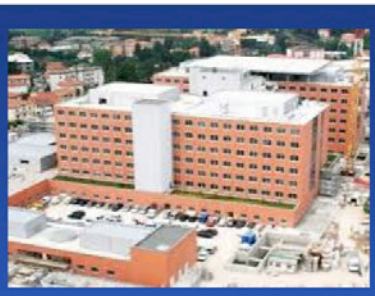
3° convegno di anticoagulazione.it
Bologna, 26 gennaio 2018



L'aderenza delle Terapie Anticoagulanti: problemi e prospettive

Alessandro Squizzato

Centro di Ricerca 'Malattie Tromboemboliche e Terapie Antitrombotiche'

Dipartimento di Medicina e Chirurgia
Università dell'Insubria - Varese

Impact of
on Morta

P. Michael Ho, MD,
Eric D. Peterson, MD

Background: Non
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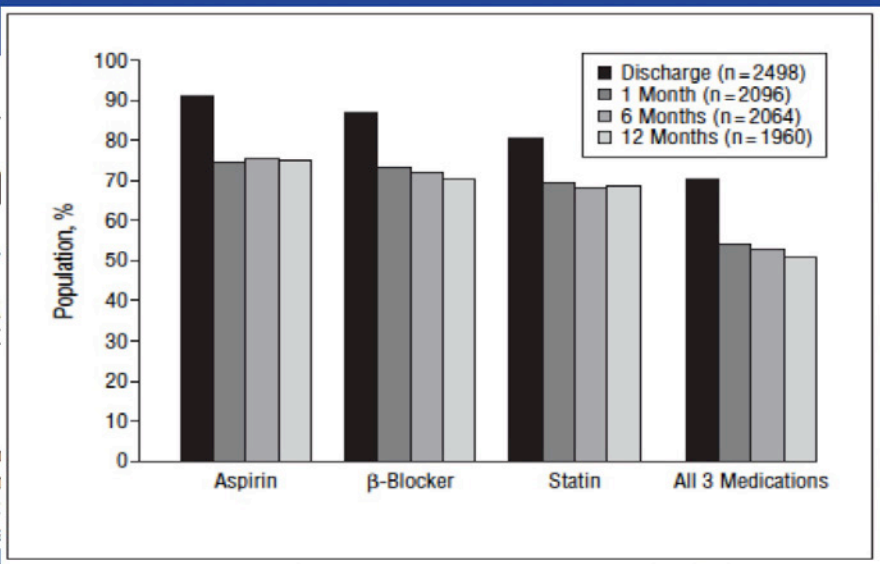


Figure 1. Rates of medication use for the entire cohort. $P<.001$ for trend for the 4 measurement periods (hospital discharge and 1, 6, and 12 months) for aspirin, β-blockers, statins, and all 3 medications.

on

. Reid, MS;
sfeld, MD, PhD

ns. The effect of in-
discontinuation was
CI, 1.34-2.34) than
). Patients who dis-
1 month had lower
-rank $P<.001$) com-

Arch Intern Med. 2006;166:1842-1847

Drugs don't work in patients who don't take them.

C. Everett Koop, M.D.

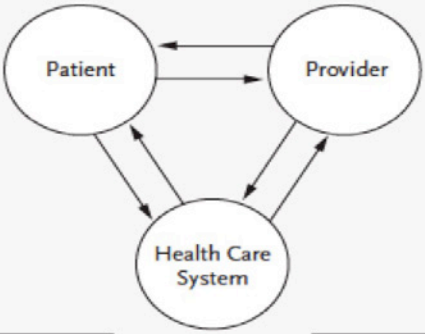
N Engl J Med 2005;353:487-97.

Table 2. Major Predictors of Poor Adherence to Medication, According to Studies of Predictors.

Predictor	Study
Presence of psychological problems, particularly depression	van Servellen et al.,[51] Ammassari et al.,[52] Stilley et al.[53]
Presence of cognitive impairment	Stilley et al.,[53] Okuno et al.[54]
Treatment of asymptomatic disease	Sewitch et al.,[55]
Inadequate follow-up or discharge planning	Sewitch et al.,[55] Lacro et al.[56]
Side effects of medication	van Servellen et al.[51]
Patient's lack of belief in benefit of treatment	Okuno et al.,[54] Lacro et al.[56]
Patient's lack of insight into the illness	Lacro et al.,[56] Perkins[57]
Poor provider–patient relationship	Okuno et al.,[54] Lacro et al.[56]
Presence of barriers to care or medications	van Servellen et al.,[51] Perkins[57]
Missed appointments	van Servellen et al.,[51] Farley et al.[58]
Complexity of treatment	Ammassari et al.[52]
Cost of medication, copayment, or both	Balkrishnan,[59] Ellis et al.[60]

N Engl J Med 2005;353:487-97.

Poor provider–patient communication
- Patient has a poor understanding of the disease
- Patient has a poor understanding of the benefits and risks of treatment
- Patient has a poor understanding of the proper use of the medication
- Physician prescribes overly complex regimen



Patient's interaction with the health care system
- Poor access or missed clinic appointments
- Poor treatment by clinic staff
- Poor access to medications
- Switching to a different formulary
- Inability of patient to access pharmacy
- High medication costs

Physician's interaction with the health care system
- Poor knowledge of drug costs
- Poor knowledge of insurance coverage of different formularies
- Low level of job satisfaction

N Engl J Med 2005;353:487-97.

