Flagging Monitoring Global Report #01

CONTENT

EMPOWER IVD●GLOBE

Flagger Report #01 27/11/2015

Background

Goal

Stability monitoring of IVD assays by plotting the moving medians of daily hypo- and hyper flagging rates.

Data

We collect instrument-specific daily hypo- and hyper-flagging rates calculated from outpatient results of 22 commonly measured analytes in serum or plasma: albumin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), calcium, chloride, C-reactive protein (CRP), creatinine, free T4 (FT4), γ-glutamyl transferase (GGT), glucose, inorganic phosphorus (phosphate), lactate dehydrogenase (LDH), magnesium, potassium, sodium, thyroid-stimulating hormone (TSH), total-bilirubin, total-cholesterol, total-protein, urea, and uric acid (urate).

User interface

www.theflagger.be (demo: username = demolab; password = demo1234)

Related activity

Patient Percentile Monitoring (www.thepercentiler.be). Stability monitoring of IVD assays by plotting the moving medians of daily patient medians.

Project status (November 2015)

Participants

Total: 42 participants (24 sites in Belgium; 18 sites international) with ~100 instruments:

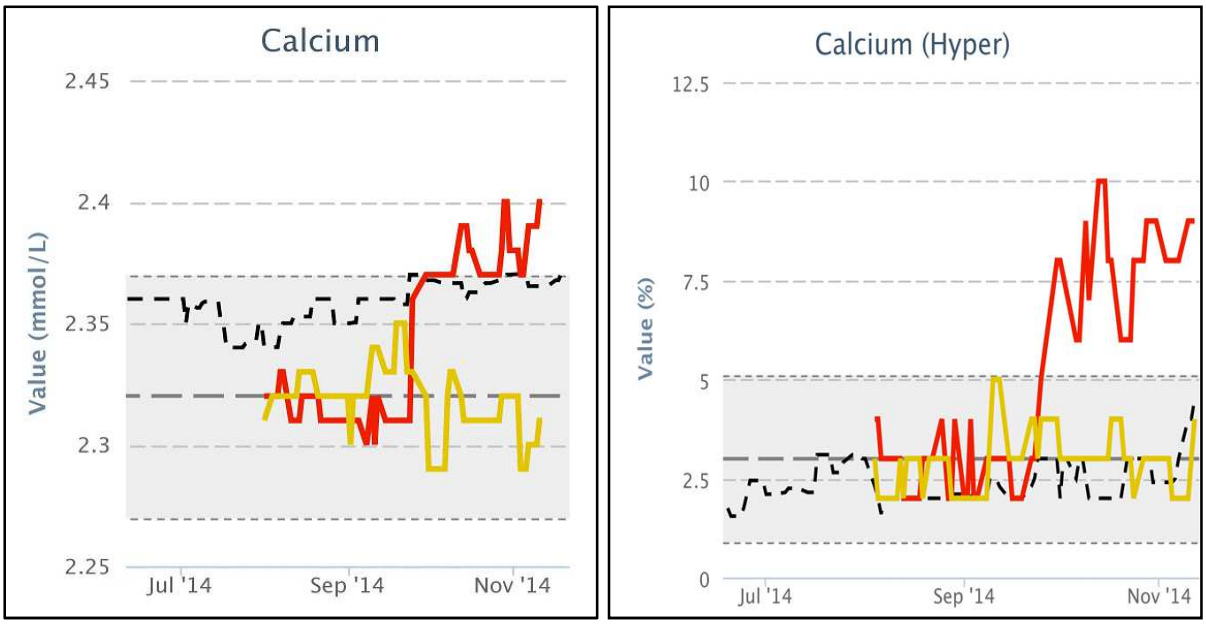
Advia	3	Integra	3
Architect	3	Modular	2
AU	7	Synchron	1
Cobas	79	Vista	0
Dimension	0	Vitros	2

IT status

LIS solutions (IT connectivity) for: GLIMS, Data Innovations, and local solutions.

Application concept

Whilst patient percentile and flagging monitoring are separately extremely suited to follow the stability of the individual instrument, combing the two tools together has the additional potential to translate analytical shifts into their effect on the flagging rate.
Example: hypercalcemia surrogate medical decision - triplication of flagging rate in period with high vs. low median values.



The left figure presents a graph from the Percentiler that shows stable patient medians for the yellow instrument. The red instrument started stable but then a shift occurred to higher values (~0.06 mmol/L higher). In the Flagger (right graph) you can observe the effect of that shift on the hyper-flagging rate; a triplication going from 2.5 to 7.5%.

