STAND UP FOR PATIENT SAFETY
NATIONAL PATIENT SAFETY FOUNDATION

Massachusetts Coalition for the Prevention of Medical Errors

Anticoagulation Management In The Ambulatory Setting: Recommendations from the Massachusetts Coalition for the Prevention of Medical Errors

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Stand Up for Patient Safety Audio-web Conference
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Anticoagulation Management in Massachusetts

Identified as a top priority for Coalition

- **Goal - *"Change Agent" Campaign: Transform healthcare across settings to eliminate harm due to anticoagulation management in Massachusetts***
  - Eliminate preventable adverse events due to anticoagulation, by December 2011
  - Reduce adverse events related to anticoagulation during hospital stays and after discharge by 75% by December 2008
  - Reduce preventable adverse events from anticoagulation in all healthcare settings by 50% by December 2009
  - 100% participation by hospitals, 90% participation by long term care facilities, and 100% participation by large group practices

A Massachusetts Collaboration

- **Partnership includes:**
  - MA Coalition for the Prevention of Medical Errors
    - Investigating current practice, networking with experts and partners, identifying clinical and payment issues, establishing best practices, and determining implementation strategies
  - Massachusetts Medical Society
    - Conducted MA physician survey of current practices
    - Planning CME initiative with MA Coalition
  - Massachusetts Association of Health Plans
    - Discussed problem and strategies regarding barriers related to coverage

Outline

1. Clinical Context
2. Management Options and Effectiveness
3. Cost-Effectiveness
4. Barriers
5. Specific Clinical Issues
   - Genetic Testing
   - Surgeries Performed on Warfarin
6. Massachusetts Approach
7. Conclusion and Next Steps

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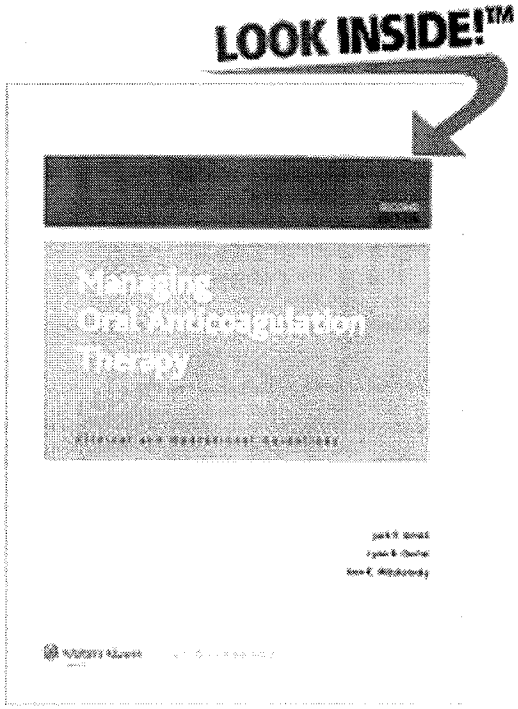
Clinical Context

Managing Oral Anticoagulation Therapy



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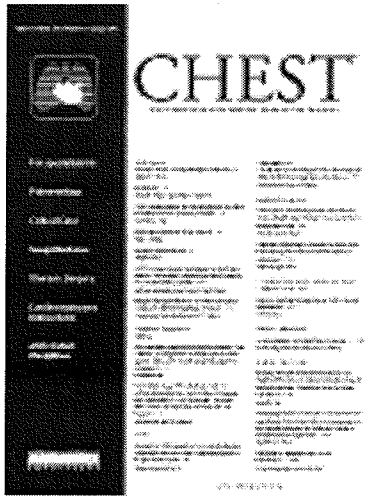

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Clinical Context: The Problem[1,2]

Warfarin is a Dangerous Drug

- Requires frequent and careful monitoring of the clotting parameter affected by warfarin, namely the prothrombin time, expressed as the International Normalized Ratio (INR)
- Risk of adverse outcomes enhanced by
  - **Over Treatment**
    - » Results in bleeding (especially intracranial bleeding)
    - » Often fatal, but whose incidence is <1%
    - » Risk can be cut by more than 50% with proper monitoring
    - » Risk can be cut another 30-50% through the use of patient home blood tests (INR Self Testing or Self Management)
  - **Under Treatment**
    - » Only 50% of chronic or paroxysmal atrial fibrillation (AF) patients are on warfarin (untreated)
    - » Risk of thrombotic blood clot or stroke when INR is < 2.0 (undertreated)
    - » Fear of warfarin contraindications do not fully account for level of under-use
    - » Physicians don't feel comfortable trying to monitor and manage their patients on warfarin

Clinical Context: Scope of... Healthcare Settings Affected[3,4,5,6]

- **Joint Commission National Patient Safety Goal – 3E**

  Reduce the likelihood of patient harm associated with the use of anticoagulation therapy in ambulatory, hospital, and long-term care facilities (September 24 Sentinel Event Alert)

  - **Ambulatory Settings**
    - MA physicians are in the advance guard of those "doing the right thing", i.e., engaging the patient and family in deciding what is best choice, based on recent MA Medical Society Survey of physicians.
  - **Inpatient Settings**
    - Medication Reconciliation issue for patients admitted on long-term warfarin[6]
    - Issue for patients started on warfarin during an admission and/or with new potentially interacting medications added
  - **Nursing Home Patients**
    - Large percentage (12 -15%) of patients maintained on warfarin [6]
    - Serious, life threatening or fatal events occurred at a rate of 2.49/100 resident months; 57% of these more serious events were considered preventable
  - **Care Across Transitions of Settings**
    - Acute hospital admissions, discharges, transfers to SNFs/Extended Care Facilities
    - The times of "baton passing", when the patient moves from home to hospital to Extended Care Facility and back home, are especially vulnerable times from a patient safety perspective
    - Need to have excellent and completely reliable communication systems for transmitting information in real time

Clinical Context: Scope of… Patients Affected[9,10,46]

