POC INR: From Professional Use to Patient Self Testing

Sheila K. Coffman BSMT (ASCP)

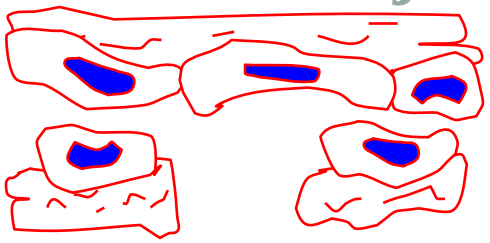
Objectives:

After participation in this presentation, you should be able to:

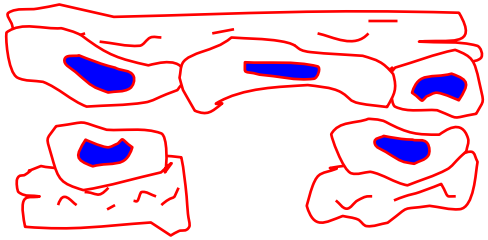
- Understand the basic criteria for selecting a POC PT/INR device
- Understand the implementation requirements
- Provide troubleshooting of POC PT/INR testing
- Explain the process of Patient Self Testing (PST)

Clot Formation

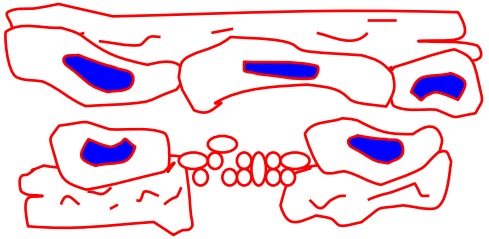
Vessel Wall Injury



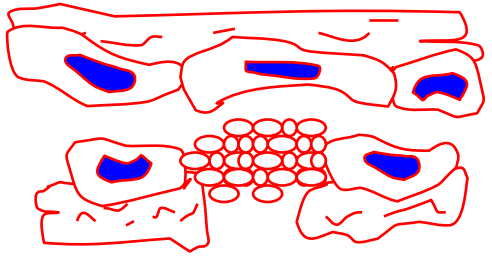
Vessel Wall Contraction



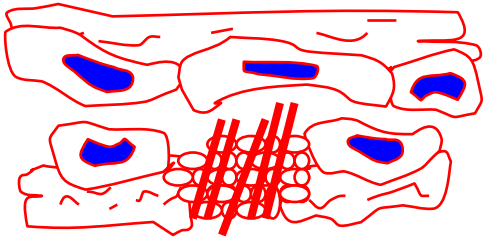
Platelet Adhesion



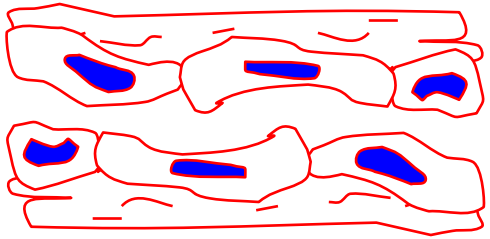
Platelet Aggregation



Fibrin Formation



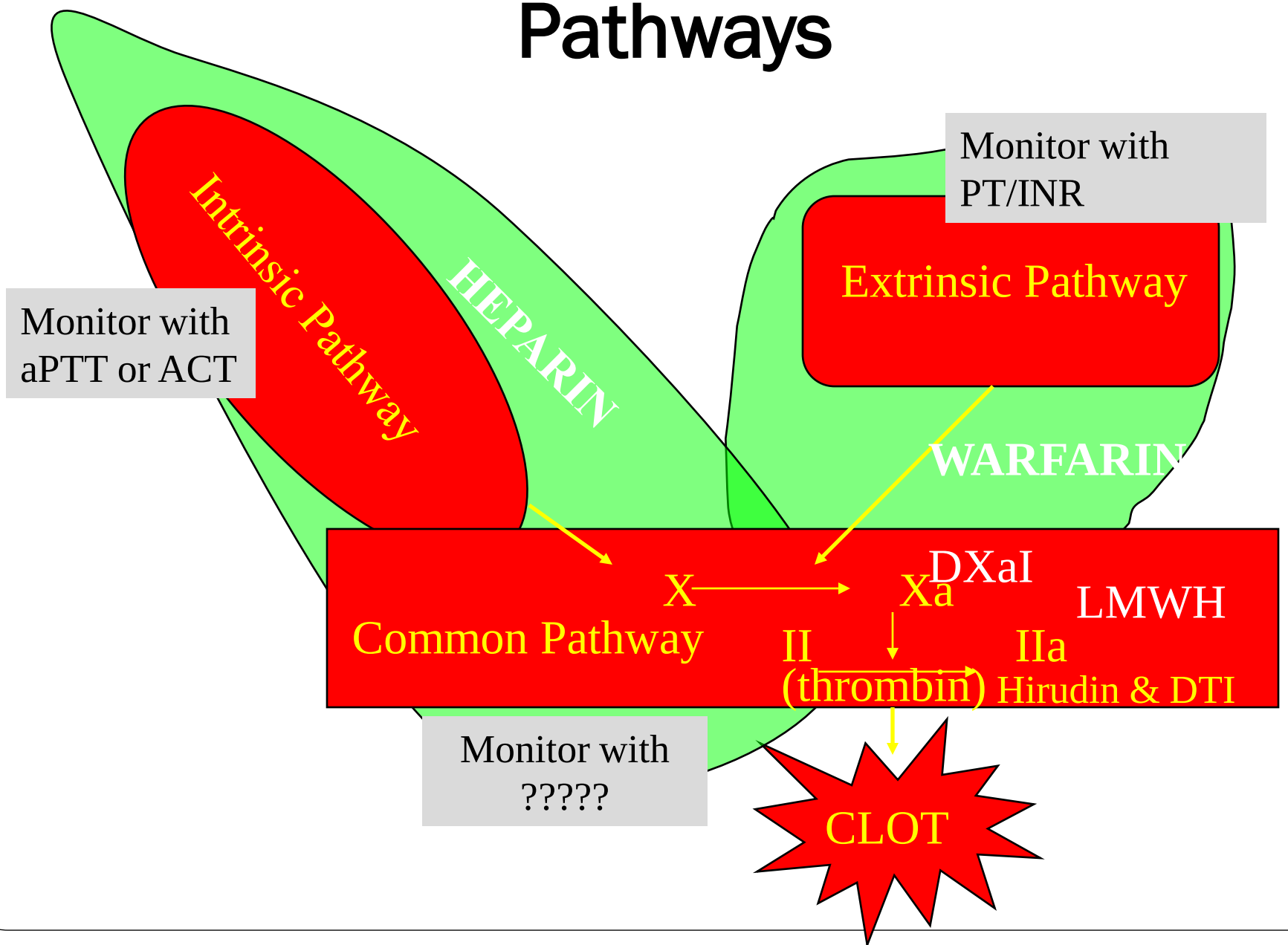
Fibrinolysis & Repair



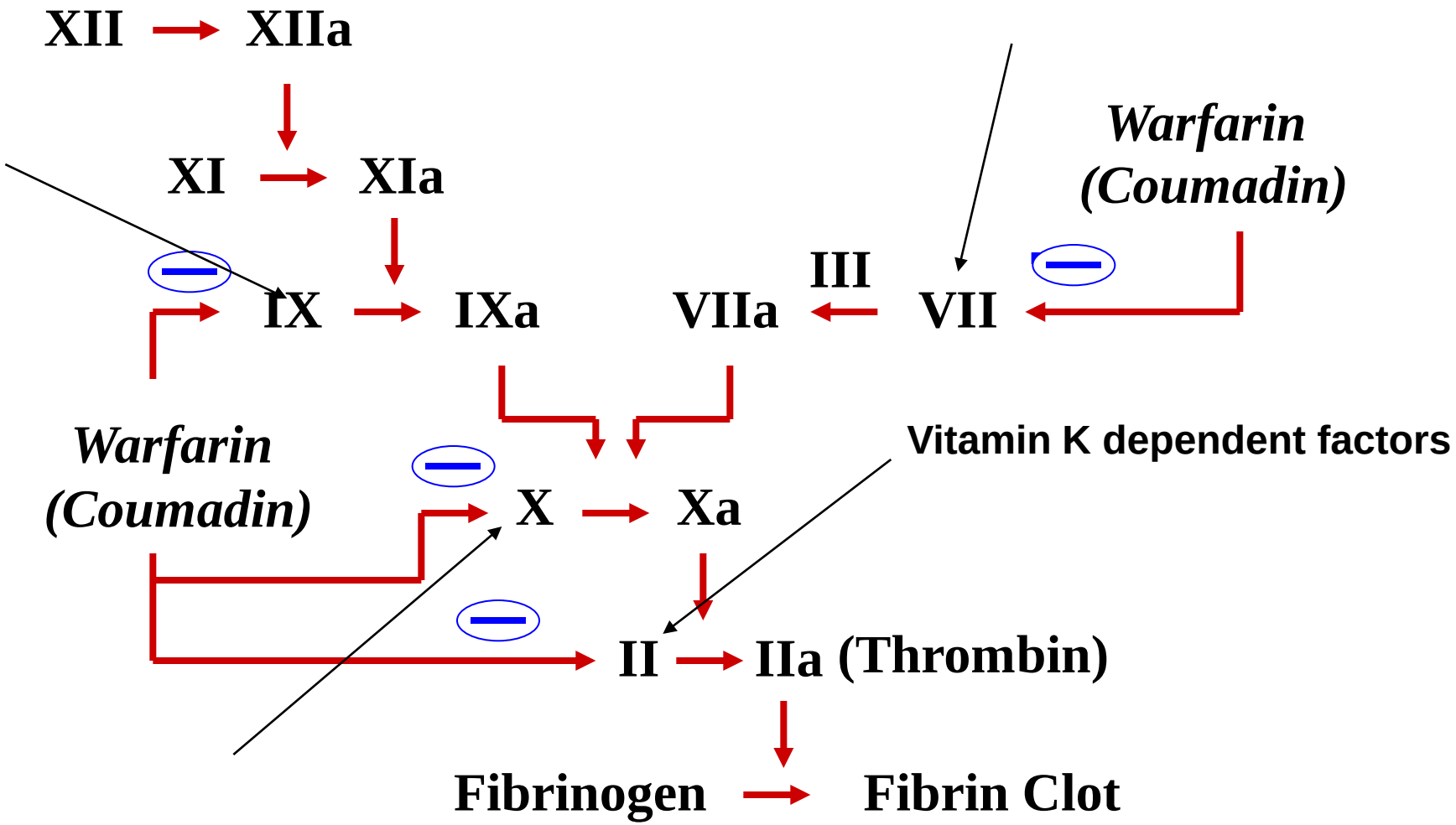
Clotting Associated with Disease States

- Artificial heart valve replacement
- Heart attack
