INR Patient Self-Testing: Yesterday, Today and Beyond

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Agenda

- Patient Self-Testing/Patient Self-Management Beginnings
- Warfarin
  - Management Challenges
  - Testing Variability
- Anticoagulation Management Models
- THINRS PST Clinical Trial
- RE-LY Clinical Trial
  - First Fixed Dose, Non-Monitored Anticoagulant
- Patient Self-Testing
- Futures
- Conclusions

INR Self Management in Germany

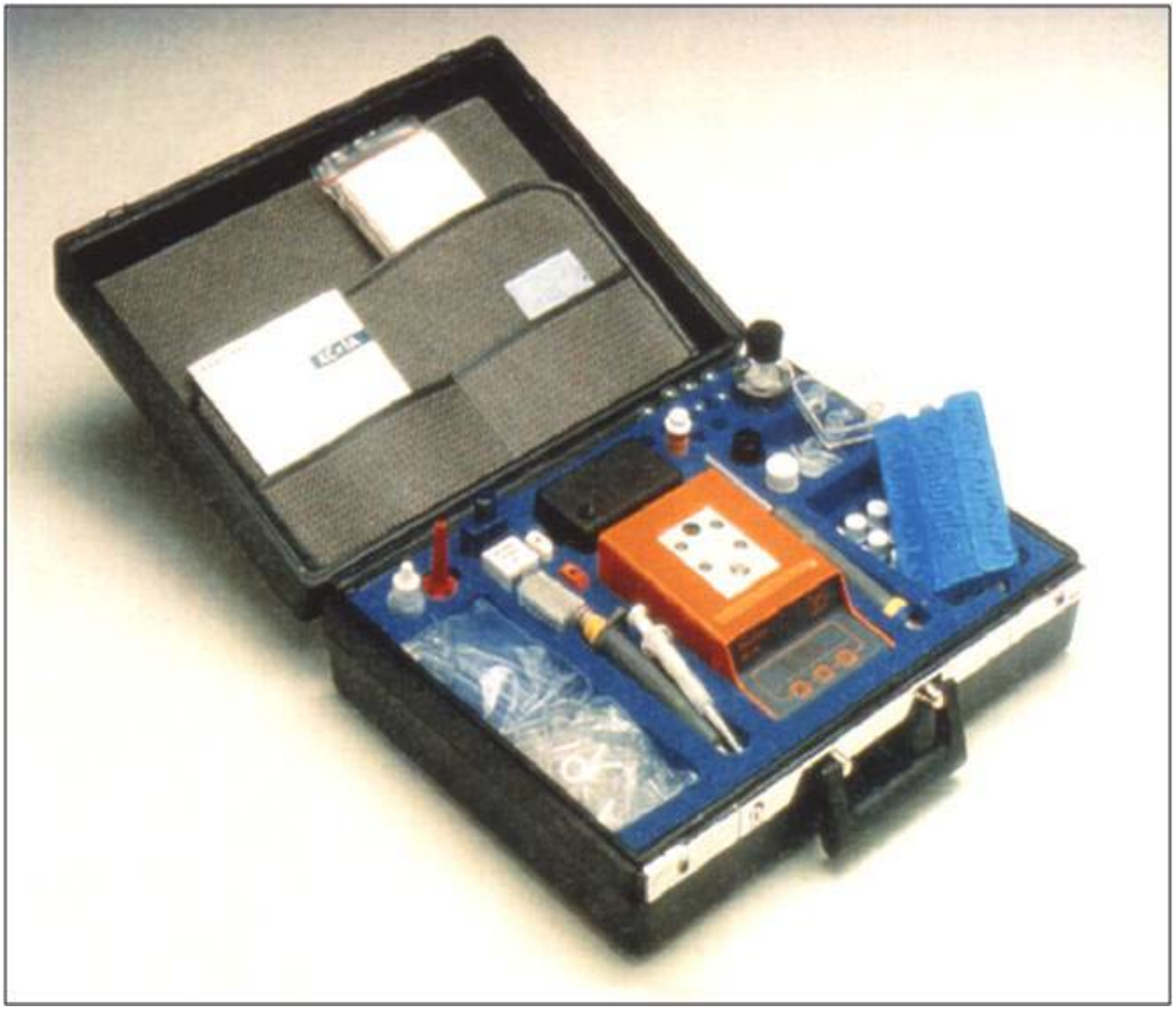
1986: A student Heike Moeller demonstrated during a doctor-patient seminar that she was able to monitor her INR results by herself.

Cardiovascular clinic Bad Berleburg: the first rehab center to teach INR self-management

Dr. Carola Halhuber, former director of the cardiovascular clinic decided to adopt the idea of INR Self-management

Heike Moeller-Jung

Amelung KC-1A

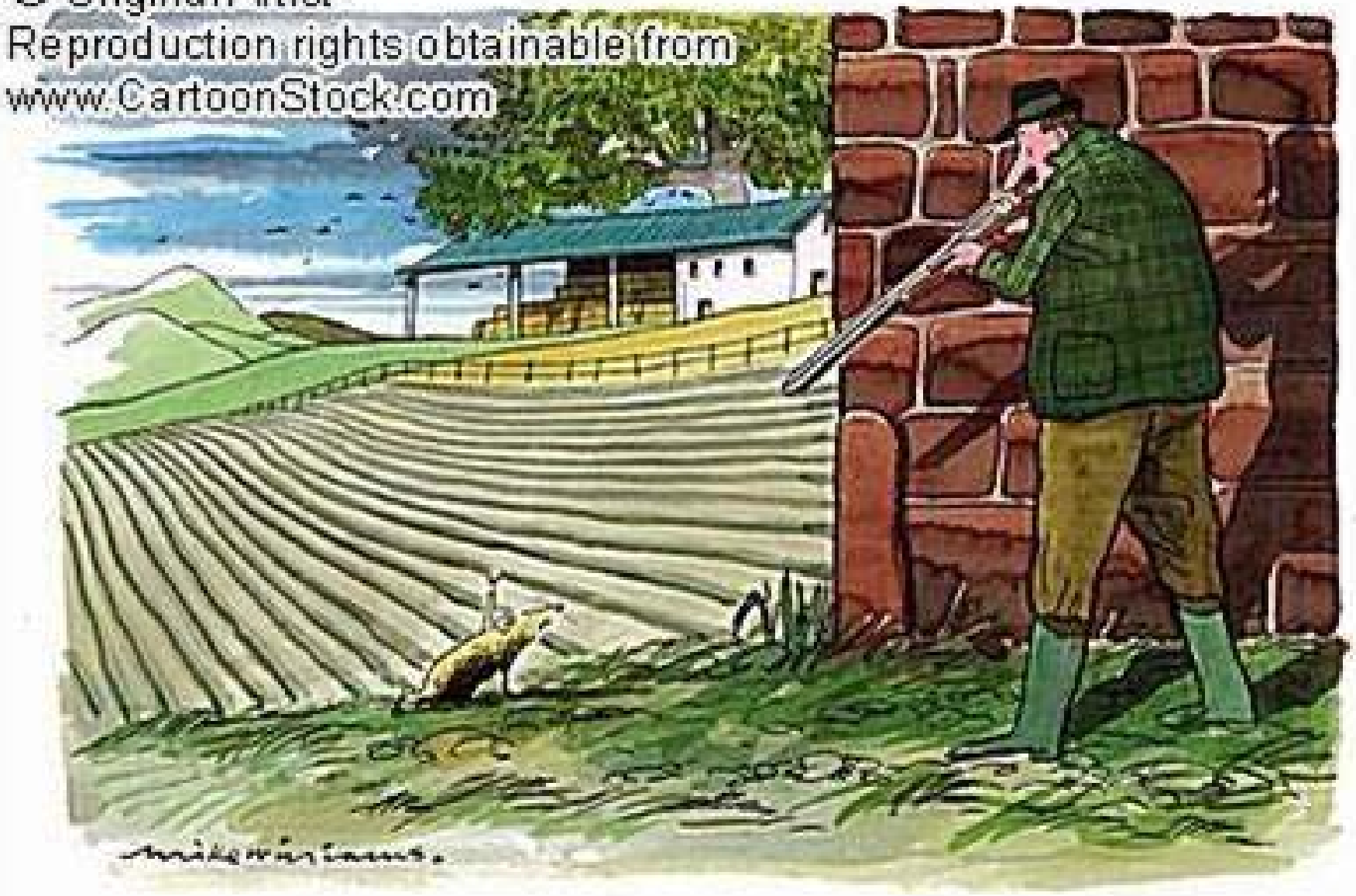


Warfarin: What is it and why is it difficult to manage?

Crystalline Warfarin Sodium

(Coumadin®)

- In the 1920's … cattle were dying due to unknown hemorrhagic disease.
- Traced to improperly cured sweet clover.
- Active agent is dicumarol, which is derived from coumarin, a sweet-smelling but coagulation-inactive chemical found in clover.
- A Vitamin K antagonist or VKA.
- Therapeutic agent – Named for discovery by the Wisconsin Alumni Research Foundation and the ending *-arin,* indicating its link with coumarin.
- Initially and today marketed as a pesticide against rats and mice.
- Approved for use as a medication in 1954.
- Warfarin or trade name Coumadin marketed by DuPont until sold to BMS in 2001.
- Barr was first generic to enter the market in 1997.



"Hold it, I wonder if I might try the warfarin again?"

Crystalline Warfarin Sodium
(Coumadin®)

- Considered a narrow therapeutic index drug (NTI).
- Therapeutic effect sensitive to:
  - Diet, alcohol
  - Exercise
  - Concurrent and intercurrent diseases
  - Competing/conflicting drugs
- Management challenges tend to be independent of clinical indications

Crystalline Warfarin Sodium
(Coumadin®)

- > 50 % of patients within a practice will be out of the therapeutic range at any given time.
- Atrial fibrillation (AFib) – affects >2.0MM Medicare beneficiaries.
- Patients are more commonly under dosed for “safety” reasons
  - Cause of 20-25% of all strokes
- Warfarin under dosed despite clear indications for it use.
- Usage estimates vary but conventional wisdom puts it at <60% in diagnosed A Fib patients.

Primary Goal of AC Therapy is to Maintain Patient in the Therapeutic Range

- Recommended range has been empirically determined over the last several decades.
- Defined as the range where the greatest benefit coincides with the fewest adverse events.
- Conversely, fewer AEs occur if patient is maintained in the therapeutic range.
- Patient can get out of range quickly and unpredictably.

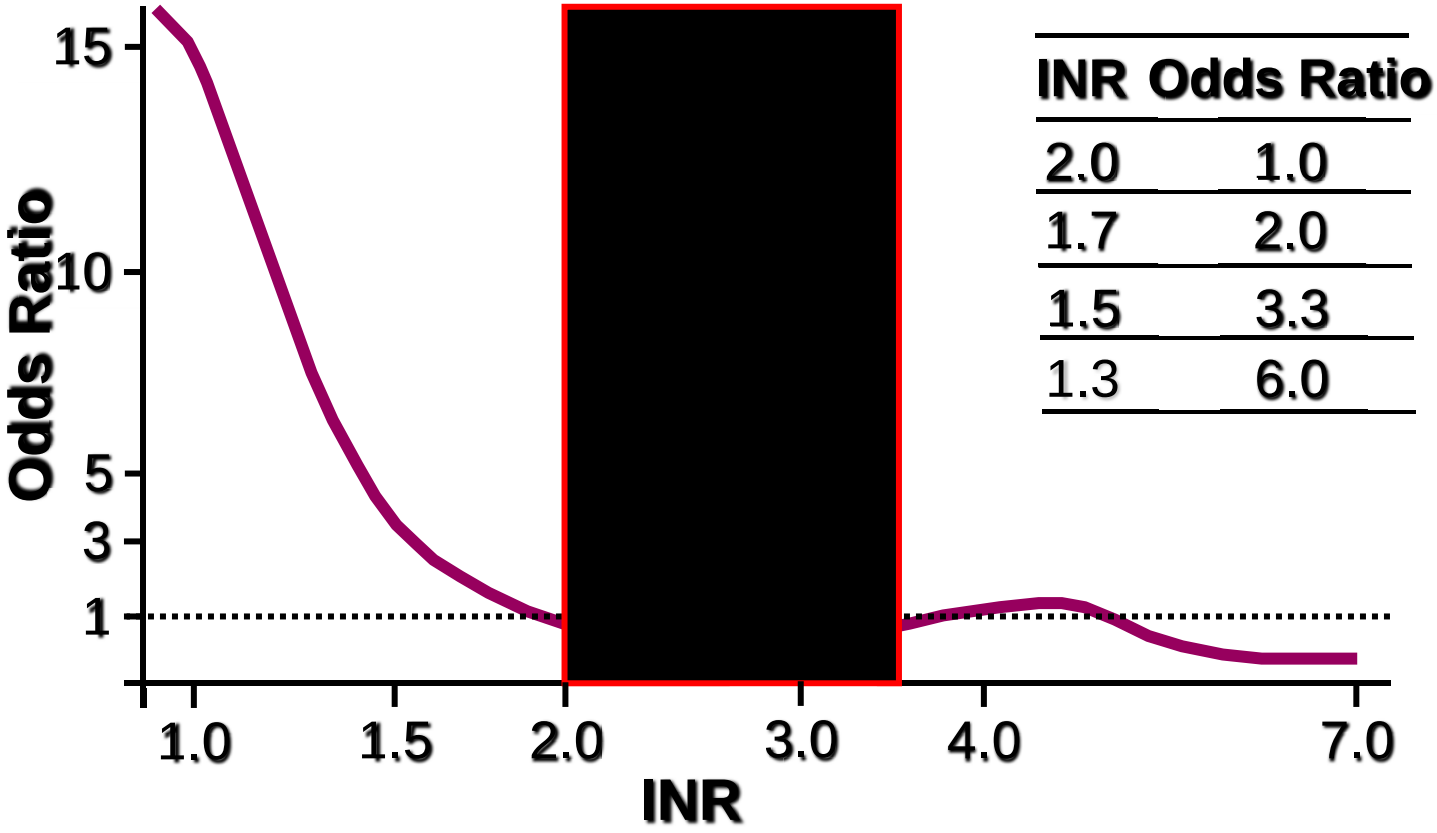
“The general recommendation for warfarin monitoring to be performed once every 4-6 weeks is not based on the pharmacokintitics nor clotting factor half life but rather by the practical constraints of access and cost balanced against complications”.