- **Adult Patients**
  - Atrial Fibrillation (AF) patients make up about 75% of the population who should be on warfarin
    - Prevalence of AF is 0.4-0.1% in general population and increases with age
      - Under age 40 less than 0.1%
      - Over age 80 = more than 8.0%
      - Median age of AF patients = 75 years
    - 75% of patients who are, or should be, on warfarin are Medicare beneficiaries
      - Roughly 80% of the AF population is over age 65
  - Other common indications in adult populations include:
    - DVT/PE
    - Hypercoagulable States
    - Mechanical Heart Valves
    - Post Total Hip Replacement, Total Knee Replacement
  - Only about 50% of population who have AF are on long term warfarin
    - Reasons commonly cited:
      - an overestimate by physicians of the risk of hemorrhage
      - absence of an AMMS to offload the work associated with use of warfarin

Clinical Context: Scope of… Patients Affected

- **Pediatric Patients**[3]
  - **Most common indications for this population include:**
    - Coagulopathy
    - DVT/PE
    - Upper Extremity DVT due to recent use of Vascular Access lines
    - Congenital Vascular Malformation
    - Heart Valves:
      - Mitral > Aortic
      - Now mostly using bioprosthetics which do not require long-term anticoagulation
    - Kawasaki Disease
  - **More commonly use Lovenox rather than warfarin**
- **For individual adult and pediatric patients, physicians face a conundrum in trying to determine what the risk/benefit tradeoffs are**

Clinical Context[7]

- **Desired Therapeutic Ranges**
  - For most patients, the desired range is 2.0-3.0
  - For high risk patients it can be 2.5-3.5
    - with mechanical heart valves and/or with systemic emboli
- **INR Testing**
  - Initial testing should be every couple days until the INR is stabilized
  - Once stabilized, subsequent testing is generally recommended once a month
  - Better control can be achieved with home self testing (ST) and self management (SM) in which the patient self adjusts dose based on a written protocol from his/her physicians
  - When the INR is outside the targeted therapeutic range, and a dose adjustment is made, it should be rechecked within 1-4 days

Clinical Context:
Randomized Trials of Anticoagulation for Atrial Fibrillation [8]

Table 19-1 Overview of the Randomized Trials of Anticoagulation for Atrial Fibrillation: Efficacy

Trial	AFASAK	BAATAF	CAFA	SPAF	SPINAF	EAFT
Anticoagulation:						
Target	INR 2.8-4.2	PTR 1.2-1.5	INR 2.0-3.0	PTR 1.3-1.8	PTR 1.2-1.5	INR 2.5-4.0
No. of subjects	335	212	187	210	260	225
No. of emboli	10	2	7	6	4	20
Annual rate	2.30%	0.41%	3.00%	2.30%	0.88%	3.90%
Control:						
No. of subjects	336	208	191	211	265	214
No. of emboli	22	13	11	18	19	50
Annual rate	5.60%	3.00%	4.60%	7.40%	4.30%	12.30%
Preventive efficacy	59%	86%	35%	69%	79%	66%
95% confidence interval	15-81%	51%-96%	(-64)-75%	27%-85%	52%-90%	43%-80%

Note: Preventive efficacy is the relative risk reduction calculated as 1 - RR) x 100, where RR is the annual rate in the anticoagulation group divided by the annual rate in the control group.

Clinical Context:

Pooled Analysis of the First Five Atrial Fibrillation Trials: Efficacy of Warfarin by Risk Category[8]

Table 19-2: Pooled Analysis of the First Five Atrial Fibrillation Trials: Efficacy of warfarin by Risk Category

Risk Category	No. of Strokes Untreated Control	Rate (95% CI)	No. of Strokes Treated w/Warfarin	Rate(95%CI)
Age <65 years:				
No risk factor	3	1.0% (0.3-3.1)	3	1.0% (0.3-3.0)
>=1 Risk factor	16	4.9 (3.0-8.1)	6	1.7% (0.8-3.9)
Age 65-75 years:				
No risk factor	16	4.3% (2.7-7.1)	4	1.1% (0.4-2.8)
>=1 Risk factor	27	5.7 (3.9-8.3)	7	1.7% (0.9-3.4)
Age >75 years:				
No risk factor	6	3.5% (1.6-7.7)	3	1.7% (0.5-5.2)
>=1 Risk factor	13	8.1 (4.7-13.9)	2	1.2% (0.3-5.0)

Note: The first five trials are listed in Table 19-1. Risk factors are history of hypertension, diabetes, or prior stroke or transient ischemic attack. Rate is annual rate; CI is Confidence Interval

Clinical Context:

Stroke Risk in Patients With Nonvalvular AF Not Treated According to CHADS2 Index [9]

Table 9 Stroke Risk in Patients With Nonvalvular AF Not Treated With Anticoagulation According to the CHADS2 Index

CHADS2 Risk Criteria	Score
Prior Stroke or TIA	2
Age >75 years	1
Hypertension	1
Diabetes mellitus	1
Heart failure	1

Patients (N=1733)	Adjusted Stroke Rate (%/y)* (95% CI)	CHADS2 Score
120	1.9 (1.2 to 3.0)	0
463	2.8 (2.0 to 3.8)	1
523	4.0 (3.1 to 5.1)	2
337	5.9 (4.6 to 7.3)	3
220	8.5 (6.3 to 11.1)	4
65	12.5 (8.2 to 17.5)	5
5	18.2 (10.5 to 27.4)	6

Clinical Context:
Antithrombotic Therapy for Patients With Atrial Fibrillation [9]

Table 10. Antithrombotic Therapy for Patients With Atrial Fibrillation

Risk Category	Recommended Therapy
No risk factors	Aspirin, 81 to 325 mg daily
One moderate-risk factor	Aspirin, 81 to 325 mg daily, or warfarin (INR 2.0 to 3.0 target 2.5)
Any high-risk factor or more than 1	Warfarin (INR 2.0 to 3.0, target 2.5)*

Less Validated or Weaker Risk Factors	Moderate-Risk Factors	High-Risk Factors
Female gender	Age greater than or equal to 75 y	Previous stroke, TIA or embolism
Age 65 to 74 y	Hypertension	Mitral stenosis
Coronary artery disease	Heart Failure	Prosthetic heart valve*
Thyrotoxicosis	LV ejection fraction 35% or less	
	Diabetes mellitus	

*If mechanical valve, target international normalized ratio (INR) greater than 2.5. INR indicates international normalized ratio; LV, left ventricular; and TIA, transient ischemic attack.