- Atrial fibrillation (Afib) ~ abnormal rhythm and rate of the heart
- Deep Vein Thrombosis (DVT) ~ clots in leg or pelvic veins causing swelling and discomfort
- Pulmonary embolus ~ a blood clot that travels to the lungs
- Hereditary disorders ~ deficiencies in blood proteins or production of antibodies that cause the blood to clot or prevent the blood from clotting

Pathways


Monitor with
PT/INR
Intrinsic Pathway
HEPARIN
Extrinsic Pathway
Monitor with
aPTT or ACT
WARFARIN
X
Xa
DXaI
LMWH
Common Pathway
II
IIa
(thrombin)
Hirudin & DTI
Monitor with
?????
CLOT

Inhibition of the Coagulation Cascade by Warfarin



How Long Until Warfarin Affected Factors Decrease?

Factor	*Approximate Half Life*
VII	4 - 7 hours
IX	12 - 24 hours
X	40 - 45 hours
II	60 – 70 hours

Black Box Warning

Bristol Myers Squibb Company

Rx only

COUMADIN® TABLETS
(Warfarin Sodium Tablets, USP) Crystalline

Anticoagulant

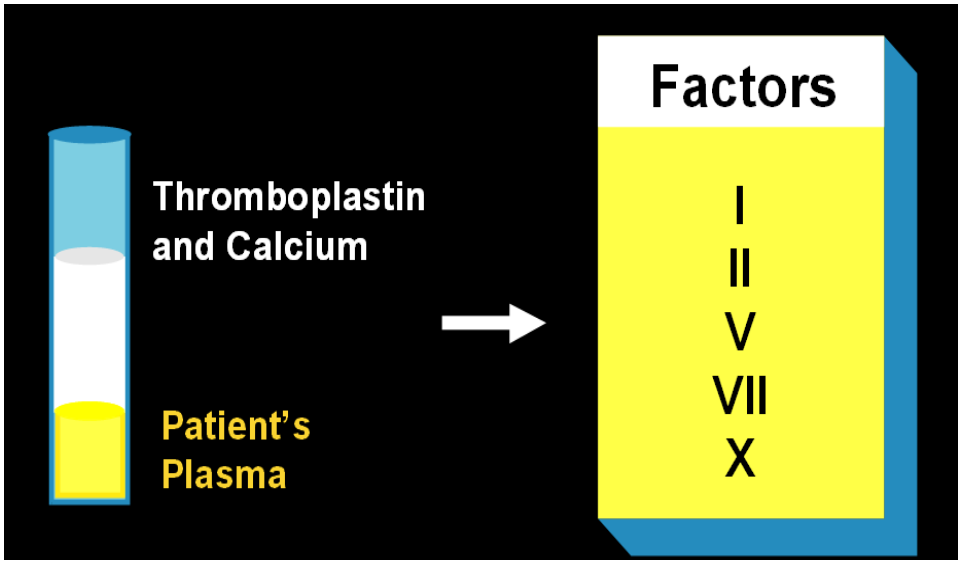
COUMADIN® FOR INJECTION
(Warfarin Sodium for Injection, USP)

WARNING: BLEEDING RISK

Warfarin sodium can cause major or fatal bleeding. Bleeding is more likely to occur during the starting period and with a higher dose (resulting in a higher INR). Risk factors for bleeding include high intensity of anticoagulation (INR >4.0), age ≥65, highly variable INRs, history of gastrointestinal bleeding, hypertension, cerebrovascular disease, serious heart disease, anemia, malignancy, trauma, renal insufficiency, concomitant drugs (see **PRECAUTIONS**), and long duration of warfarin therapy. Regular monitoring of INR should be performed on all treated patients. Those at high risk of bleeding may benefit from more frequent INR monitoring, careful dose adjustment to desired INR, and a shorter duration of therapy. Patients should be instructed about prevention measures to minimize risk of bleeding and to report immediately to physicians signs and symptoms of bleeding (see **PRECAUTIONS: Information for Patients**).

