What do we learn from the RCTs regarding **venous recanalisation** ?

How to design a trial which really moves the field forward ?

Disclosure

Speaker name:

.....Sebastian Schellong.....

I have the following potential conflicts of interest to report:

- [X] Consulting (Boehringer, Bayer, BMS, Daiichi Sankyo, Aspen)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [X] Other: speaker fees (Boehringer, Bayer, BMS, Daiichi Sankyo, Aspen)

- [ ] I do not have any potential conflict of interest

Therapy of VTE

initial early maintenance long term maintenance

Anticoagulation

Compression Therapy

Thrombolysis

Surgery

Treatment goals for DVT

- **Prevention of PE**
- **Relief from complaints**
- **Prevention of recurrence**
- **Prevention of PTS**

Effects of anticoagulation

- **Prevention of PE**
- **Prevention of recurrence**

Effects of compression therapy

- **Relief from complaints**
- **Prevention of PTS**

Sox trial

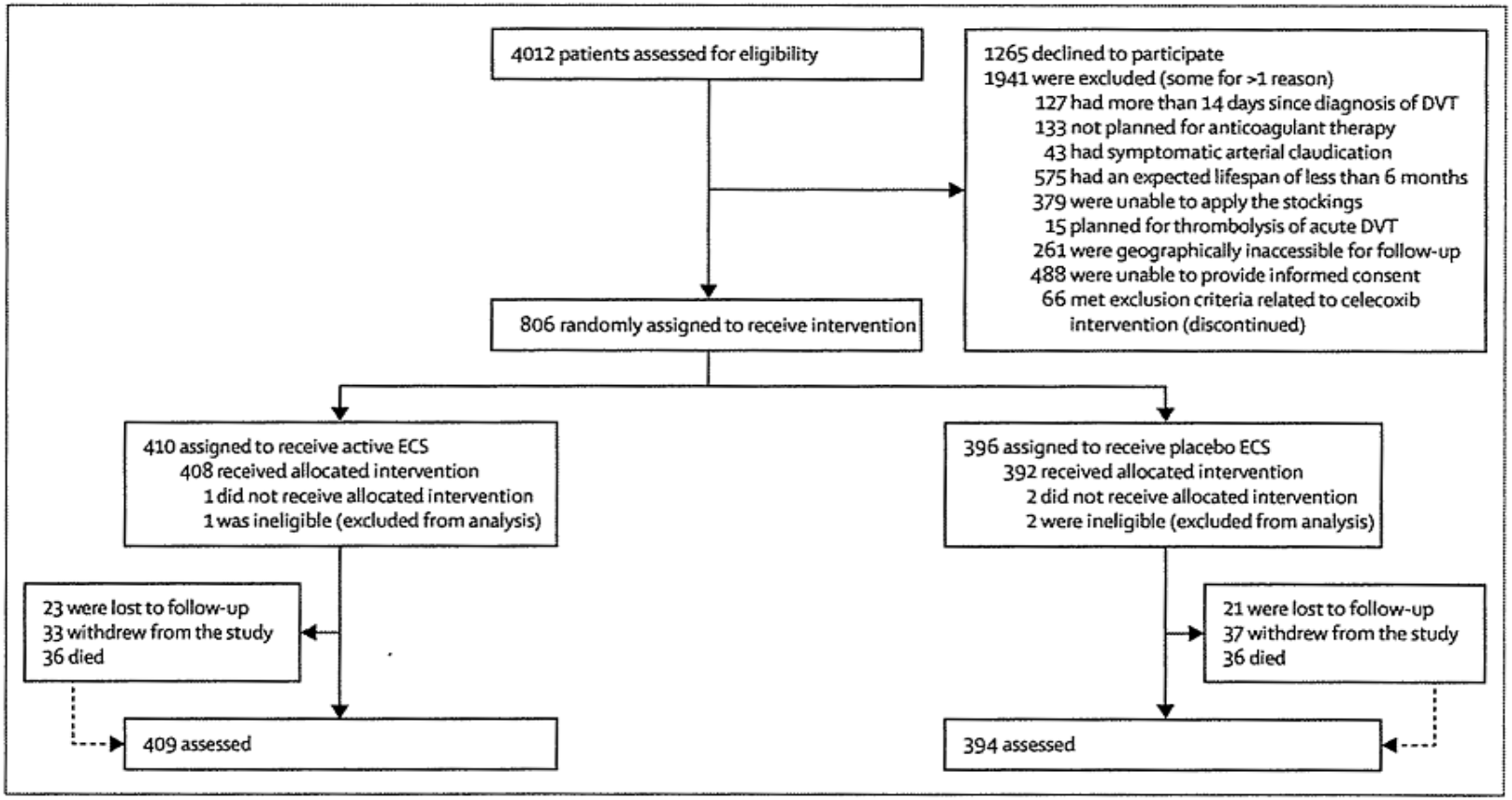
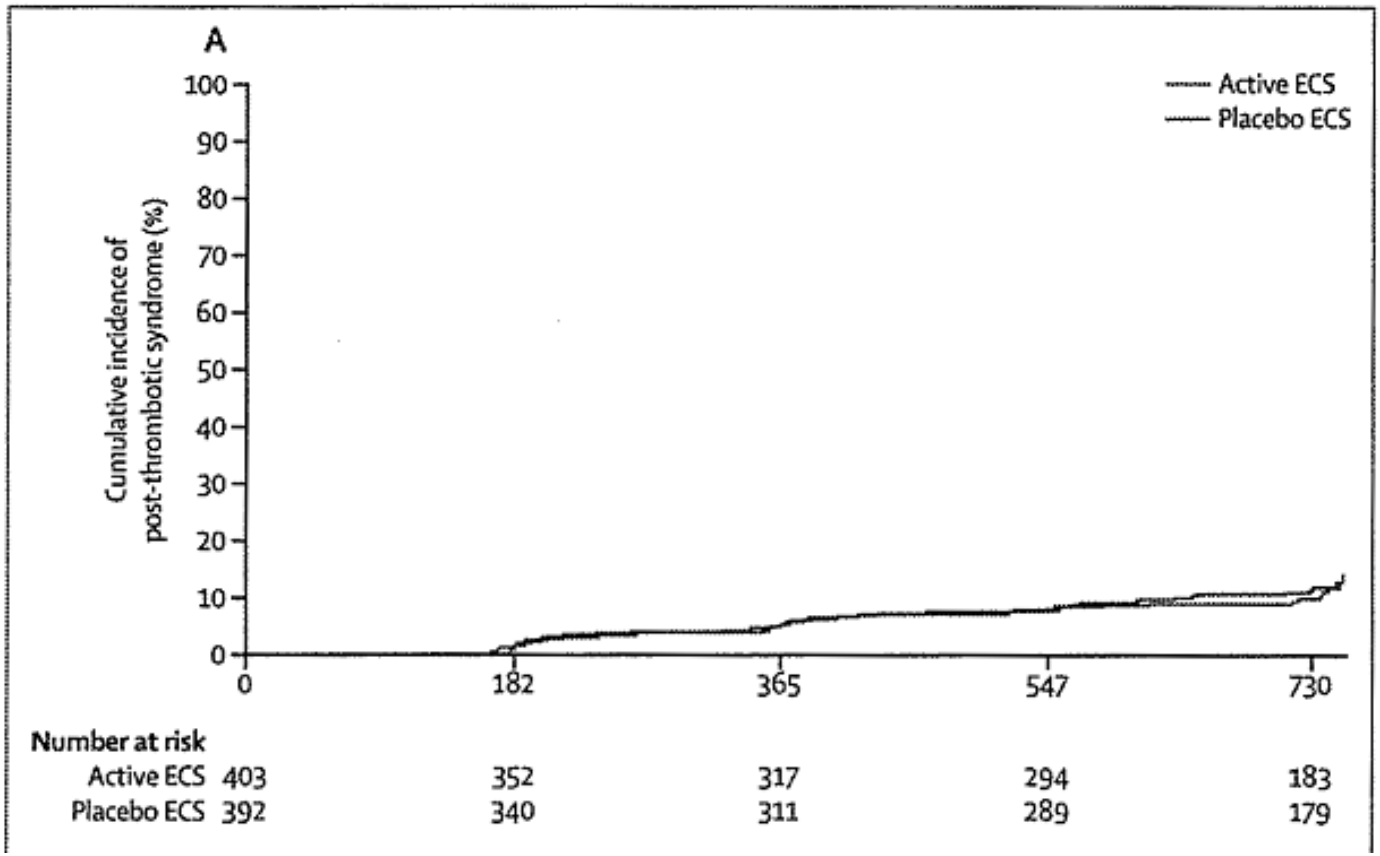