Table 3. Strategies for Improving Adherence to a Medication Regimen.*

Identify poor adherence
- Look for markers of nonadherence: missed appointments ("no-shows"), lack of response to medication, missed refills
- Ask about barriers to adherence without being confrontational

Emphasize the value of the regimen and the effect of adherence

Elicit patient's feelings about his or her ability to follow the regimen, and if necessary, design supports to promote adherence

Provide simple, clear instructions and simplify the regimen as much as possible

Encourage the use of a medication-taking system

Listen to the patient, and customize the regimen in accordance with the patient's wishes

Obtain the help from family members, friends, and community services when needed

Reinforce desirable behavior and results when appropriate

Consider more "forgiving" medications when adherence appears unlikely†
- Medications with long half-lives
- Depot (extended-release) medications
- Transdermal medications

Problemi

- VKA

- DOACs

Initiator of anticoagulant treament:

- Sets indication for anticoagulation;
- Chooses anticoagulant, based also on patient preferences;
- Decides on need of proton pump inhibitor;
- Baseline hemoglobin, renal and liver function;
- Provides education;
- Hands out anticoagulation card;
- Organises follow-up (when, by whom, what?);
- Remains responsible coordinator for follow-up.

first FU: 1 month

Follow-up: GP; anticoagulant clinic; initiator of therapy; ...

- Checks:
  1. Adherence (remaining pills; NOAC card; ...);
  2. Thrombo-embolic events;
  3. Bleeding events;
  4. Other side effects;
  5. Co-medications and over-the-counter drugs.
  6. Need for blood sampling?

1 month?
3 months
max. 6 months

In case of problems: contacts initiator of treatment.

Else:
- fills out anticoagulation card
- sets date/place for next follow-up: interval depends on patient factors like renal function.

EUROPEAN SOCIETY OF CARDIOLOGY

Europace
doi:10.1093/europace/euv309

Table 3 Checklist during follow-up contacts of AF patients on anticoagulation[a]

	Interval	Comments
1. Adherence	Each visit	Instruct patient to bring NOAC card and remaining medication: make note and assess average adherence Re-educate on importance of strict intake schedule Inform about adherence aids (special boxes, smartphone applications, etc.)
2. Thromboembolism	Each visit	Systemic circulation (TIA, stroke, and peripheral) Pulmonary circulation
3. Bleeding	Each visit	'Nuisance' bleeding: preventive measures possible? (PPI, haemorrhoidectomy, etc.). Motivate patient to diligently continue anticoagulation Bleeding with impact on quality of life or with risk: prevention possible? Need for revision of anticoagulation indication or dose?
4. Other side effects	Each visit	Carefully assess relation with NOAC: decide for continuation (and motivate), temporary cessation (with bridging), or change of anticoagulant drug
5. Co-medications	Each visit	Prescription drugs; over-the-counter drugs, especially aspirin and NSAID (see 'Drug–drug interactions and pharmacokinetics of non-vitamin K antagonist anticoagulants' section) Careful interval history: also temporary use can be risky!
6. Blood sampling	Yearly 6-monthly x-monthly On indication	Haemoglobin, renal and liver function ≥75–80 years (especially if on dabigatran or edoxaban), or frail[b] If renal function ≤60 mL/min: recheck interval = CrCl/10 If intercurrent condition that may impact renal or hepatic function

TIA, transient ischaemic attack; PPI, proton pump inhibitor; CrCl, creatinine clearance (preferably measured by the Cockcroft method).
[a]For frequency of visits: see *Figure 2*.
[b]Frailty is defined as three or more criteria of unintentional weight loss, self-reported exhaustion, weakness assessed by handgrip test, slow walking speed, or low physical activity.[34]
On online frailty calculator can be found at http://www.biomedcentral.com/1471-2318/10/57 under Additional Files.

Europace
doi:10.1093/europace/euv309

Adherence and outcomes to direct oral

Patient Characteristics	All *n* = 2882	Dabigatran *n* = 2096 (72.7%)	Rivaroxaban *n* = 571 (19.8%)	Apixaban *n* = 215 (7.5%)	*p*
Adherence					
Mean (SD) pill count per dispensed supply	38.1 (20.9)	38.2 (20.8)	38.2 (22.0)	36.4 (18.7)	<0.01
Proportion of Days Covered (mean + SD)	0.85 (0.19)	0.84 (0.20)	0.86 (0.18)	0.89 (0.14)	<0.01
PDC < 80% n (%)	796 (27.6%)	604 (28.8%)	143 (25.0%)	49 (22.8%)	0.05

Ryan T. Borne[1], Colin O'Donnell[2], Mintu P. Turakhia[3,4*], Paul D. Varosy[1,2], Cynthia A. Jackevicius[5], Lucas N. Marzec[1], Frederick A. Masoudi[1], Paul L. Hess[1,2], Thomas M. Maddox[6] and P. Michael Ho[1,2]