Clinical Context:
Guidelines for Antithrombotic Therapy for Atrial Fibrillation[10]

Table 23-2 American College of Chest Physicians - Guidelines for Antithrombotic Therapy for Atrial Fibrillation

Risk Factors	Number	Recommendation
High a	1	Warfarin b
Moderate c	>1	Warfarin b
	1	Warfarin b or aspirin
None	0	Aspirin d

a = Prior transient ischemic attack, stroke or systemic embolus, hypertension, poor left ventricular function, congestive heart failure, rheumatic mitral valve disease or prosthetic heart valve, diabetes mellitus, or age >75 years.
b = Warfarin target international normalized ratio: 2.5 (range 2.0-3.0)
c = Age 65-75 years, diabetes mellitus, coronary artery disease with preserved left ventricular systolic function
d = Aspirin, 325 mg/day.

Clinical Context:

RMC vs. AMS [44]

Frequency of Hemorrhage and Thromboembolism with Routine Medical Care versus Anticoagulation Management Service

Trial	Year	Indication	Major Hemorrhage	Recurrent TE	Combined Events
Retrospective					
Cortelazzo	1993				
RMC		MHV	4.7	6.6	11.3
AMS		MHV	1.0	0.6	1.6
Chiquette	1998				
RMC		Mixed	3.9	11.8	15.7
AMS		Mixed	1.6	3.3	4.9
Witt	2005				
RMC		Mixed	2.2	3.0	5.2
AMS		Mixed	2.1	1.2	3.3
Randomized					
Matchar	2002				
RMC		AF	1.6	7.4	9.0
AMS		AF	1.7	5.2	6.9
Wilson	2003				
RMC		Mixed	0.9	1.8	2.7
AMS		Mixed	1.8	0.9	2.7

RMC=Usual Care; AMS= Anticoagulation Management Service; AF=Atrial Fibrillation; MHV= Mechanical Heart Valve; TE=Thromboembolism

Clinical Context:
Study

Death and Disability from Warfarin-Associated Intracranial and Extracranial Hemorrhages [7,12,13]

- **Objectives:**
  - Rates of death and disability resulting from warfarin-associated intracranial and extracranial hemorrhages in a large cohort of patients with atrial fibrillation
    - Anticoagulation therapy with warfarin can reduce the risk for ischemic stroke by 68%, but, also increases the risk for major hemorrhagic complications
    - Rates of ischemic stroke in patients with atrial fibrillation who are not taking warfarin can be as high as 12% per year
    - Proportion of patients who have major functional disability after an atrial fibrillation-related ischemic stroke is substantial, as high as 59%

Clinical Context:
Study

Death and Disability from Warfarin-Associated Intracranial and Extracranial Hemorrhages[7,12,13]

- **Results:**
  - 72 intracranial and 98 major extracranial hemorrhages occurring in more than 15,300 person-years of warfarin exposure
  - At discharge, 76% of patients with intracranial hemorrhage had severe disability or died compared with only 3% of those with major extracranial hemorrhage
- **Conclusions:**
  - Intracranial hemorrhages caused approximately 90% of the deaths from warfarin-associated hemorrhage and the majority of disability among survivors
  - When considering anticoagulation, patients and clinicians need to weigh the risk of intracranial hemorrhage far more than the risk of all major hemorrhages

Clinical Context:
Study

Death and Disability from Warfarin-Associated Intracranial and Extracranial Hemorrhages[7,12,13]

- **Discussion:**
  - Data demonstrates…
    - Intracranial hemorrhage (ICH) overwhelmingly determines poor outcomes from warfarin
    - As a result, the risk of extracranial hemorrhage (ECH) should have a relatively small effect on decisions about warfarin therapy in atrial fibrillation.
  - Rates of ICH on warfarin observed…
    - Still considerably lower than the rates of ischemic stroke while the patient was not taking warfarin
    - Rate of thromboembolism occurring without warfarin therapy was 2.5 per 100 person-years in the overall ATRIA cohort and even higher in other cohorts
    - Rates are reduced by more than 50% by warfarin therapy.
    - Benefit exceeds additional risk of warfarin-associated ICH
      - 0.47 per 100 person-years with warfarin therapy compared with 0.29 per 100 person years without warfarin

Clinical Context:

Drugs Commonly Implicated in Adverse Events Treated in ERs [14,15,16]

Table 5 Number of Cases and Annual Estimate of Drugs Most Commonly Implicated in Adverse Events Treated in Emergency Departments, United States, 2004-2005

Drug	Cases, No.	Annual Estimate, No.	Annual Estimate %
Insulins	1577	55819	8.0%
Warfarin	1234	43401	6.2%
Amoxicilin	1022	30135	4.3%
Aspirin	473	17734	2.5%
Trimethoprim-sulfamethoxazoie	447	15291	2.2%
Hyrocodone-acetaminophen	420	15512	2.2%
Ibuprofen	526	14852	2.1%
Acetaminophen	497	12832	1.8%
Ciopidogrel	241	10931	1.6%
Cephalexin	293	10628	1.5%
Penicillin	270	9275	1.3%
Amoxicillin - clavulanate	274	8959	1.3%
Azithromycin	255	8794	1.3%
Levoflaxacin	230	8682	1.2%
Naproxen	245	8634	1.2%
Phenytoin	238	7937	1.1%
Oxycodone-acetaminophen	227	7328	1.0%
Metformin	179	6678	1.0%

*Drugs implicated in >=1% of adverse events. For 434 cases (annual estimate, 15784 (2.2%) 2 of these 18 drugs were implicated in the adverse event.