Prothrombin Time

- PT Introduced in 1935 by A.J. Quick
- A "Global Screening Assay"



40 Years Later....

- Thromboplastin isolated from:
  - Different species
    - pig; cow; human; etc.
  - Different organs
    - brain; thymus; lung; etc.
- All yield different results
  - Results vary by instrument system in use
    - Manual tilt tube "gold standard"
    - Fibrometer; automated coagulation systems

PT Standardization

- 1977 – 1st IRP developed
  - International reference thromboplastin preparation
- 1983 – Kirkwood describes method to calibrate local thromboplastin to IRP
  - Define reagent ISI
    - International sensitivity index
- 1983 – WHO and ISTH recommend the use of the INR to standardize PT result reporting

INR

International Normalized Ratio (INR)

ISI = international Sensitivity Index

$$INR = \left(\frac{PT_{patient}}{PT_{meannormal}} \right)^{ISI}$$

Using the INR, **theoretically,** eliminates differences between PT reagents by standardizing to the WHO and allows results to be compared between labs regardless of the type of thromboplastin.

and ISI Values

PT seconds vs. ISI				
INR	ISI = 1.0	ISI = 1.4	ISI = 1.8	ISI = 2.0
1.00	13.05	12.75	12.45	12.30
1.50	19.58	17.03	15.60	15.06
2.00	26.10	20.92	18.30	17.39
2.50	32.63	24.53	20.71	19.45
3.00	39.15	27.95	22.92	21.30
3.50	45.68	31.20	24.97	23.01
4.00	52.20	34.32	26.89	24.60

The INR was designed to “normalize” results so that any result from any lab would lead to the same treatment decision.

POC INR Professional Use

The Joint Commission (TJC)

The Joint Commission of Accreditation of HealthCare Organization's National Patient Safety Goal 3E requirements call for the reduction in harm associated with the use of anticoagulation therapy through 2009.

The Joint Commission (2007). *2008 National Patient Safety Goals, Ambulatory Care.* Retrieved January 9, 2008, from the Joint Commission Web site: http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/08_amb_npsgs.htm

Choosing an Instrument

- **CLIA licensure**
  - Waived vs. Moderately complex
- **Features**
  - OID
    - Operator lock-out
  - PID
    - Patient lock-out
  - QC
    - On board controls
    - External liquid controls
    - EQC
  - Connectivity

Instrument Selection

- Go to each vendor website or operator's manual to get instrument specifications.
- Take this information and drop it into an Excel spreadsheet.
- Have the clinic highlight those criteria most important to them and then the POCC should do the same.

PST- instrument selection is at the discretion of the prescribing health care provider. The laboratory should feel comfortable making recommendations for testing devices.

What is the sample being tested?

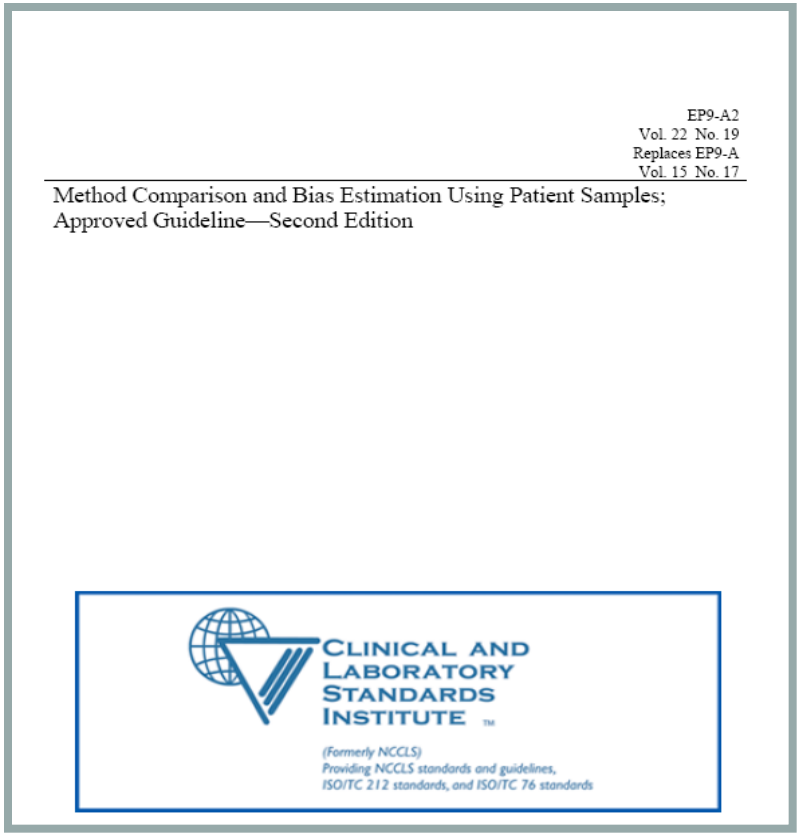
- **For most systems, the sample is fresh, non-anticoagulated venous whole blood, obtained either by finger stick or by venipuncture.**
- For some systems, there is an option for citrated whole blood
- For some systems, there is an option for citrated plasma
- Serum, which is clotted plasma and therefore depleted of several of the clotting factors, is never an option for coagulation testing

What is the clot detection in the POC device?

- Clot formation resists plunger that moves through the sample
- Thrombin from coagulation cascade releases an electroactive compound
- Impedance
- LED detects restriction in a channel
- Clot formation prevents movement of iron particles in a magnetic field
- Thrombin from coagulation cascade cleaves a chromogenic substrate releasing fluorescent rhodamine.

