

Autoverification

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Disclosures

- In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturers of the products or providers of the services that will be discussed in my presentation.

Objectives

- **Learning Outcome 1:**
 - Participants will be able to recognize the benefits and challenges of auto-verification of clinical laboratory results.
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- **Learning Outcome 2:**
 - Participants will be able to identify the parameters in clinical laboratory testing that are amenable to auto-verification.
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- **Learning Outcome 3:**
 - Participants will be able to describe how to design, validate, and implement auto-verification rules using CLSI guidelines as a guide.

Growing pressures on clinical laboratories

- “Do more with less!”
- Multiple factors are placing strain on clinical laboratories
 - Aging workforce
 - Insufficient numbers of new employees entering laboratory medicine
 - Continual pressure to reduce labor and supply costs
 - Declining revenue streams

Opportunities to increase efficiency

- Automated instruments
- Auto-verification
- Removing redundant practices
- Tackle mis-utilization of laboratory testing

- In general, optimize manual efforts of laboratory staff

Common time-consuming practices

- Manual verification of results
- Calls to clinical services
 - Critical values
 - Suboptimal specimens
- Manual re-run of specimens
- Dilution of specimens to obtain exact analyte concentration if not clinically useful
- Segregation of specimens into stat vs. routine

Critical values

Critical results (values)

- Joint Commission: “a pathophysiologic state at such variance with normal as to be life threatening if an action is not taken quickly and for which an effective action is possible”
- Critical result policies vary based on institution with no clear national guidelines
 - Influenced by population being tested and on-site test menu

Two common practices

- 1. Analysis repeated for specimens with critical values
- 2. Manual verification of all critical results—
not auto-verified

Critical results must be re-analyzed

- Get the data!
 - How often does repeat analysis change results?
- If data does not support - why delay reporting of the most time-sensitive results?
- Just because result is physiologically abnormal doesn't mean analysis is suspect
 - Distinguish from potentially “absurd” values (e.g., contaminated specimens)
 - Many critical results are well within analytical measuring range (AMR)
 - E.g., Serum K^+ of 2.4 or 7.5 mEq/L is generally well within AMR of most assays

“Critical results cannot be auto-verified”

- Common misconception – many believe that manual result release and notification of clinical service need to be coupled
- Auto-verification is acceptable by regulations and in fact can lead to better clinical care
- Still need to notify clinical service and document appropriately

Auto-verification

Research Article

Autoverification in a core clinical chemistry laboratory at an academic medical center

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University of Iowa Hospitals and Clinics (UIHC)

- 735 bed medical center located in Iowa City, IA
- Multi-specialty outpatient facility in nearby Coralville, IA
- Level 1 trauma center
- Referral center for many specialties

UIHC clinical laboratories

- Approximately 4 million billable tests per year
- LIS – Cerner Classic
- Several main laboratory sections
 - Core laboratory with chemistry, hematology, and flow cytometry
 - Microbiology and molecular pathology
 - DeGowin Blood Center
 - Anatomic pathology