Therefore, these 18 drugs accounted for adverse events in 8214 cases (annual estimate, 277/636 (39.6%). Estimates with coefficient of variation

Estimates with coefficient of variation >30% warfarin, 32.5% clopidogrel 36.6%.

Clinical Context:

Avoiding Over anticoagulation: Knowing your Antibiotics [17]

Warfarin Use is Complicated by a Relatively High Risk of Bleeding

- Bleeding rate is 5 to 15 per 100 patient years
  - Life threatening bleeds occurring at a rate of 1 to 2 per 100 patient years
- Rapidity of over-anticoagulation is an issue
- Standard recommendation - patients on warfarin therapy have an INR performed within 1 week of starting an antibiotic, but…
  - Over anticoagulation can occur within 3 days of starting some antibiotics

Clinical Context:
Avoiding Over anticoagulation: Knowing your Antibiotics [17]

- Evidence for interaction and risk of over-anticoagulation was considered highly probable for **co-trimoxazole, erythromycin** and **ciprofloxacillin**
  - For **erythromycin** and **ciprofloxacillin** this is in contrast to the findings in patients receiving acenocoumarol and phenprocoumon in whom these antibiotics were used frequently without a single episode of over-anticoagulation

Clinical Context:
Avoiding Over anticoagulation: Knowing your Antibiotics[17]

- Relative risks significantly increased for:
  - amoxicillin and sulfamethoxazole-trimethoprim,
- Highest relative risk 1-3 days after start of use were:
  - clarithromycin, norfloxacin, and trimethroprim (one of the two components in Bactrim)
- Relative risks of over-anticoagulation most strongly increased >=4 days after start of:
  - amoxicillin, doxycycline, sulfamethoxazole-trimethoprim (Bactrim)

Management Options

- **Routine Medical Care (RMC) or Usual Care (UC)**
- **Anticoagulation Monitoring and Management Service (AMMS)**
- **Patient Self-Management**
  - Self Testing (ST)
  - Self Monitoring (SM)

Management Options and Effectiveness[18]

Routine Medical Care (RMC) or Usual Care (UC)

- Patient managed by PCP, internist, cardiologist, etc.
- Many practices don't have processes in place to ensure patient is tracked and tested monthly;
- Low percent of time in therapeutic range

Management Options and Effectiveness[19]

Routine Medical Care: Quality of Clinical Documentation and Anticoagulation Control in Patients With Chronic Nonvalvular Atrial Fibrillation in Routine Medical Care[18]

- **Objective:** Anticoagulation quality and record documentation retrospectively assessed in chronic nonvalvular atrial fibrillation (CNVAF) patients managed in a routine care setting
- **Findings:** Two thirds of INRs > 3.0 or < 2.0 had no recorded dose change, nor did 45% of INRs > 5.0
- **Conclusion:** Serious deficiencies in quality and documentation of routine medical care of anticoagulation for patients with CNVAF continue to exist

Effectiveness of Management Strategies

Anticoagulation Monitoring and Management Services (AMMS) significantly improves clinical outcomes[20]

- Coordinated and focused approach to management of therapy by AMMS or these type of programs improves therapeutic control and time-in-therapeutic range (TTR)
  - Lessens the frequency of hemorrhage or thrombosis and decreases use of medical resources leading to more cost-effective therapy
  - Observational studies indicate a > 50% reduction in both major hemorrhage and thrombosis compared to usual care

Management Options and Effectiveness

Elements of a Well Run AMMS [41]

1. **Registry**
   - of patients who are on warfarin and enrolled in the AMMS
2. **Defined Program of Patient Education**
3. **Written Set of Guidelines**
   - for PA/RNs/RPhs to manage and monitor patients and simply notify MD if warfarin dose needs to be adjusted
4. **Specification of Targeted INR Range for Each Patient**
   - risk of bleeds can be dropped by 50%
5. **Follow-up Phone Calls by an RN, PA, or Pharmacist When;**
   - patient is overdue for an INR test or
   - the INR result is outside the targeted therapeutic range

Management Options and Effectiveness

Elements of a Well Run AMMS [41]

6. Algorithm for Dose Adjustments

- made when the INR is outside the targeted therapeutic range

7. Communication to MD

- Critically elevated INR test results especially if associated with bleeding, dose changes made, timing of next INR test, etc.
- MDs to notify AMMS if patient on new meds, esp. antibiotics

8. Software Package

- Incorporating above elements and reporting percent of time patient's INR's is below, within, and outside therapeutic range

9. Program for Measuring and Improving Performance

Estimated Average Annual Cost (Harvard Vanguard Medical Associates AMMS)

- $550-$650 per patient for AMMS
- Does not include cost of testing, warfarin prescriptions, and home INR self testing or self monitoring

Management Options and Effectiveness

AMMS: Effect of a Centralized Clinical Pharmacy Anticoagulation Service on the Outcomes of Anticoagulation Therapy[21]

- **Objective:** To compare clinical outcomes associated with anticoagulation therapy provided by this service to usual care
- **Results:** Patients in these services were 39% less likely to experience an anticoagulation therapy-related complication than were patients in the control group
  - Additional analyses revealed that improved outcomes associated with this service were mediated largely through improved therapeutic INR control
  - Patients in this service spent 63.5% of study period days within their target INR range compared to 55.2% in the control group
- **Conclusion:** A centralized, telephonic, pharmacists-managed anticoagulation monitoring service reduced the risk of anticoagulation therapy-related complications (major bleeds, thromboembolic, or fatal events) compared to that with usual care.
  - Cumulative evidence supporting the superior care associated with implementing a this service was sufficient to recommend wide-spread implementation

Management Options and Effectiveness

AMMS: Effect of a Centralized Clinical Pharmacy Anticoagulation Service on the Outcomes of Anticoagulation Therapy[21]

- **Comments:**
  - Most patients who experienced strokes while receiving anticoagulation therapy had subtherapeutic INR values.
  - Rate of stroke in control group was approximately 3 X that of the intervention group.
  - Most patients receiving warfarin therapy in U.S. are not enrolled in a structured AMMS
  - A coordinated, systematic approach to anticoagulation therapy may be more important than the method of management (i.e., telephone or in-person).
  - Models that include a systematic process utilizing a knowledgeable provider, reliable laboratory monitoring, and an organized system for timely patient follow-up and education will result in improved outcomes regardless of model type.

