Patient Percentile Monitoring Global Report #01

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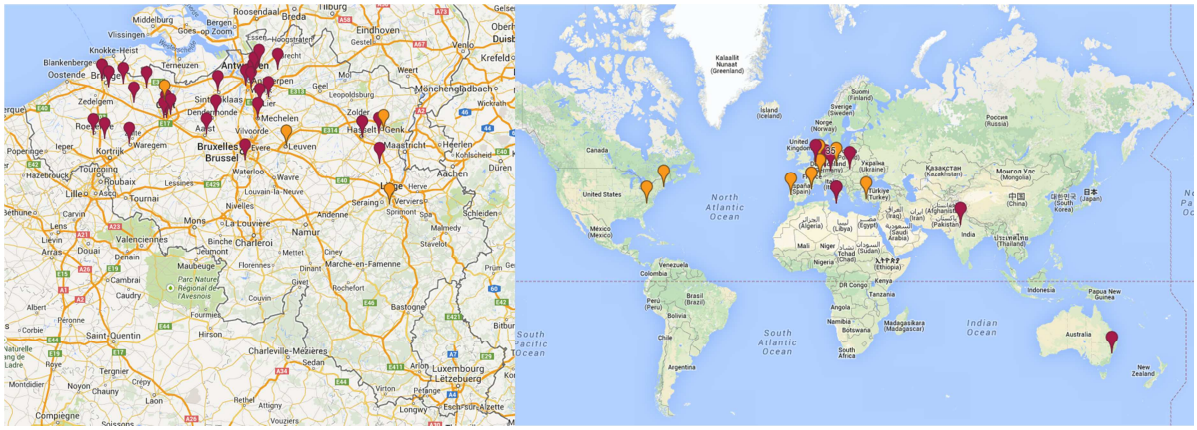
Project status (Nov 27 2013)

Participants (laboratory sites and number of instruments)

-Total 39 participants with 76 instruments:

Advia	1	Integra	5
Architect	5	Konelab	1
AU	6	Modular	2
Synchron	1	Vista	2
Cobas	38	Vitros	15

-31 sites in Belgium (4 more confirmed); 8 sites international (8 more confirmed)



IT status

-LIS solutions: GLIMS, Cegeka, IZASA, Vision4Health (Molis, Test phase)

-e-mail connection ready (Bruno Neckebroek: neckebroek.bruno@telenet.be); readable formats: mail embedded, EXCEL attachment, text attachment.

-User interface: January 2014 (Bruno Neckebroek).

Outlook

-Global contact to laboratories

-Contact to several LIS providers

-Contact to main manufacturers

-Support by BVKC/SBCC

Related activity

Master comparison 2014

Patient percentile monitoring compared to internal quality control (IQC) monitoring

The Table compares typical CV-values for IQC-monitoring and percentile-monitoring (daily medians).

The CV's for patient data are, generally, greater than for IQC data (ratios >1). Exceptions are the "high-volume" analytes with narrow biological variation (calcium, chloride and sodium).

Therefore, daily QC decisions will have to rely on IQC data in most laboratories.

However, applying moving medians with "tailored" *n*, will reduce the variability by SQRT[n]. This makes percentile monitoring applicable for mid-to long-term monitoring of analytical variability.

The actual number of daily medians required for reliable monitoring will depend on the number of outpatient results available in a laboratory, in combination with the population variation of a certain analyte (again, analytes wil low biological variation allow lower "*n*" to be used).

	IQC	Percentile	
	CV	CV	CV-ratio
ALB	0.9	2.0	2.3
ALKFOS	1.1	5.4	4.8
ALT	2.8	5.8	2.1
AST	1.9	4.7	2.4
BILTOT	2.2	12.1	5.6
CA	1.0	1.2	1.2
CHOL	1.5	5.4	3.6
CL	0.4	0.6	1.2
CRP	2.6	23.5	8.9
GGT	1.8	11.1	6.2
GLUC	0.6	2.8	4.4
K	0.4	1.4	3.7
CREAT	1.6	4.7	3.0
LDH	1.3	4.9	3.8
MG	0.9	2.6	3.1
NA	0.3	0.4	1.4
P	1.0	3.7	3.8
PROT	0.9	1.9	2.1
UREA	1.2	4.8	4.0
URIC ACID	0.5	5.3	10.5

We will have the choice between *n* = 5, 8, and 16 in the forthcoming user interface.

