Wednesday, August 3, 2016

Poster Session: 9:30 AM - 5:00 PM

Automation/Computer Applications

B-007

Standardization of Ask At Order Entry Questions: A Prudent Question is One-Half of Wisdom

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Background: The United States federal mandates for achieving Meaningful Use (MU) cause numerous work groups in the industry to discuss how to best represent actual content with standardized terminology. During the development of the Laboratory Orders Interface (LOI) and the electronic Directory of Services (eDOS) implementation guides in the Standards and Interoperability Framework's (S&I Framework) laboratory related initiatives, the need for guidance, expansion and harmonization of Ask at Order Entry (AOE) questions became evident. The primary goal is to provide a suite of harmonized standards for electronic messaging of laboratory data for the US realm for inclusion in MU regulations. A secondary goal is the reduction of variations in how the same AOE question is asked. Use cases considered for this project were ambulatory laboratory test ordering as well as Public Health reporting, such as pediatric lead level reporting. Engagement of subject

matter experts who help with consolidating duplicate AOE questions into a standard format for representation as a single concept provides further harmonization and enhanced interoperability. In addition, this project will establish a review process prior to submission for standard codes when new AOE questions are needed.

Methods: During the course of LOI and eDOS implementation guide development, commonly used AOE questions were collected from several national laboratories, Public Health laboratories and Public Health agencies. AOE questions were consolidated and standard codes were assigned from the Logical Observation Identifiers Names and Codes (LOINC®) database, maintained by the Regenstrief Institute, where appropriate codes existed. AOE questions where the required information could be communicated in other parts of the HL7 message were also identified. Several of the AOE questions were asking the same questions in different ways and this duplication creates confusion and hinders semantic interoperability. The entire AOE collection was shared with the Laboratory Messaging Community of Practice (LMCoP), a forum comprised of laboratory and standards experts from state and federal Public Health laboratories, national clinical laboratories, the National Library of Medicine and professional organizations, whose purpose is to resolve lab related issues from a laboratorian's viewpoint. The LMCoP, acting as a conduit to lab related professional organizations, provided its recommendations for subsequent review by appropriate laboratory domain content experts from the American Society for Clinical Pathology (ASCP), the Association for Molecular Pathology (AMP), and the College of American Pathologists (CAP) for completeness and proper LOINC® code assignment, as well as identification of a preferred single concept representation where overlap existed.

Results: The current iteration of AOE questions contains 131 questions, a 37% reduction from the 210 originally collected. Fifty eight (58) new terms have been submitted to the Regenstrief Institute; in addition twenty three (23) existing LOINC® terms were revised, removing trial status or survey-specific method information as result of this review.

Conclusion: The curated list of AOE questions, properly mapped to LOINC® terminology, has been published in the eDOS Implementation Guide and is available to laboratories when implementing electronic data exchange.

B-008

iRICELL® fully automated and integrated platform - correlations between chemistry and microscopy system, comparison with manual microscopy and the clinical diagnostic significance

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Objective: The main goal of our study was to compare the automated microscopy with manual microscopy, evaluation of the performance of the **iRICELL®** system in the clinical significance, correlations between chemistry and microscopy system. In our study, we emphasize the clinical performance of the **iRICELL** system and their diagnostic importance. ***Relevance:*** The analysers use reactive test strips for analysing and providing volumetric determination of the chemical parameters of the urine; density, pH, nitrites, proteins, glucose, ketone bodies, urobilinogen, bilirubin. The urinary erythrocytes and leukocytes, their investigation being useful for the localization and the source of haematuria and leukocyturia. The analyser is a fully automatic instrument, it is fast (it processes 100 samples/hour), it automatically recognizes and analyses quantitatively 2 elements, indirectly (without human intervention). The role of the automated analysis systems for the urinary sediment is that of eliminating the error sources described below: the centrifugation of the samples can cause a variable degree of loss of the urinary sediment elements, the placement of the urinary sediment between the slide and cover glass can also induce various errors through the lysis of the elements, the non-uniform distribution of the sediment elements under the cover glass, as well as their embedment in the mass of mucus, the counting of elements between the slide and cover glass is subjective. ***Methodology:*** The samples were first screened using the ***iRICELL*** fully automated and after that the selected pathological samples were examined using (for comparation) the manual microscopy at a higher power (x 400). Initially, we utilised on a normal microscope but with reduced light with the condenser placed at a lower position to increase the contrast. We selected 50 photos, representing the most important cases. The investigation was performed by using different microscopic techniques (bright field, phase contrast and interference contrast) in the observation of the sediment elements in both unstained and stained samples (May-Grünwald-Giemsa stain, Sternheimer-Malbin stain). ***Validation:*** Our results are based on the study of 800 patients, who were admitted to our hospital between January 2012 and September 2015. The patients were diagnosed with various types of renal diseases and were hospitalized in either the Nephrology or Dialysis Departments. Each photograph belongs to one patient. For urinalysis we used either the first or the second morning urine specimen. The microscopic examination revealed the presence of the same pathological urinary sediment element like the the ***iRICELL*** system. ***Conclusions:*** Our study shows that the ***iRICELL*** system compared to the classic examination of urine has greater relative sensitivity, increases the analytical accuracy and the credibility of the results, thus decreasing the workload of the microscopist and supporting the physicians. The relatively high incidence of chronic kidney disease is explained by the fact that in our laboratory we examine a relative high number of samples received from the Department of Nephrology. The benefits of use of ***iRICELL*** system are the following: it is an accurate non-invasive technique, it eliminates the risk associated with invasive methods and decreases costs.

B-009

Computational Approaches for Inpatient Mortality Predictive Modeling in a Swiss Cohort

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Background: Decision support systems that apply electronic health record (EHR) data for calculating of the risk of inpatient mortality are proposed as a "big data" computational approach for efficient patient care. Scoring systems like the Acute Laboratory Risk of Mortality Score (ALaRMS) as well as statistical learning techniques are competing approaches. We assessed predictive accuracy and model calibration of different approaches by applying them to a big biomedical dataset in a large Swiss University Hospital.

Methods: We used the complete hospital admissions database of the Inselspital Bern from 2012 to 2015, including more than 100'000 entries. Admission laboratory profiles, age, and sex were included, the outcome was inpatient mortality. The decision-support systems were used to assess mortality risk for a specific patient based on baseline data and clinical laboratory results at admission. We compared the ALaRMS score, generalized linear modeling (GLM) procedures, and non-linear and tree-based methods, and provide robust statistical models for inpatient mortality predictive modeling.

Results: ALaRMS AUC was comparable to the expected accuracy (AUC=0.858). A bias-corrected ALaRMS score yielded results comparable to a simplified 3-parameter logistic regression model (AUC=0.819 vs 0.801). Logistic regression methodology with penalization provided a robust model (AUC= 0.872). Artificial neural networks and random forest methodologies showed similar accuracy.

Conclusion: Todays GLM procedures provide calibrated unbiased models that can be used as efficient decision support tools for inpatient mortality prediction. Electronic Health Record (EHR) data is a pivotal resource for decision support in clinical practice and might aid preemptive patient triage.

B-010

Web-based Method Comparison for Clinical Chemistry

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Background: Method comparison and bias estimation are daily activities for Clinical Chemists and Pathologists. Software required for compliance with guidelines, such as CLSI EP09 A3, are commercially available but are sometimes expensive. Among the open-source alternatives for method comparison studies are those employing the R programming language. The additional R package mcr, written by Roche Diagnostics, is based on CLSI EP09-A3 but using it requires some basic knowledge of programming to use. Recognizing this as a limitation to its use, we have developed a dashboard-style web-interface to mcr requiring no programming knowledge.

Methods: In our application, Shiny, Shiny Dashboard, rhandsontable and dt packages are used for the construction of a graphical user interface and the Rmarkdown package produces the output documents: PDF, MS Word or HTML. The mcr package—the work-horse of the website—processes the user-defined data to generate both Bland-Altman and scatter plots and provides a statistical report. The dashboard allows manual data entry cutting and pasting from spreadsheet applications. The user selects the desired regression procedure from drop-down menus (Table 1), calculations are performed by a server, and the results appear interactively.