David Matchar, MD

Director, Duke Center for Clinical Health Policy Research
Professor and Director, Health Services Research at Duke University

Co-Principal Investigator THINRS Clinical Trial

Lowest Effective Intensity for Warfarin Therapy

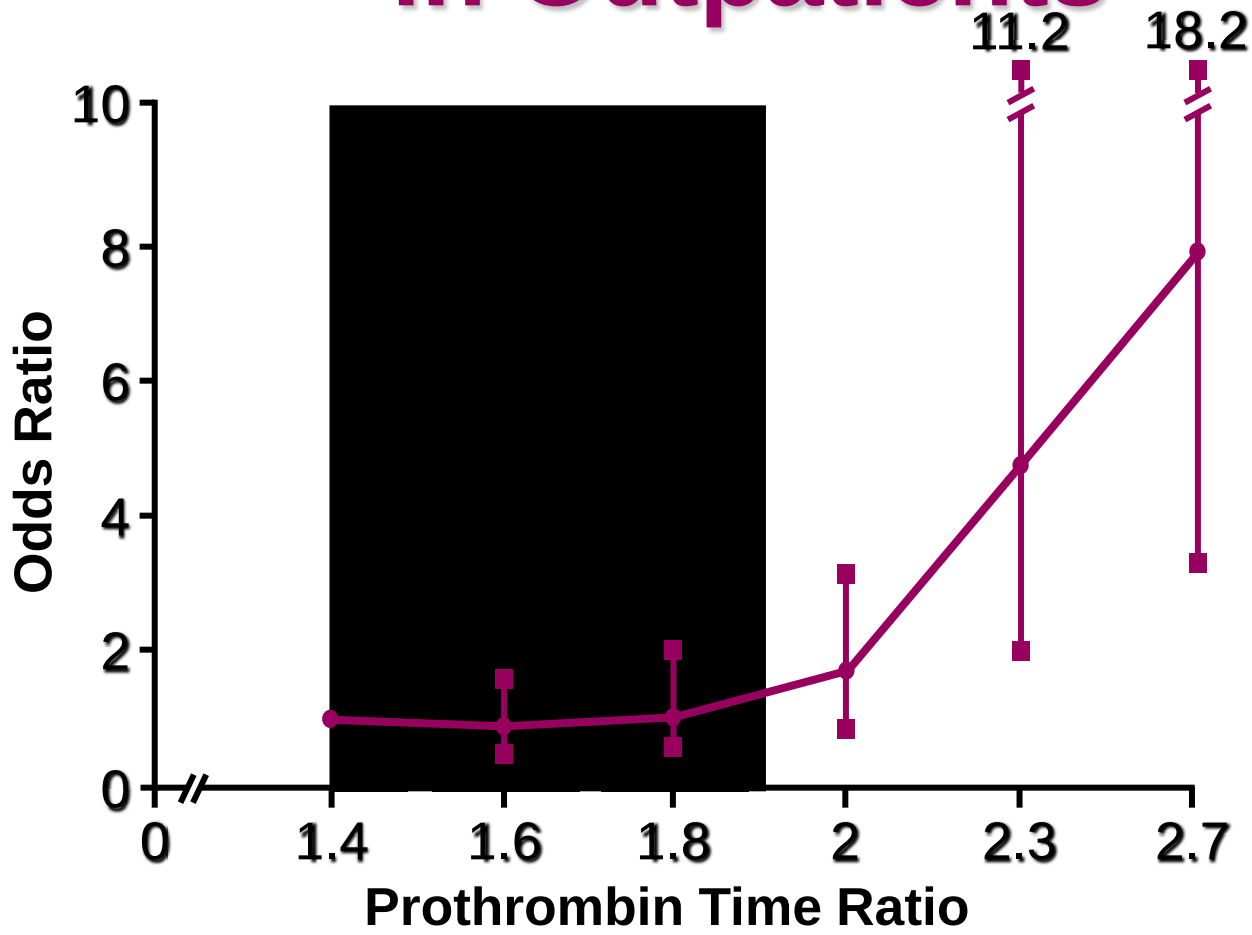


INR	Odds Ratio
2.0	1.0
1.7	2.0
1.5	3.3
1.3	6.0

- INR below 2.0 results in a higher risk of stroke

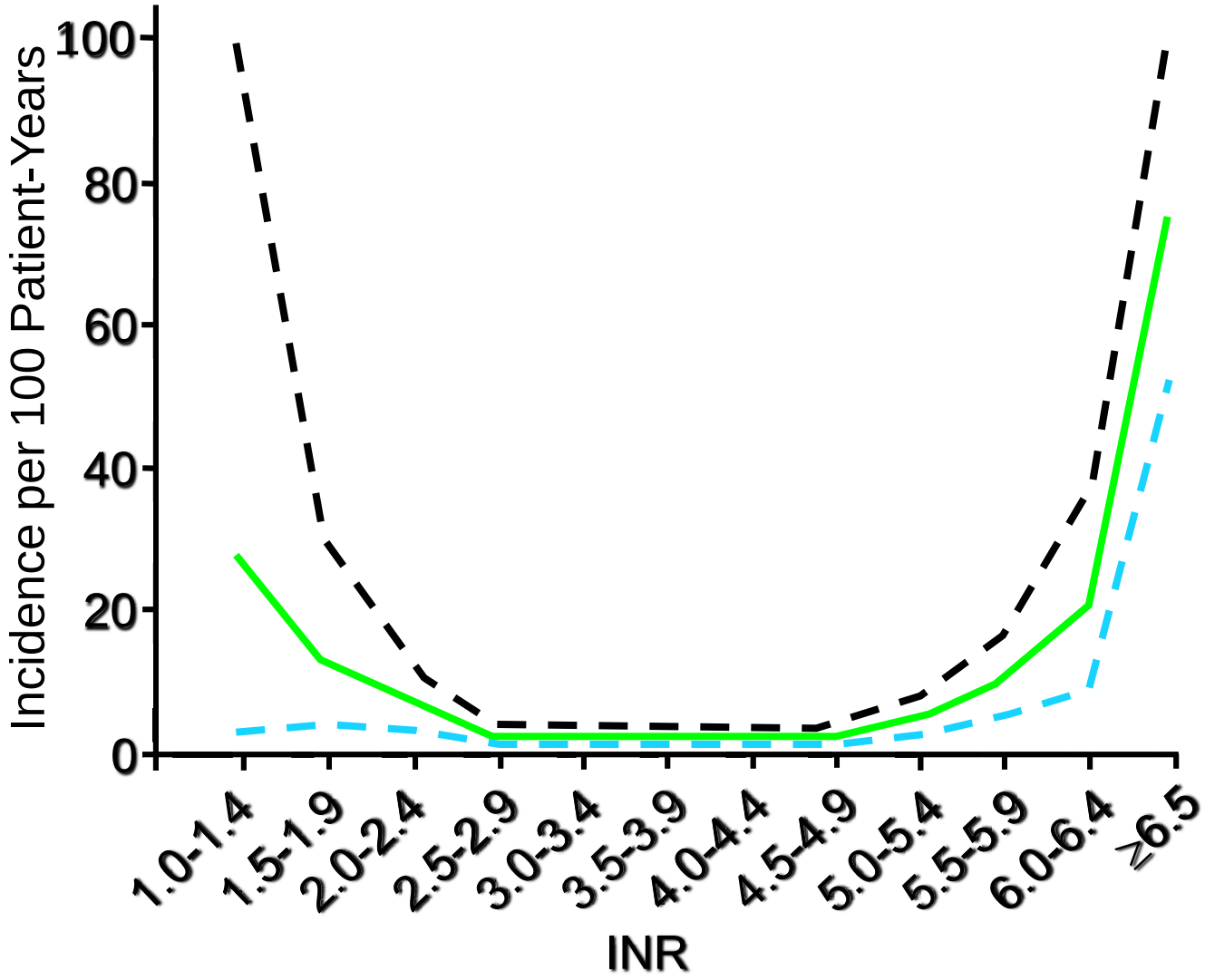
Hylek EM, et al., NFJM 1996;335-540-546

Risk of Intracranial Hemorrhage in Outpatients



- PTR above 2.0 (INR of 3.7 to 4.3) increases the risk of bleeding
- The estimated odds ratio of subdural hemorrhage increased 7.6 fold as the PTR increased from 2.0 to 2.5

Hylek EM, Singer DE, AnnIntMed 1994;120:897-902



INR-Specific Incidence of All Adverse Events (All Episodes of Thromboembolism, All Major Bleeding Episodes, and Unclassified Stroke). The dotted lines indicate the 95 percent confidence interval.

Cannegeiter et al

Why is VKA Therapy So Dangerous?

- Is it because VKAs are used in the wrong patients or for the wrong indications? ***Unlikely***
- Is it because VKAs are maintained in the wrong therapeutic range? ***Unlikely***
- Is it because VKA dosing and patient communications are not managed appropriately? ***Likely***

