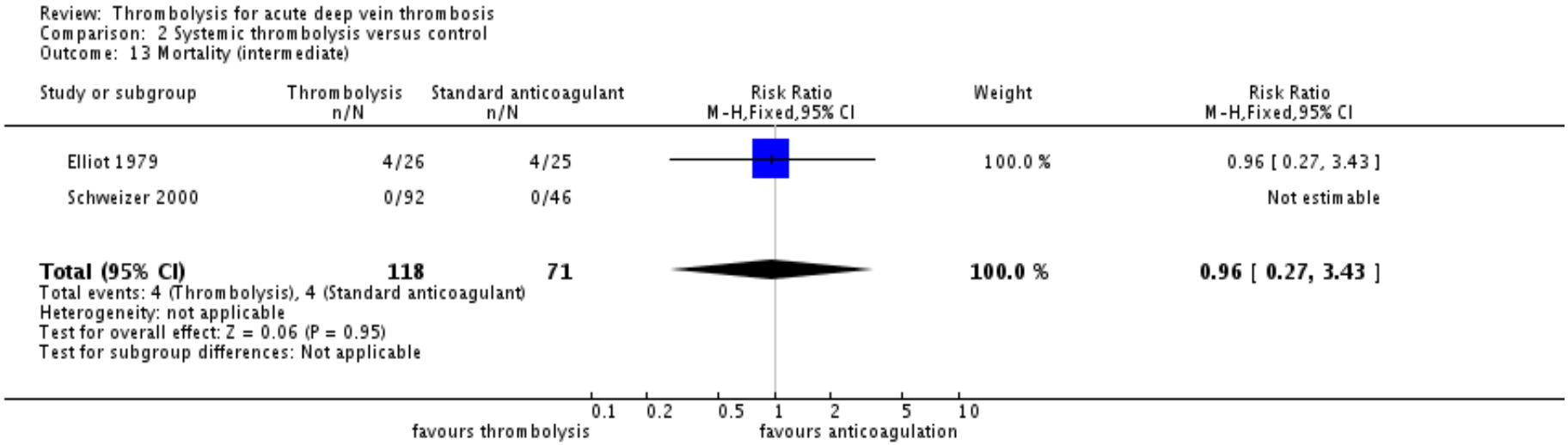
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00211

Thrombolysis for acute deep vein thrombosis



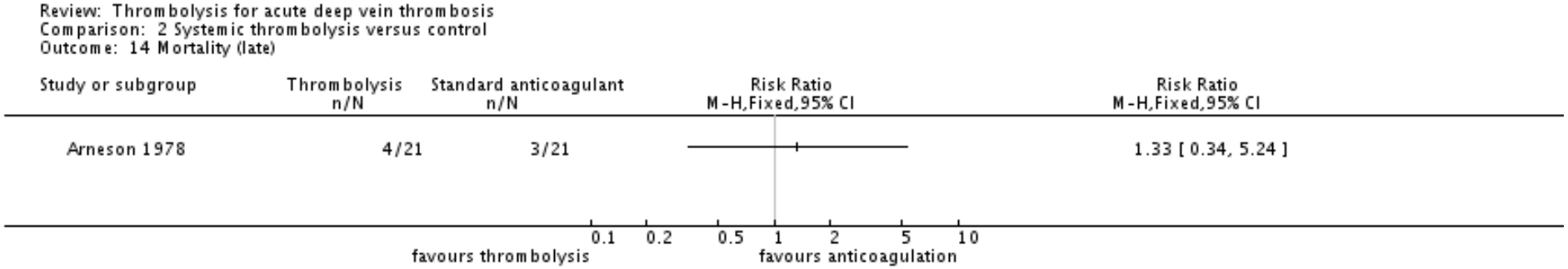
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00212

Thrombolysis for acute deep vein thrombosis



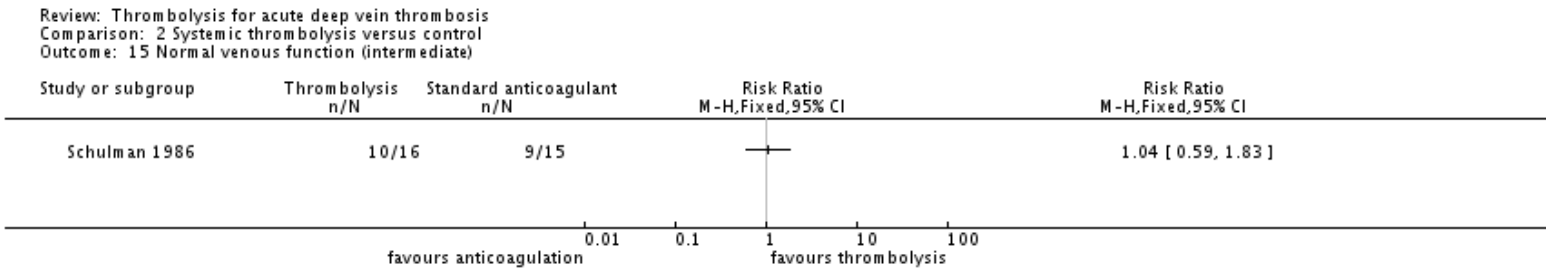
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00213

Thrombolysis for acute deep vein thrombosis



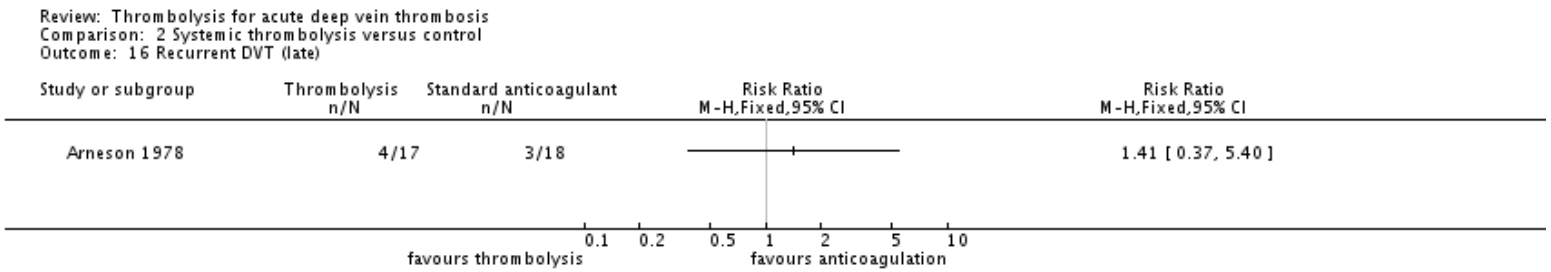
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00214