Results: Any web browser can be used to access the website and generate graphics and statistics. https://bahar.shinyapps.io/method_compare

Conclusion: In summary, we have developed a website for method comparison studies using R and various R packages. The site offers a simple, yet inexpensive way to evaluate the relative analytical performance of two analytical methods.

Table 1. Options provided for plots and statistics.

Bland-Altman	**CI**
X vs. Y-X	Analytical
X vs. (Y-X)/X	Jacknife
0.5*(X+Y) vs. Y-X	Bootstrap
0.5*(X+Y) vs. (Y-X)/X	Nested Bootstrap
rank(X) vs. Y-X	
rank(X) vs. (Y-X)/X	
sqrt(X*Y) vs. Y/X	**Bootstrap CI**
0.5*(X+Y) vs. (Y-X) / (0.5*(X+Y))	Quantile
	Student
	Bias Corrected and Accelerated
Regression	Bootstrap-t
Ordinary Least Square	
Weighted Ordinary Least Square	
Deming	**Correlation**
Weighted Deming	Pearson
Passing-Bablok	Kendall
Passing-Bablok Large Data	Spearman

Abbreviations: CI = confidence interval, X = method 1 (reference method), Y = method 2 (test method), sqrt = square root

B-011

Use of patient registry and automated notifications to improve genetic test utilization

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Background: Repeat testing for the same germline mutation or allele is unnecessary. However, previous results may be unavailable or overlooked causing redundant testing and delay in diagnostic evaluations. This study evaluated the use of a multi-institutional patient registry and automated notification system to improve genetic test utilization.

Methods: A national genetic test registry was created for patients enrolled in the Veteran Affairs (VA) healthcare system that contained 15 years of test results from the VA Corporate Data Warehouse, which was updated daily thereafter. Tests included hemochromatosis (HFE), factor V Leiden (FVL), prothrombin G20210A gene mutation (PT G20210A), HLA-B27 and *HLA-B*57:01*. An automated system performed daily searches for registry patients having new orders that triggered an email notification to designated laboratory personnel at specific VA facilities where testing was requested. Alerts contained patient identification, date, location and results of previous test(s). Test cancellation rates after notifications were compared to a control group of VA facilities that did not receive alerts.

Results: Between February, 2015 and January 2016, 22 VA laboratories received 232 notifications for duplicate orders over 1 to 11 months, depending on date of entry into program. This included 39 HFE, 53 FVL, 14 PT G20210A, 56 HLA-B27 and 70 *HLA-B*57:01* tests. Previous testing was performed at a different facility in 87 (37.5%) cases. A total of 142 (61.2%) tests were cancelled that included 30 (76.9%) HFE, 35 (66.0%) FVL, 9 (64.3%) PT G20210A, 23 (51.8%) HLA-B27 and 39 (55.7%) *HLA-B*57:01* tests. The median laboratory cancellation rate and 90th percentile range was 66.7% (22.8%-100%). A total of 949 duplicate orders were observed among 101 facilities in the control group which included 313 HFE, 202 FVL, 94 PT G20210A, 164 HLA-B27 and 176 HLA-B 5701 tests. Previous testing was performed at a different facility in 280 (29.5%) cases. A total of 32 (3.4%) orders in the control group were cancelled as duplicates that included 3 (1.0%) HFE, 12 (8.3%) FVL, 10 (10.6%) PT G20210A, 3 (1.8%) HLA-B27 and 4 (2.3%) *HLA-B*57:01* tests. The median laboratory cancellation rate and 90th percentile range in the control group was 0.0% (0.0%-14.2%). **Conclusion:** A national patient registry with automated notification system was found to be an effective strategy for improving utilization of genetic tests. This intervention reduced unnecessary retesting and provided more rapid information for diagnostic evaluations. However, cancellation rates for laboratories in the intervention group varied widely. This was not evaluated but may have been due to local practices or how alerts were administratively managed by the laboratory. Finally, interoperability of the VA laboratory information system enhanced the effectiveness of this intervention since over one-third of notifications involved results reported from another facility.

B-012

Analytical performance evaluation of newly developed immunoassay analyzer "LUMIPULSE® L2400"

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Background: For efficient operations in clinical laboratories, Immunoassay analyzer intends to have random-access system and also implement space-saving, short-time of assay and the module system with clinical chemistry analyzers. This time, we developed fully chemiluminescent enzyme Immunoassay (CLEIA) system "LUMIPULSE L2400" and, we report the evaluation results of the basic performances on this system. The features of L2400 are as follows. The processing capability is up to 240 tests per hour as maximum. It is able to access 24 analytes with full random-access, and immunoreaction time is approximately 20 minutes. Also, measurement in a short-time that is about 12 minutes is available to shorten the reporting time. (Reagent for short time assay are in development).Regarding its extensibility, it can be connected with clinical chemistry analyzer and it also implements flexible system connection by adopting external sampling method.

Methods: Fully automated CLEIA system LUMIPULSE L2400 was used for the measurement and LUMIPULSE PrestoII (FUJIREBIO INC.) was used for the system comparison. Dedicated regents used for this study were Lumipulse Presto AFP, CA19-9, BNP, HBsAg-HQ, and TP (FUJIREBIO INC., Japan). The reproducibility tests (N=6) of the above five analytes were executed to calculate coefficient of variation. (C.V.) The correlation tests of the above five analytes were carried out using more than 30 specimens for the instrument comparison of L2400 versus PrestoII.

Results: Basic evaluation for Lumipulse Presto AFP, CA19-9, BNP, HBsAg-HQ, TP was performed on L2400. The results are as follows. Reproducibility: C.V. (%): AFP: 0.9-1.9%, CA19-9: 1.1-1.8%, BNP: 0.7-1.8%, HBsAg-HQ: 1.2-3.0%, and TP: 0-1.0%. Correlation between L2400 and PrestoII is that AFP: regression y=1.00x, correlation coefficient r=1.000, CA-19-9: regression y=0.92x-0.23, correlation coefficient r=1.000, BNP: regression y=0.94x-1.30, correlation coefficient r=0.998, HBsAg-HQ: regression y=1.04x-0.26, correlation coefficient r=0.998, and TP: regression y=0.92x-0.57, correlation coefficient r=0.997.

Conclusion: The results of basic evaluation for AFP, CA19-9, BNP, HBsAg-HQ, and TP on LUMIPULSE L2400 were excellent. These results demonstrated that LUMIPULSE L2400 is sufficiently applicable for routine laboratory tests. *note: LUMIPULSE L2400 and the reagents were approved by PMDA in Japan. Not approved by US-FDA, CE-IVDD.

B-013

Automated IFA methods compare well with established manual IFA screening and titration for ANA HEp-2

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Background: Often, only basic nuclear patterns like homogenous, speckled, nucleolar, centromere or cytoplasmic are reported by laboratories. The detection of other patterns requires well trained readers. As a result, different systems have been developed which automate part of or the complete IFA method and reading process. Methods: This study compares 2 commercially available HEp-2 antinuclear antibody (ANA) indirect fluorescent antibody (IFA) assays using a sensitivity panel (120 clinically determined patients) and a specificity panel consisting of 80 clinically confirmed negative patients. We compared the NOVA View® system from INOVA with the HELIOS® IFA Processor from AESKU.Systems/AESKU.Diagnostics to assess their capability for screening and titration of these samples. The automated method was directly compared to manual reading of the same processed slides on respective microscopes and also compared with the known clinical information.

Results: The results of the two automated methods were in good agreement. The HELIOS® system detected 188 samples correctly from negative and positive samples (versus 187 detected by the NOVA View® system). The falsely detected positive samples were all of low titer (1:80). The HELIOS® system found 157 patterns in agreement to the target pattern (NOVA View® 156). From 80 negative samples AESKU detected 73 correctly (NOVA View® 71). Conclusion: Both systems resulted in an overall sensitivity >95% and a specificity of 91.25 and 88.75 (for AESKU HELIOS® versus NOVA View®). The pattern recognition also showed only minor aberrant findings resulting in a slightly better detection of cytoplasmic and nuclear membrane patterns by the Helios-system while NOVA View detected slightly better the centromeric pattern.