Method Validation

The "Correlation" Study



EP9-A2
Vol. 22 No. 19
Replaces EP9-A
Vol. 15 No. 17

Method Comparison and Bias Estimation Using Patient Samples;
Approved Guideline—Second Edition

CLINICAL AND LABORATORY STANDARDS INSTITUTE ™

(Formerly NCCLS)
Providing NCCLS standards and guidelines,
ISO/TC 212 standards, and ISO/TC 76 standards

Method Validation

Overview of the General Comparison Experiment

Evaluating an analytical method requires the following:

- Sufficient time for the operators to become familiar with the device's operation and maintenance procedures.
- Sufficient time for the operators to become familiar with the evaluation protocol.
- Assurance that both the test and the comparative methods are in proper quality control throughout the evaluation period.
- Sufficient data to ensure representative results for both the test and the comparative methods.

Method Validation

Comparison of Methods Experiment

Test Samples

Collect and handle patient samples according to accepted laboratory practice and manufacturer's recommendations.

Storage

The duration and conditions of storage depend on the stability of the measure and to be analyzed. Avoid storing samples, if possible.

Excluded Samples

If a sample is excluded, record the reason for the exclusion.

Method Validation

Range of Measurement

Evaluate the test method over the clinically meaningful range, i.e., where medical decisions are made. In general, this range extends from below to substantially above the expected reference range.

Therapeutic Range INR 2-4 and thus evaluation should cover INR 1- 6 minimally.

Analyte concentrations should be distributed over the analytical measurement range to the extent possible. The analytical measurement range is the analyte concentration interval claimed by the manufacturer to provide acceptable performance.

Method Validation

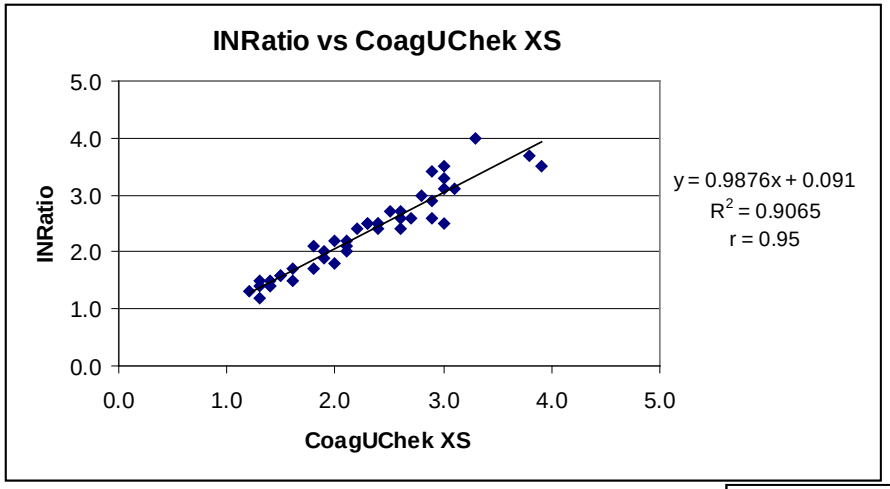
Number of Samples

Analyze 20-40 samples that meet the criteria. More samples will improve the confidence in the statistical estimates and increase the opportunity to incorporate the effects of unexpected interfering substances (individual idiosyncratic biases).

Time and Duration

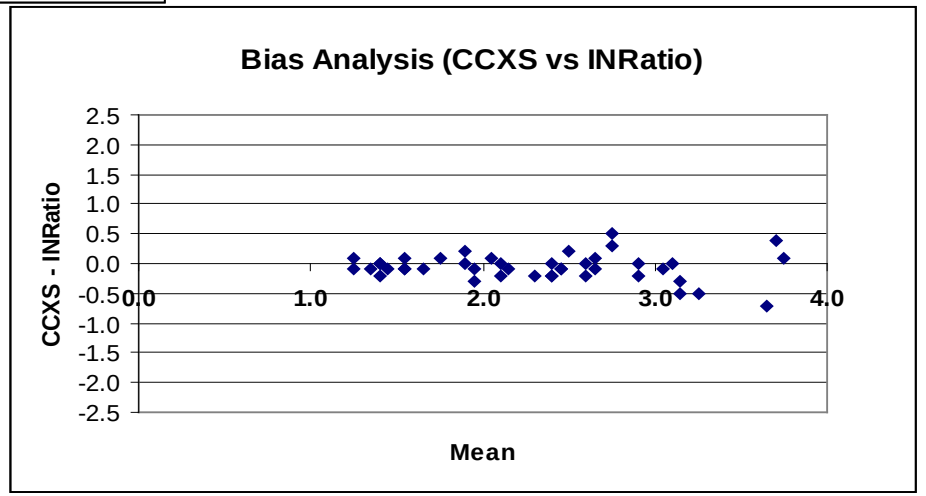
For a given sample, analysis by the comparative and test methods should occur within a time span consistent with the analyte stability.