Borne *et al. BMC Cardiovascular Disorders* (2017) 17:236

	Rivaroxaban		Dabigatran		Apixaban	
3 Months						
PDC,[a] mean (SD)	0.84	(0.24)	0.77	(0.28)	0.82	(0.26)
≥0.80, n (%)	2,521	(73.0)	783	(62.0)	354	(70.2)
0.50-0.79, n (%)	424	(12.3)	202	(16.0)	67	(13.3)
<0.50, n (%)	510	(14.8)	279	(22.1)	83	(16.5)
Gaps,[b] n (%)						
≥15 days	336	(9.7)	170	(13.5)	72	(14.3)
≥30 days	123	(3.6)	61	(4.8)	33	(6.6)
≥60 days	18	(0.5)	8	(0.6)	7	(1.4)
Switch,[c] n (%)						
Other OAC	198	(5.7)	179	(14.2)	32	(6.4)
Antiplatelet	59	(1.7)	31	(2.5)	6	(1.2)
6 Months						
PDC,[a] mean (SD)	0.75	(0.31)	0.67	(0.33)	0.75	(0.29)
≥0.80, n (%)	1,711	(63.5)	561	(53.6)	201	(61.9)
0.50-0.79, n (%)	429	(15.9)	173	(16.5)	63	(19.4)
<0.50, n (%)	554	(20.6)	312	(29.8)	61	(18.8)
Gaps,[b] n (%)						
≥15 days	483	(17.9)	268	(25.6)	102	(31.4)
≥30 days	252	(9.4)	128	(12.2)	62	(19.1)
≥60 days	84	(3.1)	51	(4.9)	19	(5.9)
Switch,[c] n (%)						
Other OAC	224	(8.3)	195	(18.6)	30	(6.7)
Antiplatelet	67	(2.5)	40	(3.8)	8	(2.5)
9 Months						
PDC,[a] mean (SD)	0.70	(0.34)	0.62	(0.35)	0.71	(0.32)
≥0.80, n (%)	838	(55.0)	309	(46.7)	63	(56.8)
0.50-0.79, n (%)	229	(15.0)	97	(14.7)	21	(18.9)
<0.50, n (%)	457	(30.0)	256	(38.7)	27	(24.3)
Gaps,[b] n (%)						
≥15 days	366	(24.0)	225	(34.0)	45	(40.5)
≥30 days	220	(14.4)	124	(18.7)	27	(7.3)
≥60 days	106	(7.0)	60	(9.1)	14	(12.6)
Switch,[c] n (%)						
Other OAC	153	(10.0)	129	(19.5)	12	(10.8)
Antiplatelet	48	(3.2)	29	(4.4)	4	(3.6)

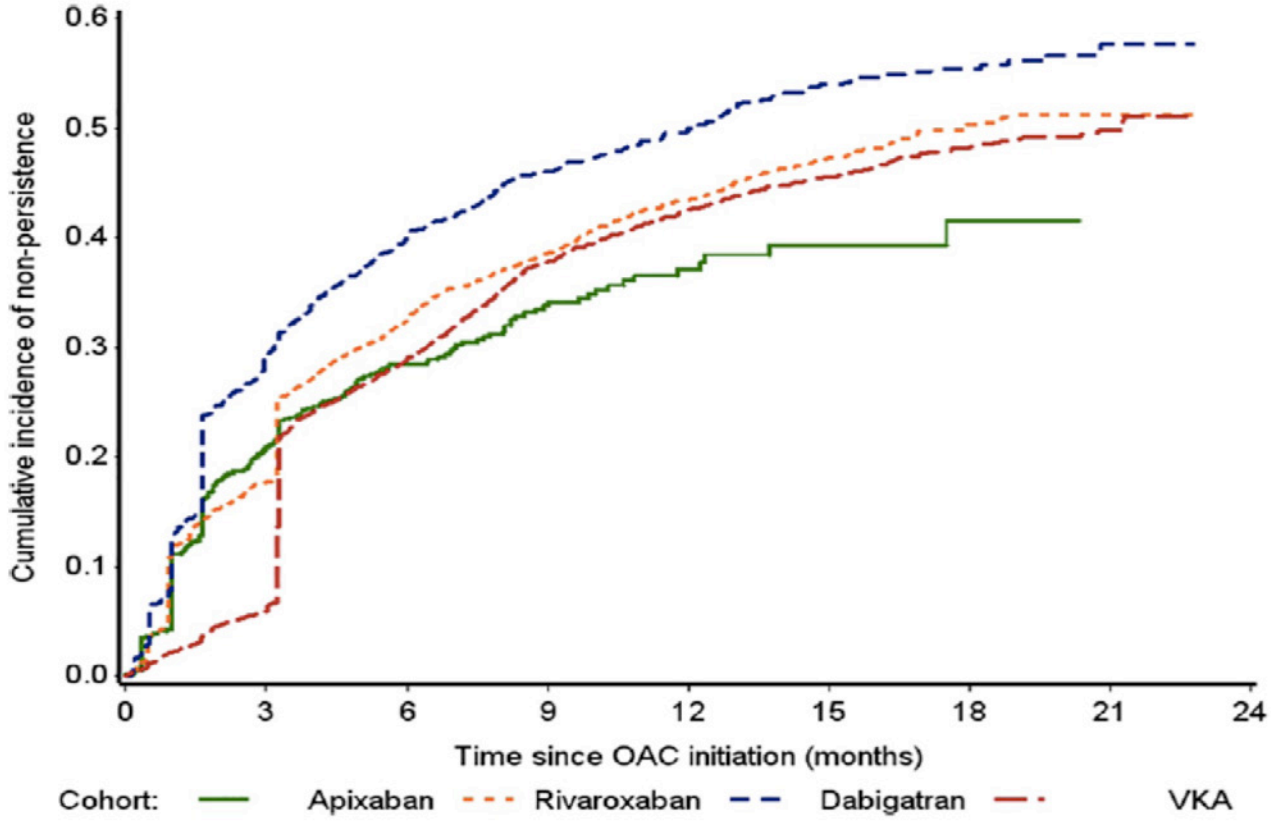
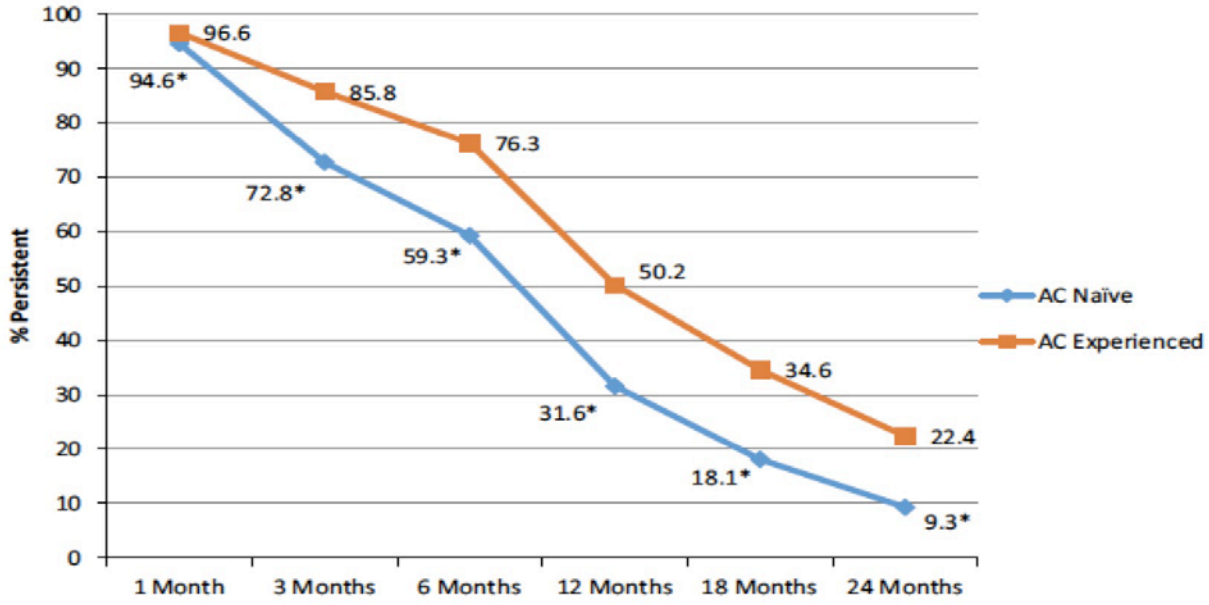