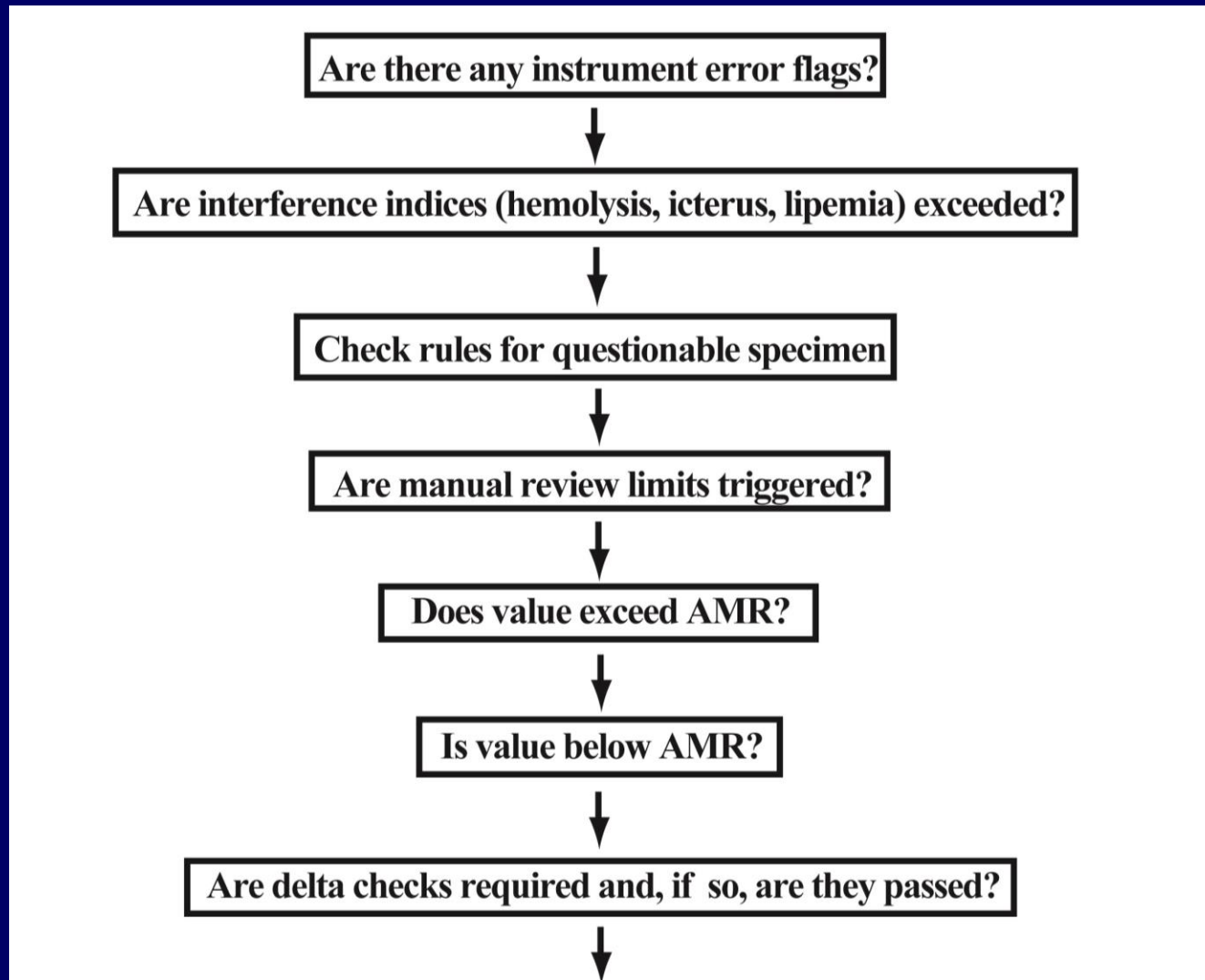
Auto-verification

- Verification of results without manual human action
 - Reduces time spent manually reviewing results
- Use pre-defined rules (indices, reference ranges, critical values) to govern release of results
 - Rules can define whether to auto-release results or hold for human intervention
 - Standardize result review (need to consider screen fatigue from staff manually reviewing hundreds or thousands of results per day)