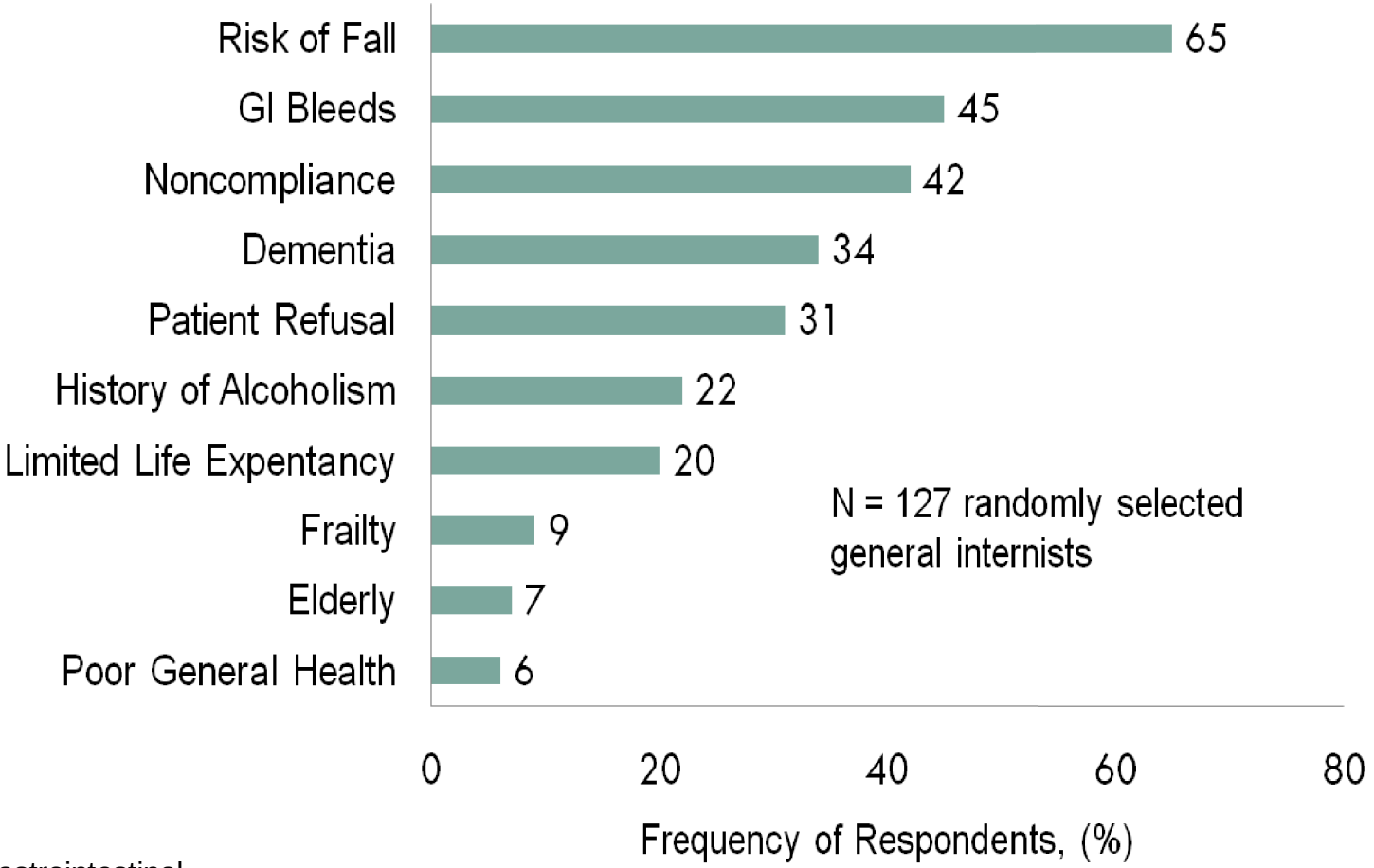
A drug with a narrow therapeutic range and a therapeutic level that is influenced by many factors requires **high quality dose management**.

Ansell JE et al. *Chest.* 2004;126:204S-233S.

Consequences of problems with oral anticoagulants?

- Non - treatment of some conditions
  - Atrial Fib (~ 50% of AF population not treated)
- Inadequate treatment of many conditions
  - Atrial Fib, Heart Valves, etc. (only 30 - 50 % TTR) leads to Increased complications
- Hemorrhage & thrombosis (3% - 15% rate of major AEs)

Top 10 Reasons For Not Prescribing Warfarin to AF Patients



GI = gastrointestinal

Sum of responses is greater than sample size because respondents were instructed to select up to 3 reasons.

Gross CP, et al. *Clin Ther*. 2003;25:1750-1764.

Current state of AC Management (VKA Therapy)

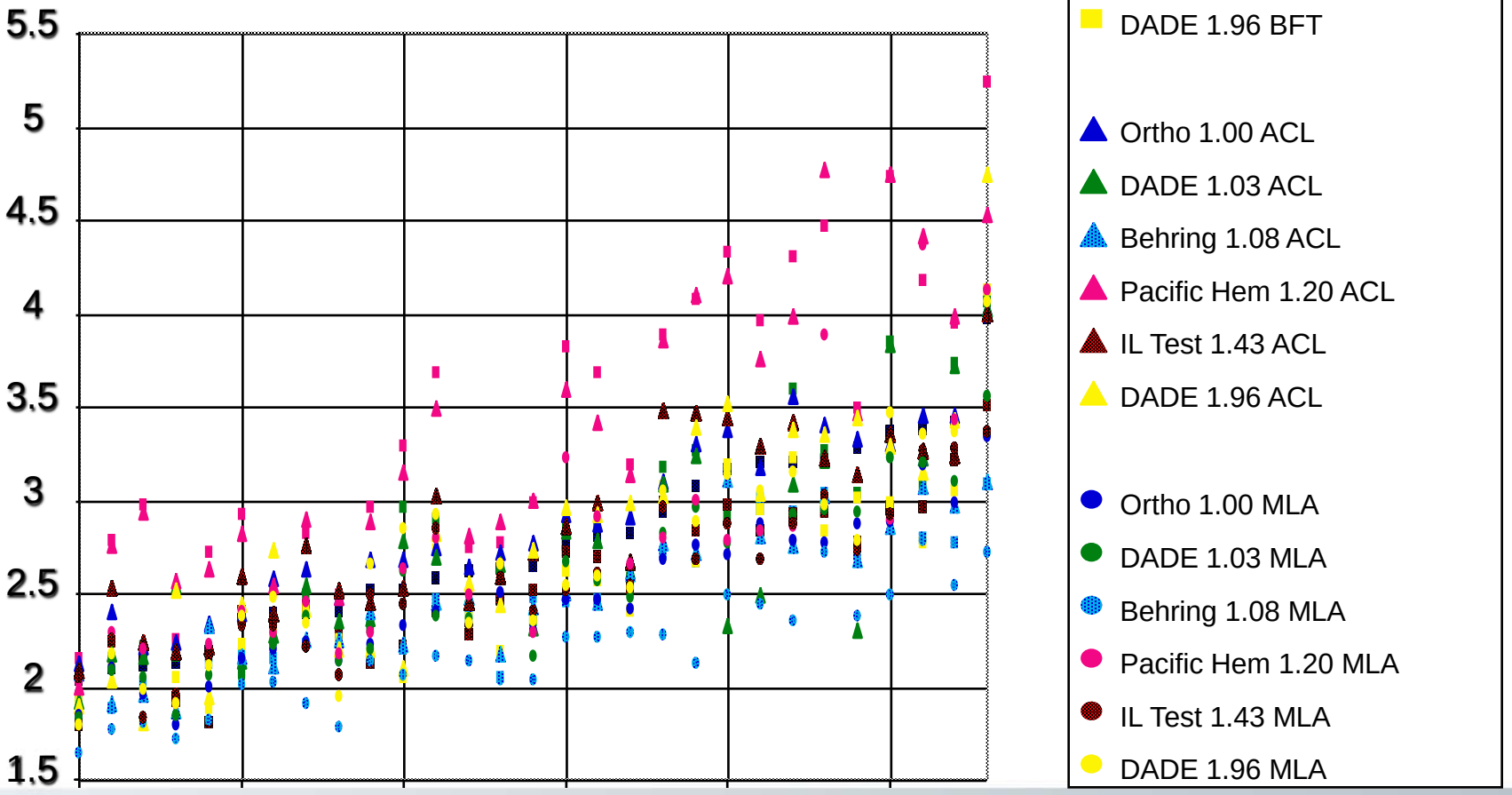
- Little progress in oral anticoagulants has been made and choices have been limited to vitamin K antagonists.
- Warfarin and other vitamin K antagonists were the only oral anticoagulants for >70 years.
- Warfarin has limitations:
  - Large dosing differences between patients
  - Narrow therapeutic window
  - Dietary and drug interactions
  - Routine monitoring necessary
  - Poor management leads to high adverse event rates

Ansell et al. Chest 2004;126(Suppl):202S-231S

Testing Variability


Not all rabbits are alike.
WARING

Thromboplastin/Reagent Combinations & Observed Variation in INR



Source: A. Jacobson, MD

CAP Proficiency Testing Summary Extract CG1-01 High Therapeutic

	# labs	Low	Median	High
Dade Innovin	715	3.1	3.8	4.6
Dade C+	826	2.2	4.3	5.7
Recombiplastin	289	2.9	4.0	4.9
IL-PT-FIB 1.8	542	3.6	5.2	6.9

Models of AC Management

Models of AC Management

- **Routine Medical Care (Usual Care)**
  - AC managed by physician or office staff w/o any systematic program for education, follow-up, communication, and dose management. May use POC device or laboratory INR
- **Anticoagulation Clinic (ACC)**
  - AC managed by dedicated personnel (MD, RN or pharmacist) with systematic policies in place to manage and dose patients. May use POC device or laboratory INR
- **Patient Self-Testing (PST)**
  - Patient uses POC monitor to measure INR at home. Dose managed by UC or ACC
- **Patient Self-Management (PSM)**
  - Patient uses POC monitor to measure INR at home and manages own AC dose

Campbell PM et al. *Dis Manag Clin Outcomes.* 2000;2:1-8;.
Ansell JE. In: Ansell JE, Oertel LB, Wittkowsky AK, eds. *Managing Oral Anticoagulation Therapy*. 2nd ed. St. Louis, Mo: Facts and Comparisons; 2003;44:1-6.

Defining an AC Clinic

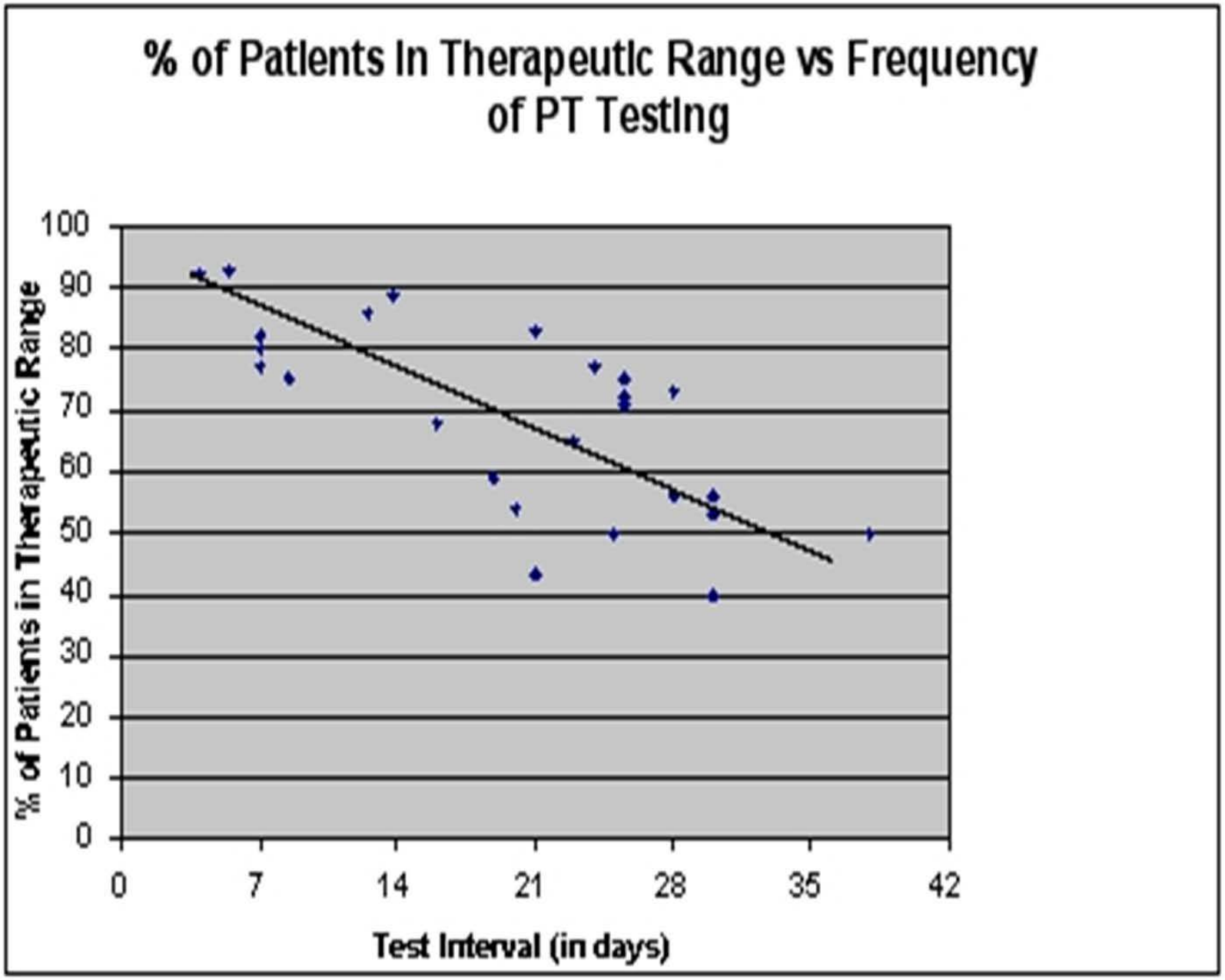
- The key features of an anticoagulation clinic that distinguishes it from other types of anticoagulation management, and allows it to achieve excellent outcomes, includes…..
  - Active vs passive care
  - Dedicated patient manager
  - Expert dosing decisions
  - Documentation, tracking, follow-up
  - Initial and ongoing patient education

AC Management Models and TTR

Model of Care	Time in Therapeutic Range*
Usual Care	~30-60%
Anticoagulation Management Service (AMS)	~50-80%
Patient Self-Testing	~55-70%
Patient Self-Monitoring	~55-90%

* Increased frequency of testing improves TTR.