Fig 3. Cumulative incidence of OAC non-persistence.



AC Naïve (N)	29,148	22,432	18,268	9,743	5,591	2,870
AC Experienced (N)	34,064	30,269	26,891	17,707	12,203	7,885

Prospettive

- VKA
- DOACs

Cardiovascular Perspective

Reimagining Anticoagulation Clinics in the Era of Direct Oral Anticoagulants

Geoffrey D. Barnes, MD, MSc; Brahmajee K. Nallamothu, MD, MPH;
Anne E. Sales, PhD, RN; James B. Froehlich, MD, MPH

Abstract—Anticoagulation clinics were initially developed to provide safe and effective care for warfarin-treated patients with atrial fibrillation, venous thromboembolism, and mechanical valve replacement. Traditionally, these patients required ongoing laboratory monitoring and warfarin dose adjustment by expert providers. With the introduction of direct oral anticoagulants (dabigatran, rivaroxaban, apixaban, and edoxaban), many have questioned the need for anticoagulation clinic. However, we think that the growing number of oral anticoagulant choices creates an urgent need for expanding the traditional role of the anticoagulation clinic. We outline 3 key purposes that a reimagined anticoagulation clinic

Circ Cardiovasc Qual Outcomes. 2016;9:182-185.

1. Nuovi modelli organizzativi

2. Nuovi modelli di servizi

Modelli organizzativi

- GP-based
- Nurse-based
- Pharmacist-based
- Junior doctor/Resident-based

Perché i Centri Emostasi hanno ridotto ...

Visite in PS

Ospedalizzazioni

Episodi tromboembolici

Episodi emorragici

Rudd KM et al. Pharmacotherapy 2010

Anticoagulation clinic: 3 finalità ...

1. Selezionare il migliore AC (TAO/DOAC) al dosaggio ottimale

2. Minimizzare il rischio emorragico

   (fattori di rischio, farmaci concomitanti, funzione renale/epatica, gestione periprocedurale)

3. Incoraggiare l'aderenza alla terapia

Pros

(anticoagulation clinic)

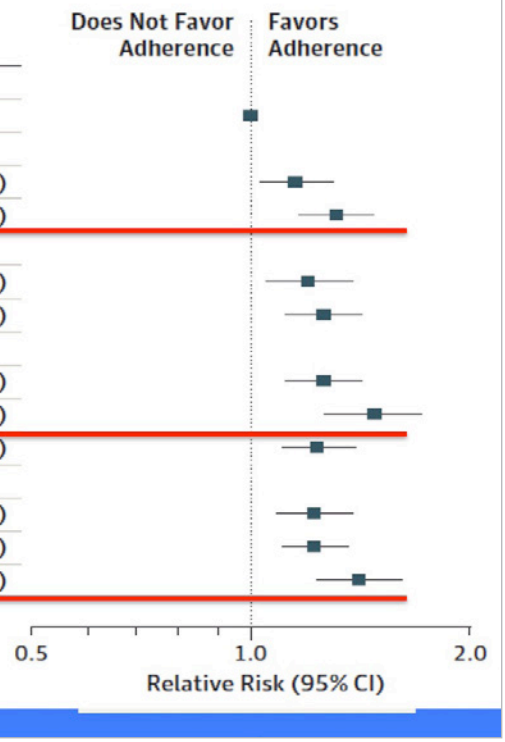
Più tempo a disposizione per i pazienti +
Risposte più rapide e precise =
Aumenta l'aderenza

Controllo esami ematici (20% IR in FA) =
Meno emorragie

Centralizzazione delle sospensioni =
Minimizzazione dei rischi e meno 'lavoro' per MMG, cardiologo, anestesista, chirurgo, etc.