Parameters often included in auto-verification rules

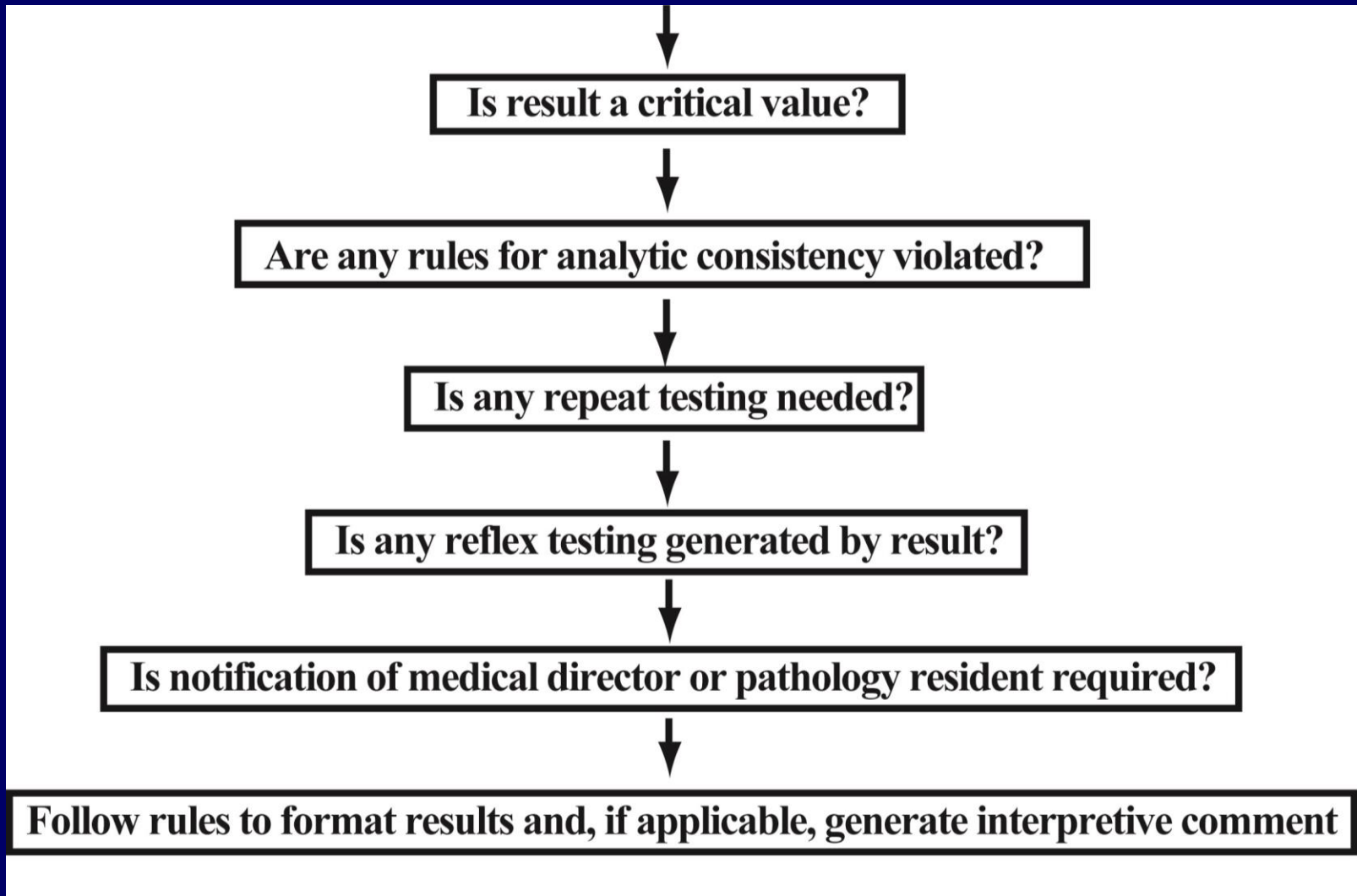
- Analyte reference (normal) ranges
- Instrument flags (short sample, possible bubble or clot, etc.)
- Indices (hemolysis, lipemia, icterus)
- Delta checks
- Calculations
- Conditions for re-analysis
 - Repeat measurement
 - Dilutions
 - Assays that occasionally give erroneous ‘fliers’

Example autoverification scheme



Ref: Krasowski MD et al. J Pathol Inform 5: 13, 2014.

Example autoverification scheme (cont.)



Ref: Krasowski MD et al. J Pathol Inform 5: 13, 2014.

Delta checks

- Comparing current patient result to previous results on same patient
 - Manual verification required if delta check limits exceeded
 - May be only way to detect mis-identified specimens (e.g., wrong patient label on a tube)
- However, if not set up well, can dramatically reduce rate of auto-verification
 - Can be especially tricky if testing a wide variety of patients (e.g., outpatients and ICUs)

Reference Change Value (RCV)

- May be used to determine delta check limits using analytical and biological variation

$$RCV = 2^{0.5} * Z * (CV_A^2 + CV_I^2)^{0.5}$$

- Z score = 1.96 at 95% probability and 2.58 at 99% probability
- CV_A = analytical variation
- CV_I = intra-individual variation (see <http://www.westgard.com/biodatabase1.htm> or find in published literature)

Example RCV calculation

- Albumin has a CV_A of 2.0% at 3 g/dL
- CV_I is 3.2% (Westgard website)

RCV at 99% =

$$1.414 * 2.58 * (2^2 + 3.2^2)^{0.5} = 13.8\%$$

- If the lab is interested in large variations in albumin ($P < 0.01$), a delta check limit of 13.8% or greater change in serial results could be set. This is equivalent to absolute difference of ~0.4 g/dL at 3 g/dL levels.