Ansell J, et al. Chest, 2008; 133: 160S-198S.


% of Patients In Therapeutic Range vs Frequency of PT Testing
% of Patients in Therapeutic Range
100
90
80
70
60
50
40
30
20
10
0
0
7
14
21
28
35
42
Test Interval (in days)

UC vs AMS

Study	Indication	#		Major Bleed (%) U C	AMS	Recurrent TE (%) U C	AMS
UC: Retrospective Trials							
Gitter 1995	Mixed	261		8.1		8.1	
Beyth 1998	Mixed	264		5.0		NA	
Steffensen 1997	Mixed	682		6.0		NA	
Willey 2004	VTE	2,090		2.8		6.2	
Total		**3297**		**4.4**		**6.4**	
AMS: Retrospective Trials							
van der Meer 1993	Mixed	6,814			3.3		NA
Cannegeiter 1995	MHV	1,608			2.5		0.7
Veeger 2005	VTE	2,304			2.8		6.3
Total		**10,726**			**2.9**		**1.7**
AMS: Prospective Trials							
Palareti 1996	Mixed	2,745			1.4		3.5
Abdehafiz 2004	AF	402			1.7		1.5
Total		**3,147**			**1.5**		**3.0**
UC vs AMS: Retrospective Trials (before/after)							
Cortelazzo 1993	MHV	271	271	**4.7**	**1.0; p<0.01**	**6.6**	**0.6; p<0.01**
Chiquette 1998	Mixed	142	82	**3.9**	**1.6; p<0.5**	**11.8**	**3.3; p<0.05**
Witt 2005	Mixed	3,322	3,323	**2.2**	**2.1; p=NS**	**3.0**	**1.2; p<0.05**
UC vs AMS: Prospective Randomized Trials							
Matchar 2002	AF	190	173	**1.6**	**1.7; p=NS**	**7.4**	**5.2; p=NS**
Wilson 2003	Mixed	106	112	**0.9**	**1.8; p=NS**	**1.8**	**0.9; p=NS**

Author Year	Intervention	# Patients	TTR (% or time in range)	Major Hemorrhage	Thrombo-embolism
PST vs UC					
Beyth 2000	PST/ams* vs UC	163 vs 162	56 vs 32 p<0.001	12 % vs 5.6% p=0.049	8.6 % vs 13% p = 0.2
PST vs AMS					
White 1989	PST/ams* vs AMS	23 vs 24	93 vs 75 p=0.003	0	0
Kaatz 2001	PST/ams* vs AMS		63 vs 65 p=NS		
Gadisseur 2003	PST/ams* vs AMS	52 vs 60	63.9 vs 61.3 p=0.14	0 vs 1 event	0
THINRS 2009	PST /ams vs AMS		~68% vs 63% p = NS		
PSM vs UC					
Kortke 2001	PSM vs UC	305 vs 295	78.3 vs 60.5 p=≤0.001	1.7 % vs 2.6% p=NS	1.2% vs 2.1% p=NS
Sidhu 2001	PSM vs UC	34 vs 48	76.5 vs 63.8 p<0.0001	1 event vs 0	1 event vs 0
Sunderji 2004	PSM vs UC	69 vs 70	71.8 vs 63.2		
Voller 2005	PSM vs UC	101 vs 101	67.8 vs 58.5 p=0.0061	2 events vs 0	0 vs 1 event
PSM vs AMS					
Watzke 2000	PSM vs AMS	49 vs 53	84.5 vs 73.8	1 event vs 0	1 event vs 0
Gadisseur 2003	PSM vs AMS	47 vs 52	66.3 vs 63.9 p=0.14	1 event vs 1 event	0
Khan 2004	PSM vs AMS	40 vs 39	71.1 vs 70.4		
Menendez-Jandula 2005	PSM vs AMS	368 vs 369	58.6 vs 55.6 p=NS	4 events vs 7 events	4 events vs 20 events

Cooperative Studies Program #481

The Home INR Study (THINRS): Primary Results

Palo Alto Cooperative Studies Program
Coordinating Center (CSPCC)

Introduction

- Warfarin is effective if managed well
  - Warfarin is underutilized
  - Quality of management can be poor
- Frequent home INR monitoring (weekly patient self testing (PST)) is a promising strategy to improve outcomes
  - Increasing test frequency to more quickly identify and respond to out-of-range INRs
  - Promoting patient engagement in their own care

The Home INR Study (THINRS)

- Key question: does PST notably improve major health outcomes over currently recommended practice (high quality anticoagulation management (HQACM)?)
  - Primary outcome: time to first major event (stroke, major bleed, death)
  - Powered to identify a 32% relative risk reduction in annual rate of major events (from 5.5 to 3.75% (1.75% absolute reduction)

Study Setting

- 28 VA Medical Centers
- Had an anticoagulation clinic (AC) which met MAST* guidelines and managed >400 patients

Study Population

- Atrial fibrillation (AF) or mechanical heart valve (MHV)
- On warfarin for indefinite duration
- Patient or caregiver is competent in performing PST based on Part I evaluation (training, 2-4 week of testing, formal competency evaluation)

*Matchar, Samsa, Cohen, Oddone, Jurgelski. American Journal of Medicine. 2002; 113(1):42-51.

Randomization

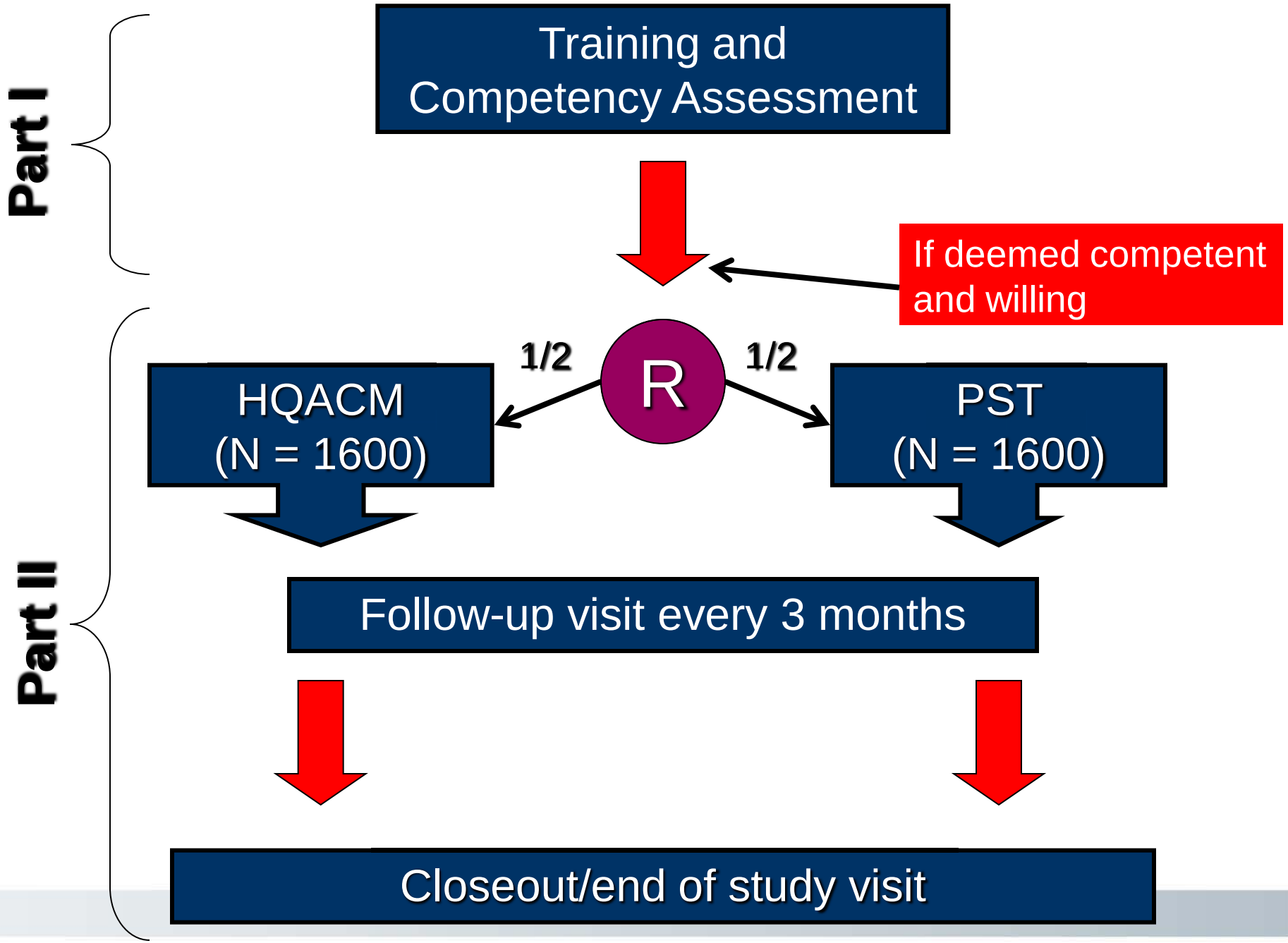
- Performed using adaptive allocation
- Stratified by length of anticoagulation (<3 vs. ≥ 3 months) and indication (AF only, MHV) within site
- Intervention could not be masked but major outcomes were assessed by independent adjudicators

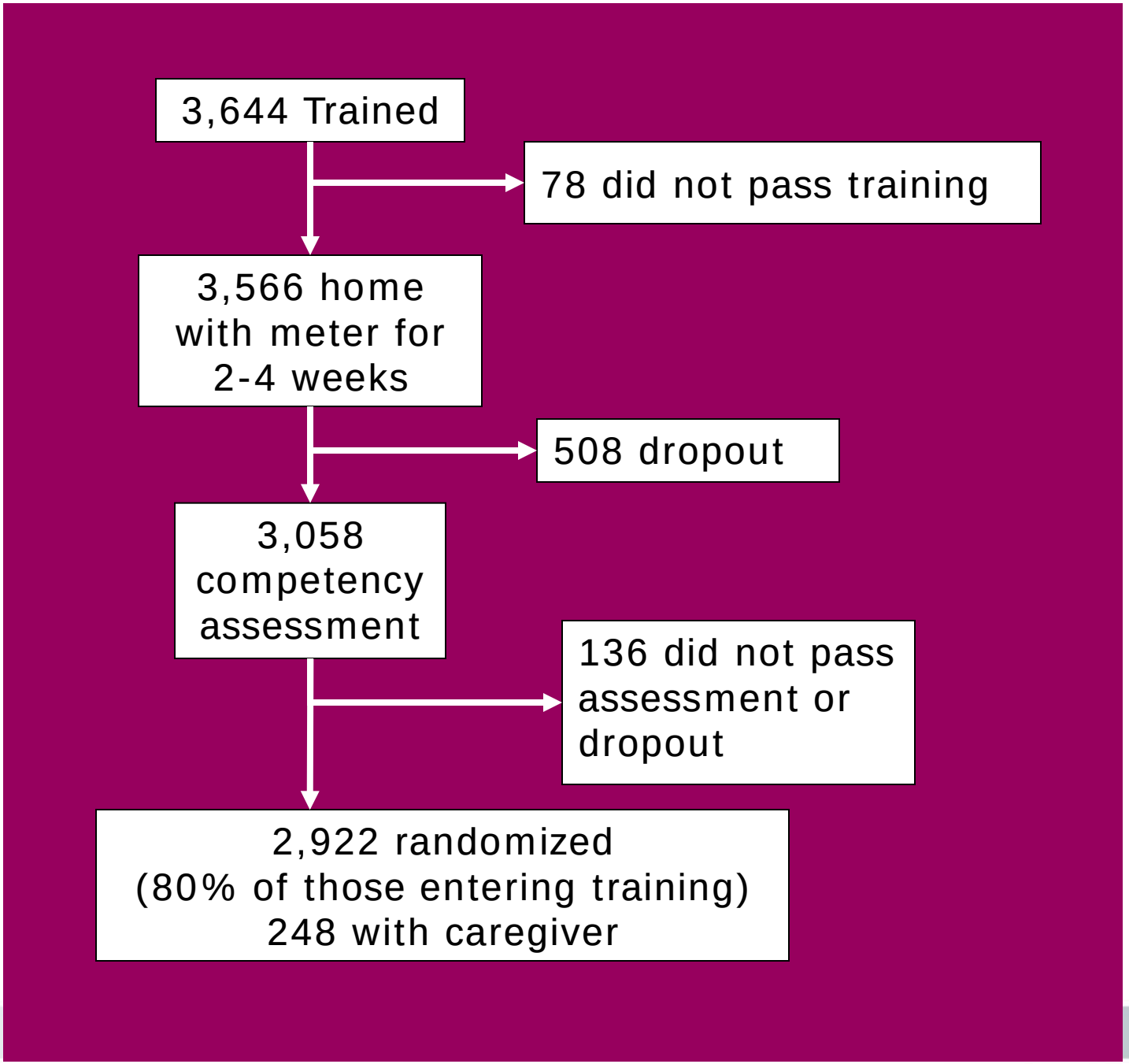
Interventions

- HQACM (monthly INR)
  - Designated, trained staff person
  - Local, standard management algorithm
- PST (Weekly INR)
  - Interactive voice response reporting system with web-based local monitoring