Management Options and Effectiveness

Patient Self Management [22, 29]

- **Self-Testing**
  - Patient uses home kit to test INR
  - 30% reduction in complications
  - Can self-test more than monthly
    - Results in a higher percent of INRs in the therapeutic range
  - Cost = $2000 per patient kit
  - Does not include phone call to patient for follow up
- **Self-Monitoring**
  - Patient uses home kit to test INR
  - Patient monitors INR range
  - Patient adjusts warfarin dose based on INR result

Effectiveness of Management Strategies[23,24]

- "Self management (SM) results in a control of anticoagulation that is at least as good, and potentially superior, to control by a specialized anticoagulation service in a randomized cross-over trial"

- Fewer than 1% of patients managed by anticoagulation clinics use self-testing (ST) or SM
  - Primary barrier to ST and SM is the limited health insurance coverage (except for patients with mechanical heart valves)
    - Self-testing might be more prevalent if reimbursement were improved
  - Percent of patients willing and able to do ST or SM varies widely in clinical trials, but generally is below 25%.

Management Options and Effectiveness

ST and SM: Patient Self Testing and Management is much better than Routine Care and even better than AMMS[44]

Table 44-1 Studies of Patient Self-Testing and Patient Self-Management of Oral Anticoagulation Stratified by Whether the Comparator Group Is Routine Medical Care or an Anticoagulation Management Service Model of Care

Study	Study Groups	Time in Range
Horstkotte et al (1996) (RCT)	PSM vs RMC	92% vs 59%
Sawicki et al (1999) (RCT)	PSM vs RMC	57% vs 34%
Kortke et al (2001) (RCT)	PSM vs RMC	78% vs 61%
Sunderji et al (2004) (RCT)	PSM vs RMC	72% vs 63%
Beyth et al (2000) (RCT)	PST* vs RMC	56% vs 32%
Watzke et al (2000) (RCT)	PSM vs AMS	85% vs 74%
Ansell et al (1995) (cohort)	PSM vs AMS	88% vs 66%
Gadisseur et al (2003) (RCT)	PSM vs AMS	66% vs 64%

*Dose management for PST group performed by an anticoagulation management service.
RCT=randomized control trial; PST=patient self-testing; PSM=patient self-management; RMC=routine medical care; AMS=anticoagulation management service;

Management Options and Effectiveness

Long Term Self Management of Oral Anticoagulation [25, 27]

Several clinical studies determined that self-testing of INR is associated with improvements in time in range

Table 44-2 Long Term Patient Self-Management of Oral Anticoagulation

Clinical Outcomes	Self-Managed Patients	Control Patients	pValue
Number of patients	20	20	
Weekly warfarin dose	37.5 mg	34.8 mg	>.10
Mean duration in study (Mo.) (Range)	44.7 (3-87)	42.5 (3-86)	>.10
Number of PTs (mean/patient)	2153 (107.7)	1608 (80.4)	>.05
Mean interval between PTs (days)	13.8	16	>.10
PTs above range	5.2%	10.3%	<.001
PTs below range	6.30%	21.8%	<.001
PTs in range	88.6%	68.0%	<.001
Dose changes	10.7%	28.2%	<.001

Note: 20 patients followed over a period of 7 years measured their own PTs and adjusted their own warfarin doses based on guidelines provided by study investigators. Patient outcomes are compared with 20 matched controls.

Effectiveness of Management Strategies

Relationship Between Frequency of Testing and Outcomes [25]

- Recent clinical trials suggest that Time in Therapeutic Range (TTR) and fewer adverse drug events (ADEs) can be achieved by more frequent testing
  - While studies are neither definitive nor entirely generalizable, they do consistently support the hypothesis that frequency of testing improves outcomes
- Increased education and engagement of patients doing ST or SM are also important contributors towards the reduction of ADEs

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Cost-Effectiveness

Cost Effectiveness [44]

- All studies show reduced rates of thrombotic and hemorrhagic strokes in AMMS' vs. routine medical care.
  - The savings in "backend" costs more than offset the "front-end" costs.
- Capitated medical groups, e.g., Harvard Vanguard Medical Associates and Fallon Clinic in MA uniformly implement AMMS and save $ on these patients
  - Harvard Vanguard spent $1.2M for 3200 patients
- FFS medical groups (Mercy Hospital in Scranton) that operate an AMMS generally do so at a financial loss to the practice but do so to improve the quality of care their patients receive and the use of time of their physicians

Cost Effectiveness[31]

Economic Analysis of Systematic Anticoagulation Management vs. Routine Medical Care for Patients on Oral warfarin Therapy

- Anticoagulation therapy effectively reduces the risk of thromboembolism by more than two thirds for patients with atrial fibrillation
- A systematic approach to anticoagulation management has been shown to reduce rate of hemorrhagic events while reducing the risk of thromboembolic mortality and morbidity
- For a cohort of 1000 atrial fibrillation patients on warfarin therapy:
  - Total cost of systematic anticoagulation management was estimated to be $1,202,824.00.
    - Included cost of all anticoagulation-related adverse events
  - The total cost of routine medical care for anticoagulant therapy for this same cohort was $2,027,006.00