B-014

Comparison between the performance of the HELMED® Blot Module and the HELIA® using the *AESKUBLOTS*® ANA-17 Pro

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Background: Immunoblotting is a common method for efficient profile testing of autoimmune and infectious diseases. Automation offers higher throughput testing, therefore AESKU.SYSTEMS developed two solutions to facilitate automated immunoblot testing.To compare the performance of the HELMED® Blot Module that is a fully automated Blot processor, and the HELIA®, an automated analyzer for line immunoassays.

Methods: 39 routine samples were tested on the *AESKUBLOTS*® ANA-17 Pro (AESKU.DIAGNOSTICS) utilizing in parallel the HELMED® Blot Module and the HELIA® system (both AESKU.SYSTEMS, Wendelsheim). By performing samples with the HELMED® Blot Module the *AESKUBLOTS*® were analyzed by the AESKU. SCAN® software

Results: 28 samples were found to be positive for one or more parameters. 2 samples showed equivocal results and 9 were completely negative for all ANA antigens. Overall agreement (concordance correlation coefficient) between the HELMED® Blot Module and the HELIA® system was 0.9476 (95% CI: 0.9216 to 0.9652). Notably, all discordant samples were characterized by very borderline signal. Comparing the level of immunoreactivity of the different coated antigens and sample diversity the Pearson precision (ρ) was 0.9718 (95% CI: 0.9547 to 0.9825; p<0.0001).

Conclusion: The HELMED® Blot Module and the HELIA® system are able to identify the ANA positive samples with the same level of band intensity of the coated antigens. Both approaches are able to reduce inter-laboratory variability and time required to perform ANA testing, especially in high throughput laboratories.

B-015

Multicenter evaluation of a new high-throughput HbA1c testing platform

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Background: This non-interventional, multicenter study with anonymized leftover patient samples was performed to evaluate the reliability and analytical performance of the novel HbA1c cobas c 513 analyzer. Methods: A performance evaluation was carried out at three European study centers to validate the overall system functionality, user interaction and analytical performance of the new cobas c 513 analyzer using the Tina-quant® HbA1c Gen. 3 assay. This established assay is standardized against the approved IFCC reference method for measurement of HbA1c in human blood and is approved for monitoring of long-term blood glucose control in individuals with diabetes mellitus, as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. The HbA1c determination is based on the turbidimetric inhibition immunoassay for hemolyzed whole blood. The novel analyzer has the capacity to process up to 400 closed whole blood or hemolysate samples for HbA1c testing per hour. Results are reported in mmol/mol hemoglobin A1c (IFCC) and %HbA1c (DCCT/NGSP). Method comparisons were performed with commercially available dedicated HbA1c analyzers COBAS INTEGRA 800 CTS, Tosoh G8 and Menarini HA-8180V using fresh and frozen anonymized residual samples from routine. The evaluation also covered usability testing and practicability assessment. **Results:** HbA1c applications for both whole blood and hemolysate samples show a very stable analyte recovery of assigned target values ±1 SD (~5.5 % ± 0.34 and ~10 % ± 0.6) and high precision using both quality control materials and different concentrations of whole blood pools or hemolysates. The repeatability and intermediate precision for the whole blood and hemolysate applications in %HbA1c was 0.4 - 0.7 % and 0.8 - 1.5 % respectively. The comparison of HbA1c Gen. 3 on cobas c 513 to HbA1c Gen. 2 on COBAS INTEGRA® 800 CTS using 10052 whole blood samples from two labs combined shows high concordance (slope (95%CI) = 1.00 (1.00, 1.01); intercept (95%CI) = -0.15 (-0.13, -0.18)). Moreover analyte concentrations as measured by the cobas c 513 and Tosoh G8 (slope (95%CI) = 0.94 (0.94, 0.95); intercept (95%CI) = 0.21 (0.16, 0.26); n=500) and Menarini HA-8180V (slope (95%CI) = 0.96 (0.94, 0.97); intercept (95%CI) = 0.29 (0.19, 0.40); n = 249) are comparable. The cobas c 513 also proved to reveal reliable results with system handling provocations as they can occur during routine use. Recovery rates of 98.2 to 102.6% were obtained with IFCC reference materials. The HbA1c Gen. 3 whole blood application on cobas c 513 moreover exhibited linearity in the tested range of 4.8 - 14.0 % HbA1c. The quantification of HbA1c Gen. 3 on cobas c 513 was not influenced by common Hb variants HbAS, HbAC, HbAD, HbAE and HbA2. The cobas c 513 system was rated with "exceeds expectations" in 92.3% of questions by operators with regard to practicability and usability. **Conclusion:** The cobas c 513 has proven to be a reliable system that yields excellent analytical performance of the Tina-quant® HbA1c Gen. 3 assay in high throughput laboratories. Additionally, operators have rated the system usability as exceeding expectations.

B-016

New protocol for quantification of alpha1-antitrypsin stool using a commercial kit for human serum

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Background: Alpha1-antitrypsin (A1A) is an alpha1-A globulin that circulates in the blood and protects the tissues of the body from being damaged by substances contained in white blood cells (e.g., trypsin, elastase, collagenase and other proteolytic enzymes). The synthesis of alpha1-antitrypsin is controlled by a pair of genes at the proteinase inhibitor locus that is inherited as co-dominant alleles. Since A1A is resistant to degradation by digestive enzymes, it is used as an endogenous marker for the presence of blood proteins in the intestinal tract. An elevated A1A clearance suggests excessive gastrointestinal protein loss and an A1A deficiency states often have a genetic cause. Gastrointestinal protein enteropathy has been associated with regional enteritis, sprue, Whipple intestinal lipodystrophy, gastric carcinoma, allergic gastroenteropathy, intestinal lymphangiectasia, constrictive pericarditis, congenital hypogammaglobulinemia and iron deficiency anemia associated with intolerance

to cow's milk. Although there are some commercial kits available to quantify A1A in stool, none has *registration* at BrazilianHealth Surveillance Agency (ANVISA), making difficult the implementation of this test on Brazilian market. **Objective**: On this project, we aimed to validate the N Antiserum to Human α1-Antitrypsin Kit (Siemens Healthcare Diagnostics) to quantify A1A instool by means of immunonephelometry on the BN Systems (Siemens). This kit is an *in vitro* diagnostic reagent used for the quantitative determination of α1-antitrypsin (α1-proteinase inhibitor) in human serum. **Methods**: A different method of sample preparation and some modifications of manufacturer's instructions were necessary to validate the utilization of this kit for stool samples. Fresh stool samples were collected from 40 healthy patients. The samples were homogenized and separated in two aliquots of 0.5 g each: an aliquot was maintained in an incubator at 37°C for three hours and the other one was diluted in a solution of NaCl 0.9%.The homogenate was centrifuged at 5,000 rpm for 20 minutes. The supernatantwas centrifuged at 13,200 rpm, for 20 minutes and used for analysis. An aliquot was performedimmediately and other was frozen and sent to a reference laboratory to compare the results. **Results**: Two samples were selected for precision analysis. The intra-assay variation of the test was calculated from 20 replicate determinations on each one of two samples. The inter-assay variation was calculated from data on two samples obtained in 20 different assays over a period of ten days. To the precision test, the following coefficients of variation (CV) were obtained: 3.24% (intra-assay); 7.32% and 7.69% (inter-assay). Comparison of the results between the two laboratories yielded a coefficient of correlation 0.816 (CI = 95%; ρ= 0.0012, Spearman). **Conclusion:** These results reveal that the N Antiserum to Human α1-Antitrypsin Kit was efficient for quantitative determination of α1-antitrypsin in stool after the necessary preparation, unfolding a good alternative to the execution of this test.

B-017

Process Management Opportunities for Lab IT Solutions

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Background: Laboratories are turning to information technology (IT) for automation and software solutions to help manage increasing cost pressure and improve the percentage of timely, accurate, and reliable test results. While many IT solutions currently used in the laboratory offer streamlined solutions that manage data from the medical devices and middleware (data management), laboratory personnel are missing opportunities for adopting IT solutions that optimize their laboratory's overall efficiency (process management).