Analysis Plan

- Primary outcome: time to first major event (stroke, major bleed, death)
  - Intention-to-treat
  - Log-rank test and Cox regression
  - Sample size: 1 year enrollment/min 2 yrs FU to discern a 32% relative drop in major events with 90% power; 3,200 target. Actual 2,922 with 2.75 yrs enrollment and mean FU 3 years
- Secondary outcomes:
  - Time in target range
  - Satisfaction with anticoagulation (Duke Anticoagulation Satisfaction Scale (DASS))
  - Quality of Life (Health Utilities Index Mark 3)


Part I
Training and Competency Assessment
If deemed competent and willing
Part II
1/2
R
1/2
HQACM (N = 1600)
PST (N = 1600)
Follow-up visit every 3 months
Closeout/end of study visit


3,644 Trained
78 did not pass training
3,566 home with meter for 2-4 weeks
508 dropout
3,058 competency assessment
136 did not pass assessment or dropout
2,922 randomized
(80% of those entering training)
248 with caregiver

Subject Characteristics - Demographics

	HQACM	PST	p-Value
Number Randomized, n (patient-years)	1,457 (4,235)	1,465 (4,495)	
Gender, Male (%)	1,431 (98%)	1,440 (98%)	0.87
Age, Mean (SD)			
Total	67.4 (9.4)	66.6 (9.7)	0.05
AF	68.3 (9.1)	67.9 (9.1)	0.30
MHV	64.2 (9.7)	62.4 (10.4)	0.02
Range	33 - 99	23 - 89	
Ethnicity, Hispanic/Latino (%)	90 (6%)	108 (7%)	0.20
Race, White (%)	1,347 (92%)	1,347 (92%)	0.61
Transport to Clinic, Did Not Drive Self (%)	229 (15%)	228 (15%)	0.52

Subject Characteristics - Comorbidities

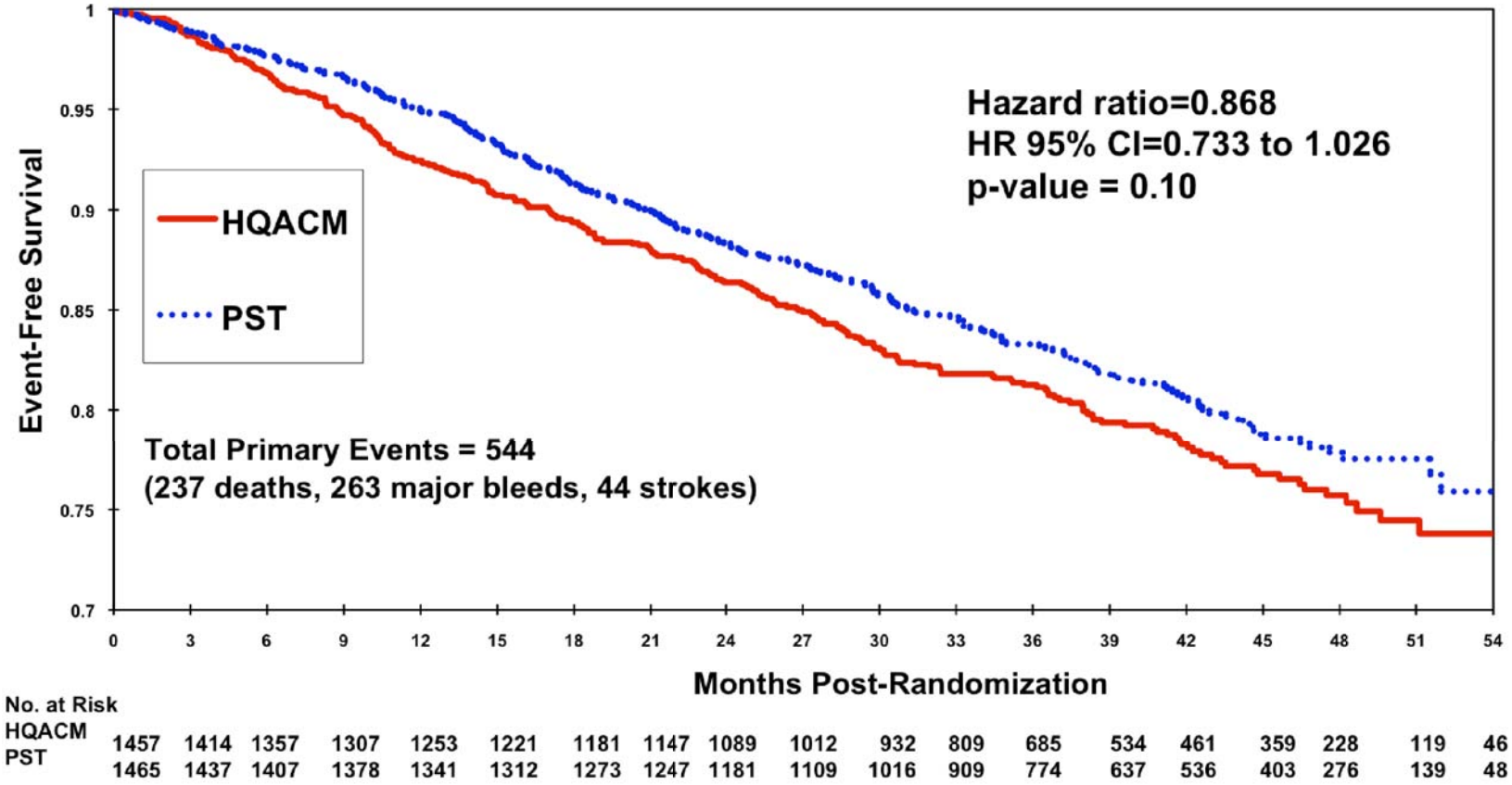
	HQACM	PST	p-Value
Cardiac Disorders			
AF	1,221 (84%)	1,201 (82%)	0.19
CHADS2, mean	1.82	1.79	0.74*
Mechanical Valve	334 (23%)	351 (24%)	0.51
Aortic	256 (18%)	278 (19%)	0.33
Mitral	90 (6%)	91 (6%)	0.97
Other	0 (0%)	0 (0%)	
Arrhythmia, Not AF	160 (11%)	158 (11%)	0.87
CHF	434 (30%)	404 (28%)	0.19
Diabetes Mellitus	495 (34%)	472 (32%)	0.31
Hypertension	1,010 (69%)	1,041 (71%)	0.31
Previous Stroke	140 (10%)	136 (9%)	0.76

*Chi-square for distribution

Subject Characteristics - Medications

	HQACM	PST	p-Value
Average Weekly Warfarin Dose, mg Mean (SD)	36.1 (15.9)	37.1 (16.3)	0.16
Median	35	35	
Range	5 - 112	3.2 - 135	
Antiplatelet Rx			
Aspirin	426 (29%)	429 (29%)	0.98
Clopidogrel	25 (2%)	27 (2%)	0.80
Ticlopidine	1 (0%)	0 (0%)	0.50
Amiodarone	128 (9%)	129 (9%)	0.99

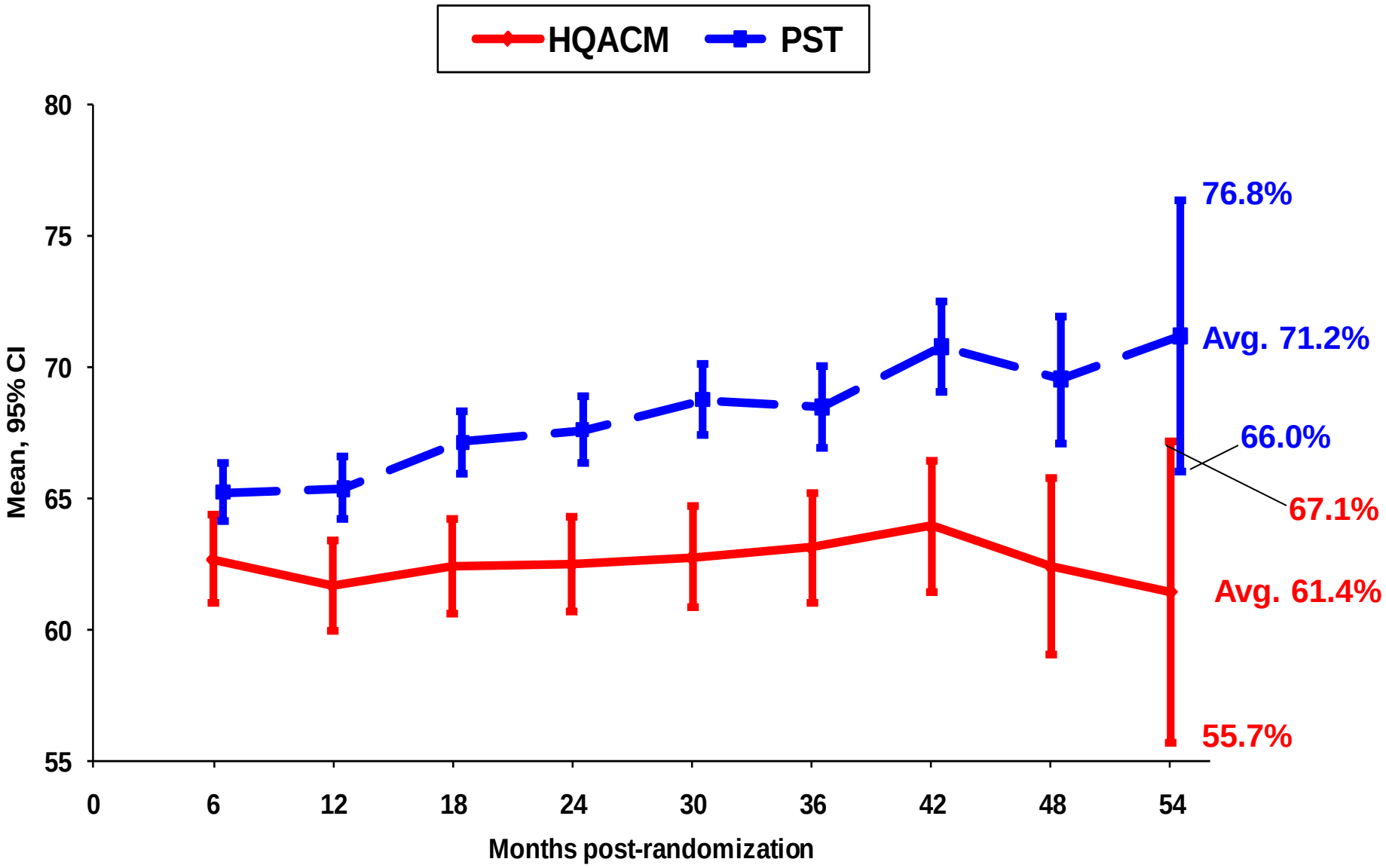
Primary Outcome: Time to first event



Total Events

Total events by intervention						
	HQACM (4,235 pt-yrs)		PST (4,495 pt-yrs)		Total (8,370 pt-yrs)	
Event type	N	Rate per pt-yrs	N	Rate per pt-yrs	N	Rate per pt-yrs
Stroke	32	0.76%	31	0.69%	63	0.72%
Major bleed	189	4.46%	173	3.85%	362	4.15%
Death	157	3.71%	152	3.38%	309	3.54%
Total	378	8.93%	356	7.92%	734	8.41%

Time in target range



THINRS Conclusions

- Compared with monthly clinic INR testing, weekly home INR monitoring does not improve the aggregate outcome of stroke, major bleed, or death to the extent suggested by previous studies
- Such monitoring improves time in target range and patient satisfaction with anticoagulation therapy
- A high proportion (80%) of subjects are able to successfully demonstrate competency, either on their own, or with the assistance of a care provider.