Thrombolysis for acute deep vein thrombosis



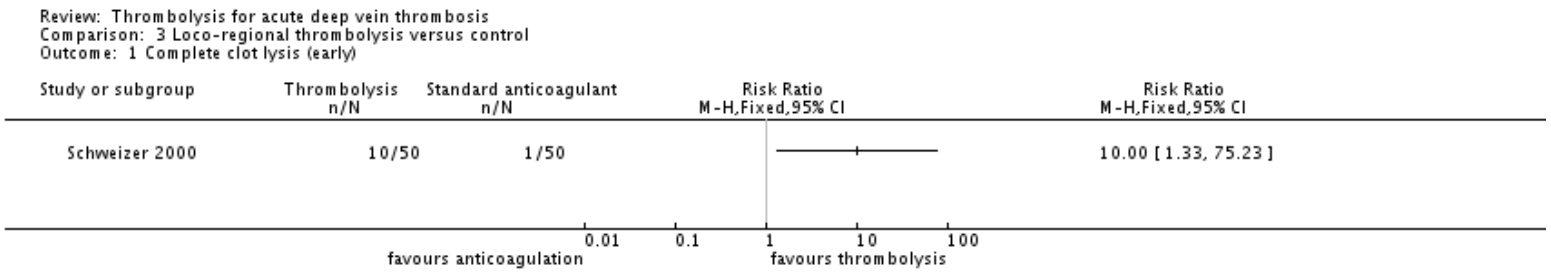
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00215

Thrombolysis for acute deep vein thrombosis



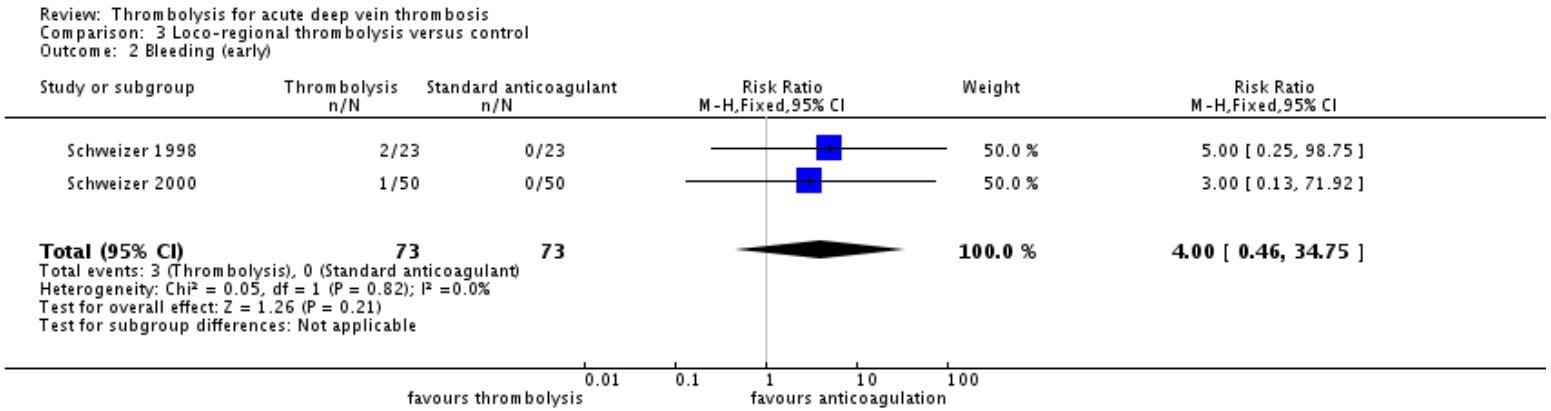
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00216

Thrombolysis for acute deep vein thrombosis



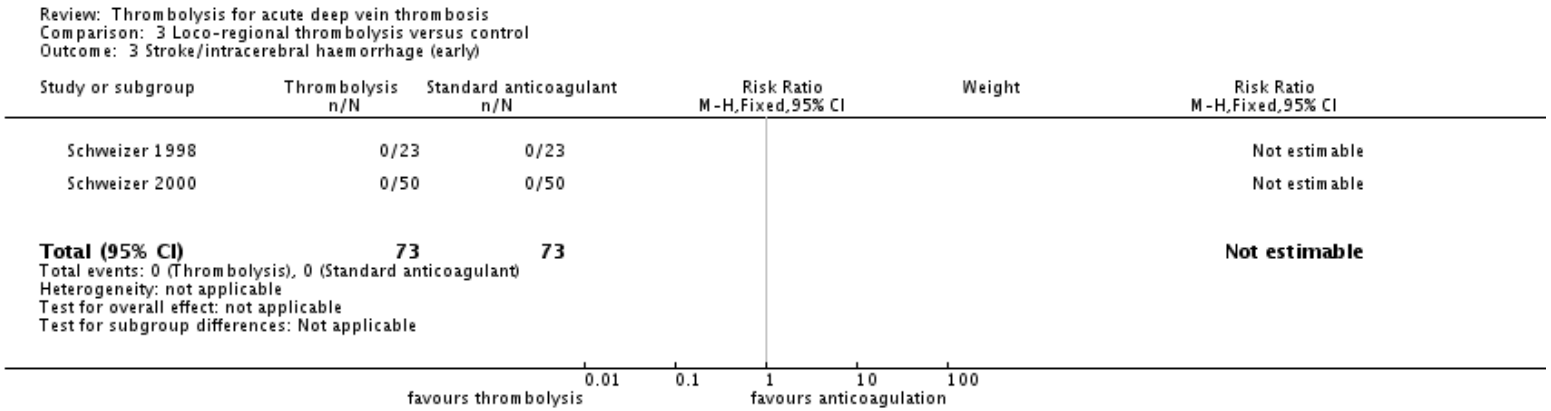
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00301