Objective: Obtain laboratory-management feedback on opportunities for IT solutions that would improve the overall efficiency of the laboratory. Use this feedback to determine feature sets for future IT solutions.

Methods: Online surveys and field interviews were conducted with laboratory managers from five countries (USA, Germany, UK, Italy, and Spain). Four specific feature opportunities were tested: workflow intelligence, increased productivity, centralized control, and centralized visibility. The collected feedback was used to determine if the:

- Overall appeal of the feature opportunity matches their laboratory's needs
- Feature opportunity is unique
- Laboratory manager is motivated to learn more about a solution that addresses this feature opportunity

Results: 95 laboratory managers were interviewed. The percentages of those who believed that the feature opportunity is extremely likely or very likely to meet the needs of their laboratory are listed in the table below:

	Overall Appeal		Uniqueness		Ability to Motivate	
	%	Rank	%	Rank	%	Rank
Workflow intelligence	89	2	57	1	57	1
Increased productivity	90	1	47	2	47	2
Centralized control	81	4	39	3	39	3
Centralized visibility	82	3	34	4	34	4

Conclusion: Based on the high overall appeal of the four feature opportunities, the following features were identified as having high value for improving the laboratory's efficiency and overall quality:

- Workflow intelligence and increased productivity: Advanced reporting for turnaround times, samples, tests, and automation utilization; real-time information about priority samples
- Centralized control and visibility: Consolidated inventory and alert management; ability to remotely control the medical devices within the laboratory

B-018

Optimized Handling of Every Tube through Machine-vision-guided Automation

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Background: Sample-container variation poses a significant challenge to the reliability and performance of automated in vitro diagnostic equipment. Historically, manufacturers have chosen to respond by restricting the variety of tube types supported by each instrument. However, modern clinical laboratories receive patient samples from an ever-increasing array of sources and often have minimal influence over the containers they must process. This forces them to expend considerable time and resources on the error-prone task of transferring samples from one container to another to overcome the different limitations of each device.

For its [product name]*, [company name] has invested in the development of a machine-vision system that fully characterizes each sample container as soon as it is loaded onto the instrument. This allows the platform to support more than 30 tube types, including 5 varieties of capillary tubes and a tube-top sample cup (TTSC) that can be placed in any supported vessel.

Methods: The Drawer Vision System (DVS) images every tube while the operator is closing the drawer. STAT samples are recognized and prioritized in less than 10 seconds. Within 30 seconds, every tube in the drawer is characterized as capped, uncapped, or uncapped with a TTSC. Tubes with a TTSC are moved more gently and handled with special care through all stages of processing. Capped tubes that are accidently placed on systems are sorted into user-configurable exception trays. For all tubes, the sample-transfer robot dynamically adjusts the pick location in the drawer based on the measured center of the top of the tube, ensuring that tube tilt is minimized and jostling reduced. Empty slots in the tray are automatically detected and skipped, improving system throughput and eliminating the need to load tubes in a specific pattern.

Results: More than 10,000 sample vessels were evaluated during the development of the DVS. Images of each of these tubes are maintained in an image library, and any algorithm change is validated against all of them before it is released. Routine tubes were correctly identified 99.96% of the time. In the remaining 0.04% of cases, irregularities such as severely peeling barcode labels and tubes leaning in tray slots prevented the tube from being classified with a high degree of certainty. After manual intervention to correct these anomalies, all tubes were correctly identified. Empty tray slots, capped tubes, and tubes with TTSCs were correctly identified in all evaluated cases. The absolute mean error for tube diameter measurement was 0.40 mm, with a standard deviation of 0.37 mm. The maximum error for 99.6% of tubes was 1.99 mm.

Conclusions: Using its custom-developed machine-vision system, the [product name] is capable of optimizing the handling of every tube. This frees the operator from the burden of presorting samples, because loading the instrument is as simple as placing any supported tube in any location. Laboratories no longer need to adjust their workflows in order to overcome the limitations of their equipment.

*Under development. Not available for sale.

B-019

Multivariable Statistical QC Techniques for Detecting Unnatural Behavior of a Method Performed on Several Instruments. A Practical Example with Direct Bilirubin Performed on Two Cobas c311® and two Cobas c501®.

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Background: In two laboratories, one associated with an emergency room, the other associated with a hospital, two cobas c311® and two cobas c501® analyzers are used interchangeably to assay direct bilirubin. Consequently, the same reagent lot and the same QC material lot are used on the four analyzers to ensure interchangeability of the results. This study illustrates the usefulness of multivariable QC statistical techniques to detect an unnatural behavior of the analytical method. ***Methods*:** Instruments, two Cobas c311 and two cobas 501 (Roche). Reagent, ROCHE D Bili® lot# 610028 exp.8/31/2016 (Roche) was prepared and maintained on the instruments for 14 days according to manufacturer's instructions. QC material, Liquichek® pediatric control level 2 lot# 21632 exp. 8/31/2017 (Bio-Rad) was assayed once every shift of eight

hours; the QC values were stored and analyzed with Unity Real Time® 2.0 (Bio-Rad). The quality control values collected in a month were electronically transferred to Minitab® (Version 17, Minitab Inc.) statistical software for numerical and graphic multivariable data analysis. ***Results:*** While for the Unity Real Time QC monthly summary statistics (z score < 2.5, CV ratio <1.5) were acceptable and the L-J chart for all four instruments did not display any abnormal behavior of the method, the T-squared chart, as obtained with the values of all four instruments, clearly showed parallelism (Otelling's T-square P <<0.05 for 20 of 31 of the comparisons). The parallel boxplots by day and the L-J chart, as generated by Minitab, gave for all four instruments an immediate visualization of two parallel down trends of seven days period. These trends were clearly shown by the locally weighted scatterplot smoother applied to the L-J charts. Interestingly, the newly reconstituted reagent brought back the QC values around the mean performance for only seven days. The reagent's stability was suspected as the assignable cause and it was decided to use the reagent for only seven days. This corrected the behavior of the method. ***Conclusions:*** Since the mean function of a QC process is an arbitrary function of time, sometimes the detection of a trend departing from the white noise is not an easy task. This practical example showed that the use of multivariable statistics and their graphic representations gave a warning that prompted further studies. These indicated that the instability of the reagent was the most probable assignable cause . The discrepancy between visual impressions obtained with the L-J charts of Unity Real Time and Minitab is most probably explained with the ratio of the length of y axis to the length of x axis. While the y/x ratio for the three types of L-J charts, as produced by Unity Real Time, is 0.11, 0.2 and 0.3, that for L-J chart as produced by Minitab is 0.55. In general, it is more difficult to visualize some parallel down trends using narrow, stretched charts. In conclusion, the use of multivariable statistical techniques and their graphic representations may be useful for monitoring the behavior of a process. The availability of statistical software, like Minitab, is obviously of paramount importance.

B-020

Multicenter Study of the Sysmex CS-2100i and CS-5100 Systems Compared to the Sysmex CA-1500 System Using Siemens Healthcare Reagents

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Background: The objective of this study was to compare the performance of two automated coagulation analyzers, the Sysmex® CS-2100*i* and Sysmex CS-5100 Systems (CS-2100*i* and CS-5100), to the Sysmex CA-1500 System (CA-1500) using Siemens reagents. Performance characteristics of the systems for prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, antithrombin (AT), and D-dimer were compared.

Methods: Three U.S. laboratories participated in method comparison (MC) studies. Result comparability was investigated using leftover samples.* MC of CS-5100 and CS-2100*i* versus CA-1500 was based on a total of 2510 and 2423 results respectively (sum of results over all parameters). In addition, reference intervals were determined at the three U.S. sites in accordance with CLSI guideline EP28-A3c. Determination of the reference intervals was based on at least n = 60 samples per site, with a controlled ethnical distribution representing the ethnical distribution among the U.S. population.

Results: Analysis of MC data was done by Passing-Bablok regression and difference plot and revealed very good agreement to CA-1500, showing slopes between 0.957 and 1.083 and correlation coefficients ≥0.993 (depending on instrument and application). Reference intervals showed good comparability between the predicate device, CA-1500, and the two test devices, CS-2100*i* and CS-5100.