Figure 3. Forest Plot Showing Association Between Various Monitoring Strategies and Patient Adherence to Dabigatran

Adjusted Association With Adherence	Total No. of Patients	No. of Adherent Patients (Unadjusted, %)	Relative Risk (95% CI)
Treatment management strategy			
No monitoring	1042	679 (65.2)	1 [Reference]
Tailored management			
No tailoring to nonadherent	826	610 (73.8)	1.15 (1.03-1.29)
Tailored to nonadherent	1117	885 (79.2)	1.31 (1.16-1.47)
Provider			
Outpatient pharmacists	472	352 (74.6)	1.20 (1.05-1.37)
Anticoagulation clinic	1471	1143 (77.7)	1.26 (1.12-1.42)
Mode of contact			
Telephone or face to face	320	257 (80.3)	1.26 (1.11-1.42)
Face to face	198	167 (84.3)	1.47 (1.26-1.72)
Telephone only	1425	1072 (75.2)	1.24 (1.10-1.39)
Duration of monitoring, mo			
3	1176	880 (74.8)	1.22 (1.08-1.38)
6	362	278 (76.8)	1.23 (1.10-1.37)
>12	405	337 (83.2)	1.41 (1.23-1.61)



Nostra esperienza ...

- GP-based
- Nurse-based
- Pharmacist-based
- Junior doctor/Resident-based


CARTELLA INFERMIERISTICA
2007


EFFETTO DOTTOR HOUSE...
NON MI FIDO

Results Before nurse monitoring, INR values were out of range 20.4% of the time; after nurse monitoring they were out of range 19.2% of the time ($P=.115$); the time between sequential INR readings also did not differ before and after implementation of nurse monitoring (23.9 vs 21.6 days, $P=.789$).

Conclusion Nurse-led monitoring of INR is as effective as traditional physician monitoring. Advantages of nurse-led monitoring might include freeing family physicians to see more patients or to spend less time at work. It might also represent potential cost savings.

examined.

Intervention Implementation of nurse-led monitoring in a primary care network in place of standard family physician INR monitoring.

EDITOR'S KEY POINTS

- Given warfarin's narrow therapeutic index, it requires extensive monitoring through measurement of the international

Can Fam Physician 2012;58:e465-71

Neth Heart J (2014) 22:297–300
DOI 10.1007/s12471-014-0529-9

SHORT COMMUNICATION

Practical introduction of novel oral anticoagulants through an anticoagulation nurse. The Leeuwarden model

R. J. Folkeringa · L. M. Geven · T. Veldhuis · M. Hoogendoorn · S. H. Hofma · E. Van Roon

Sistema Socio Sanitario
Regione Lombardia
ASST Sette Laghi

PER QUALI PAZIENTI?

PAZIENTI SELEZIONATI DAL PERSONALE MEDICO:

- Che non necessitano di valutare la durata della terapia

- STABILI ALLE VISITE PRECEDENTI:
  - Esami ematochimici nella norma
  - Non note necessità di procedure/interventi

Sistema Socio Sanitario
Regione Lombardia
ASST Sette Laghi
Ospedale di Circolo Fondazione Macchi

Ospedale di Circolo e Fondazione Macchi
AZIENDA SOCIO SANITARIA TERRITORIALE DEI SETTE LAGHI

Facoltà di Medicina e Chirurgia

Centro Trombosi ed Emostasi
Responsabile: Prof. Walter Ageno

Centro Trombosi ed Emostasi
Dirigenti Medici
Dr. Luigi Striuli
Prof. Walter Ageno
Prof. Alessandro Squizzato
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Infermieri Professionali
Emanuela Longo
Rosy Maffei
Gabriele Pinnagro
De Iorio Laura

Segreteria Centro Trombosi ed Emostasi
Rita Lombardo
Tel 0332-278831
Fax 0332-278118
Orari:
da Lun a Ven h. 9.00-14.00
Orari prenotazioni telefoniche:
da Lun a Ven h. 10:00-14:00

Ambulatori
Sorveglianza terapie antitrombotiche
Trombofilia
Ecografia Vascolare Venosa
Follow-up nuove terapie anticoagulanti

Controllo terapeutico – DOACs - Scheda infermieristica

Data:

NOME:	COGNOME:
DATA DI NASCITA:	TEL:
E-MAIL :	

PATOLOGIA:
FARMACO ASSUNTO: DOSE GIORNALIERA:

Data del piano terapeutico:

Aderenza alla terapia	
Dimenticanze	
Variazioni terapia domiciliare	
Sanguinamenti	
Nuovi eventi tromboembolici	
Effetti collaterali	
Necessità di sospensione	

Esami ematici eseguiti in data:

Hb (g/dL)		PTL/mm3	
AST/GOT		ALT/GPT	
Anni compiuti		Peso	
Creatinina (mg/dL)		Clearance della creatinina mL/min	

L'Infermiere Refertante:

Cons
(anticoagulation clinic nurse-based)

Normativo: impossibilità prescrittiva

Formativo: non completa indipendenza

Culturale: 'Voglio il dottore !'