Figure 1: **Trial profile**
Three patients were ineligible and excluded from the analysis (in the active ECS group, one patient had no DVT [did not receive study stockings] and in the placebo ECS group, one patient had previous DVT [did not receive study stockings] and one was moribund [received study stockings]). Three patients did not receive their allocated intervention. Because of leg shape, one patient in each group could not be fitted with stockings; they did not receive stockings but continued in the trial. One patient in the placebo ECS group received active ECS at the baseline visit due to an error at the stockings distribution centre—the patient insisted on using the same type of stockings throughout the trial without knowing if it was active or placebo. ECS=elastic compression stockings. DVT=deep venous thrombosis.

Kahn SR et al., Lancet 2014; 383:880-8

Sox trial



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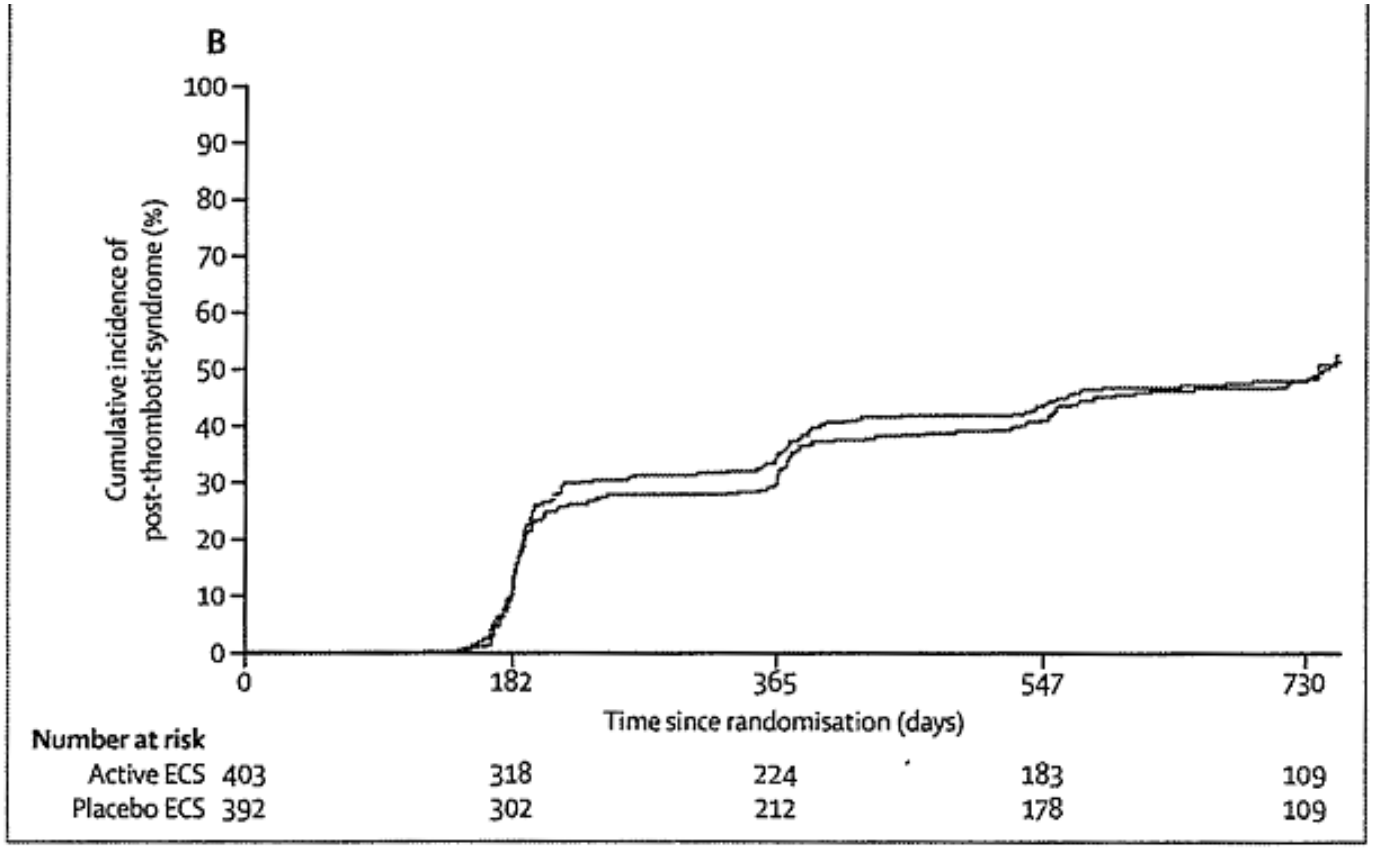
Sox trial