Note

We foresee IQC-monitoring in a later phase of the project.

Comparison of outpatient/all patient monitoring

The Table shows the differences between all-patients and outpatients in typical hospital laboratories and the CV-ratio of those 2 groups.

There is a considerable difference in the median of outpatients and all patients for most of the analytes. Note, however, only outpatients will give medians that can be compared with “target” medians from reference interval information.

The CV-ratios All-/Out-patients are typically <1, meaning that monitoring all patients would result in better stability.

We decided, however, to continue with outpatient monitoring because only outpatients may give comparable values between different laboratories, allowing the assessment of laboratory/peer group bias. The somewhat higher variability can be compensated by a slightly higher “*n*” for the moving medians.

	%-Diff Out/All	CV Ratio All/Out
ALB	14.2	1.76
ALKFOS	-7.0	**0.69**
ALT	-4.6	0.79
AST	-4.5	0.83
BILTOT	-7.3	**0.68**
CA	3.0	1.18
CHOL	1.6	0.90
CL	0.2	0.76
CREAT	1.9	0.74
CRP	-93.2	1.27
GGT	-23.6	0.89
GLUC	-5.2	0.87
K	2.8	**0.58**
LDH	-5.0	0.83
MG	1.6	**0.61**
NA	0.4	0.89
P	0.7	**0.65**
PROT	7.0	1.13
UREA	3.4	**0.65**
URIC ACID	4.4	0.78

Stability limits

The stability limits refer to limits that should not be violated longer than 1 week. These limits are guided by the systematic error limits based on biological variation ("desirable" values; see Westgard website). However, we took the current capability of diagnostic manufacturers into account and expanded these limits for analytes with narrow biological variation, such as sodium, chloride, calcium, etc. Note, we set a general upper limit of ~10% for analytes with very high biological variation (CRP).

	Bias Biology (%)	Bias Empower (%)	Bias Biology (unit)	Bias Empower (unit)	Unit	Median "SI"
ALB	1.3	2.3	0.56	1	g/L	43.0
ALKFOS	6.4	7.0	4.6	5	U/L	71.9
ALT	11.4	11.0	2.1	2	U/L	18.1
AST	5.4	4.9	1.1	1	U/L	20.4
BILTOT	11.4	12.2	0.94	1	µmol/L	8.21
CA	0.8	2.1	0.019	0.05	mmol/L	2.38
CHOL	4	4.1	0.20	0.2	mmol/L	4.91
CL	0.5	1.0	0.51	1	mmol/L	102.0
CRP	21.8	11.0	0.40	0.2	mg/L	1.82
GGT	10.8	9.4	2.3	2	U/L	21.2
GLUC	2.2	3.8	0.12	0.2	mmol/L	5.24
K	1.8	3.4	0.08	0.15	mmol/L	4.44
CREAT	4	4.1	2.9	3	µmol/L	73.0
LDH	4.3	5.4	7.9	10	U/L	183.6
MG	1.8	3.5	0.015	0.03	mmol/L	0.85
NA	0.3	0.7	0.42	1	mmol/L	140.6
P	3.2	3.6	0.036	0.04	mmol/L	1.11
PROT	1.2	1.4	0.83	1	g/L	69.5
UREA	5.5	5.5	0.30	0.3	mmol/L	5.45
URIC ACID	4.9	4.7	15.5	15	µmol/L	317

The actually chosen numbers were "tailored" to the SI-units; for albumin and total-protein, for example, we chose 1 g/L; the respective %-ages were then calculated at the median concentration, resulting in "non-integer" numbers: 2.1% for calcium, 3.8% for glucose.

The limits should be regarded as preliminary working numbers and should be matter of discussion among the participants.