Cost Effectiveness[30]

Economic Analysis of Systematic Anticoagulation Management vs. Routine Medical Care for Patients on Oral Warfarin Therapy

- **Systematic anticoagulation management can provide revenue potential to the physician if:**
  - PT/INR test is provided at the point of care; and
  - physician or staff provides anticoagulation-related evaluation and management services
- **Some health care payers have established specific policies for the frequency of anticoagulation services for specific clinical indications**

Cost Effectiveness[31,32,33]

- **Physicians bear financial burden for tracking and record-keeping components of systematic anticoagulation management when a PT/INR result is reported to the physician from a standard reference laboratory**

- **Conversely, when the PT/INR test is performed at the point of care, the physician can be reimbursed for both the test and anticoagulation services**
  - Point-of-care PT/INR testing also has the additional benefit of being an enabling technology for systematic anticoagulation management by putting patient, physician, and test results in the same place at the same time, enabling proper patient evaluation and education

Cost Effectiveness [9,29,33]

Home Self Test

- Reduction in thrombotic and hemorrhagic complications below those achieved by an AMMS do not uniformly result in savings to the health care system, but do uniformly produce better health care outcomes.

- Cost effectiveness of home INR (POC) self-testing (ST) and self-management (SM) is uniformly favorable when patients' and family costs (mainly time of travel to a lab) are included in the analysis.

- CMS recently extended coverage of home INR testing beyond patients with mechanical heart valves to include patients with atrial fibrillation and DVT/PE…by far the most common indications for long term warfarin.

Cost Effectiveness[31,32]

Management Strategies

- **Usual Care vs. Anticoagulation Clinic (AMMS)**
  - 1.7 thromboembolic events and 2.0 hemorrhagic events avoided per 100 patients over 5 years (3.7 events avoided)
  - Resulted in a cost-effectiveness ratio of $31,327 per avoided event
- **Anticoagulation Clinic vs. Patient Self-Testing**
  - Another 4.0 thromboembolic events and 0.8 hemorrhagic events avoided per 100 patients over 5 years (4.8 events avoided)
  - Resulted in a cost-effectiveness ratio of $24,818 per avoided event
  - Resulted in overall cost savings > $140,000 per 100 patients
- **Net Result**
  - Discounted incremental cost-effectiveness ratios differ substantially depending on whether the costs incurred by patients (mainly the value of their time) and caregivers are included.
  - Costs presented above do not include long term costs associated with skilled nursing care and nursing home care for patients unable to take care of themselves due to a stroke

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Barriers

Potential Barriers

- **Physicians**
  - Not aware of available anticoagulation management and monitoring (AMMS) programs
  - Processes not established for management of patients in routine medical care (i.e., in the individual physician's office practice setting)
- **Reimbursement**
  - Coverage for providing an AMMS service
    - Can physicians and their staff be paid for all the non face-to-face services (example, phone calls) to monitor and manage patients?
      - Payment of new codes **99363 / 99364** would accomplish this
      - How can performance be evaluated to determine percentage of time patients are INR range?

Barriers

Barriers to Patient Self-Testing of Prothrombin Time: National Survey of Anticoagulation Practitioners [29,33]

- 60% of anticoagulation clinics prohibited INR self-testing for enrolled patients
- <1% of patients being managed by U.S. anticoagulation clinics use self-testing to obtain INR results
- Primary barriers were:
  - Cost of self-testing instruments (78.7% of respondents)
  - Cost of reagent cartridges (60.4%)
  - Fear self-testing might lead to unintended self-management (35.7%)
- Over 75% of respondents believed that some reimbursement for the cost of self-testing devices and supplies would increase the likelihood that anticoagulation clinics would recommend INR self-testing

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Specific Clinical Issues

- Genetic Testing
- Surgeries Performed on Warfarin

Genetic Testing

Pre-warfarin Treatment – Should It Be Standard Practice? [34,35]

- The FDA has issued a black box warning

  "In our view, evidence of a greater risk of not achieving a stable INR as quickly as possible during the induction period, and an increased risk of over and under anticoagulation shortly after commencing warfarin therapy, attributable to not considering pharmacogenetics is substantial; it is necessary to communicate this information in the label in a way that is supported by the scientific and clinical evidence".

- Most researches and clinicians remain unconvinced from NHLBI

  "After strong association between genotype and drug sensitivity have been identified, trials must be conducted to evaluate the clinical efficacy of the gene-based prescribing strategy and to determine whether the increment in efficacy or safety warrants the cost of genetic testing".

Genetic Testing

Why The Concern?[42]

- "....patients carrying VKORC, haplotype A had significantly higher INR values in the first week than did non-A homozygotes, the VKORC, haplotype predicted both the time to the first INR within the therapeutic range and the time to the first INR of >4.

Why/To Whom Is This a Risk?

- Cerebral Amyloid angiopathy (CAA)...involves the superficial vessels of the cortex...and is an important contibutor to warfarin associated lobar hemorrhage. The majority of the hemorrhages occur from a particular vascular predisposition, rather than from excessive anticoagulation.

- Elevated risk of CAA and ICH in elderly is counter balanced however, by a parallel increase with age in risk of thromboembolic stroke.