Organizzativo: Visita DOAC-based

Modelli di servizi

Insufficiente: prescription clinics

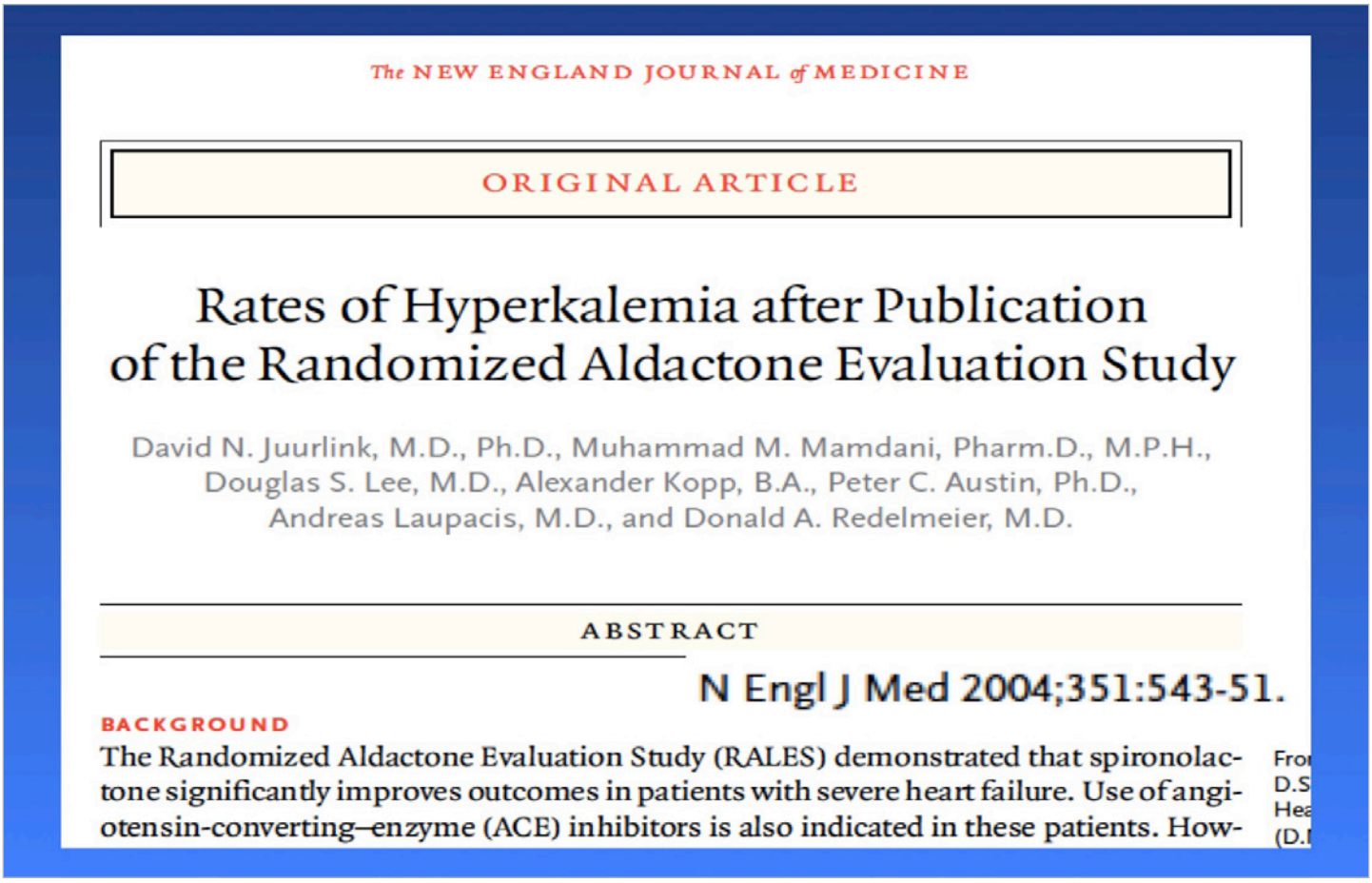
Medication safety clinics

Anticoagulante

Antiaritmico (e.g. amiodarone)

Diuretico (e.g. antialdosteronico)

Polifarmaco terapia
(e.g. diuretico, antiipertensivo, FANS)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rates of Hyperkalemia after Publication of the Randomized Aldactone Evaluation Study

David N. Juurlink, M.D., Ph.D., Muhammad M. Mamdani, Pharm.D., M.P.H., Douglas S. Lee, M.D., Alexander Kopp, B.A., Peter C. Austin, Ph.D., Andreas Laupacis, M.D., and Donald A. Redelmeier, M.D.

ABSTRACT

N Engl J Med 2004;351:543-51.

BACKGROUND

The Randomized Aldactone Evaluation Study (RALES) demonstrated that spironolactone significantly improves outcomes in patients with severe heart failure. Use of angiotensin-converting–enzyme (ACE) inhibitors is also indicated in these patients. How-