Index of Individuality

- Indicates which analytes are more likely to fluctuate within an individual
- Ratio of intra-individual variation (CV_I) and between-individual variation (CV_G)

$$=(CV_I/CV_G)$$

Ratio < 0.6 indicates analyte values are tightly regulated within an individual although they may vary between individuals

Index of Individuality

Analyte (units) ^a	Index of individuality ^b	Method CV _i , %
Alanine aminotransferase ^c (U/L)	0.47	3.2
Albumin (g/L)	0.31	3.4
Alkaline phosphatase ^c (U/L)	0.13	6.5
Apolipoprotein A (g/L)	0.39	4.8
Apolipoprotein B (g/L)	0.34	2.7
Aspartate aminotransferase ^c (U/L)	0.52	3.4
β -Carotene ^c (μ mol/L)	0.36	7.4
β -Cryptoxanthin ^c (μ mol/L)	0.35	7.7
Bicarbonate (mmol/L)	0.83	2.4
Bilirubin, total ^c (μ mol/L)	0.56	3.0
C peptide ^c (nmol/L)	0.43	7.2
Calcium, ionized ^c (mmol/L)	0.67	1.4
Calcium, total ^c (mmol/L)	0.70	2.2
Chloride (mmol/L)	0.61	1.0
Cholesterol, total ^c (mmol/L)	0.37	2.3
Creatinine ^c (μ mol/L)	0.36	1.0
Creatinine, urine ^c (mmol/L)	0.70	2.2

Ref: Lacher DA et al. Clin Chem 51(2): 450-2, 2005.

Analytes with low intra-individual variability often used for delta checks

- Alkaline phosphatase
- Bilirubin
- Creatinine
- MCV

Limitations of delta checks

- May not have access to prior results (e.g., transferred patients)
- Limited aid in outpatients with infrequently performed labs
- Patients may show dramatic changes in analytes that are part of disease process or due to treatment (e.g., dialysis, transfusions, chemotherapy)

Define potentially absurd values

- Examples depend on clinical population
- Very low plasma glucose (e.g., < 10 mg/dL)
 - May have different limits for infants vs. adults
- $K^+ > 11$ mEq/L often artefactual
- [Direct bili] \gg [total bili]
- Creatinine very abnormal with normal BUN
- [Albumin] $>$ [Total protein]
- AST and ALT very discordant

Auto-verification rules packages

- Some vendors offer pre-set rules packages
 - Can provide starting point for labs new to auto-verification
- Wise to start simply and then build from there
- Takes time to build comfort level and expertise with auto-verification

Validation plan for auto-verification

- Pre-testing
- Simulated patient testing
- Testing using clinical specimens
- Approval of documentation
- Implementation and maintenance of rules

- *CLSI Autoverification of Clinical Laboratory Test Results; Approved Guideline (AUTO10-A)*

Validation challenges

- Generally wise to have “test” environment
- Cannot test every scenario
- But make best effort to test every:
 - Test code
 - Upper and lower limits (including “boundaries”)
 - Rules individually and in combination
 - Result integrity to LIS
 - Result reporting to HIS

Testing Clinical Specimens

- Pays to collect “unusual” specimens
- Especially valuable to save specimens with:
 - Abnormal results
 - Interferences (hemolyzed, icteric, and lipemic)
 - Results less than analytical measurement range (AMR), if available; otherwise, may need to dilute
 - Values exceeding AMR (e.g., test auto-dilution protocols)

Regulations/guidelines – CAP

- CAP GEN.43850 Autoverification approval
 - There is a policy signed by the laboratory director approving use of auto-verification procedures
- CLSI Autoverification of Clinical Laboratory Test Results; Approved Guideline (AUTO10-A)
 - Qualified Laboratory Director must establish policies and procedure for allowing auto-verification

Practical challenges

- Determine scope of project
 - Identify key staff
 - Will auto-verification be done in middleware or LIS or both?
 - Allocate time for rule writing and testing
- Benefits of auto-verification unfold over time
 - May save 5-20 secs of manual time hundreds of times per day
- Coordinate with LIS operation

Auto-verification in middleware or LIS?

- Depends on instrumentation, informatics capability within clinical laboratory, and functionality of LIS
- Where are the informatics personnel resources?
 - Can resources be “home-grown”?

Potential value of middleware

- May be more easily under control by clinical laboratory staff
- Technologists can quickly intervene (e.g., suspending auto-verification rules) if problem arises
- If using LIS for auto-verification, how much will this task compete with hospital computing services resources?