Interpretation

- These results support that home testing is an acceptable alternative to high-quality clinic care and may be preferable when patient access is difficult (e.g., due to disability or geographic distance)

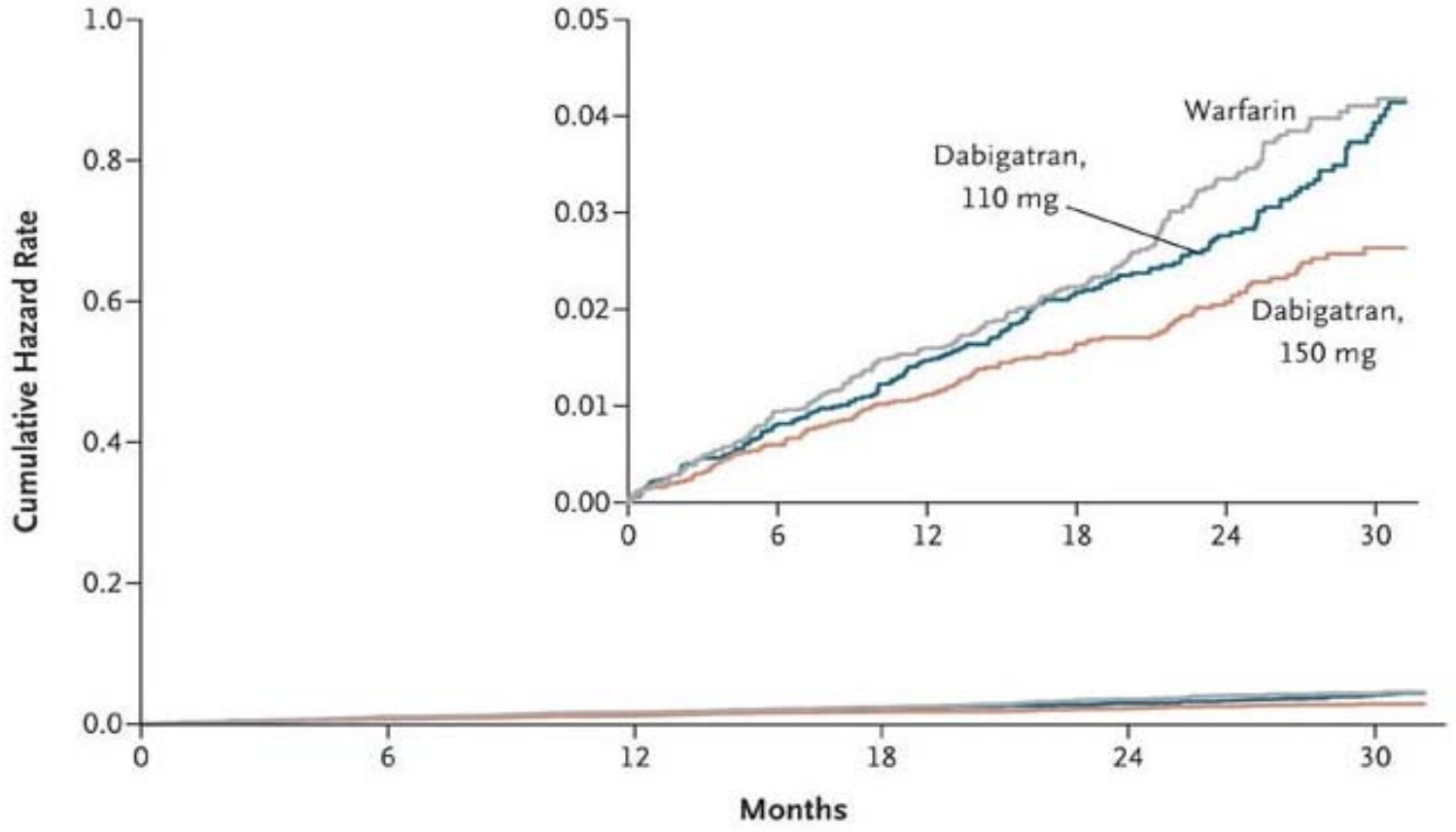
Randomized **E**valuation of **L**ong Term Anticoagulant Therap**y** the RE-LY Trial

Dabigatran Etexilate manufactured by Boehringer Ingelheim

RE-LY Trial

- Randomized Evaluation of Long Term Anticoagulant Therapy (RE-LY) With Dabigatran Etexilate manufactured by Boehringer Ingelheim.
- Dibigatran marketed as Pradaxa is a Factor Xa (10A) inhibitor.
- 18,113 patients were enrolled between Dec. 22, 2005 and Dec 15, 2008.
- Patients were recruited from 951 clinical centers in 44 countries.
- Three treatment groups: two fixed doses of dibigatran, 110 mg and 150 mg administered in a blinded manner and taken twice per day (b.i.d.) and open–label use of warfarin managed by the attending physician.

Pradaxa vs. warfarin in AFib



No. at Risk

Warfarin	6022	5862	5718	4593	2890	1322
Dabigatran, 110 mg	6015	5862	5710	4593	2945	1385
Dabigatran, 150 mg	6076	5939	5779	4682	3044	1429

- **TTR: 64%**

Connolly SJ, et al. N Engl J Med, 2009; 361: 1139-51.

Renal Insufficiency

- Renal excretion of unchanged dabigatran is the predominant elimination pathway, with ~80% of a single dose being excreted in the urine.

Creatinine Clearance	Recommended Dose*
>30 mL/min	150 mg orally, twice daily
15-30 mL/min	75 mg orally, twice daily
<15 mL/min	No dose recommendation

* Package Insert

Special Populations and Pradaxa

- Patients with prosthetic heart valves
  - No data.
- Pediatric patients
  - Safety and Tolerability of Dabigatran Etexilate in Adolescents (clinicaltrials.gov #NCT00844415), June, 2011.
  - Safety and Tolerability of Dabigatran Etexilate Solution in Children 1 to < 12 Years of Age (clinicaltrials.gov #NCT01083732), Dec. 2011.
- Pregnancy
  - Pregnancy Category C.
  - Unknown if excreted in human milk.

Drug Discontinuation and AEs with Pradaxa

Variable	Dabigatran, 110 mg (n=6015)	Dabigatran, 150 mg (n=6076)	Warfarin (n=6022)	P
Discontinued at 1 yr	862 (15%)	935 (16%)	608 (10%)	<0.001
Discontinued at 2 yr	1161 (21%)	1211 (21%)	902 (17%)	<0.001
Discontinued due to serious adverse event	163 (2.7%)	166 (2.7%)	105 (1.7%)	<0.001
Dyspepsia as an adverse event	707 (11.8%)	688 (11.3%)	348 (5.8%)	<0.001

Connolly SJ, et al. N Engl J Med, 2009; 361: 1139-51.

Dosing and Therapeutic Compliance*

Dosing	Took Most Doses	Took Doses on Time
Once daily	79%	74%
Twice daily	69%	58%
3 times daily	65%	46%
4 times daily	51%	40%

* Averaged from 76 studies using electronic monitoring.

Garner JB. Am J Cardiol, 2010; 105: 1495-1501.

AC Therapy Costs

Anticoagulant	Cost for 30 days of therapy
Dabigatran, 150 mg twice a day	$202.50 $2,430.00/yr
Coumadin, 5 mg/day	$50.30 $603.60/yr
Jantoven, 5 mg/day	$18.99 $227.88/yr
Warfarin, generic, 5 mg/day	$13.99 $167.88/yr

- Cost for one month of therapy with dabigatran is the Wholesale Acquisition Price, which is less than the price to the consumer.
- Cost for 30 days of Coumadin, Jantoven, and generic warfarin (5 mg/day) from Drugstore.com.

RE-LY Study Conclusions

- The new thrombin and factor Xa inhibitors provide safe and effective alternatives for many patients on chronic warfarin therapy.
- These agents will not work for all patients, however, for a variety of reasons.
- Optimal management approaches using warfarin (e.g., AMS, PST/PSM) provide safe and effective strategies for patients needing chronic antithrombotic therapy.

Pradaxa Recent Developments

- FEBRUARY 4, 2011
  - Pradaxa in bottles must be used within 30 days
- FEBRUARY 15, 2011
  - Dabigatran joins US atrial-fib guidelines
  - However, the guideline contained a new statement that cautions warfarin may still be appropriate for some patients. "Because of the twice-daily dosing and greater risk of nonhemorrhagic side effects with dabigatran, patients already taking warfarin with excellent [international normalized ratio] INR control may have little to gain by switching to dabigatran," it states.

Patient Self-Testing

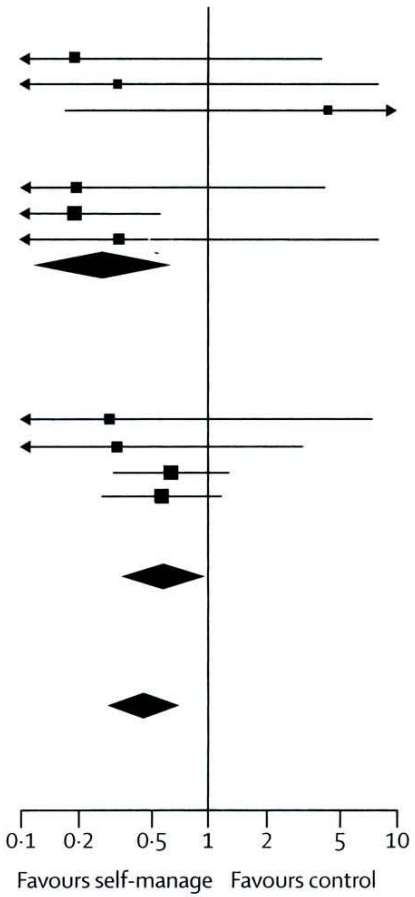
Why would PST achieve better outcomes?

- Access to testing
  - Frequency (convenience), timeliness
    - Greater Time-in-Range
    - Increased complinace
- Consistency of testing
  - Instrument & thromboplastin
    - Consistent Results
- Awareness of test results
  - Knowledge, empowerment, compliance
    - Greater Time-in-Range

Jacobson AK. In: Ansell JE, Oertel LB, Wittkowsky AK, eds. *Managing Oral Anticoagulation Therapy*. 2nd ed. St. Louis, Mo: Facts and Comparisons; 2003;45:1-6.