Surgeries That Can Be Performed on Warfarin [36,37]

Dental

- Restorations
- Endodontics
- Prosthetics
- Uncomplicated extractions
- Dental hygiene treatment
- Peridontal therapy

Ophthalmologic

- Cataract extractions
- Trabeculectomies
- Dermatologic
- Mohs micrographic surgery
- Simple excisions and repairs

GI

- Upper endoscopy with/out biopsy
- Flexible sigmoidoscopy with/out biopsy
- Colonoscopy with/out biopsy
- ERCP without sphincterotomy
- Biliary stent insertion without sphincterotomy
- Endosonography without fine-needle aspiration
- Push enteroscopy of the small bowel

Orthopedic

- Joint aspiration
- Soft tissue injections
- Minor podiatric procedures

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The Massachusetts Approach

Warfarin Related Morbidity [38]

- Hospital admissions due to major bleeds and thrombotic strokes during 12 months ending 10/1/01 (patients on warfarin at least 90 days)

- Combined claims data for Fallon and Tufts HMO members, N=980,000

Patients on warfarin	**10,449**
Hospital Admissions	**491**
Hospital Days	**2,192**

- Can expect approximately one major bleed or thrombotic stroke annually for every 20 patients on warfarin

Preventable Warfarin Morbidity [38]

- **Fallon study reviewed transaction data and inpatient and outpatient charts for all serious ADEs over 12 months in a population of 28,000 seniors**
  - All records judged by two independent physician reviewers.
- **Warfarin misadventures judged to be preventable in 36% of cases**
  - More frequently than other ADEs
- **Most common errors related to prescribing and monitoring of therapy, with patient compliance problems noted as well**

Statewide Implications [38]

- Using the combined Fallon/Tufts data, and 2002 census data for Massachusetts, the following projections are made for people on warfarin treatment:
  - **3200 major bleeds and thrombotic strokes annually**
  - **1150 potentially preventable, including hundreds of permanent disabilities and deaths**
- This is a major public health problem!

Anticoagulation Management in Massachusetts

Identified as one top priority for Coalition

- **Goal - *"Change Agent" Campaign: Transform healthcare across settings to eliminate harm due to anticoagulation management in Massachusetts***
  - Eliminate preventable adverse events due to anticoagulation, by December 2011
  - Reduce adverse events related to anticoagulation during hospital stays and after discharge by 75% by December 2008
  - Reduce preventable adverse events from anticoagulation in all healthcare settings by 50% by December 2009
  - 100% participation by hospitals, 90% participation by long term care facilities, and 100% participation by large group practices

A Massachusetts Collaboration

- **Partnership includes:**
  - MA Coalition for the Prevention of Medical Errors
    - Investigating current practice, networking with experts and partners, identifying clinical and payment issues, establishing best practices, and determining implementation strategies
  - Massachusetts Medical Society[39]
    - Conducted MA physician survey of current practices
    - Planning CME initiative with MA Coalition
  - Massachusetts Association of Health Plans
    - Discussed problem and strategies regarding barriers related to coverage

MA Physician Survey 39

MA Medical Society partnered with MA Coalition in the physician warfarin survey to:

- determine the current state of MA physician practices related to the monitoring and management of patients who might be candidates for long term anticoagulation

Survey sent to MMS members in the specialties judged most likely to write warfarin prescriptions:

- **Cardiology**
- **Family Medicine**
- **Geriatrics**
- **Internal Medicine**
- **Neurology**
- **Oncology**
- **Orthopedics**

MA Physician Survey [39]

- Survey distributed to 1508 Massachusetts physicians
- 185 responded (12.3% response rate)
- Concerns regarding how representative the respondent sample was
  - Respondents came from large group and hospital-based practices rather than solo or small group practices
- PCP's (Family Medicine. Geriatrics and Internal Medicine) accounted for 73% of the patients on warfarin
  - Other specialties together accounting for only 27%
- 72% of the respondents had >10 patients in their practice on warfarin
- Three most common clinical indications for warfarin together accounted for >75% of the patients on this drug:
  - Atrial Fibrillation (AF)
  - Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE); and
  - Mechanical heart valves (MHV)

MA Physician Survey [39]

- **35% of patients with "a history of a CVA and/or TIA, but without a documented history of AF", were reported to be on warfarin**
  - Not considered a valid indication for warfarin
  - Aspirin is the drug of choice for these patients
- **The % of patients with chronic or paroxysmal AF reported to be on warfarin (76.7%) is far higher than the usually reported national experience (45-55%)**
- **23.2% of respondents said they maintained <2/3 of their patients with AF on warfarin**
- **Of the patients maintained on long term warfarin therapy:**
  - 78.1% reported using point-of-care (POC) testing
    - mostly done in their office (29.4%) or their lab (48.6%)
    - very few (only 6.6%) reported using it in their patients' homes

MA Physician Survey [39]

- **100% of those using an AMMS said it included specification of the targeted therapeutic range**
- **15-20% using an AMMS lacked 1 or more of the desired elements of a well run AMMS**
- **Reasons given for not treating all patients with clinical indications for the use of warfarin included:**
    a) history or risk of falls
    b) high risk for ICH
    c) history of poor compliance

MA Physician Survey 39

- **Actions requested of MMS:**
  a) work with payers to improve reimbursement
  b) provide opportunities to learn about "best practices" in MA
  c) identify an AMMS in my practice region to which I could refer my patients
  d) provide me instructions (a toolkit) to enable me to set up an AMMS within my current practice setting

- **Use web-based learning and written materials**
  – rather than conferences held away from my practice

The Massachusetts Initiative…

Will Cross Health Care Settings and Include:

- Improvement to Delivery System
  - Large Practices/Small Practices
    - ➢ Patient Referral to an AMMS
  - Guidelines
    - ➢ Clinical, Management and Monitoring, Transitions, Measures, Patient Education, Provider Education
  - Toolkit
  - Curriculum
- Payer Incentives
- Communications
    - ➢ Patients, Providers, Anticoagulation Clinics, Health Centers, SNFs, Nursing Homes
- Evaluation

Guidelines

Clinical [41]

- **Provider Competencies**
  - Suggesting minimum requirements be met
- **Qualifications of Personnel**
- **Supervision**
- **Patient Assessment and Selection**
  - Criteria will be shared
- **Initiation of Therapy**
  - Maintenance and Management of Therapy
  - Management and Triage of Therapy-Related and Unrelated Problems

Guidelines

Management & Monitoring [41]

- **Care Management and Coordination**
  - Communication and Documentation
  - Laboratory Monitoring
  - Patient Outcomes

