Antithrombotic stewardship:
The proof of the pudding…….

Patricia van den Bemt

March 24th 2021

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Disclosures

No recent financial or other conflicts of interest to disclose

Introduction

- Antithrombotic therapy carries high risks for patient safety[1,2]
- Studies on the implementation and (cost-)effectiveness of a multidisciplinary antithrombotic team are scarce
  - Reardon et al – main focus on prevention of HIT
  - Newer studies – focus on DOACs
  - Older studies – pharmacist based; focus on VKA
- A hospital-based multidisciplinary antithrombotic team (S-team) may improve the effect and safety of antithrombotic therapy during and after hospitalization

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1.Xu Y et al. Thromb Res 2019 and Chest 2017; 2. Bajorek et al. J Am geriatr 2005

Objectives

To study the effect of implementing a hospital-based multidisciplinary antithrombotic team (S-team) on the efficacy and safety of antithrombotic therapy during and after hospitalization.

To determine the cost-effectiveness of such a team.

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Method - study population

- Prospective, multicenter before-after intervention study

- Inclusion criteria
  - Age ≥18 years
  - Hospitalization in two Dutch hospitals
  - Informed consent
  - Treatment with therapeutic anticoagulant medication
  - Only the first hospitalization was included

- Exclusion criteria
  - Hospitalization <24 hours
  - Admission to the ICU without admission to a regular ward
  - Patients treated with LMWH only for thrombosis prophylaxis
  - Patients treated with a single dose of an anticoagulant medicine

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Studyflow

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Multidisciplinary antithrombotic team

S-team

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Intervention: medication reviews

- Medication reviews by hospital pharmacist
- Focused on anticoagulation/antiplatelet
  - Bodyweight
  - Renal function
  - Combinations

Intervention: protocols

- Anticoagulation portal within hospital system
- Reduction of overload of department based protocols
- Towards hospital based protocols

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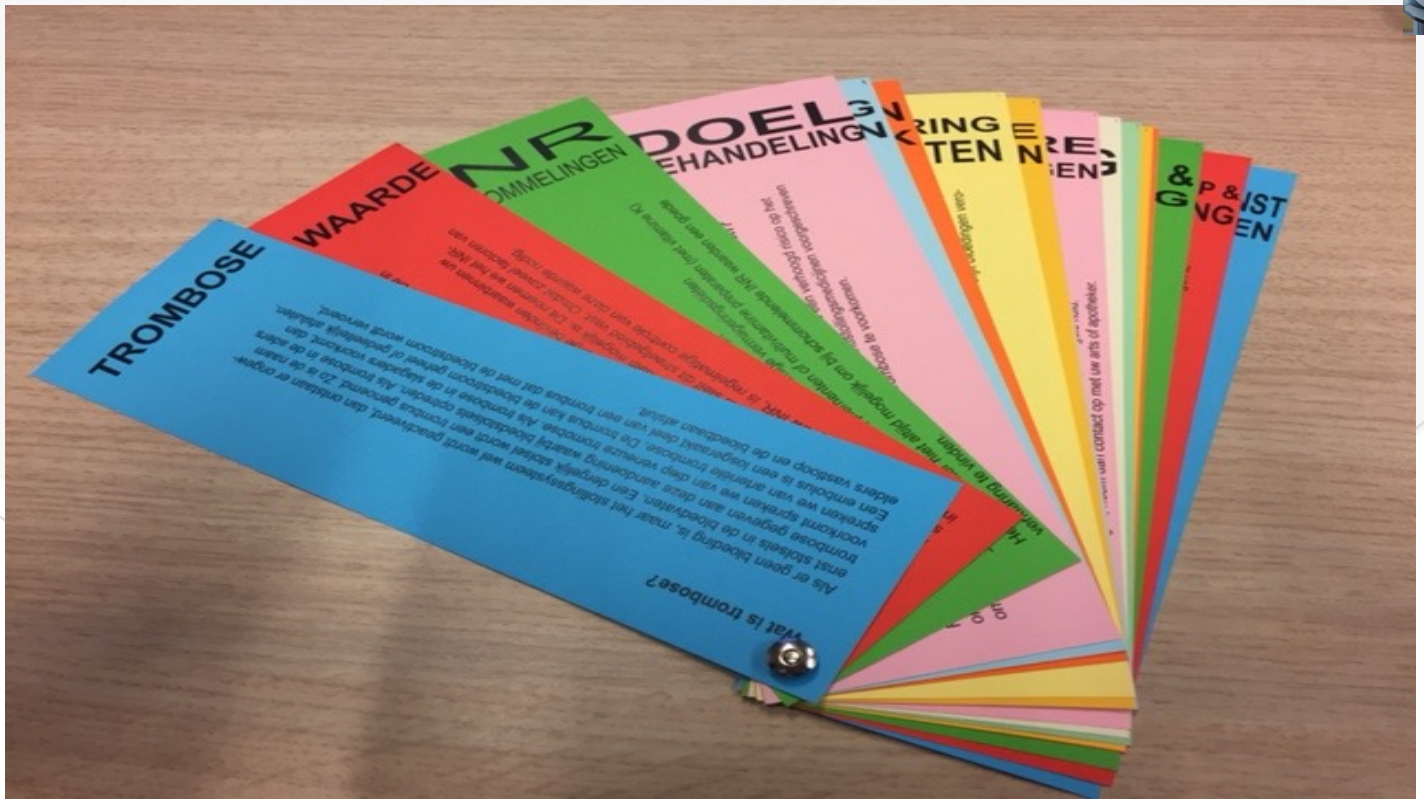
Intervention: patient education