Maintenance of auto-verification

- Need ability to shut off autoverification if necessary
- Annual audits
- Strongly recommend robust backup system with downtime procedure
 - Using middleware, can sometimes maintain operations even with LIS entirely down for scheduled or unscheduled downtimes

Key goals to success

- Realize significant investment is needed, including nurturing of staff with informatics skills
- Good project management
- Robust validation
- Ownership by lab staff (may find some staff uncomfortable initially with change in practice)

UIHC experience

- Beginning in 2005, began putting significant investment into informatics
 - Team of 4 technologists within core laboratory developed and validated ~1,500 rules governing auto-verification of results
 - Some technologists moved to hospital informatics over time
- Moved to lithium heparin plasma separator tube for most chemistry tests
 - Avoid micro-clots

UIHC Core Chemistry

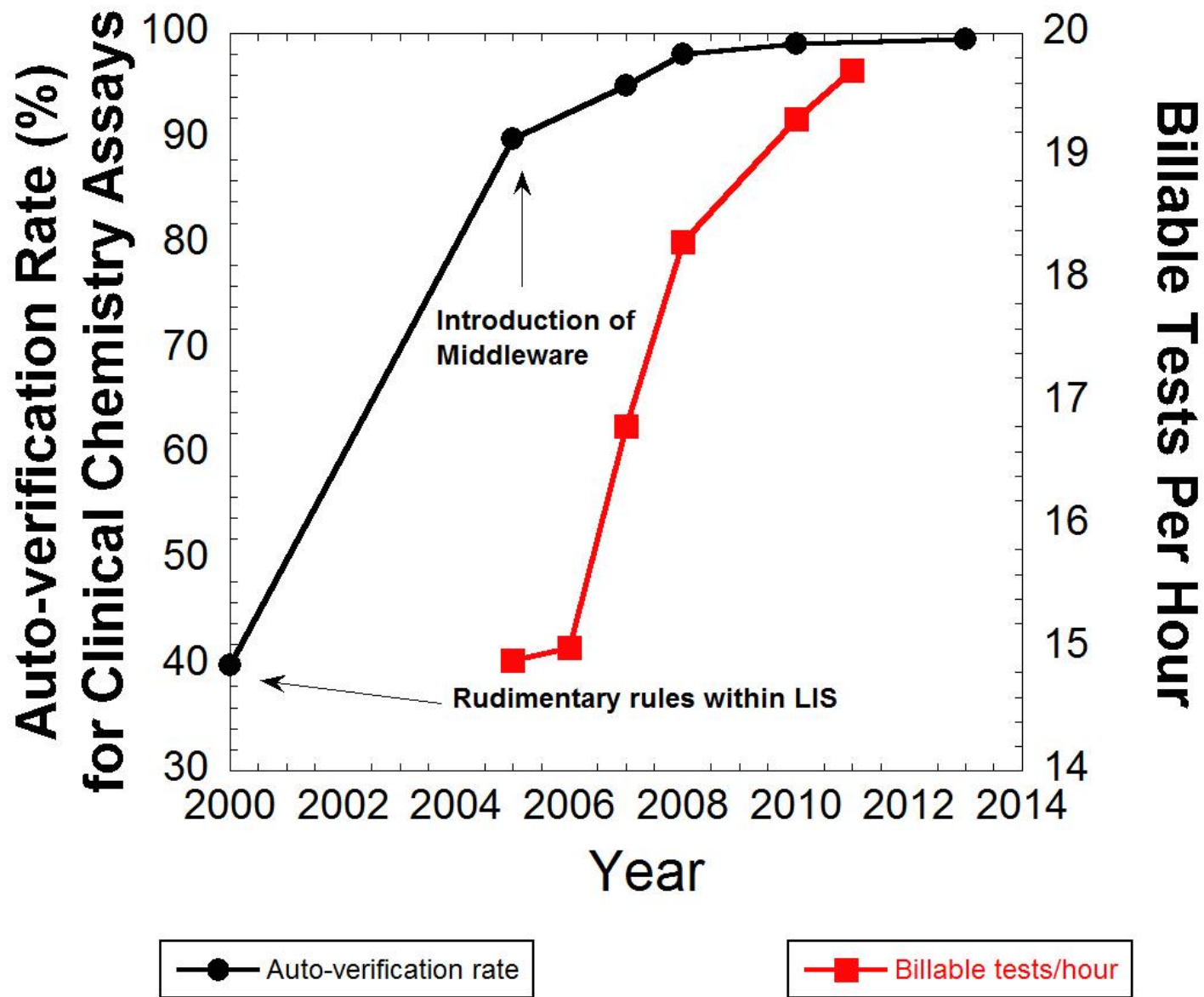
- Systematically evaluated a variety of practices
 - Critical look at all manual process by literature review and own studies
 - Repeating analysis of critical values
 - Defining potentially “absurd” values (e.g., plasma potassium of 15 mEq/L)