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Compression therapy
Open label study

194 outpatients with symptomatic proximal DVT
Compression stockings *vs* no stockings for at least 2 years
Mean follow up 76 months
Assessment of post-thrombotic syndrome by score system

Mild-to-moderate	**20%**	***vs***	**47%**	**(p<.001)**
Severe	**11%**	***vs***	**23%**	**(p<.001)**
Ulcer	**1%**	***vs***	**3%**	

Almost all cases of PTS detectable within 24 months

Brandjes et al, Lancet 1997;349:759-62

Compression therapy
Open label study

180 outpatients with first episode of proximal DVT
Compression stockings *vs* no stockings for at least 2 years
Follow up 60 months
Assessment of post-thrombotic syndrome by score system

All PTS	**24%**	***vs***	**49%**
Severe	**3%**	***vs***	**11%**

HR 0.49 (95%CI 0.29-0.84); p = 0.011

All but one cases of PTS detectable within 24 months

Prandoni et al, Ann Int Med 2004;141:249-56

Effect of recanalisation therapy

- **? ? Additional prevention of PTS ? ?**

Results of systemic thrombolysis

- **PTS:** **RR 0.66 (95%CI: 0.47–0.94)**
- **Major bleed:** **RR 1.7 (95%CI: 1.04-2.09)**
- **Mortality:** **1.5%**

CaVenT trial

- CDT with rt-PA
- N=209, multicenter, randomised

- significant benefit regarding:
  - PTS: 41 vs. 56% (NNT=7) FU 24 Mo
  - Iliofemoral patency: 66 vs. 47% FU 6 Mo

- CDT with 20 bleeds
  - major: n=3
  - clinically relevant: n=5

Enden T et al.: Lancet 2012;379:31-8

ATTRACT trial

Outcome (24 mo)	PCDT (n=336)	no PCDT (n=335)	P value
Any PTS	**46,7 %**	**48,2%**	**0.56**
Recurrent VTE	12,5%	8,5%	0.09
Generic QOL (SF-36 PCS)	11,8	10,1	0.37
VENOUS QOL (VEINES)	27,7	23,5	0.08
Moderate or Severe PTS	17,9%	23,7%	0.035
MS-PTS IFDVT	18,4%	28,2%	
MS-PTS FPDVT	17,1%	18,1%	
Major bleed	1,7%	0,3%	0.049
Any bleed	4,5%	1,7%	0.049

PTCD less effective in patients ≥65 years (p = 0.038)

S. Vedantham et al, N Engl J Med 2017;377:2240-2252

WARNING !

- **The term “iliofemoral” is a mixed bag**
- **which causes confusion.**

Types of DVT

1 – ascending
2 – transfascial
3 – descending

Ascending vs descending DVT

	ascending	descending
Age	mean 60 yrs	20 – 30 yrs
Sex	f = m	f >> m
Trigger	60 : 40	? (90 : 10)
Complaints	insidious	acute
Recanalisation	slowly, incomplete	Iliac veins: hardly Femoral veins: quickly
PTS	50 / 25 / 5 Typical	? / ? / ? Atypical

Consequence 1:

- **The term “iliofemoral” should be abandoned**

Consequence 2:

A consensus has to be reached on

- **which population to be included**
- **how to measure PTS**
- **when to measure PTS**
- **which procedure exactly to be studied**

The ideal trial on venous recanalisation

Randomised controlled trial

- **Population: acute descending DVT only**
- **Primary outcome: PTS after 2 years**
- **Measure: venous claudication + Villalta severe**
- **Procedure: catheter directed thrombolysis + stent**
- **Background therapy: compression**
- **Methodology: open label, blinded outcome**
- **Methodology: superiority design, 50% reduction**

Discussion