Intervention: healthcare provider education

- Protocols
- Risks and benefits
- PR for the antithrombotic stewardship team
- Introducing the ”coagula-phone”

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Intervention: information transfer

- Thrombotic services
  - High quality network in The Netherlands
  - Monitoring vitamin K antagonists
  - However….when hospitalised loss of information
- Information from thrombotic service on usual dosage regimen transferred to responsible physician
- With this information (re)start of vitamin K antagonist

- And vice versa (all anticoagulants):
  - To thrombotic service
  - To GP
  - To community pharmacist

Primary outcome

Proportion of patients with a composite end point consisting of one or more bleeding episodes or one or more thrombotic event from hospitalization until three months after hospitalization

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Secondary outcomes and subgroup analyses

- Separate components of the composite endpoint
- Primary outcome only during hospitalization
- Primary outcome only after hospitalization
- All-cause mortality
- Length of hospitalization
- Costs

- Subgroupanalyses:
  - Type of antithrombotic therapy
  - Type of hospital

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Data analysis

- IBM Statistics SPSS version 21
- The primary outcome was analysed using segmented regression analysis for the interrupted time series data
- Secondary outcomes: relative risk and 95% CI
- Costs: healthcare perspective
  - calculation of non-major bleeding costs in- and excluding costs of hospitalisation

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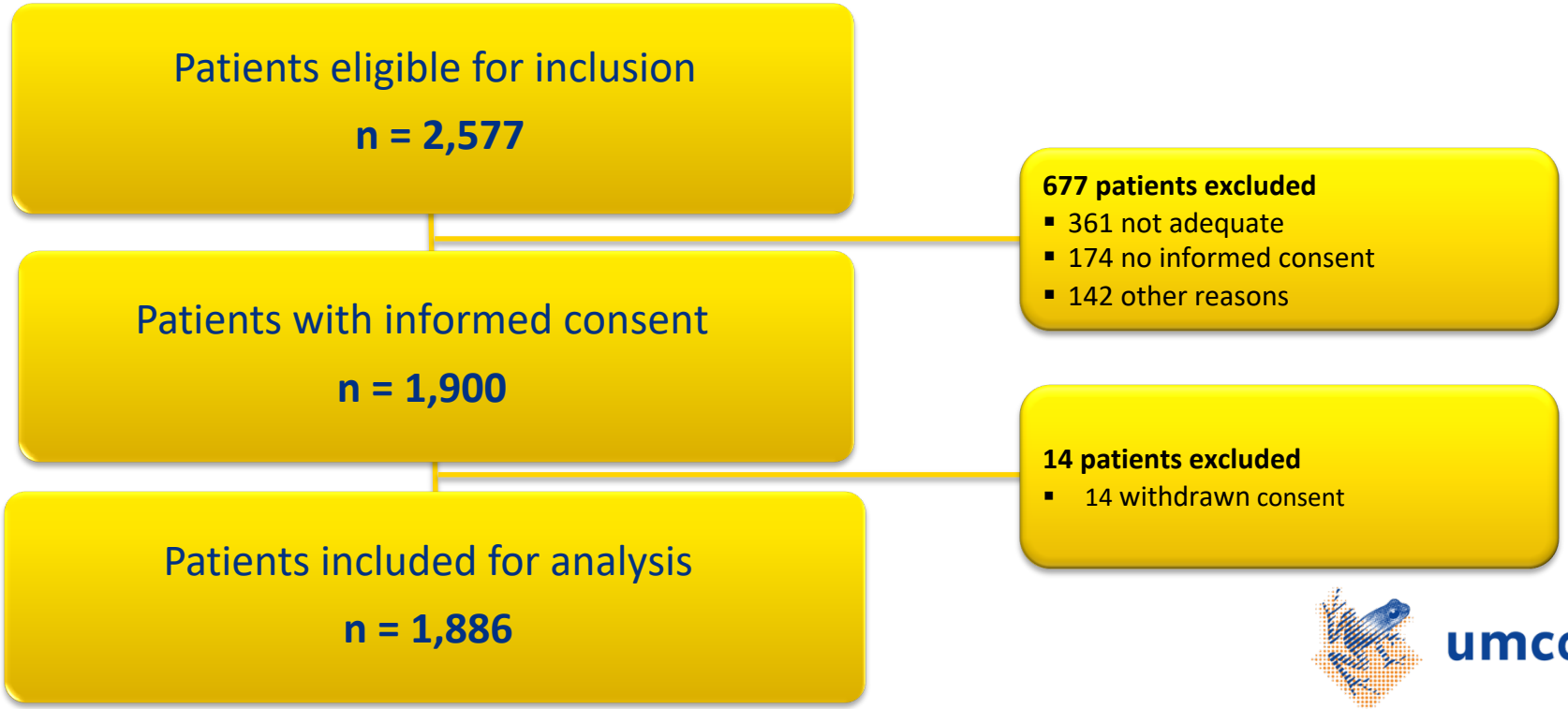
Study flow