Target values (laboratory, peer, manufacturer reported reference interval, trueness-based)

Target values are structured according hierarchy: long-term laboratory median, peer group moving median, and a “reference” target. The latter, however, is difficult to define. There is only one source we know that claims “trueness-based” reference intervals (http://pweb.furst.no/norip/). The reliability of that source is high for analytes such as sodium and calcium. The information for some enzymes has to be used critically (changes in the IFCC procedures; no uniform adaptation of IFCC procedures). We also compiled reference interval information from manufacturers’ data sheets. Cross comparison with the NORIP data may help to define some preliminary “reference” targets for several analytes (see Table below).

	Median		Diff
	NORIP	Assays	(%)
ALB (g/L)	41.5	42.8	**3.1**
ALP (U/L)	63.0	73.2	16.2
ALT (U/L)	21.0	21.5	**2.3**
AST (U/L)	23.0	22.6	**-1.9**
BILTOT (µmol/L)	10.0	8.6	-13.8
CA (mmol/L)	2.34	2.33	**-0.3**
CHOL (mmol/L)	5.20	-	-
CL (mmol/L)	-	*102.5*	-
CRP (mg/L)	-	-	-
GGT (U/L)	22.0	17.5	-20.6
GLUC (mmol/L)	4.87	4.80	**-1.5**
K (mmol/L)	4.05	4.25	4.9
CREAT (µmol/L)	70.7	77.0	8.9
LDH (U/L)	152	176	15.6
MG (mmol/L)	0.83	0.86	**3.6**
NA (mmol/L)	141.1	140.6	**-0.4**
P (mmol/L)	1.13	1.12	**-0.9**
PROT (g/L)	69.8	73.2	4.9
UREA (mmol/L)	4.89	4.96	**1.4**
URIC ACID (µmol/L)	282	272	**-3.5**

Current analytes with “reference” targets could be albumin, ALT, AST, calcium, glucose, magnesium, sodium, phosphate, urea, uric acid.

We will also ask manufacturers about their long-term target values for patient medians, because several manufacturers routinely monitor their lot-stabilities by use of patient data.

Structure of the individual reports

The individual reports that you receive are based on workdays, only. We also omitted "coarse" outliers because these reports are based on EXCEL-templates where we have to use moving averages instead of moving medians (in the user interface). The data are presented in figures for visual interpretation and described in a written report.

Structure of the figures

The figures show the "moving average" of the daily medians (values on *y*, date on *x*) for the 20 analytes (Saturdays and Sundays excluded; coarse outliers removed). Analytes that were measured on different instruments were combined in one figure; in that way, a minimum number of "virtual instruments" were created. The figures show further the long-term laboratory mean (blue, long-broken line) and the limits around (short-broken blue lines). Finally, a Peer group mean is indicated by the pink broken line. Currently, this is available for the Cobas group, only.

Written report

The written report addresses:
-Basic variability of the patient median
-Systematic differences between instruments (when more than 1 is monitored)
-General comments on stability
-Specific points of attention/problems
-Peer difference (where applicable)

Preliminary observations for enzymes

We see 2 clearly separated groups for LDH (most probably IFCC- and GSCC-procedures). In turn, we will need a detailed description of the procedures used, in particular, for the ALT/AST procedures (with or without pyridoxal phosphate) where the differences are not that big.

We will make a general inquiry about the procedures used, as different procedures are offered from the same manufacturer for several analytes (albumin, creatinine, etc.).

Example

The example below shows a laboratory with low median variation (high numbers of results making up the median; clearly stratified outpatient population). Characteristically, even the daily medians are most often found between the stability limits. Typically, the *n* for the moving average can be 5. These conditions are advantageous for the detection of analytical instabilities (shifts, drifts). For smaller hospital laboratories, with greater intrinsic median variation, a higher *n* (7, 10, or more) has to be chosen for the moving average/median; consequently, they need longer observation times to uncover analytical instabilities and they loose some shorter-term information. But percentile monitoring is also a very useful mid- to long-term quality management tool for smaller laboratories.

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