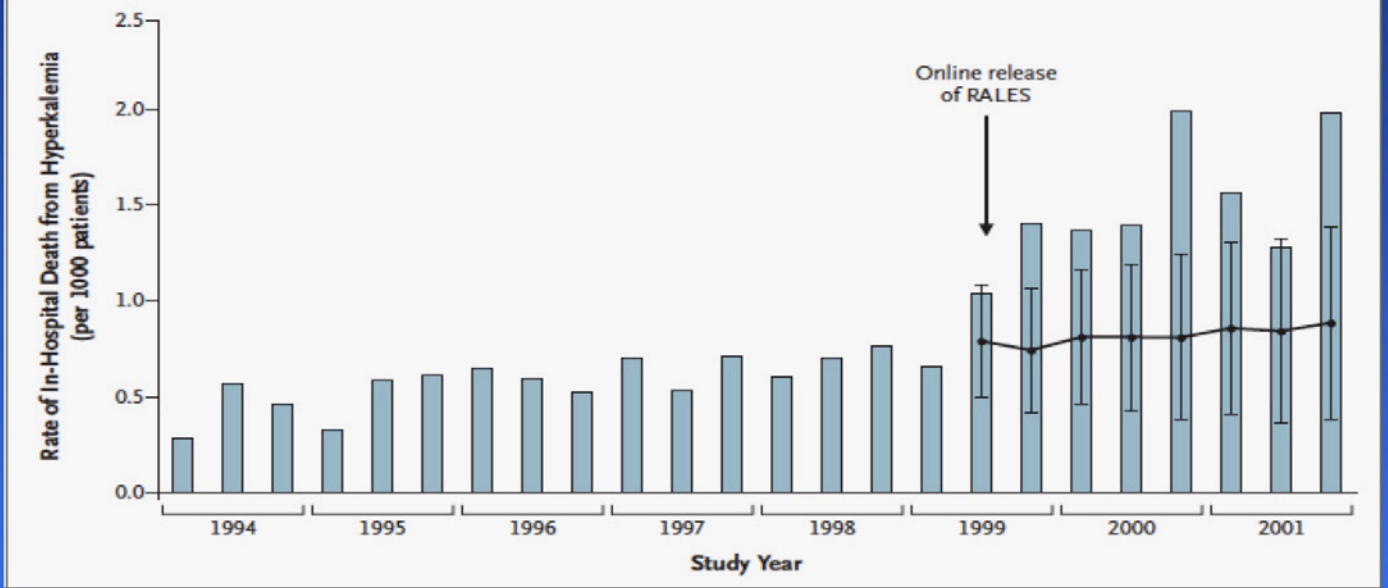


Figure 3. Rate of In-Hospital Death Associated with Hyperkalemia among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Each bar shows the rate of in-hospital death associated with hyperkalemia per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 shows projected death rates derived from interventional ARIMA models, with I bars representing the 95 percent confidence intervals.

Table 1. Observed Laboratory Testing of Potassium and Creatinine Levels Among Patients Initiating Mineralocorticoid Receptor Antagonist Therapy for Heart Failure

	No. (%) of Patients (N = 10 443)
Preinitiation testing (120 d before drug initiation)	
Appropriate[a]	9564 (91.6)
None	879 (8.4)
Early postinitiation testing (1-10 d after drug initiation)	
Appropriate[b]	1384 (13.3)
Any	4661 (44.6)
None	5782 (55.4)
Extended postinitiation testing (11-90 d after drug initiation)	
Appropriate[c]	3122 (29.9)
Any	8115 (77.7)
None	2328 (22.3)
Received all appropriate testing	756 (7.2)
No preinitiation or postinitiation testing	280 (2.7)

[a] Defined by the presence of at least 1 laboratory claim (or hospitalization) within 120 days before drug initiation.

[b] Defined by the presence of 2 laboratory claims (or hospitalizations or 1 laboratory claim plus hospital discharge within 3 days before initial outpatient prescription fill) within 10 days after drug initiation.

[c] Defined by the presence of 3 laboratory claims (or hospitalizations) within 11 to 90 days after drug initiation.

Bleeding Risk with Dabigatran in the Frail Elderly

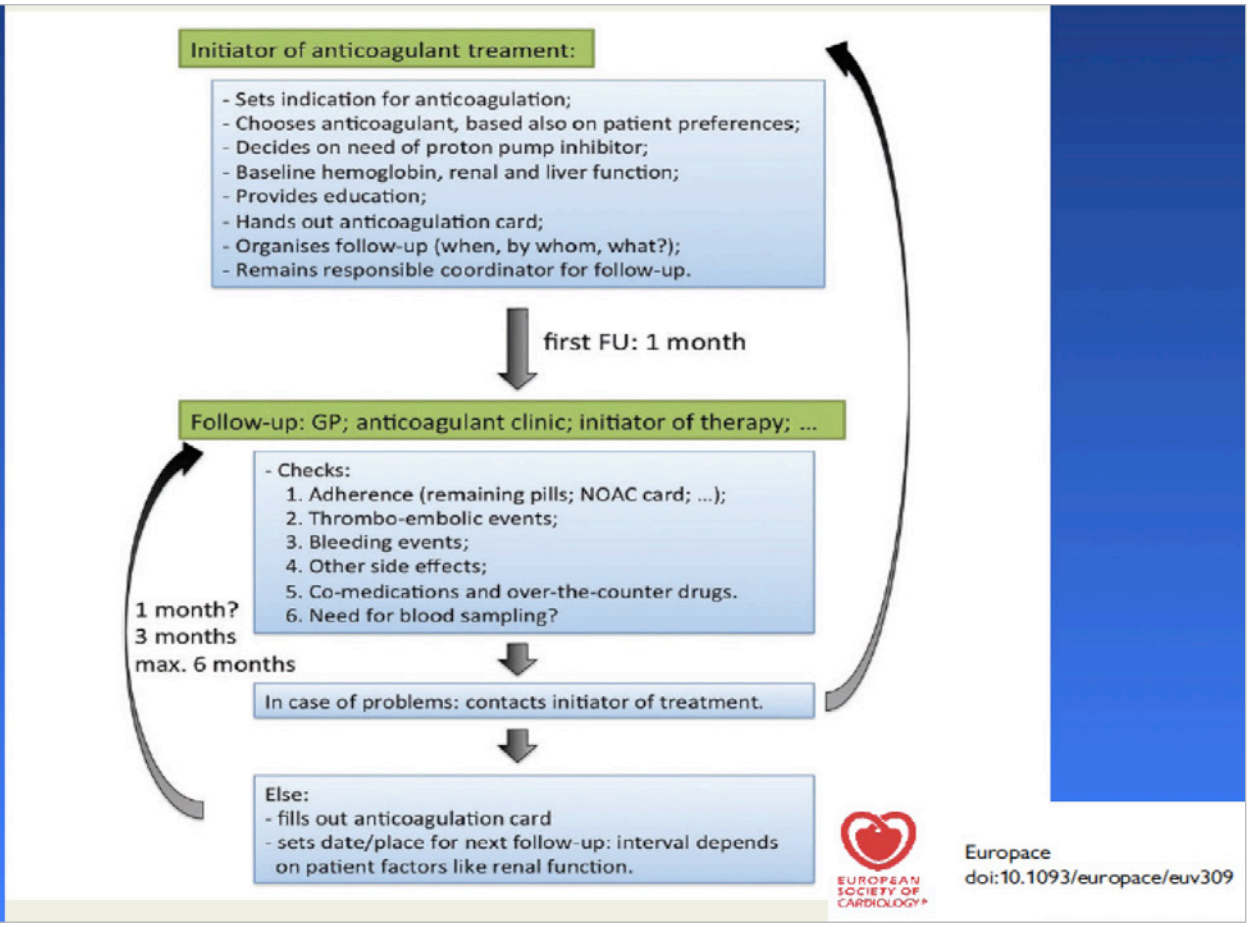
TO THE EDITOR: Since July 1, 2011, the thrombin inhibitor dabigatran has been available in New Zealand for stroke prevention in patients with atrial fibrillation. There are no restrictions on prescribing, and access is free to patients through government funding. Approximately 7000 patients started treatment in the first 2 months.