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Patient characteristics (n=1,886)

Characteristic	Usual care period (n=941)	Intervention period (n=945)	p-value
Male gender	562 (59.7)	578 (61.2)	0.522
Age, years	69 [59-77]	69 [59-77]	0.665
Bleeding in history	198 (21.0)	269 (28.5)	< 0.001
Thrombotic event in history	448 (47.6)	461 (48.8)	0.610
Hospital type, University Medical Center	472 (50.2)	472 (49.4)	0.927
Bodyweight, kg	80 [70-91]	80 [70-93]	0.177
e-GFR, ≤50 ml/min/1.73m²	301 (33.0)	266 (30.1)	0.189
Readmission within 3 months after discharge	294 (31.2)	291 (30.8)	0.833
Surgery	340 (36.1)	330 (34.9)	0.583
Type of anticoagulant therapy*			
- Vitamin K antagonist	647 (68.8)	552 (58.4)	< 0.001
- Direct oral anticoagulant	80 (8.5)	263 (27.8)	< 0.001
- Low-molecular-weight-heparin	488 (51.9)	423 (44.8)	0.002

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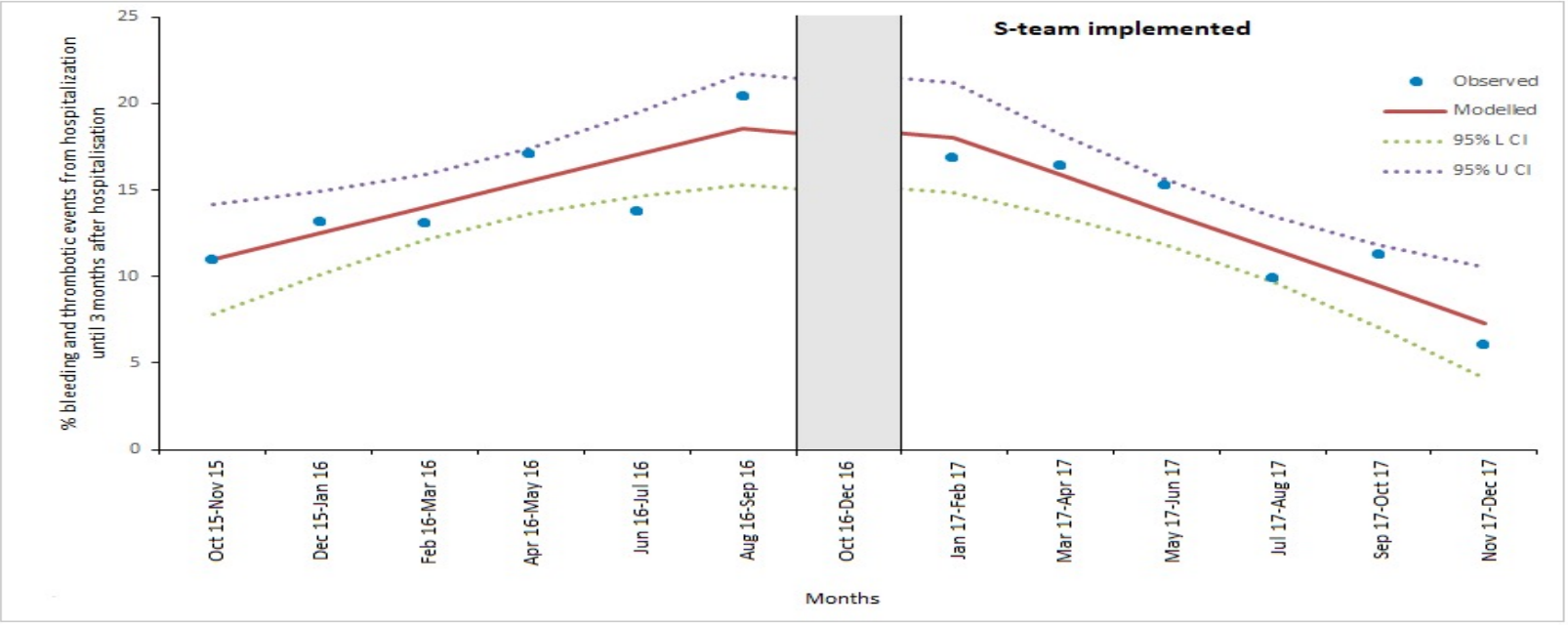
Primary outcome