Thrombolysis for acute deep vein thrombosis



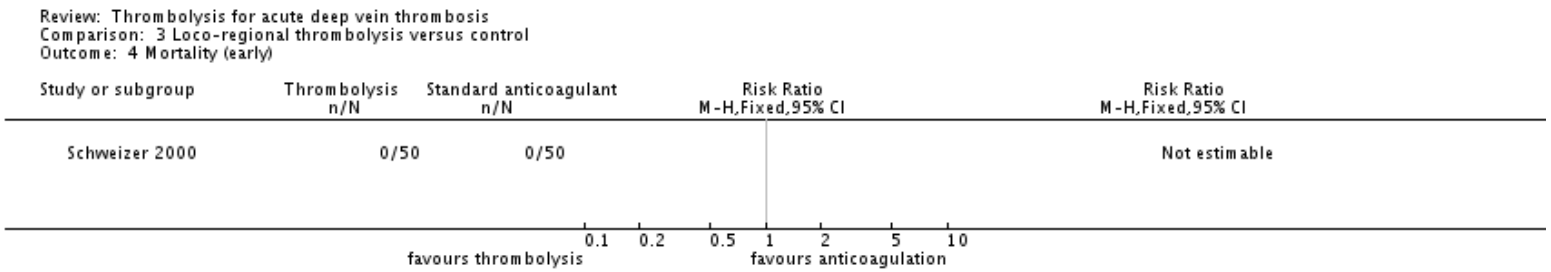
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00302

Thrombolysis for acute deep vein thrombosis



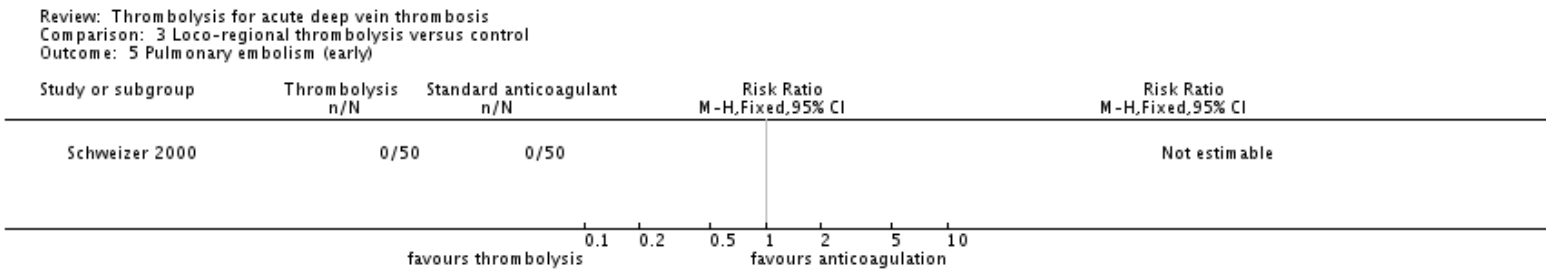
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00303

Thrombolysis for acute deep vein thrombosis



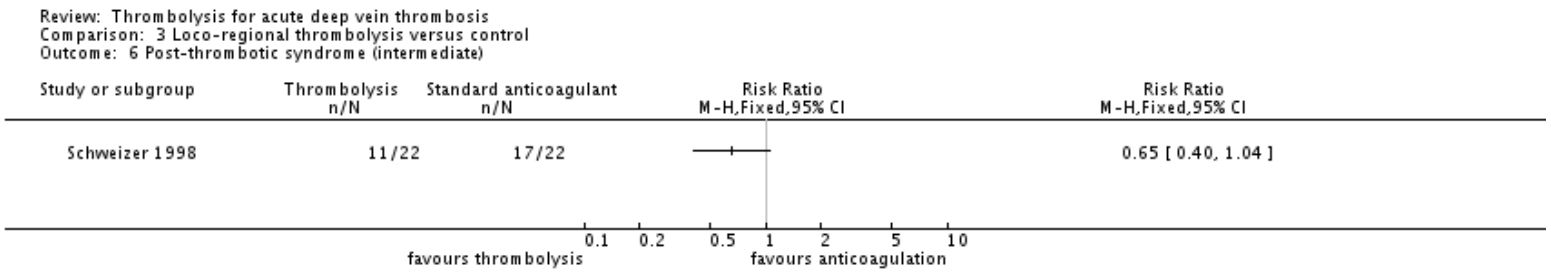
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00304

Thrombolysis for acute deep vein thrombosis



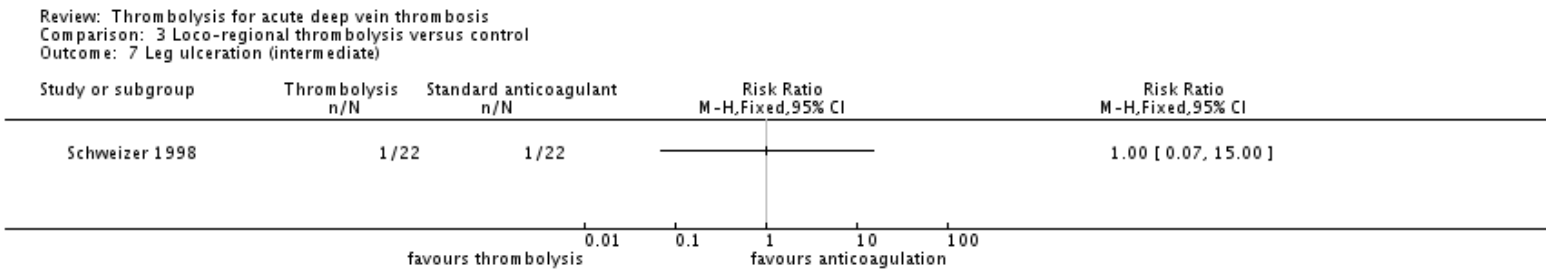
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00305