Actions taken

- Completely eliminated ability to request assays stat (everything routine – “one-piece flow”)
- Auto-verification of critical values
- Eliminated routine practice of repeating critical values except when past evidence showed this had value

Auto-verification at UIHC

- By 2010, over 99% of chemistry results were being auto-verified
 - This included nearly all critical values
- Performed rigorous variance review
- Common reasons for manual review include:
 - Specimen errors (bubbles, clot, short sample)
 - Need for manual dilution
 - Possible contamination flag



Rates of autoverification

Test(s)	Annual volume	Autoverification rate (%)
All chemistry tests	3,805,000	99.5%
Basic metabolic panel	114,140	99.6%
Electrolyte panel	1,320	98.6%
Lipid panel	31,000	98.6%
ACTH	830	98.6%
Bilirubin, direct	20,560	97.6%
Free light chains, serum	4,180	88.0%
Gentamicin	2,450	94.0%
Hepatitis B surface antigen	12,050	97.8%
Methotrexate	1,200	89.6%
SS-A	1,540	100%
Troponin T	17,910	99.2%

Ref: Krasowski MD et al. J Pathol Inform 5: 13, 2014.

Common reasons preventing autoverification

Test(s)	Most common reasons preventing autoverification
Basic metabolic panel	Contamination flag, specimen error*, delta check failure
Electrolyte panel	Contamination flag, specimen error*, delta check failure
Lipid panel	Specimen error*
ACTH	Specimen error*
Bilirubin, direct	Exceeded AMR – manual dilution
Free light chains, serum	Exceeded AMR – manual dilution
Gentamicin	Exceeded AMR – manual dilution
Hepatitis B surface antigen	Repeat testing for positives and grayzones
Methotrexate	Exceeded AMR – manual dilution
Troponin T	Specimen error*

* Examples include bubble, clot, short specimen, etc.

Ref: Krasowski MD et al. J Pathol Inform 5: 13, 2014.

Comments from core laboratory staff

“Autoverification saves time for the filing person. It eliminates mistakes by people when interpreting results.”

“Autoverification lessens the workload at the filing bench to allow me to perform other tasks required in the immediate area.”

“One person can run chemistry by themselves, the others can help where needed.”

'Push' technology

- Printouts generated by LIS or Middleware provide clear instructions what to do
 - Critical values
 - Confirmatory testing
 - Manual dilutions
 - Situations to contact laboratory director or pathology resident
 - Can be especially helpful for rare scenarios by 'scripting' actions to take

Example print-out #1:
notification to staff (either call
center or main laboratory) to call
critical value that has already
been auto-verified

Example print-out #1

- Patient name: Patient ID:
- Location: D.O.B.:
- Accn # Draw time:

Ordering physician:

A CRITICAL K⁺ result has been resulted for this patient. Call area and document in RIA.

Example print-out #2

- Less common scenario
- Total bilirubin very discrepant from icteric index
- Can be caused by monoclonal gammopathy, most often IgM (package insert data)

Example print-out #2

The BILT minus ICT is > 4 . Possible interference of bilirubin measurement due to abnormal proteins. If repeated BILT is now within 4 of ICT, reorder BILT, and file BILT result. If repeated BILT is still > 4 of ICT, review results and check LIS to see if evidence of myeloma (SPE, SIFE).

If any evidence of myeloma, access cancelled BILT in LIS and add phrase 'Interference due to myeloma protein'. Present findings to Path resident and [Clinical Chemistry Director]."

Clinical implications

- In many cases, clinicians are seeing critical values before we even make the call (especially in ICU and emergency center)
 - Makes the phone notification much easier and is consistent with regulatory initiatives to speed reporting of critical values
- Very few complaints about turnaround time
 - TAT issue is almost always due to delay in sample getting to lab
 - Consistency in TAT is also important

Upfront investment pays off

- Much of the upfront work is rule writing and verification
 - This expertise can be transferred to other instrumentation
- Have been able to handle increased volumes without increase of staff in chemistry

Be prepared for downtimes

- Invest effort in preparing and practicing for downtimes
 - Backup servers
 - Developed clear downtime procedures and practiced
 - Incorporate into disaster drills

Summary

- **Autoverification: 99.5%**
 - Increased from 40% with LIS
- **Volume Increased 18.5%**
 - 2.7M in 2005 to 3.2M in 2010
- **32% Increase in Billables per Tech**
 - \$14.9 to \$19.7 billable tests per hour
- **Rules for Esoteric Patient Conditions**

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