	Y_0 (95% CI) (mean percentage at time=0)	$ß_1$ (95% CI) (baseline trend)	$ß_2$ (95% CI) (immediate change)	$ß_3$ (95% CI) (change in trend)
Bleeding and thrombotic events	9.49 (5.36 to 13.61)	0.75 (0.23 to 1.28)	1.63 (-3.60 to 6.85)	-1.83 (-2.58 to -1.08)

Bleeding and thrombotic events

	Usual care (n=941) N (%)	Intervention period (n=945) N (%)	RR (95% CI)
Bleeding events	136 (14.5)	130 (13.8)	0.95 (0.76-1.19)
Thrombotic events	25 (2.7)	20 (2.1)	0.80 (0.45-1.42)

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During vs after hospitalization
composite endpoint

	Usual care (n=941) N (%)	Intervention period (n=945) N (%)	RR (95% CI)
During	73 (7.8)	65 (6.9)	0.89 (0.64-1.22)
After	66 (7.0)	66 (7.0)	1.00 (0.72-1.38)

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Mortality and length of hospitalization

	Usual care (n=941) N (%)	Intervention period (n=945) N (%)	RR (95% CI)
Mortality	108 (11.5)	81 (8.6)	0.75 (0.57-0.98)
Length of hospitalization (days±SD)	11.8 (13.7)	10.7 (12.5)	P=0.08 (t-test)

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Subgroup analysis: type of antithrombotic

	Usual care (n=941) n/N (%)	Intervention period (n=945) n/N (%)	RR (95% CI)
Vitamin K antagonist	96/647 (14.8)	74/552 (13.4)	0.90 (0.68-1.20)
Direct oral anticoagulant	8/80 (10.0)	33/263 (12.5)	1.25 (0.60-2.61)
Low Molecular Weight Heparin	81/488 (16.6)	74/423 (17.5)	1.05 (0.79-1.40)

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Subgroup analysis: type of hospital

	Usual care (n=941) n/N (%)	Intervention period (n=945) n/N (%)	RR (95% CI)
General teaching hospital	53/469 (11.3)	47/473 (9.9)	0.88 (0.61-1.27)
University Medical Centre	82/472 (17.4)	77/472 (16.3)	0.93 (0.66-1.30)

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Mean costs per admission

	Usual care period €	Intervention period €
General teaching hospital		
• Labour costs S-Team	-	89
• Hospitalization costs	9360	8580
• Bleeding costs	944	908
• Thrombotic event costs	169	143
TOTAL	**10470**	**9680**
University Medical Centre		
• Labour costs S-Team	-	71
• Hospitalization costs	3970	3570
• Bleeding costs	600	514
• Thrombotic event costs	109	77
TOTAL	**4680**	**4200**

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Discussion & Conclusion

- Significant upward trend in the proportion of patients with the primary endpoint in the usual care period

- Implementation of a S-team over time reduces bleeding and thrombotic events

Multidisciplinary antithrombotic teams should become a core service in hospitals

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Questions?