Conclusion: Results of both systems were in good agreement with CA-1500. Based on the data collected during these studies in combination with improved functionality, CS-2100*i* and CS-5100 provide high performance, quality, and efficiency to mid- to high-volume coagulation laboratories.

Product availability may vary from country to country and is subject to varying regulatory requirements.

*Donors gave informed consent and review boards were involved.

B-021

The Average of Deltas: Detection of Systematic Error Using the Average of Intra-Patient Differences

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Background: Traditional quality control (QC) procedures only provide a momentary glimpse of assay performance. Many laboratories employ alternate QC strategies designed to monitor assay performance for the development of systematic error (SE). One strategy, the delta check, compares a patient's most recent chemistry results to historical values but delta checks are limited in that they are best suited to detect large SE. Another strategy gaining in popularity is patient moving averages (MA). With MA the mean patient analyte value is monitored to detect development of SE. The limitation of MA is the inability to equitably detect SE in skewed patient populations. Given that delta checks and MA both have weaknesses; the objective of our study was to develop an Average of Deltas (AoD) monitoring strategy that relies on monitoring the mean difference between pairs of consecutive, intra-patient results.

Methods: From a database of 4.2 million results spanning 638 days we generated arrays containing pairs of patient results collected within 18-26 hours of each other for each assay in our study. To develop sensitive AoD protocols that detect SE equal to the reference change value for each assay we employed an simulated annealing algorithm in Matlab (Mathworks, Natick, MA) to select the number of patient pairs to average (Np) and truncation limits to eliminate large deltas. Again using Matlab, we simulated SE by adding positive or negative bias at fixed intervals in the arrays of paired patient results for serum assays of albumin, aspartate aminotransferase, amylase, bicarbonate, calcium, creatinine, potassium and magnesium. For each assay the average number of deltas to detection (ANDD) was calculated in Matlab in response to induced SE conditions.

Results: The ANDD for SE equal to the reference change value for easy assay varied between assays and between positive and negative SE. For albumin, a +0.4g/dL shift for was detected with an ANDD of 24.6 intra-patient deltas while a -0.4 g/dL SE was detected with an ANDD of 8.8. The AoD protocol with the lowest ANDD was amylase with a +20 U/L SE detected with an ANDD of 6.2 intra-patient deltas and a -20 U/L SE detected with an ANDD of 6.6. Creatinine had the highest ANDD in our validation set with an ANDD of 44.6 intra-patient deltas for a +0.3 mg/dL shift and an ANDD of 43 for a -0.3 mg/dL shift.

Conclusion: We have demonstrated that the AoD can quickly detect development of SE conditions. The AoD strategy is complimentary to other alternative QC strategies such as MA in that the AoD detects SE in assays such as amylase which are challenging for MA. AoD's limitation is that daily laboratory analyses of patients are required; however this is typically not problematic for most inpatient facilities. This initial study demonstrates the validity of the AoD strategy and we are developing further protocols to assess and optimize AOD's capabilities. It is our belief, given the power of AoD, that in the near future that AoD will be implemented in most clinical laboratory analyzers.

B-022

Evaluation of the Performance of JEOL BioMajesty JCA-BM6010/C Automated Clinical Chemistry Analyzer

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Background: Automated clinical chemistry analyzer has been designed for improved quality and speed, and to meet the various demands of different laboratory environments. The JEOL BioMajesty JCA-BM6010/C (JEOL, Japan) is a recently developed, ultra-compact automated analyzer. In this study, we evaluated the performance of JCA-BM6010/C on 11 analytes.

Methods: Precision, linearity, method comparison, accuracy and sample carryover of 11 analytes; alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransaminase (ALT), gamma-glutamyl transpeptidase (GGT), lactate dehydrogenase (LDH), calcium, uric acid, and total bilirubin were evaluated in accordance with the guidelines of the Clinical Laboratory Standards Institute (CLSI). We also further evaluated linearity using three open reagents (Sekisui, Japan) in the same JCA-BM6010/C instrument. For the correlation study, we compared the JCA-BM6010/C with Cobas 8000 modular analyzer (Roche diagnostics, Basel, Switzerland), and also compared JEOL exclusive reagents to other open reagents (Sekisui, Denka Seiken and Roche) for AST, ALT, GGT, glucose, and uric acid in the

same JCA-BM6010/C analyzer. To assess accuracy, three analytes with open reagents were evaluated (creatinine for Roche, glucose for Denka Seiken, calcium for Sekisui).

Results: The total coefficients of variation (CV) for imprecision evaluation of all analytes showed good values between 1.0 and 2.7% in the JCA-BM6010/C. Linearity was observed for all analytes over the entire analytical range ($R^2 \geq 0.99$). The JEOL exclusive reagent showed a wider linear range than the Sekisui open reagent in ALT and GGT. The JCA-BM6010/C showed good correlation coefficients ($R^2 > 0.975$) for all evaluated analytes except LDH ($R^2 = 0.945$) compared with the Cobas 8000. In the accuracy evaluation, the recovery rates were 96.6 to 101.5% (JEOL exclusive reagents) vs. 98.7 to 109.3% (open reagents) for three analytes (creatinine, glucose, and calcium). The sample carryover was less than 0.34%.

Conclusions: The JCA-BM6010/C showed excellent performance in terms of precision, linearity, comparison, accuracy, and sample carryover. Additionally, the instrument's performance is comparable with the Roche Cobas 8000. We conclude that the JCA-BM6010/C could be used well for the medical services in the routine laboratories.

B-023

implementation of new total laboratory automation system and analysis of its outcome for laboratory turnaround time: experience of a core clinical laboratory in a large tertiary care hospital

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Background: The continuous pressure to improve laboratory efficiency and reduce turnaround time (TAT) have made the use of laboratory automation pervasive in clinical laboratories and brought about continual evolution and expansion of its capabilities. Recently, our laboratory has implemented a new total laboratory automation (TLA) system and informatics tool (Aptio™ Automation and CentraLink™ Data Management System, Siemens Healthcare Diagnostics), which can automate the laboratory processes from specimen transportation to refrigerated storage and disposal. In this article, we have drawn on our experience on new TLA system in clinical chemistry and immunology at a 1400-bed tertiary care hospital, Korea, in comparison with old one (ADVIA LabCell, Siemens).

Methods: The major changes between Aptio™ and ADVIA LabCell were as follows: use of bulk input module, incorporation of centrifugation module in the TLA line (routine samples only) and implementation of refrigerated storage module (RSM) capable of automated sample storage, retrieval and disposal. To evaluate the performance of Aptio™ Automation, TAT from sample collection to reporting and intra-laboratory TAT (from sample loading to reporting) after Aptio™ implementation (October 2014-January 2015) were compared to those in the ADVIA LabCell period (October 2015-January 2016) using 3 representative chemistry (AST, TSH, and troponin I) and 1 immunology (anti-HBs) items. The benefits of RSM were evaluated using the number and intra-laboratory TAT of reflex tests arising from the results exceeding analytical measurement range, which were processed automatically (Aptio™), or manually (LabCell).

Results: During the study period, the proportion of routine vs. stat orders was 40% vs. 60%, and it meant 40% of manual centrifugation was reduced under Aptio™ system. The mean intra-laboratory TAT for stat and routine samples was 19 and 21 min (LabCell) vs. 21 and 35 min (Aptio™), while TAT from sample collection to reporting was 60 and 67 min (LabCell) vs. 66 and 72 min (Aptio™), respectively. Under both system, 0.2% of samples (4,979/2,463,709 on LabCell; 6,491/3,343,082 on Aptio™) needed reflex tests and mean intra-laboratory TAT of reflex tests was 34 (LabCell) vs. 37 min (Aptio™).

Conclusion: Our experience on the new TLA system showed that Aptio™ Automation did not shorten TAT compared to previous one, while it reduced pre-analytical and post-analytical manual process considerably with minimal delay in intra-laboratory TAT by incorporating centrifugation module and storage module. Although the new features of Aptio™ Automation were appreciated, it seems that strategies to optimize laboratory TAT are needed.