Thrombolysis for acute deep vein thrombosis



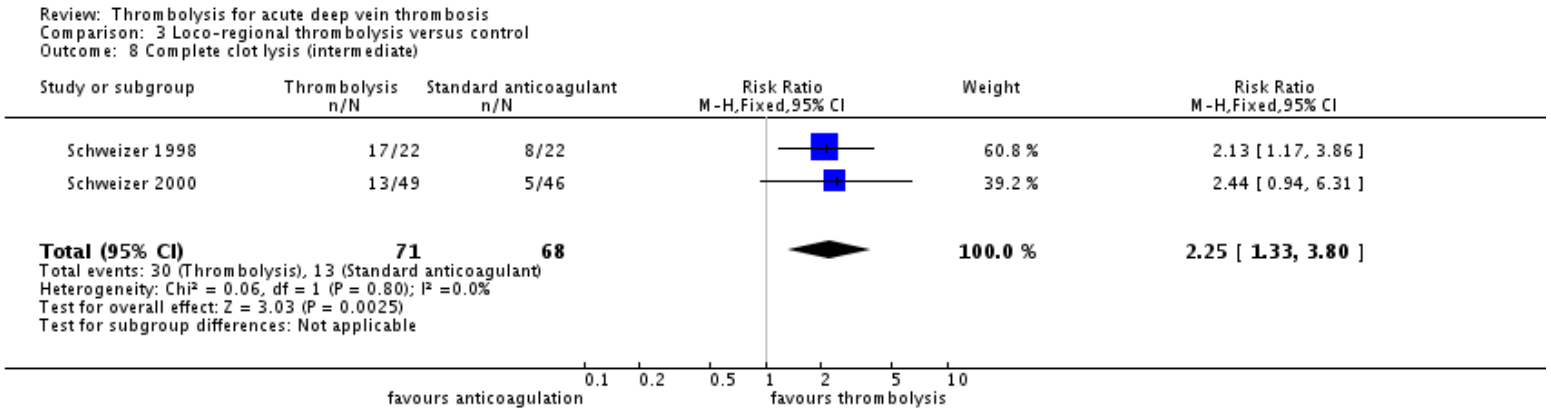
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00306

Thrombolysis for acute deep vein thrombosis



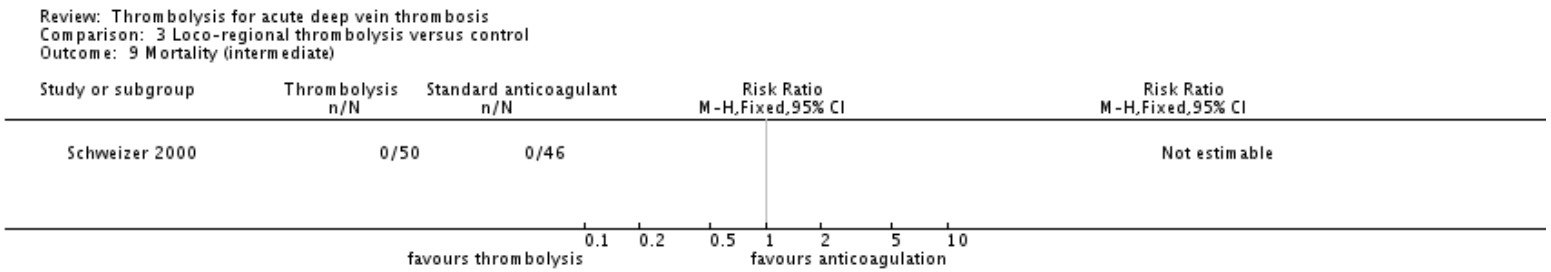
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00307

Thrombolysis for acute deep vein thrombosis



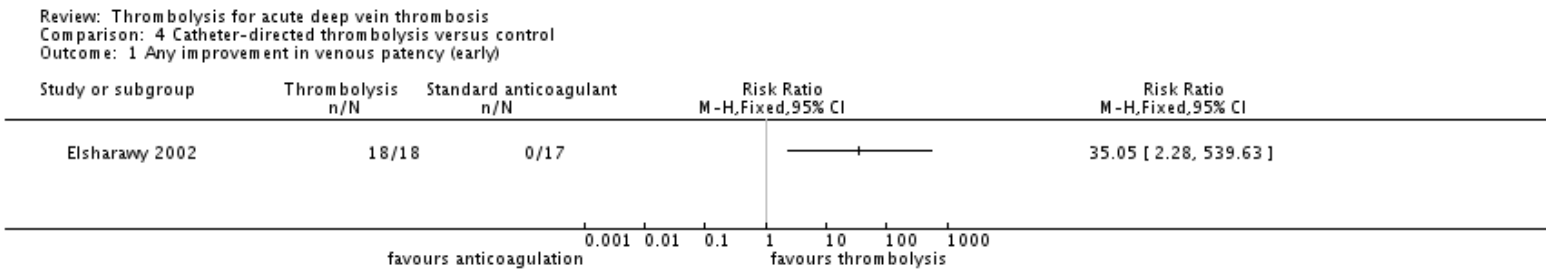
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00308

Thrombolysis for acute deep vein thrombosis



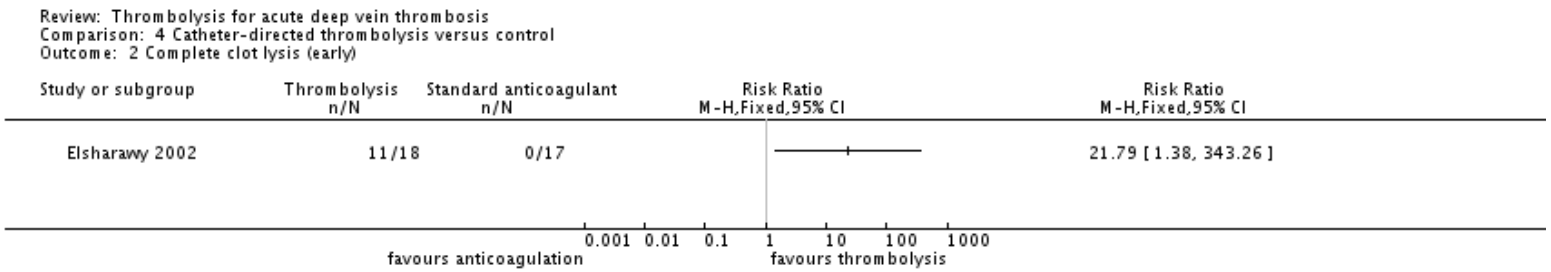
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00309