Analysis



Linear Regression

Bland-Altman



Implementation

1. Make at least one person responsible for the POC process.
2. Provide a notebook/online with SOP, QC logs, reagent logs, package inserts, POCC business card, etc.
3. Ensure QC program understanding with proper documentation
4. Organize a maintenance program and provide logs
5. Ensure method of result recording and documentation retention
6. Order Proficiency Testing material (when available)

KEY TO SUCCESS STARTS HERE:

TRAINING

Training

Training of individuals should include the following:

- Theory of the instrument
- Specimen collection and application
- Instrument calibration
- Quality Control principles and procedures
- Patient Testing
- Instrument Maintenance
- Troubleshooting

Training

- Sources of Training
  - POCC taught in service.
  - Manufacturer's on-site training (Sales Rep. or Technical Specialist).
  - Manufacturer's web based training modules.
  - Train the Trainer (POCC-> MA -> Nurse -> Provider)
  - PST-Patients phone trained or face to face in service by nurse
- Content of Training
  - Direct Observation Competency
  - Knowledge Based Competency

Training

- Direct Observation
  - Patient Preparation
  - Specimen Collection
  - Specimen Application
  - Testing
  - Recording/reporting of results
  - QC Testing
  - Instrument maintenance
  - Testing assessment through:
    - Internal blind samples, PT

- Knowledge Based
  - Theory of instrument
  - Storage Requirements
  - QC Requirements
  - Troubleshooting

Process Improvement Initiative- Competency should be adjusted periodically to account for observed errors, FAQ and package insert changes.

Procedure

- Purpose
- Clinical Significance
- Forms and Records
- Specimen Collection
- Equipment and Materials
- Calibration
- QC
- Steps in the Patient Testing
- Calculations
- Reporting of Results
- Procedure Notes
- Limitations

Including a section on troubleshooting/error codes can be very insightful to clinic personnel. This can be copy/pasted from the manufacturer operator's manual.

Quality Control

The manufacturer should develop system-specific QC recommendations that are consistent with the robustness and stability of the test system, its intended use, and with the device's process controls and available QC modalities.

NACCLS (CLSI) H49-A

Quality Control Options

- Internal Control (on board)
- External Control (liquid)
- Equivalent Quality Control (EQC)

Maintenance

- Follow manufacturer recommendations.
  - Cleaning
  - Temperature verification
  - Battery Replacement/charging

Connectivity

Connectivity can be achieved several ways-

Data Management Software:

- RALS (mod complex devices)
- Telcor (mod complex devices)

Disease Management Software:

- Standing Stone-CoagClinic
- Web INR
- ClotCare

Existing EMR

None!

“GUILTY UNTIL PROVEN INOCENT”

Troubleshooting

1. Pre-analytical Error
   - Hand warm?
   - Lancing performed correctly?
   - No over manipulation of the collection site?
   - One, large drop of blood collected?
2. Medication interference
   - Bridging Therapy (Heparin/LMWH)
     - Many PT/INR measurement systems (both lab and POC) are sensitive to Heparin and LMWH to varying degrees.
3. Disease interference
   - Antiphospholipid antibodies

The INR Equation

$$INR = (PT_{patient}/PT_{mean\ normal})^{ISI}$$

ISI: International Sensitivity Index for Thromboplastin Used for PT Determination

Example:

INR = 3.0

ISI = 2

$$3.0 = \left(\frac{17.3}{10}\right)^{2}$$

PT = 17.3 Seconds

ISI = 3

$$3.0 = \left(\frac{14.4}{10}\right)^{3}$$

PT = 14.4 Seconds

Accuracy and Comparison Issues

The following data comes from a 2006 laboratory proficiency check sample study (~3,500 labs reporting)

Sample #	Low reported result	High reported result	
1	0.8	1.0	0.2
2	2.3	3.6	1.3
3	2.3	3.7	1.4
4	2.5	4.1	1.6
5	3.9	7.5	3.6

Issues

- POC and Reference Lab results may not match
- POC Brand A & POC Brand B results may not match

Solution:

Correlation Study

Consideration:

- If Main Lab Service is optimized & phlebotomy is excellent, there may be less institutional interest in POC testing within the hospital because of the items in bullets 1 and 2 above

Bottom line

- Repeat any patient result not consistent with patient clinical presentation and history. If POC repeats and concern still exists, send to the laboratory for confirmation.
- When the result is above the "cut off", then the result SHOULD be verified by the laboratory.
- Consider adding correlated results to the correlation for a period of time.

Cost

- **POC-**
  - Typically more expensive per unit cost, but total cost is less expensive.
  - Lab pay or site pay?
    - Reagent rental, purchase, gratis devices w/ large reagent purchase?
- **PST-**
  - The burden of cost is on the patient to either pay out of pocket or support with insurance approval.

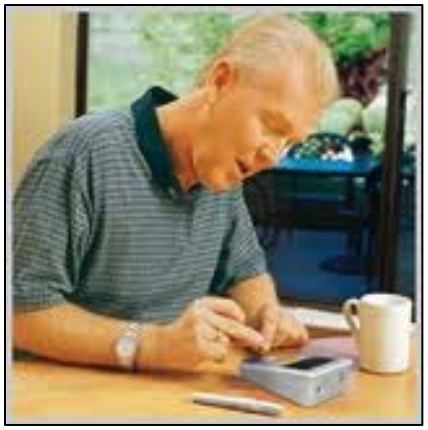
CPT **Codes**

- CPT 85610 code for Prothrombin Time .The QW Modifier indicating this is a waived test. Ohio $5.74
- Medicare reimburses for venous samples but not finger sticks. If the patient having the in-house PT test is covered by Private Insurance, you may be able to bill CPT code 36416.
- CPT 99201- 99205 E&M of New Patients.
- CPT 99211- 99215 E&M of Established Patients.
  - E/M services involve the following:
  - 1. Patient history documentation.
  - 2. Patient examination.
  - 3. Making medical decisions such as dose adjustments.