B-024

Development and application of a network glucometer quality control program for a tertiary hospital

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Background: The use of point-of-care (POC) glucometers for hospitalized patients has been increased. However, it has never been subjected to traditional quality control assessment. Here, we developed a novel network quality control program for glucometers using Unity (Bio-Rad Laboratories, Irvine, USA). We evaluated more than 200 glucometers (ACCU-CHEK, Roche Diagnostics) in service in a tertiary hospital.

Methods: Quality control (QC) data on glucometers were collected from September 2014 to June 2015. In Unity, we made the instrument number to be recognized as a lot number in a single laboratory containing more than 200 different lots. The QC data were transferred to a laboratory information system (LIS) using the Roche docking system, and then to Unity, in real time. The data were analyzed daily to detect violations of Westgard rule and monthly to get mean and standard deviation (SD) for each instrument. The acceptance criteria for accuracy and precision were, respectively, the mean±12 mg/dL or 12.5% and a coefficient of variation (CV) ≤7.1%.

Results: About 250 POC glucometers were subjected to QC each month. The mean number of QC runs for each instrument was 55.4. Pooled CVs for low and high control materials were 2.7 ~ 3.8% and 2.1 ~ 2.7%, respectively. During the study period, all the instruments met the accuracy criteria, while 0.0 ~ 0.4% and 0.3 ~ 1.6% of instruments could not meet the precision criteria for low and high QC materials, respectively. When the QC check failed, the instrument was checked and the operative given additional education on how to perform QC measurements. During the study period, seven instruments were changed because of abnormal QC results.

Conclusion: We developed a network QC program for glucometers using LIS and the Unity program. We successfully monitored QC results of POC glucometers. To our knowledge, this is the first attempt to apply QC to glucometers systematically. Our method will be useful in large hospitals with numerous POC glucometers.

B-025

Evaluation of the Analytical Performance of a Thyroid-stimulating Hormone Assay on the Atellica Immunoassay Analyzer$_1$

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Introduction: Measurement of thyroid-stimulating hormone (TSH) concentration with a high degree of sensitivity, accuracy, and precision is important in the diagnosis and management of thyroid and pituitary disorders. The primary objective of this study was to demonstrate the analytical performance of the TSH3-Ultra (TSH3-UL) assay on the Atellica™ Immunoassay (IM) Analyzer[1], an automated, high-throughput immunoassay analyzer under development by Siemens Healthcare Diagnostics.

Methods: The Atellica IM TSH3-ULassay uses the same reagents and calibrators as the ADVIA Centaur® TSH3-UL assay, a third-generation TSH assay. The Atellica IM TSH3-UL assay employs anti-FITC monoclonal antibody covalently bound to paramagnetic particles, a FITC-labeled anti-TSH capture monoclonal antibody, and a tracer consisting of another anti-TSH monoclonal antibody and acridinium ester (AE), both conjugated to BSA. The AE is a patented high quantum yield hydrophilic NSP-DMAE-HEG-Glutarate-NHS molecule. Precision of the TSH assay was evaluated for serum and plasma samples spanning the measuring range (0.034 to 132 µIU/mL) according to CLSI protocol EP05-A3. LoB, LoD, and LoQ were determined as described in CLSI protocol EP17-A2. Interference testing followed CLSI protocol EP07-A2.

Results: Detection capability for the Atellica IM TSH3-UL assay was estimated to be 0.001, 0.005, and 0.007 µIU/mL for LoB, LoD, and LoQ (functional sensitivity at 20% total CV), respectively. Observed repeatability ranged from 1.09 to 4.87% CV, and within-lab precision ranged from 1.82 to 5.95% CV over the assay range. The assay showed no significant effect (less than 5% bias) from endogenous interferences, including red blood cell lysate up to 600 mg/dL hemoglobin, triglycerides up to 2000 mg/dL, and conjugated and unconjugated bilirubin up to 60 mg/dL. There was no high-dose hook effect for the Atellica IM TSH3-UL assay in samples up to 9239 µIU/mL TSH. Comparison between the Atellica IM and ADVIA Centaur XP TSH3-UL assays yielded the following Deming regression equation: Atellica IM TSH3-UL = 1.07(ADVIA Centaur XP TSH3-UL) + 0.00 µIU/mL; n = 347 serum samples ranging

from 0.008 to 148.79 µIU/mL; r = 0.994. The on-system stability of the Atellica IM TSH3-UL reagents was determined to be at least 60 days.

Conclusion: The Atellica IM TSH3-UL assay has demonstrated excellent analytical performance capable of measuring TSH with a high degree of sensitivity, accuracy, and precision for use in the diagnosis and management of thyroid and pituitary disorders.

[1] Under development. Not available for sale.

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B-026

Total laboratory automation in a high-volume clinical laboratory: assessment of economic savings, improvement of processes and productivity increase.

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Background: In the last years, the increasing demand on clinical laboratories required improvements on workflow and cost efficiency, as well as reduction in turnaround time (TAT) and error rates. All these factors propelled to the use of total automation systems (LAS) as a solution for routine and emergency sample management. LAS also allows the laboratory manager to have a clear path of each process in the analytical area and act directly in bottlenecks to improve processes , leading to "Lean" laboratories. In order to measure whether LAS improve sample and process management, we investigated daily test release rates, productivity/staff, tube and waste reduction rates in a laboratory that produces 34 million biochemistry and immunology tests per year.

Methods: A new laboratory configuration was proposed in order to connect 17 Siemens ADVIA CentaurXP®, 8 ADVIA Chemistry 2400 ® and 2 IMMULITE 2000® to the 65 meters Siemens Aptio® LAS equipped with 3 bulk input module, 1 input/output module and 3 rack output modules. This configuration allowed sample loading onto the system without rack-placing procedure with an input up to 3,000 tubes/hour and 35,000 tubes/day. Relevant data, such as, number of tubes, exams/hour, exams/personnel and time to report results, was collected from Laboratory Information System (LIS) and CentraLink Data Management System® before and after LAS installation.

Results: After 3 months of LAS operation, 86% of biochemistry and 80% of hormone-related tests results were reported at the same day of sample collection(versus 67% and 50% in the pre-LAS condition, respectively). An increase of 55% in number of tests performed by technician/day were observed. Cost savings with tubes reached up to US$ 6,500, per month (US$80,000/year) with 97,500/month tube handling decrease and biological waste reduction to more than 1,13 tons/month. Moreover, processes involving loading, sorting, and error handling of samples were dramatically reduced.

Conclusions: Here, we describe a successful LAS implementation, with gains in TAT, number of tests/personnel and tube reduction. The workflow was substantially simplified, turning from a multi-step process to a one-way route through pre-analytical to post-analytical phases. Thus, LAS allowed significant cost reduction and raised the productivity in a high-volume laboratory.

B-027

Experience of a Laboratory Automation System in a laboratory growing up to 30% a year: reduction in blood collection tubes, biological waste, and TAT reduction.

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Background: In recent years, clinical laboratories face the challenge to increase productivity, quality and reduce Turnaround Time (TAT) and costs of operation. The use of automated systems as well dedicated software for management of laboratory orders and results represents a very useful solution. However, Laboratory Automation Systems (LAS) drastically changes the workflow and processes within a laboratory, requiring staff to rethink all laboratory processes. Examples of these changes are tube unification from different areas such as immunology, hormone and biochemistry, changing of staff roles towards management of critical results or STAT samples. This laboratory redesign facilitates the mapping of sample flow and allows the standardization and improvement of processes, augmenting the quality of data and reducing the number of process steps required to report a given test. Here we describe an experience of a laboratory which performs more than 26,000 tests/day and is growing at a pace (around) 30% annually.

Methods: A 40 meter Aptio® track system with 4 Advia CentaurXP® Immunoassay System, one IMMULITE 2000 XPi® dedicated for allergy and esoteric tests and 2 Advia® Biochemistry System all connected to the track which was originally designed to run 4,500 tubes/day. The track was also configured for sorting tubes to non-LAS connected instruments or manual tests, eliminating the need for handling. Moreover, Centralink Data Management System® was configured to auto-validate tests which show values compatible with a pre-configured normality range. In order to assess relevant changes, TAT, test autovalidation, tests/tube, laboratory disposable supplies, biological waste reduction and new sample request due to internal errors were compared between pre and post track installation. 73,09% of overall laboratory tests are analyzed trough this track system, considering initial tests volume of 575,000/month.