Thrombolysis for acute deep vein thrombosis



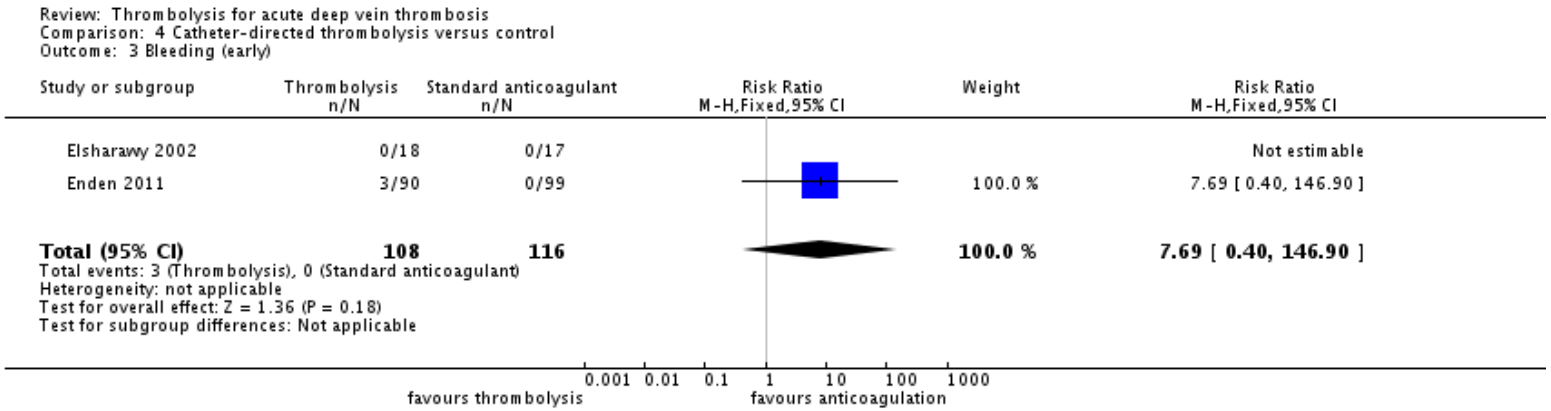
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00401

Thrombolysis for acute deep vein thrombosis



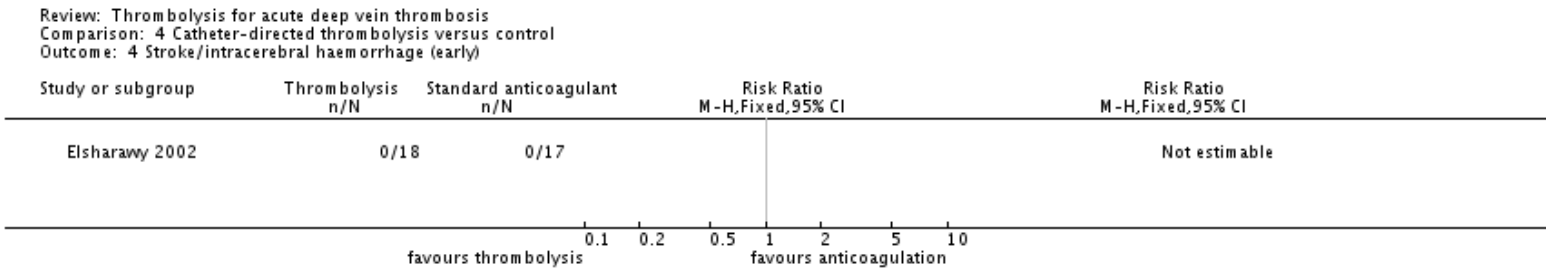
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00402

Thrombolysis for acute deep vein thrombosis



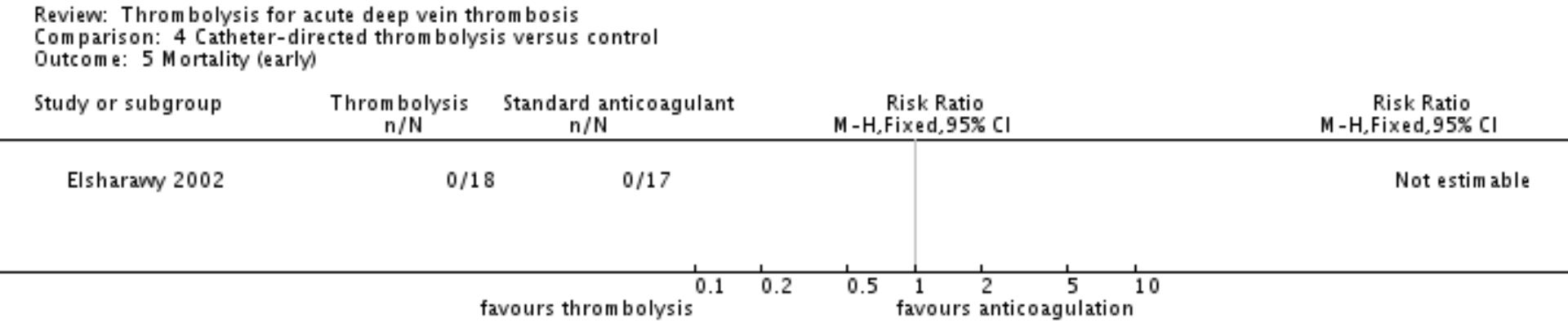
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00403

Thrombolysis for acute deep vein thrombosis



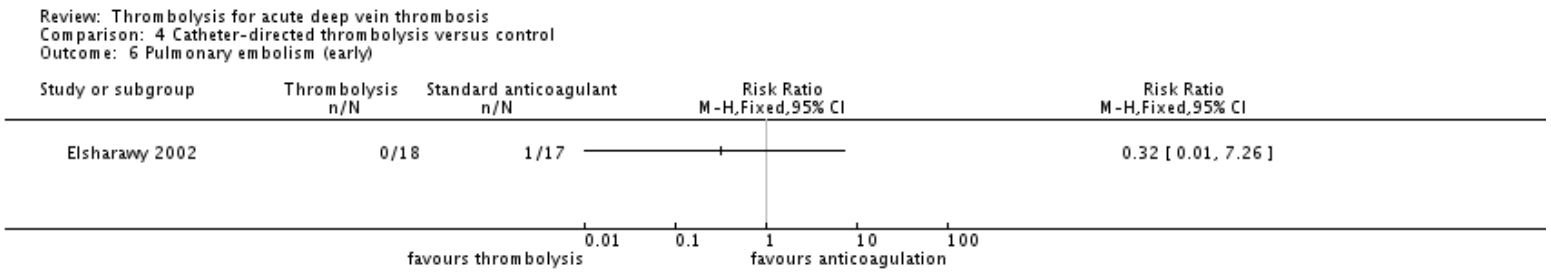
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00404