Ohio Statewide CPT Code 99211 Allowed Amount = $17.94

Source: http://cms.hhs.gov/ClinicalLabFeeSched/02_clinlab.asp

Patient Self Testing



CMS announces National Coverage Decision

Covers Home Prothrombin Monitoring

*"**Home prothrombin monitoring significantly improves time in therapeutic range** for select groups of patients, compared to physician offices or anticoagulation clinics."*

*"Increased time in therapeutic range (TTR) **leads to improved clinical outcomes** with reductions in thromboembolic and hemorrhagic events."*

Administrative File: CAG-00087C
September 18, 2001

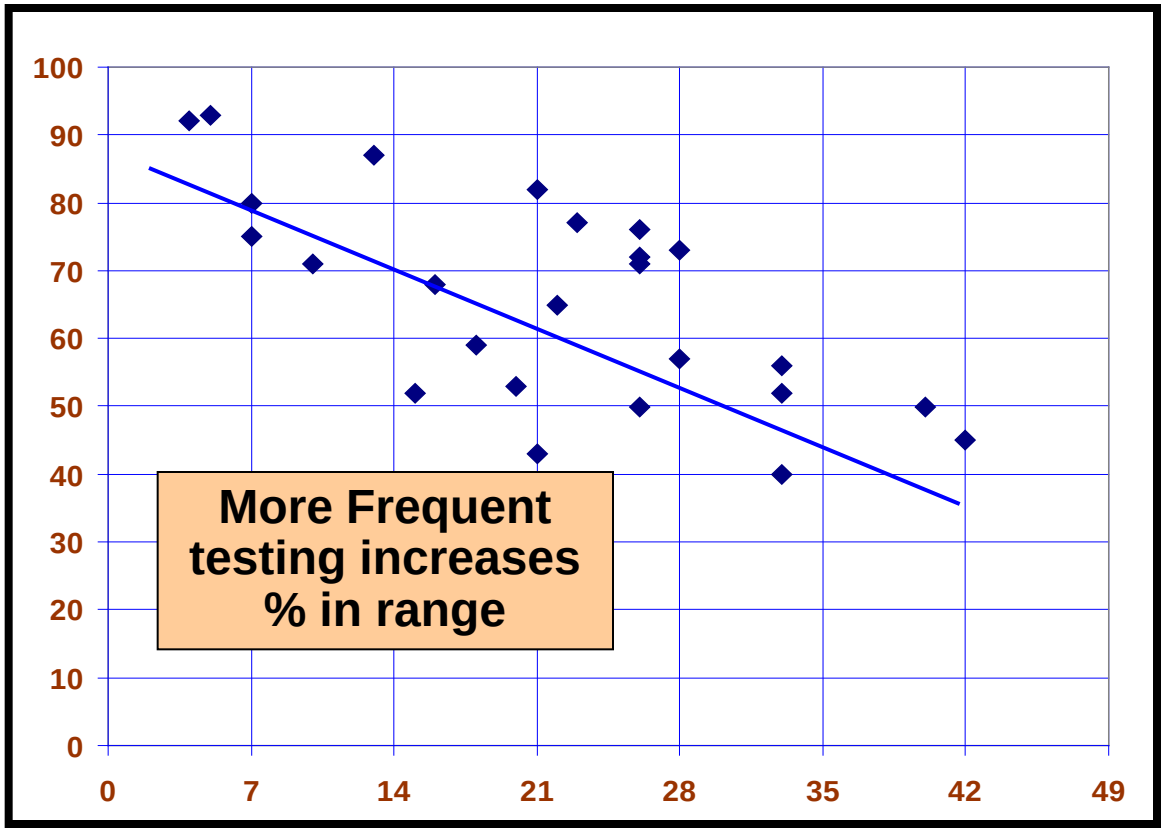
The 10 studies reviewed by CMS

Over 2,000 patients

Author, Year	Indications MHV	AF	Other	Numbers of patients	PST	PSM	Type of Study	Results Time in Range
White, 1989	X		X	50	X		RCT	17% increase
Ansell, 1995	X		X	40	X	X	Cohort	20% increase
Horskotte, '96	X			150	X	X	RCT	34% increase
Hasenkam'97	X			41	X	X	Case Ctr.	24% increase
Byeth, 1997	X	X	X	325	X	X	RCT	24% increase
Sawicki, 1999	X	X		179	X	X	RCT	23% increase
GELIA	X			278	X	X	RCT	11% increase
ESCAT	X			1,200	X	X	RCT	18% increase
Chromheecke	X	X	X	50	X	X	RCT	6% increase
Watzke, 2000	X	X	X	102	X	X	RCT	11% increase