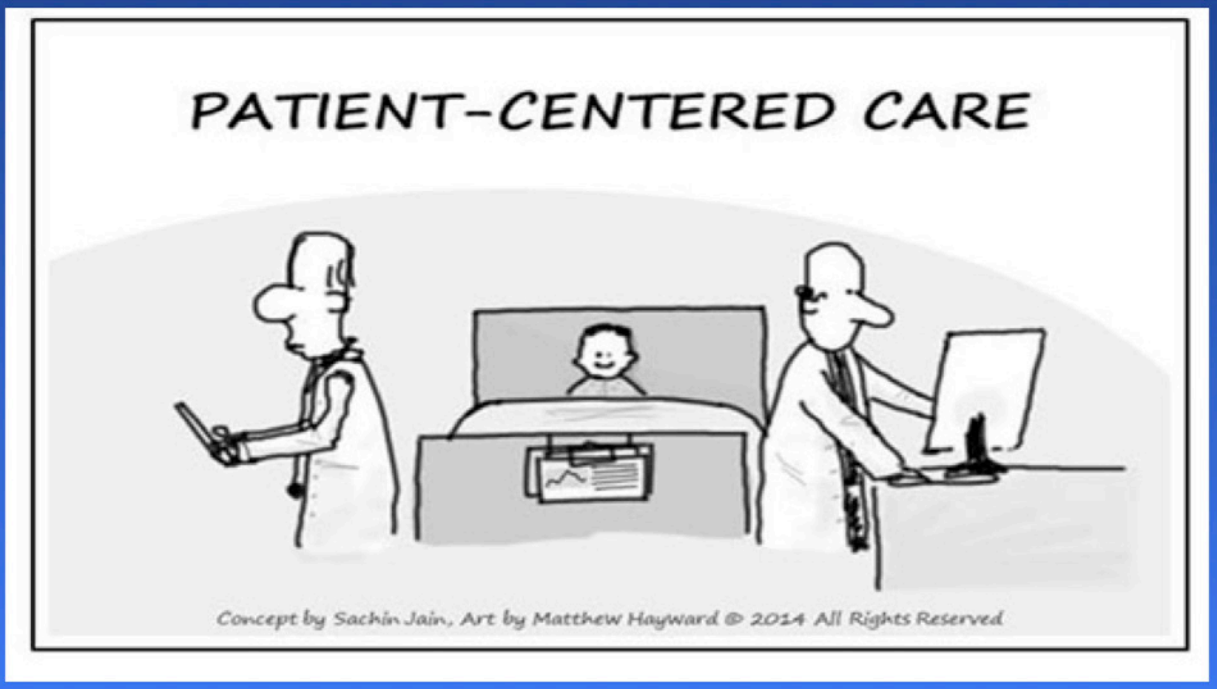
Concerns from hematologists led to an audit of bleeding events that was initiated in collaboration with the Haematology Society of Australia

Table 1. Details of Episodes of Bleeding in 44 Patients Taking Dabigatran.*

Patient No.	Age	Sex	Weight	Daily Dose†	Site of Bleeding	Degree of Renal Impairment‡	Required Blood Products§
	yr		*kg*	*mg*			
1	65	M	129	300	Mucosal	Severe	No
2¶	71	M	NA	300	Hematuria	Moderate	No
3‖	77	M	60	300	Rectal	Moderate	Yes
4	78	F	NA	220	Rectal	Moderate	No
5‖	40	M	94	220	Rectal	Mild	Yes
6	65	F	79	300	Postoperative	Mild	Yes
7	71	M	75	300	Hematuria	Mild	No
8	74	M	100	220	Hematuria	Mild	No
9	75	F	NA	220	Rectal	Mild	Yes

N ENGL J MED 366;9 NEJM.ORG MARCH 1, 2012





”I may not speak, but I have much to say”

The ‘Angel’ Pietro