Results: In spite of 30% tests volume increase after LAS installation, TAT was reduced from 11 hours to 9 hours (approximately 20% reduction), Physical Area Utilization Rate Rate increased from 3,305 to 4,297 tests/m², auto validated results increased from 70% to 90% (around 5,000 tests) and test/tube ratio increased from 6 to 9 tests/tube. This increase in test density/tube reduced the costs of blood collection tubes, reflecting in biological waste production, which was decreased by 15%. Also, TAT reduction allowed the laboratory report of iPTH tests on the same day of sample collection.

Conclusions: Upon laboratory automation system (LAS), laboratory dramatically reduced TAT while the number of overall tests increased up to 30%. Autovalidated tests and number of tests per tube increased and granted staff to gain productivity and focus on the critical samples. Overall workflow of sample processing inside the laboratory was redesigned and simplified. Track system has generated consistent savings to the laboratory in terms of blood collection and biological waste, and has allowed laboratory growth to reach up to 2,250,000 tests/month in the same physical area based on the technical expansion strategy and track system existing capabilities.

B-028

Gains in productivity and workflow with a total automation system: the experience of a brazilian clinical laboratory

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Background and objectives: Cost efficiency and increased productivity are challenges for most clinical laboratories nowadays. Even smaller laboratories can benefit from enhanced workflow and greater efficiency that an automation system provides. In this study, we evaluate the productivity and quality gains in Labimed - a 97000 tests/month clinical laboratory located in south of Brazil - after the implementation of VersaCell X3 automation system (Siemens Healthcare Diagnostics).

Methods: A VersaCell X3 connecting two imunoassays systems (IMMULITE and Advia Centaur XP) and one chemistry system (ADVIA Chemistry 1800) was implemented on Labimed in October of 2014. Relevant data, such as, number of tubes, total turnaround time (TAT) and the percentual of autovalidated results was collected from Laboratory Information System (LIS) and CentraLink Data Management System (Siemens Healthcare Diagnostics), before and after VersaCell installation. We also compared the workflow in both scenarios. Overall perception of benefits was surveyed among the laboratory staff.

Results: The productivity per technician was increased in 15% and TAT was reduced, in average, by 68%. The total number of tubes was reduced in 40%. Analyzing the workflow, less steps are necessary to process samples tubes now. Also, staff surveyed reported the perception of reduced workload.

Conclusion: Due to the automation's single tube concept, it was possible to reduce the total number of tubes in the laboratory. By automating manual tasks and creating a single, consolidated workstation for chemistry and immunoassay tests (80% of total routine is processed on VersaCell X3 platform) the workflow became much more lean, improving TAT. Besides pre and analytical gains, we also observed post-analytical improvements: with autovalidation rules configured in a dedicated middleware (Siemens CentraLink Data Management), 85% of the results are now autoverified, reducing the workload of the technicians. All in all, with the implementation of VersaCell X3, our laboratory was able to deliver faster results, save on material costs and increase staff productivity.

B-029

Analysis of kidney stones by quantitative automated method

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Background: The analysis of kidney stones (KS) are essential for management of patients with nephrolithiasis. Most KS are composed of calcium oxalate, uric acid, calcium phosphate or magnesium-ammonium-phosphate (struvite). KS are usually analyzed by semi-quantitative colorimetric manual method. The aim of this study was to evaluate the analysis of KS by automated quantitative method to identify the following type of KS: calcium oxalate, uric acid, calcium phosphate and struvite. **Methods:** KS were analyzed by two methods: 1. Reference method: manual and semi-quantitative by colorimetric analysis (Merck®), following the manufacturer's instructions and determining the components of the calculation with the highest percentage (oxalate, calcium, uric acid, phosphate, ammonium and magnesium). They were classified into calcium oxalate, uric acid, calcium phosphate and struvite. 2. Method to evaluate: automated and quantitative. KS was crushed and degraded with 100 µL of sulfuric acid. Then 50 µL of the sample degraded was diluted with 450 µL of distilled water and the following biochemical parameter were determined in the autoanalyzer Dimension EXL (Siemens diagnóstic®): calcium, uric acid, phosphorus and magnesium. Statistical analysis was performed using the software MedCalc®. **Results:** We analyzed 58 KS, 35 were calcium oxalate, 17 calcium phosphate, 5 uric acid and 1 struvite, according to the semi-quantitative method reference. The range and median of biochemical parameter determined by automated quantitative method for each type of KS is shown in the following table:

	Calcium oxalate	Calcium phosphate	Uric acid	Struvite
Calcium (mg/dL)	**55.7 (18.6-169.8)**	**63.0 (25.3-155.2)**	2.1 (0.1-4.8)	10.0
Phosphorus (mg/dL)	1.7 (0-9.6)	**18.7 (13.0-52.1)**	0.1 (0-0.1)	**21.1**
Uric acid (mg/dL)	0.2 (0-1.4)	0.2 (0-0.9)	**101.3 (44.6-296.1)**	0
Magnesium (mg/dL)	1.7 (0-5.7)	2.2 (0-2.9)	0.9 (0.4-1.0)	**55.1**

Using the Mann-Whitney test, we found statistically significant differences ($p<0.0001$) with:

a) Calcium levels to identify KS composed of calcium oxalate or calcium phosphate. b) Phosphorus levels to identify KS composed of calcium phosphate or struvite. c) Uric acid levels to identify KS composed of uric acid. **Conclusions:** This automated quantitative method can be used for analysis of KS. Calcium, phosphorus, uric acid and magnesium levels in KS identify the type of KS.

B-030

Automated Sigma Metric Analysis for Monitoring Quality in a Standardized Healthcare System.

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Background:

As healthcare systems continue to merge and expand, additional tools are needed to monitor analytical performance metrics, more efficiently and effectively. This poster demonstrates the utility of sigma metric analyses for evaluating quality across multiple instruments and assays in networked healthcare system. Automated techniques are leveraged in the analysis, demonstrating the future possibilities for quickly and efficiently capturing large amounts of quality control data for use in sigma metric calculations. In addition, this study will demonstrate the use of sigma metrics for evaluating instrument and or assay performance changes over time and which variables play a role in these changes.

Methods: This study collected 400 days of quality control data from 5 networked laboratories, comprising 284,676 quality control data points, across seven Abbott ARCHITECT platforms. In total, 25 assays were evaluated using QC levels near medical decision points. Target means were obtained through Biorad™ Unity peer data reports for bias estimates, and focused on one lot of unassayed Multiqaul control. Before sigma metrics were calculated, an outlier identification method was determined. Two methods were evaluated and compared to the number of values outside of the laboratory defined ranges. 1.) Using an instrument calculated +/- 3.5SD multiplier. 2.) Using instrument calculated mean and quartiles. To test for sigma stability or variability over time, 400 days of data were divided into ~180 day quarters. The impact of reagent lot changes, calibration lot changes, and calibrations were collected for investigating their contribution to sigma variability over time.

Results: The 3.5SD outlier method proved to be the preferred approach by successfully eliminating QC errors attributable to human error. In contrast, the Quartiles method incorrectly eliminated data when quartile widths were made extremely small due to a large number of identical QC results. Sigma metrics revealed nine assays exceeded 6 sigma for all seven analyzers over 4 quarters. Additionally, ten more analytes exhibited median sigma levels exceeding 6. Sigma metrics also revealed performance differences between instruments and over time.

Conclusion: Successful automation of sigma metrics for assessing and detecting quality changes in a networked healthcare system has been demonstrated. This data illustrates how instrument-assay combinations can be quickly obtained and reviewed for differences, prompting further investigations where needed. By collating data into statistically significant quarters, lab managers and directors can monitor performance trends over time. This tool allows a high level overview of networked instrument performance, and helps describe how robust a sigma level will be over time. Through automation tools and summary statistics such as sigma metrics information leading to QC cost reductions and improved performance will continue to play a role in clinical laboratory management.