Thrombolysis for acute deep vein thrombosis



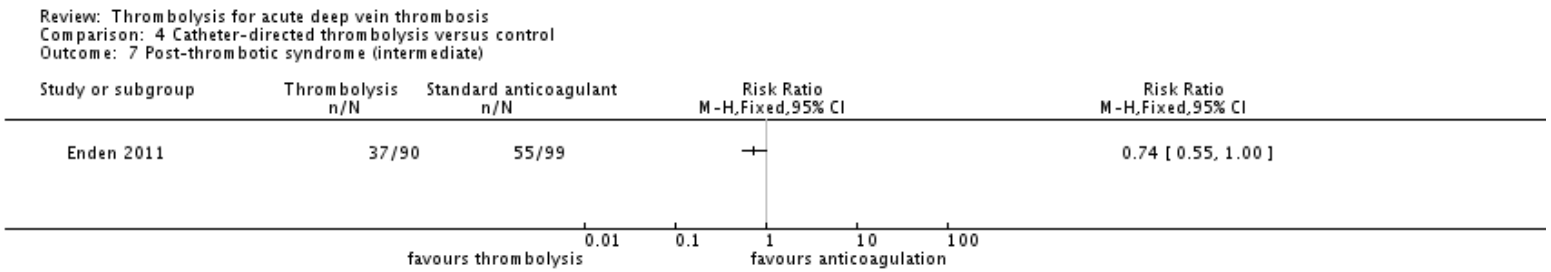
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00405

Thrombolysis for acute deep vein thrombosis



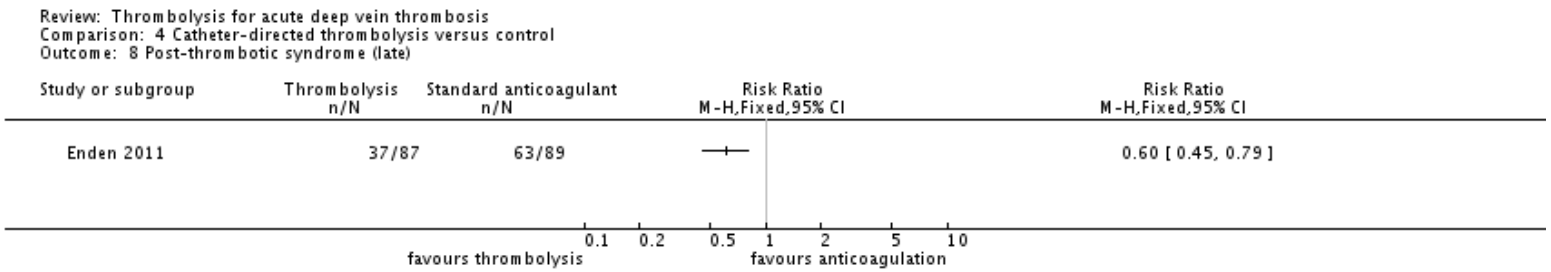
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00406

Thrombolysis for acute deep vein thrombosis



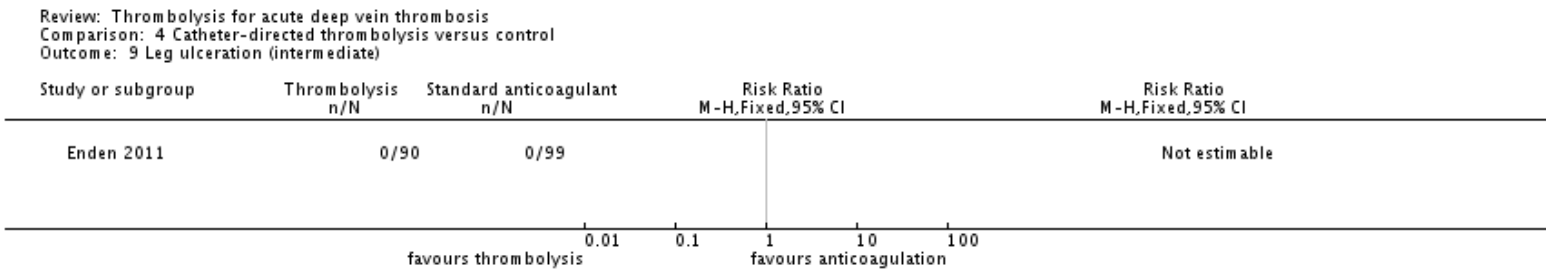
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00407

Thrombolysis for acute deep vein thrombosis



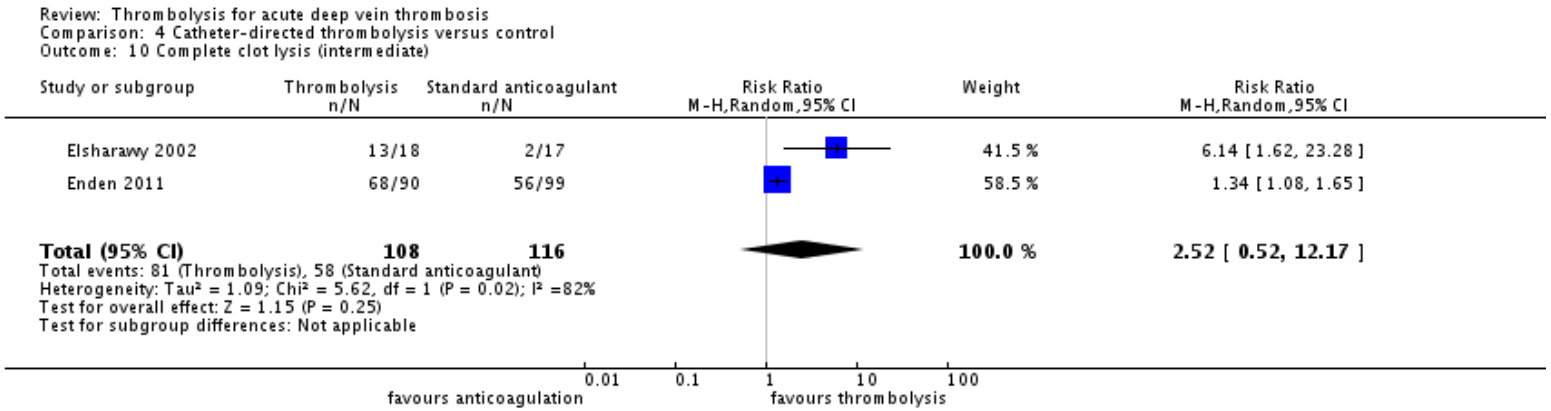
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00408