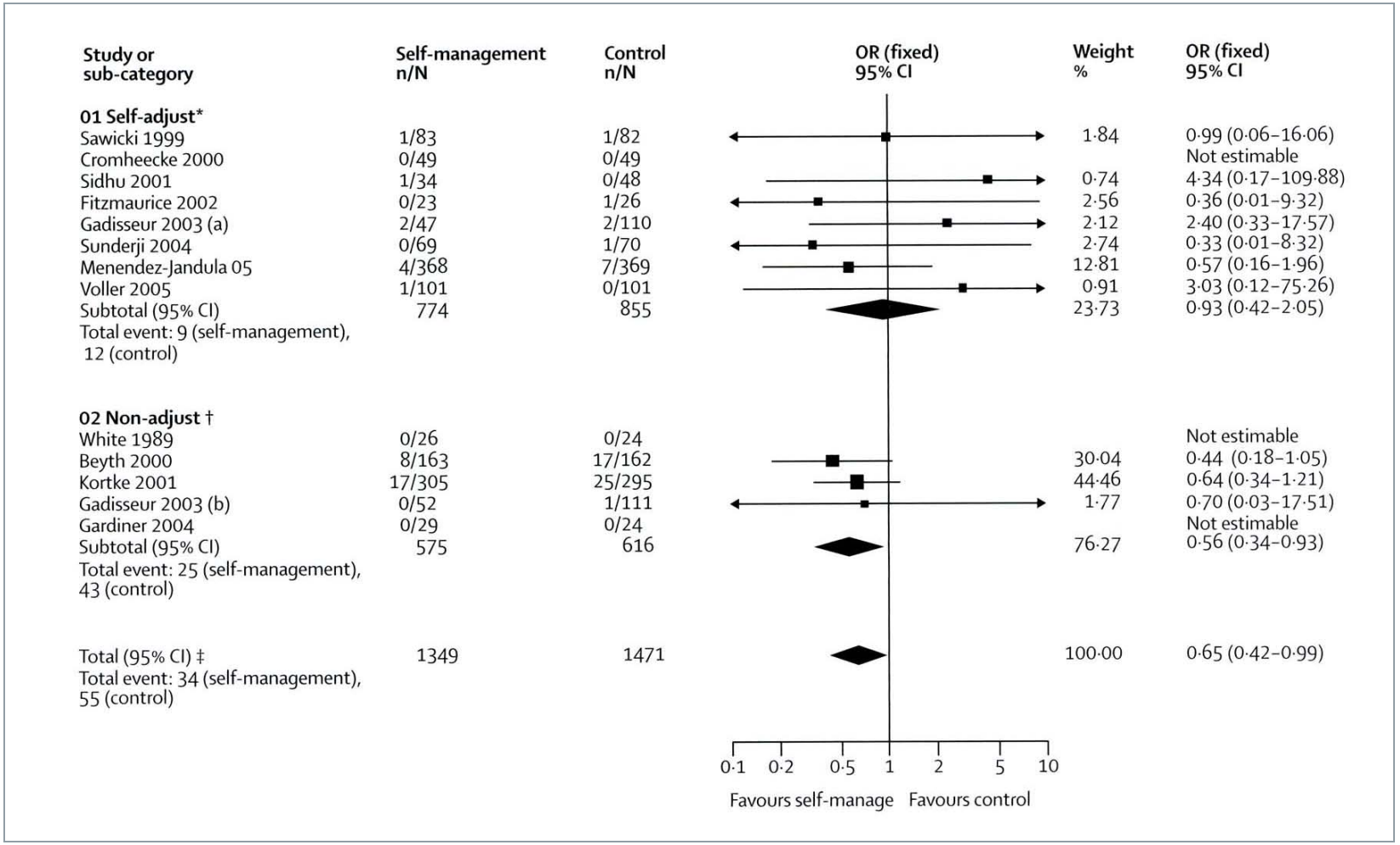
Thromboembolism with PST or PSM

Study or sub-category	Self-management n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
01 Self-adjust*					
Sawicki 1999	0/83	2/82		3·50	0·19 (0·01–4·08)
Cromheecke 2000	0/49	1/49		2·08	0·33 (0·01–8·22)
Sidhu 2001	1/34	0/48		0·56	4·34 (0·17–109·88)
Fitzmaurice 2002	0/23	0/26			Not estimable
Gadisseur 2003 (a)	0/47	0/110			Not estimable
Sunderji 2004	0/69	2/70		3·45	0·20 (0·01–4·18)
Menendez-Jandula 05	4/368	20/369		27·68	0·19 (0·06–0·57)
Voller 2005	0/101	1/101		2·09	0·33 (0·01–8·20)
Subtotal (95% CI)	774	855		39·37	0·27 (0·12–0·59)
Total event: 5 (self-management), 26 (control)					
02 Non-adjust †					
White 1989	0/26	1/24		2·14	0·30 (0·01–7·61)
Horstkotte 1998	1/75	3/75		4·15	0·32 (0·03–3·19)
Beyth 2000	14/163	21/162		26·98	0·63 (0·31–1·29)
Kortke 2001	12/305	20/295		27·37	0·56 (0·27–1·17)
Gadisseur 2003 (b)	0/52	0/111			Not estimable
Gardiner 2004	0/29	0/24			Not estimable
Subtotal (95% CI)	650	691		60·63	0·57 (0·35–0·93)
Total event: 27 (self-management), 45 (control)					
Total (95% CI) ‡	1424	1546		100·00	0·45 (0·30–0·68)
Total event: 32 (self-management), 71 (control)					



Heneghan et al. Lancet 2006;367:404

Major Hemorrhage with PST and PSM



Heneghan et al. Lancet 2006;367:404

Improving AC Outcomes at Time of Discharge

- 128 patients randomized to home POC monitoring (n= 60) or UC (n=68) after discharge. POC testing on d 2,4,6,8 vs UC on d 8

	Discharge		Day 8		
	Home Monitoring	UC Monitoring	Home Monitoring	UC Monitoring	p value
Sub-therapeutic	49%	47%	29%	33%	
Therapeutic	42%	45%	67%	41%	<0.01
Supra-therap	9%	8%	4%	26%	

Adverse events up to day 90

	Home Monitoring (n=59)	Usual Care Monitoring (n=68)	
Major Bleeding	2	10	0.05
Total Bleeding	15	36	0.009
Embolic Event	9	10	NS
Readmit due to AC Complication	3	8	0.32
Death	7	8	NS

Jackson et al. J Intern Med 2004:256:137

Considerations for Patient Selection

- Willing to:
  - Learn and perform testing procedure
  - Keep accurate written records
  - Communicate results in timely fashion
- Able to:
  - Participate in a training program to acquire
  - skills/competencies to perform self-testing
  - Generate an INR
  - Understand implications of test result
  - Maintain records
- Reliable to:
  - Perform procedure with acceptable technique to obtain accurate results

Training for PST

- CMS expanded PST coverage for patients with AF or DVT/PE stipulates and pays for patients to complete a one-time, face-to-face training program and demonstrate correct use of their INR monitor.
- Topics should included training technique for fingerstick blood collection, monitor setup, operation, performance, recording and communicating the result, obtaining supplies, and care and storage of the device and supplies.
- Patients must demonstrate correct operation of the device prior to beginning a home testing program.

Barriers to PST/PSM

- Lack of physician awareness or acceptance[1,2]
- Fear it will lead to unintended self-management[3]
- Implementation of PST/PSM[3]
- Reimbursement[3]

1. Jacobson AK. In: Ansell JE, Oertel LB, Wittkowsky AK, eds. *Managing Oral Anticoagulation Therapy*. 2nd ed. St. Louis, Mo: Facts and Comparisons; 2003;45:1-6. 2. Roche Diagnostics. *CoaguChek System: Why Use?* Available at: http://www.coaguchek-usa.com/information_for_professionals/why_use/content.html. Accessed May 12, 2006. 3. Wittkowsky AK et al. *Pharmacotherapy.* 2005;25:265-269.

INR PST Monitors

Alere INRatio2

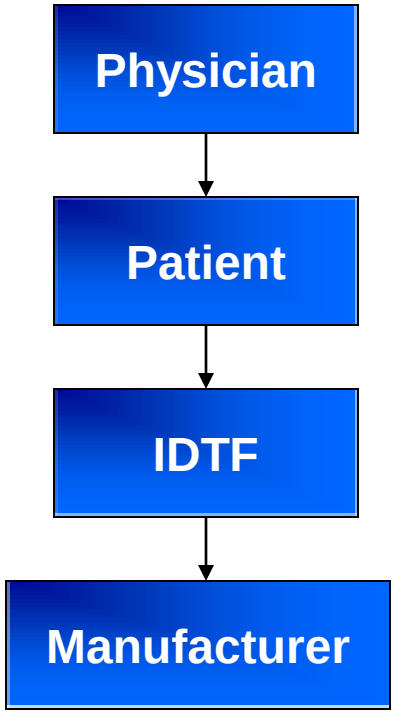
ITC ProTime

Roche CoaguChek XS

2011 PST Reimbursement

- Initiation and Training – G0248
  - *Payment = POL $139.98 - Hosp OP $128.48*
- Ongoing Monitoring, Technical – G0249
  - *Payment = POL $123.67 – Hosp OP $128.48*
- Ongoing Monitoring, Professional – G0250
  - *Payment = POL $9.17 – Hosp OP $N/A*

PST Reimbursement Flow



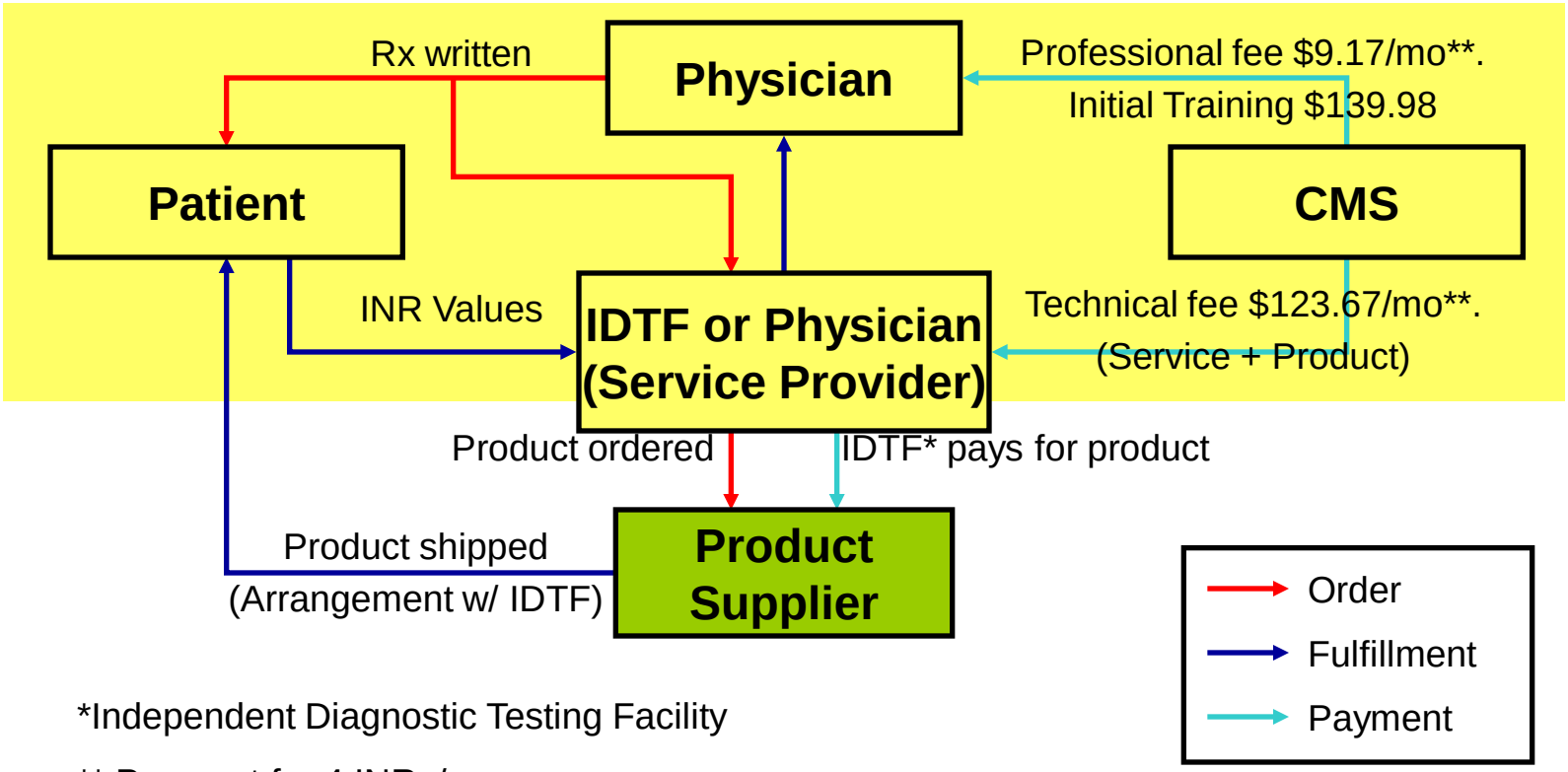
Prescribes monitor and strips for PST

Receives monitor and strips

Supplies monitor and strips

Monitor and strips sold to IDTF

Diagnostic Service Model



*Independent Diagnostic Testing Facility

** Payment for 4 INRs/mo.

INR PST Service Providers

- Alere Home Monitoring
  - http://www.coagnow.com
- CoaguChek Patient Services
  - http://www.coaguchek.com
- mdINR, a Lincare Company
  - http://mdinr.com
- Patient Home Monitoring
  - http://www.myphm.com
- Philips INR@Home Services
  - www.inrselftest.com

Futures?

Will Warfarin Still be in Use a Year from Now?