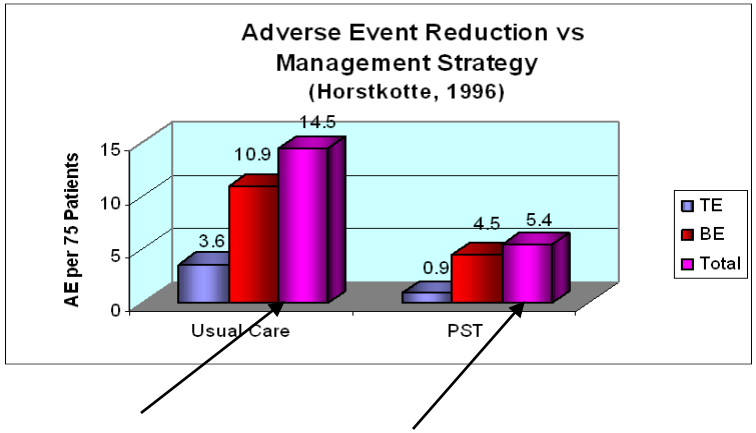
Average increase of TTR is > 19%

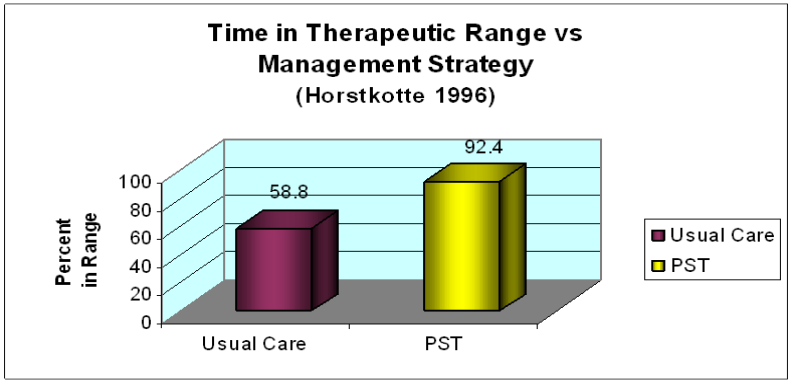
Test Interval vs % In Range

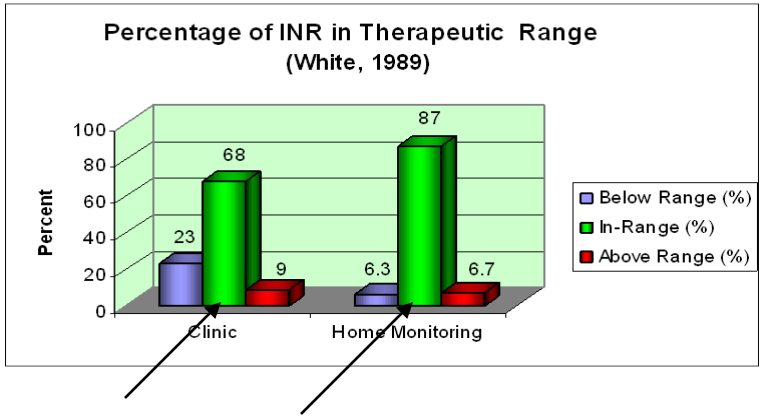


Summary 18 published studies: PST Coalition Report, July 2000

Increase TTR = Reduced Adverse Events







CMS recognized the value of Patient Self-Testing

PST Reimbursement

Eligibility:

- The patient must have been anti-coagulated for 3 months prior to use of a home INR device.
- The patient must undergo a face-to-face educational program on a/c management and must have demonstrated the correct use of the device prior to its use in the home.
- The patient continues to correctly use the device in the context of the management of the a/c therapy following the initiation of home monitoring.
- Self testing with the device should not occur more frequently than once a week.

CMS Coverage:

Benefit Component	Type	Provider	Code	Short Descriptor
Provide face-to-face training on the use of the home PT/ INR monitor	Technical	Physician or IDTF	G0248	Demonstrate use home inr mon
Issue PT/INR monitoring equipment and supplies to the patient for home testing	Technical	Physician or IDTF	G0249	Provide INR test mater/equip
Physician review and interpretation of results and patient management	Professional	Physician only	G0250	MD INR test revie inter mgmt

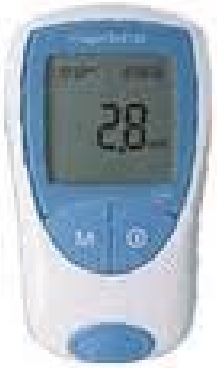
Ohio $137.86

Ohio $117.13

Ohio $9.61

PST Meters

Abbott CoaguSense



Roche CoaguChek

ITC ProTime

HemoSense INRatio

These meters are approved for professional and patient self testing.

Questions:

1. Does your institution have a Coumadin Clinic or service for A/C patients?
2. Do you use POC in this service? If yes, what were your criteria for the device?
3. What are your biggest concerns about POC INR?
4. How do you handle correlation issues?
5. Do you have connectivity for your POC INR device? PST?
6. Does your facility bill for POC INR?
7. Does your institution offer patient self testing?
8. Do you (laboratory) have any involvement in PST?

Q & A

Thank you!

Sheila K. Coffman BSMT (ASCP)

sheila.coffman@abbott.com

(407) 430-8520