Thrombolysis for acute deep vein thrombosis



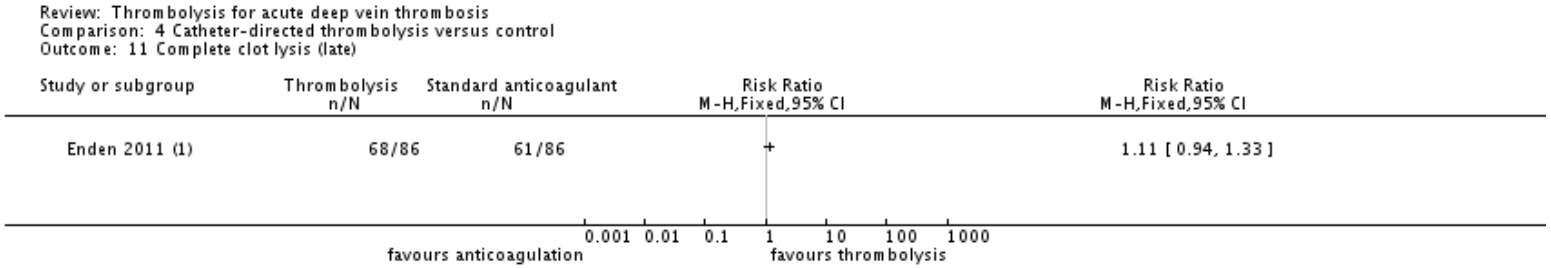
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00409

Thrombolysis for acute deep vein thrombosis



Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00410

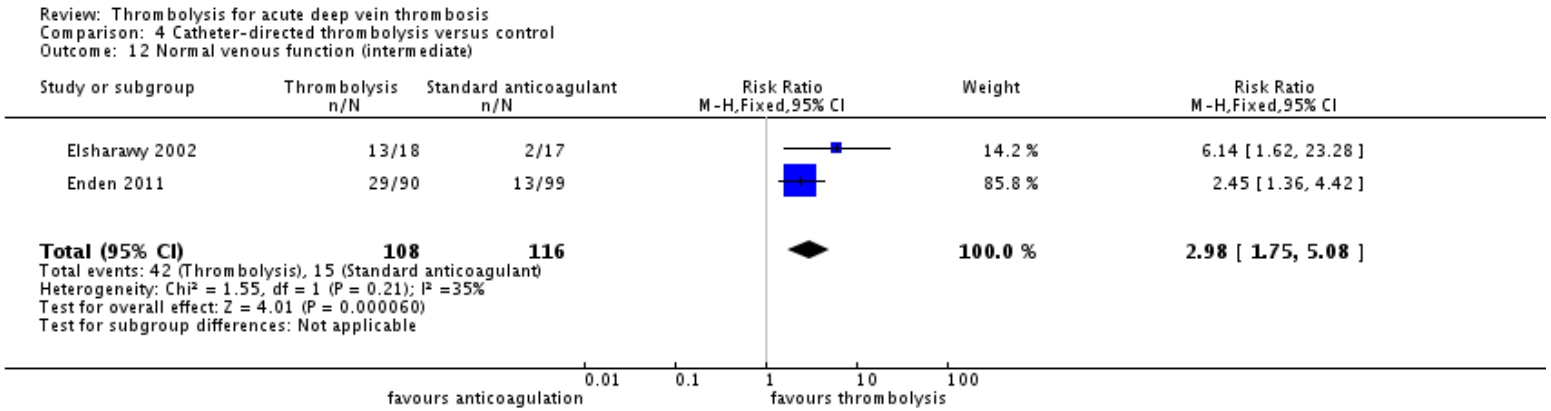
Thrombolysis for acute deep vein thrombosis



(1) Four patients had inconclusive results and not reported.

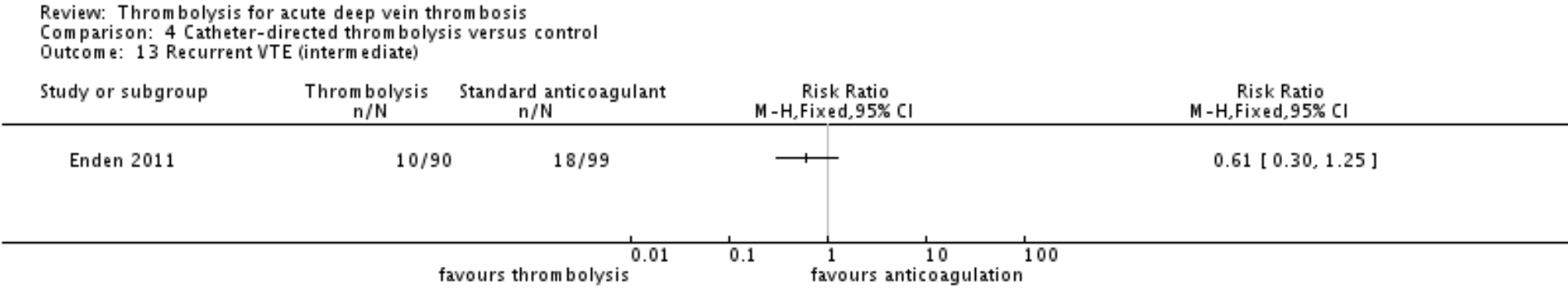
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00411