- **Review of software systems and POC devices to determine benefits**

Guidelines [4,6,21,38,,43,45]

Transitions

- Identified the transition of warfarin patients from one setting to another as problematic
  - 83.6% missing some information for discharge
    - 59.9% missing last 3 INRs with dates
    - 55% missing last 3 doses
    - Pre-initiative rate of transitions with complete information of 16.4% for all 5 hospitals (2 tertiary, 3 community) increased to 90-98% for all 5 hospitals after initiative
- Separate set of issues identified for nursing home patients on warfarin
- Patients prescribed warfarin were:
  - More than twice as likely (odds ratio of 2.6) to discontinue warfarin after an overnight hospitalization for elective surgery
  - More than one and a half times as likely (odds ratio of 1.6) to discontinue warfarin after an ambulatory procedure

Measures

- Time in Therapeutic Range
- Percent of patients tested monthly

Guidelines [41]

Patient Education

- Anticoagulation provider should have a policy and procedure pertaining to the desired goals and objectives of its educational program
  - Patient education should be individualized according to the initial assessment
  - Based on the patient's level of understanding
  - Accompanied by written information as a reinforcement
  - Reviewed on a regular basis

Provider Education

- Clinical Guidelines
- Provider Competencies
- Patient Assessment and Selection Criteria
- Patient Registries and Follow Up

Toolkit [41]

- **Guidelines for Organization and Management**
  - Qualifications of Personnel
  - Supervision
  - Care Management and Coordination
  - Communication and Documentation
  - Laboratory Monitoring
- **Guidelines for the Process of Patient Care**
  - Patient Selection and Assessment
  - Initiation of Therapy
  - Maintenance and Management of Therapy
  - Patient Education
  - Management and Triage of Therapy-Related and Unrelated Problems
- **Guidelines for the Evaluation of Patient Outcomes**
  - Organization Components
  - Patient Outcomes

Curriculum

Collaborate with MMS on physician education campaign

- Teach and share guidelines, best practices, and strategies for managing these patients according to established criteria
  - Web-based educational offering with CME credits
  - Vital Signs publication bringing awareness to issue

Communications [41]

Providers

- Develop education programs to teach and share best practices for:
  - AMMS
  - Health Centers
  - Hospitals
  - SNFs
  - Nursing Homes
- Providers should have policies and procedures regarding communications with the:
  - Patient
  - Primary care physician or other provider
  - Laboratory
  - Designated pharmacies

Communications 41

Patients

- **Educate patients, families, consumers about the relevant clinical and system issues to promote awareness of this important issue**
  - State reason for taking warfarin – relation to clot information
  - Recite name of drug (generic and trade)
  - Discuss how drug works (problems with too much or too little)
  - Explain need for blood tests and target INR
  - Recite importance of adherence, close monitoring, regular appointments, follow up
  - Describe common signs of bleeding
  - Outline precautionary measures to decrease trauma and bleeding
  - Identify diet, drug, alcohol use that may cause problems with therapy
  - Explain importance of not becoming pregnant and need for birth control measures
  - Report honestly changes in lifestyle, diet, medications, alcohol intake, disease
  - Inform provider when dental, surgical, or invasive procedures are scheduled or occur unexpectedly
  - State what to do in case of an emergency
  - Identify the specific tablet or tablets, by color and markings, the patient is taking.

Payer Incentives

Working with Massachusetts health plans

- **Activate two new codes for an AMMS**
  - 99363 for the initial 90 days on warfarin
    - covers work involved in adjusting warfarin levels based on a review of a patient's INR measurements
    - requires at least 8 INR's in the 90 day period
    - bill the code on the 90th day of management
  - 99364 for each subsequent 90-day period of management
    - requires only 3 INR measurements
- **Expand coverage of home INR testing beyond mechanical heart valve patients to include patients with AF, DVT, and PE**

Payer Incentives

Working with Massachusetts health plans

- **Pay a monthly case rate for any member on warfarin**
  - Explore the possibility of setting up a credentialing system with participation in it as a condition of receiving a monthly case payment.
  - Require the use of an agreed upon set of clinical guidelines that include:
    - patient registry
    - patient education
    - frequency of testing
    - specification of the target therapeutic range
    - tracking of every patient for missed lab tests
    - clarification of the system to be used for out of range INR's,
    - repeat testing after a dose change
    - tracking the use of any additional meds known to affect the INR

- **Explore P4P payment increments for practices**
  - For example, reporting on the % of INR values within the therapeutic range or time in therapeutic range (or other approach to measuring performance) and reward documented improvements in performance

Evaluation

Determine impact of initiative

- Evaluate overall rate of decrease in strokes and bleeds
- Determine increase in proportion of atrial fibrillation patients treated with warfarin and treated in an AMMS

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Conclusions and Next Steps

Conclusions

- Warfarin is an important, dangerous, and underused drug
- Rate of complications of long term outpatient anticoagulation with warfarin can be greatly reduced when patients are cared for in a program with the essential elements of an AMMS
- Point-of-care (POC) INR Self-Testing (ST) and Self-Management (SM) can reduce the complication rates further for selected patients once the barriers are removed

Conclusions (cont'd)

- Collaboration among patient safety organizations, regulatory and credentialing agencies, medical societies, specialty organizations,hospitals, extended care facilities, and health plans is needed to
  - establish the practice standard that all long-term anticoagulation patients should be cared for in an AMMS; and
  - promote the use of ST and SM among selected patients

Next Steps

- MA Coalition with its partners will…
  - Address anticoagulation management in the ambulatory setting first
    - Share processes and guidelines that contribute to improvement of anticoagulation management in Massachusetts
  - Address this topic in long-term care facilities
  - Work with payers to address financial concerns
  - Establish measures to evaluate improvement

Contacts

- The MA Coalition is interested in connecting with clinics and providers working to improve anticoagulation management
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