B-031

Development of a risk model to predict urgent dialysis among advanced chronic kidney disease (CKD) patients

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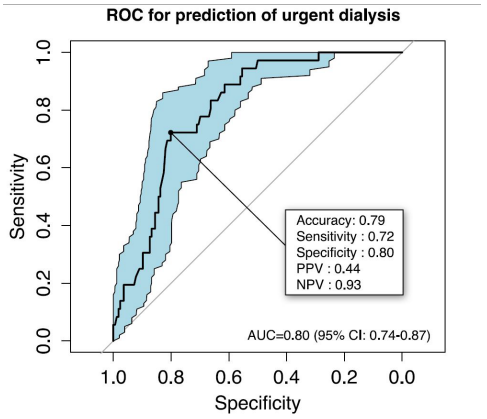
Background: Urgent in hospital dialysis starts are associated with increased costs and high morbidity and mortality. While previous studies have assessed risk factors for urgent dialysis among CKD patients, no study has developed a risk score to predict urgent dialysis. The objective of this was to develop a risk model to predict urgent dialysis among advanced CKD patients.

Methods: The study population included all advanced CKD (eGFR < 30 ml/min/1.73m^2) patients who were referred to multidisciplinary chronic kidney disease at The Ottawa Hospital between January 01, 2010 and December 31st 2014 (n=1010). This was a retrospective cohort study, which included the following data: Patient demographics (age, sex, race), physical examination variables (e.g. height, weight, blood pressure), laboratory test results (e.g. creatinine, eGFR, hemoglobin, urea, albumin); co-morbidities (e.g. coronary artery disease, hypertension, CHF); medications (e.g. anti-hypertensive, statin). A random forest (RF) classification algorithm was developed using these variables to predict patients at risk for urgent dialysis. Data were divided into training (60%), crossvalidation (20%), and test (20%) sets to optimize and test the performance of the model. The algorithm was optimized by adding features to the random forest model to maximize the ROC area-under-the-curve (AUC).

Results: The random forest model identified the following variables as the most important predictors: changes in CO2, calcium, albumin, weight, potassium, and phosphate along with age, urine protein:creatinine ratio, and creatinine. The RF model had an AUC of 0.80 (0.73-0.87), with sensitivity of 72% and specificity of 80% at maximum efficiency for prediction of urgent dialysis.

Conclusion: The model developed herein represents a potential mechanism to identify patients at risk for urgent dialysis. Identification of this population may allow for earlier interventions to improve outcomes in CKD patients progressing urgently to dialysis; implementation of this algorithm is also likely to reduce the associated costs of urgent in-hospital dialysis.



B-032

Optimizing use of business analytics and lab-oriented statistical software to establish robust and pertinent reference intervals

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Background: The patient population served by our automated chemistry laboratory has grown outside our local population due to rapid expansion of our health system, as well as the increased nationwide geographical footprint of the Cleveland Clinic's reference laboratory. Population-based reference intervals are a set of values classified by upper and lower reference parameters, which typically represents the central 95% of values from the reference population of normal, healthy, control subjects. Given our growing and likely evolving patient population, our existing reference intervals were re-evaluated for their appropriateness. Various challenges accompany the process of validating or verifying reference ranges. Traditional approaches may have some limitations, including a lack of laboratory resources, inadequate availability of specimens from normal, healthy subjects (especially for partitioned reference intervals, e.g. due to patient demographics), insufficient or inefficient access to LIS or EMR data, or inappropriate starting point reference intervals based on literature or vendor-provided information. Establishing *de novo* reference intervals for common metabolic analytes was preferred (vs. verifying other intervals) because the new ranges would reflect the actual patient population being served. The goal of this study was to establish laboratory-specific *de novo* reference intervals for 12 common metabolic analytes by leveraging multiple software tools and existing patient results. This is an example of how laboratories can efficiently utilize analytics to drive better patient care. **Methods:** This study utilized Altosoft (*Kofax*, Irvine, CA), "code-free" business intelligence software to readily identify suitable existing patient samples where results were stored in our laboratory information system (*Sunquest*, Tucson, AZ). Data was exported into Excel (*Microsoft*, Redmond, WA) and filtered according to pre-defined, medical director-approved qualifications (including visit-related diagnosis codes) which resulted in the datasets used for further analysis. The datasets were evaluated using an EP Evaluator® (*Data Innovations*, South Burlington, VT) statistical module, entitled "Establish Reference Interval (EST)." This Establish RI module uses the nonparametric method in accordance with CLSI: C28-A guidelines to calculate the reference interval (based on central 95% of results from healthy subjects). **Results:** Reference intervals were established using analysis of historical data for 12 common metabolic analytes. The number of patient results used in establishment (N) far exceeded the traditionally recommended minimum of 140 samples, and ranged from 540 to 646 for each analyte. **Conclusions:** Data mining tools and real-time analytics utilization was used for robust establishment of reference intervals that would not be feasible to achieve with our historical methods. Improvements over our previous methodology included: 1) Establishing reference intervals for common analytes utilized large datasets to produce *de novo* ranges that are truly representative of our patient population. 2) After gaining familiarity with the analytic tools, the process proceeded quickly. 3) Readily accessible and exportable data via the business intelligence software allowed us to bypass our previous reliance on IT expertise and availability to conduct our data searches. 4) Although we utilized EP Evaluator® software in this project, the statistical analysis of the healthy population dataset could be performed in most spreadsheet programs with either default functions or via add-in packages.

B-033

Integration of steroid analysis in serum using LC-MS/MS with fully-automated sample preparation

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Background: Currently sample preparation for the detection of steroids in serum by liquid chromatography-mass spectrometry (LC-MS/MS) involves complex offline extraction methods such as solid phase extraction or liquid/liquid extraction, all of which require additional sample concentration and reconstitution in an appropriate solvent. These sample preparation methods are time-consuming, often taking 1 hour or more per sample, and are more vulnerable to variability due to errors in manual preparation. Our approach to offering a high sensitivity steroid detection method and timely, automated analysis of multiple samples is to use the automated sample preparation system coupled to the detection capabilities of a high-sensitivity triple stage quadrupole mass spectrometer.

Methods: 10 steroid hormones (cortisol, aldosterone, 11-deoxycortisol, corticosterone, 17-alpha-hydroxyprogesterone (17-OHP), 4-androstene-3,17-dione (androstenedione), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), progesterone and testosterone) in serum were verified using CHS™ MSMS Steroids Kit (PerkinElmer, USA). Serum sample was loaded directly into the automated sample preparation system (CLAM-2000 Shimadzu, Japan). The CLAM-2000 was programmed to perform protein precipitation using acetonitrile followed by filtration and sample collection. The sample is then transported using an arm from the CLAM-2000 to the HPLC without human intervention for LC-MS/MS analysis. The treated samples were trapped using a MAYI-ODS column (2mm x 5mm) and then separated by Core-Shell Biphenyl HPLC column (Kinetex Biphenyl, 100mm x 2mm, 2.6µm, Phenomenex) at 40°C with a binary gradient system at a flow rate of 0.3 ml/min in 11 min.

Results: We evaluated this system using calibrator and control serum spiked with 10 steroids in Kit and carried out concurrent analysis over a range of concentrations for each steroid: cortisol (1.51-320 ng/mL), aldosterone (0.03-7.05 ng/mL), 11-deoxycortisol (0.08-18 ng/mL), corticosterone (0.29-62 ng/mL), 17-OHP (0.12-26 ng/mL), androstenedione (0.08-18 ng/mL), DHEA (0.31-65 ng/mL), DHEAS (12.9-2750 ng/mL), progesterone (0.12-26.5 ng/mL) and testosterone (0.03-7.2 ng/mL). The calibration curves that were generated had linear regression values of r^2 >0.997 for each curve. The reproducibility (N=3) at seven concentrations, including LLOQ of each compounds was excellent (CV<10%). We found that the sample preparation time was reduced from 60 minutes to 10 minutes by the automated system.

Conclusion: We completed steroid analysis using the automated sample preparation system coupled to LC-MS/MS. The results shows the capability of the system for large sample set analyses with improved accuracy and precision by eliminating human error associated with manual sample handling.