Thrombolysis for acute deep vein thrombosis



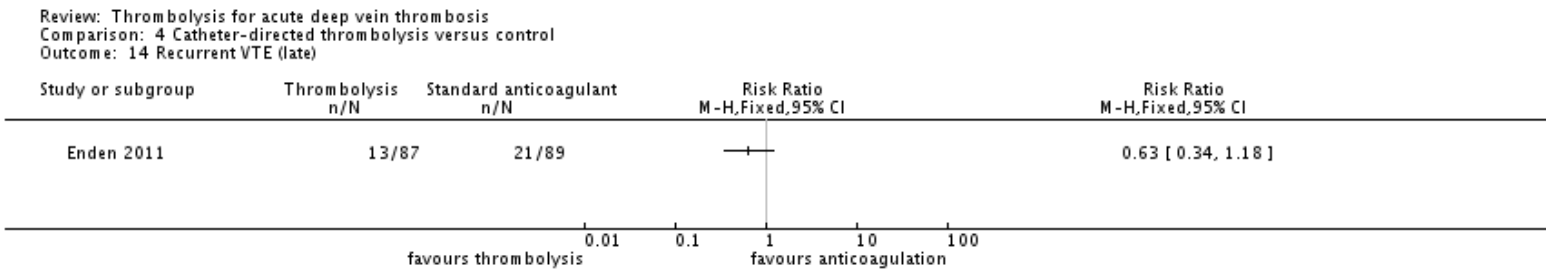
Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00412

Thrombolysis for acute deep vein thrombosis



Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00413

Thrombolysis for acute deep vein thrombosis



Cochrane Database of Systematic Reviews
10 NOV 2016 DOI: 10.1002/14651858.CD002783.pub4
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub4/full#CD002783-fig-00414

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CDT: catheter-directed thrombolysis; CI: Confidence interval; DVT: deep vein thrombosis; PTS: post-thrombotic syndrome; RCT: randomised controlled trial RR: Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1 Downgraded by one level as confidence intervals are wide around the estimate of the effect
2 Downgraded by one level as confidence intervals wide around the estimate of effect. Studies did not report any bleeding events in standard anticoagulation group
3 Results are from one small study with a small number of events. Downgraded by one level

Randomised Clinical Trial

Early Results of Thrombolysis vs Anticoagulation in Iliofemoral Venous Thrombosis. A Randomised Clinical Trial

Volume 24, Issue 3, September 2002, Pages 209-214

M. Elsharawy[a, f1], E. Elzayat[b]

European Journal of Vascular & Endovascular Surgery
esvs Journal

- 35 pts w/ iliofemoral DVT
- CDT w/ AC vs AC alone
- Streptokinase--2-4.5 million units total w/ infusion rate of 100,000 U/HR
- NO bleeding complications
- NO mortality

Randomised Clinical Trial

Early Results of Thrombolysis vs Anticoagulation in Iliofemoral Venous Thrombosis. A Randomised Clinical Trial

Volume 24, Issue 3, September 2002, Pages 209-214

M. Elsharawy[a, f1], E. Elzayat[b]

European Journal of Vascular & Endovascular Surgery
esvs Journal

- At 6 months, patency rate was better in cases treated with thrombolysis [13/18 (72%) vs 2/17 (12%), $p < 0.001$]. Venous reflux was higher in-patients treated with ONLY anticoagulant [7 patients (41%) vs 2 (11%), $p = 0.04$]

- **NICE 2012**
- *National Clinical Guideline Centre. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing. Clinical Guideline. Methods, evidence and recommendations. http://www.nice.org.uk/guidance/cg144/evidence/cg144-venous-thromboembolic-diseases-full-guideline3 (accessed 20 September 2016).*

- *DUTCH CAVA-trial. Ultrasound accelerated catheter-directed thrombolysis for primary iliofemoral deep vein thrombosis (IFDVT) compared to non-invasive conventional anticoagulant therapy alone: a Dutch randomized controlled multicenter clinical trial. https://clinicaltrials.gov/ct2/show/NCT00970619 (accessed 11 June 2015).*

Chest

Volume 149, Issue 2, February 2016, Pages 315–352

Evidence-Based Medicine

Antithrombotic Therapy for VTE Disease : CHEST Guideline and Expert Panel Report

Clive Kearon, MD, PhD[a], Elie A. Akl, MD, MPH, PhD[a, b], Joseph Ornelas, PhD[c], Allen Blaivas, DO, FCCP[d], David Jimenez, MD, PhD, FCCP[e], Henri Bounameaux, MD[f], Menno Huisman, MD, PhD[g],

Show more

http://dx.doi.org/10.1016/j.chest.2015.11.026

- *Zhang X, Ren Q, Jiang X, Sun J, Gong J, Tang B, et al. A prospective randomized trial of catheter-directed thrombolysis with additional balloon dilatation for iliofemoral deep venous thrombosis: a single-center experience. Cardiovascular and Interventional Radiology 2014;37(4):958-68*

- *Patra S. Catheter directed thrombolysis along with mechanical thromboaspiration versus anticoagulation alone in the management of lower limb deep venous thrombosis - a comparative study. Journal of American College Cardiology 2014;64(16 Suppl 1):C203*

- *Cakir V, Gulcu A, Akay E, Capar AE, Gencpinar T, Kucuk B, et al. Use of percutaneous aspiration thrombectomy vs. anticoagulation therapy to treat acute iliofemoral venous thrombosis: 1-year follow-up results of a randomised, clinical trial. Cardiovascular and Interventional Radiology 2014;37(4):969-76*

- *Bashir R. Comparative outcomes of catheter-directed thrombolysis plus anticoagulation vs anticoagulation alone to treat lower-extremity proximal deep vein thrombosis. JAMA Internal Medicine 2014;174(9):1494-501.*

- *Sharifi M, Bay C, Mehdipour M, Sharifi J. Thrombus obliteration by rapid percutaneous endovenous intervention in deep venous occlusion (TORPEDO) trial: Midterm results. Journal of Endovascular Therapy 2012;2:273-80*

Thrombolysis for acute deep vein thrombosis

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - » Fifth level

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - Fifth level

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - » Fifth level

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - » Fifth level

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - » Fifth level