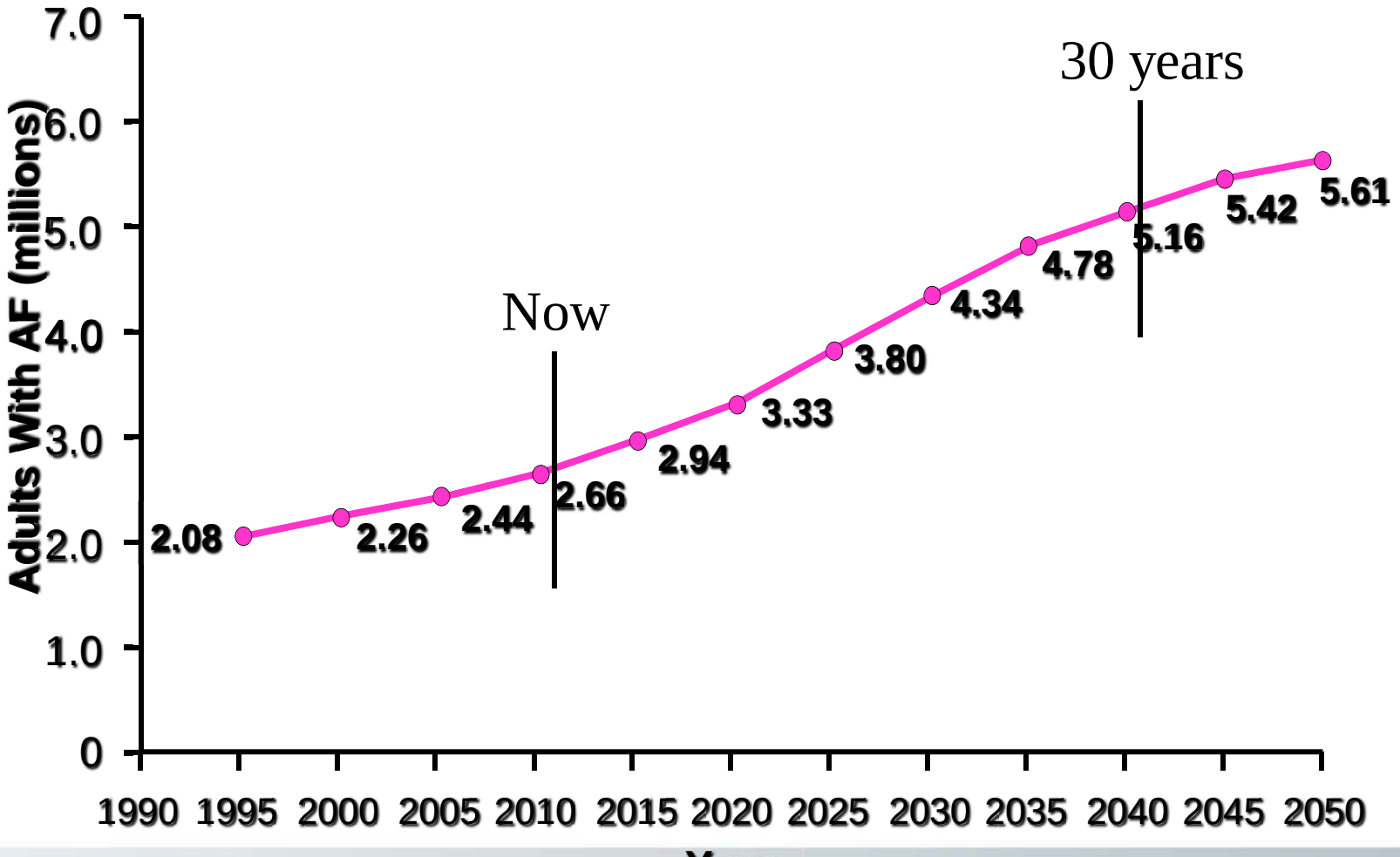
Estimated US Launch for Fixed Dose Anticoagulants

Dabigatran etexilate (Pradaxa)	2011 Released 9/10
Rivaroxaban (Xarelto)	2011-12
Apixaban	2012
Vernakalant (IV)	2012
Vernakalant (oral)	2013
Budiodarone	2012
Tecadenoson	2012
Edoxaban	2012
Tecarfarin	2013
Betrixaban	2014
YM-150	2014

Future of Atrial Fibrillation

ATRIA Study

Projected Number of Adults With AF in the US, 1995 to 2050

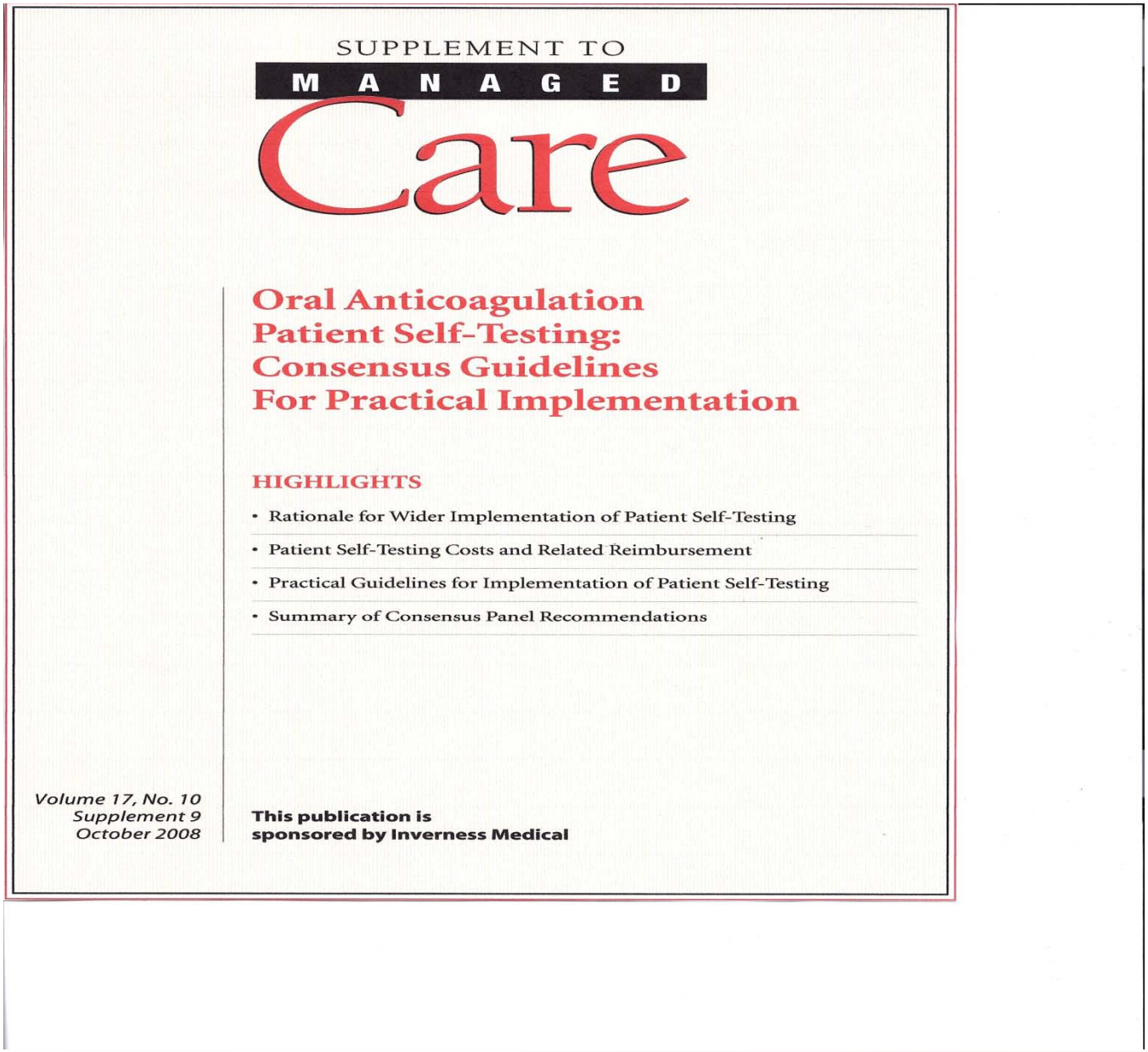


Go et al. *JAMA*. 2001;285:2370-2375.

The Future?

- CoumaWatch
- Transdermal INR
- Programmable therapeutic range
- Automatic daily dosage calculator
- Satellite communicator to primary provider

PST Conclusions



http://www.managedcaremag.com/supplements/0810_oral_anticoagulation/0810_oral_anticoagulation.pdf

PST Conclusions…

- Warfarin is often poorly managed and underutilized;
- The inpatient - outpatient transition is critical and requires labor intensive systems and processes for successful outcomes;
- AC Management models include Routine or Usual Care, AC Clinics, and PST/PSM;
- Most patients are able to perform home monitoring;
- PST monitoring requires systems in place to implement and manage results;
- Outcomes with PST are similar to those achieved by an ACC, but better than those achieved by UC;
- Patient satisfaction is higher with PST.

PST Conclusions…

- Warfarin therapy requires a systematic method of management and follow-up, including regular INR testing.
- Point-of-care testing and PST are enabling technologies that facilitate high-quality management of patients receiving long-term oral anticoagulation therapy.
- Patient self-testing enables more frequent testing that has been shown to improve INR control and reduce the incidence of bleeding and thrombotic complications.

PST Conclusions…

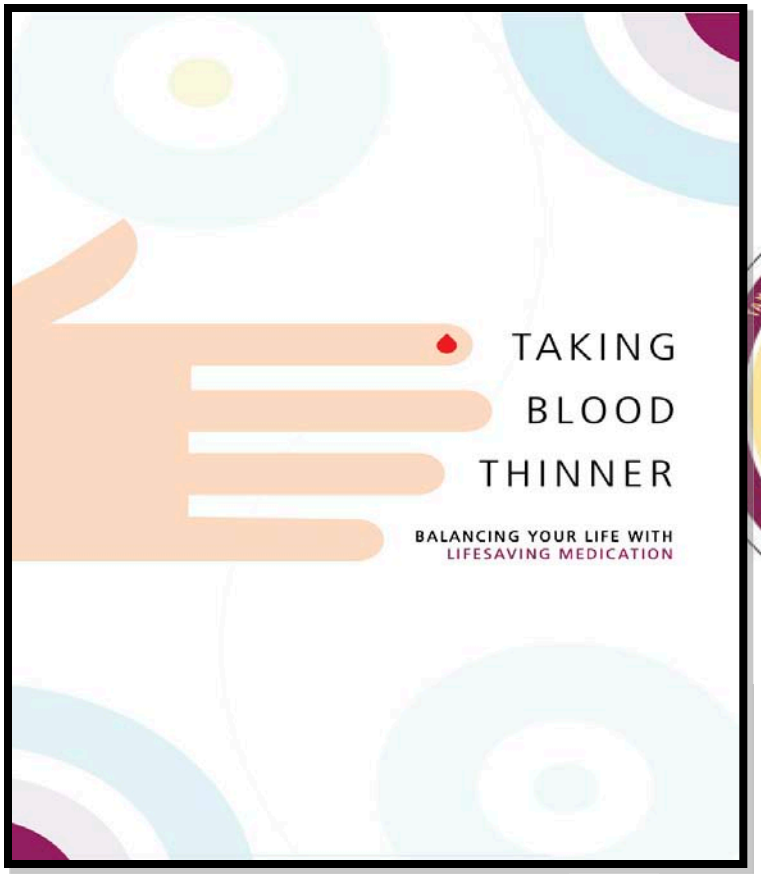
- There is compelling evidence supporting PST in the context of a comprehensive anticoagulation management plan:
- Increased time in therapeutic range;
- Reduction of hemorrhagic and thrombotic complications;
- Overall cost-effectiveness;
- Improved quality of life for patients and their families;
- PST is not an alternative to regular care provided by a medical practitioner; PST provides additional data that allows practitioners to make more informed patient-care decisions.

PST Conclusions…

- An increase in the demand for high-quality management of oral anticoagulation therapy is anticipated in the near future, and the current management methods may be inadequate to provide high-quality care to all the patients who require treatment.
- Medicare reimbursement, although imperfect, is changing in response to the growing body of clinical data supporting PST, and in response to the input of practitioners who understand the value and cost-effectiveness of PST.
- There are many options regarding all aspects of PST, allowing practitioners to tailor implementation to their needs and preferences.

PST Conclusions…

- Elements that are important to successful implementation of PST include:
  - Standardized patient selection process that focuses on the medical necessity for those patients or their caregivers who are willing and able to reliably perform PST as prescribed;
  - Reliable phone service or other means of communicating with the practitioner;
  - Initial and ongoing patient education and specific INR device training prior to initiating PST;
  - Clear, consistent communication between patients and practitioners regarding expectations of patients performing PST and consequences for nonadherence;
  - A readily accessible means for patients to communicate results to the practitioner’s office;
  - An office system for managing patient communication and follow-up;
  - Ongoing patient education and specific INR device training prior to initiating PST.



Links to obtain the DVD

www.hemosense.com
www.acforum.org
www.ptinr.com
www.stoptheclot.com

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ARTICLES

INR Patient Self-Testing: Yesterday, Today and Beyond

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