Target values

Typically, the reference interval of a laboratory is defined by the 95% of apparently healthy people. Theoretically, we expect flagging rates of about 2.5% for both hypo-, and hyper-conditions. However, for a number of analytes the normal distribution is skewed, e.g. mostly hyper-values for enzymes. For other analytes general recommendations are applied, e.g. for total-cholesterol laboratories apply age-dependent limits provided by The National Cholesterol Education Program (NCEP). As a consequence, the expected flagging rate will differ for all analytes, and due to a lack of consensus on the applied reference intervals, a target value is not provided.

Stability limits

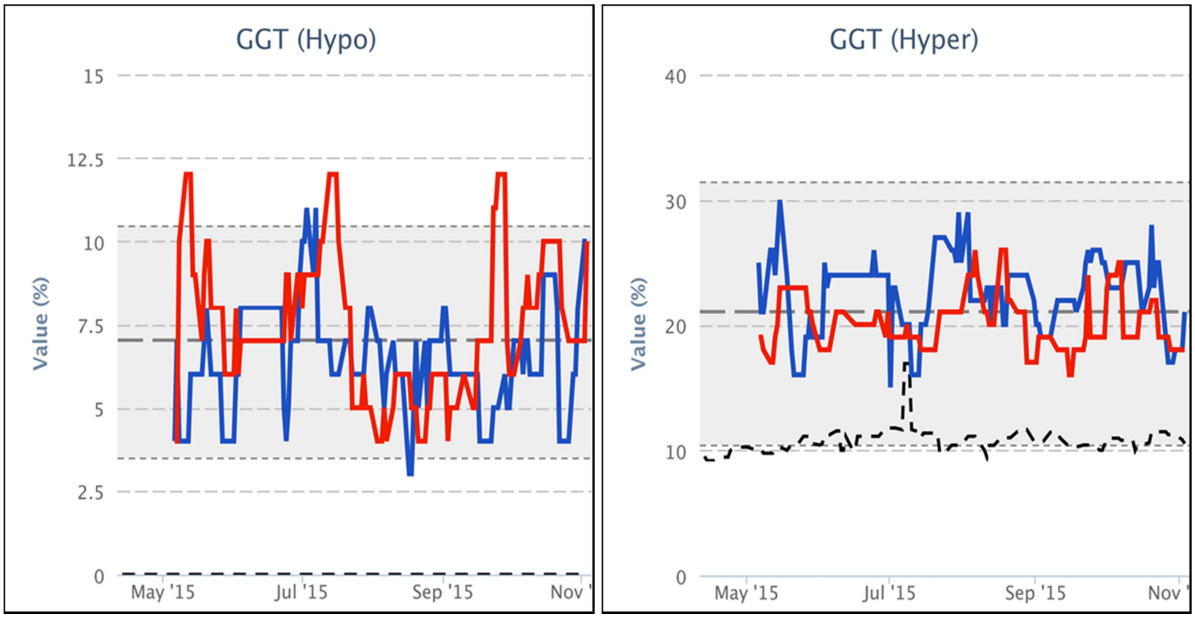
The Flagger applies limits that are calculated relative compared to the long-term flagging rate, but set an absolute minimum when the long-term flagging rate is low. For example, the relative limit for AST is 30% with an absolute minimum of 1%. This means when your long-term flagging rate equals 10%, the limits will be ± 3% (= 30% of 10%). When your long-term flagging rate equals 2.5% the limit equals the minimal 1%, and not 0.75%.

Flagger limits are chosen so that they are in agreement with current state-of the-art performance at the higher and/or lower concentration ranges. Note, these limits need to be regarded as preliminary. Right now, they are biased towards the Cobas performance.

	Percentiler		Flagger	
	Bias Biology (%)	Bias Empower (%)	Limit (Relative %)	Minimum Limit (Absolute %)
ALB	1.3	2.3	30	1
ALKFOS	6.4	7.0	40	1
ALT	11.4	11.0	30	1
AST	5.4	4.9	30	1
BILTOT	11.4	12.2	30	1
CA	0.8	2.1	70	1
CHOL	4	4.1	20	1
CL	0.5	1.0	50	1
CRP	21.8	11.0	30	1
GGT	10.8	9.4	50	1
GLUC	2.2	2.8	20	1
K	1.8	2.3	30	1
CREAT	4	4.1	30	1
LDH	4.3	5.4	50	1
MG	1.8	3.5	70	1
NA	0.3	0.7	100	1
P	3.2	3.6	70	1
PROT	1.2	1.4	60	1
UREA	5.5	5.5	30	1
URIC ACID	4.9	4.7	50	2
FT4	3.3	3.4	30	1
TSH	7.8	7.3	30	1

Comparison with overall and/or peer group median

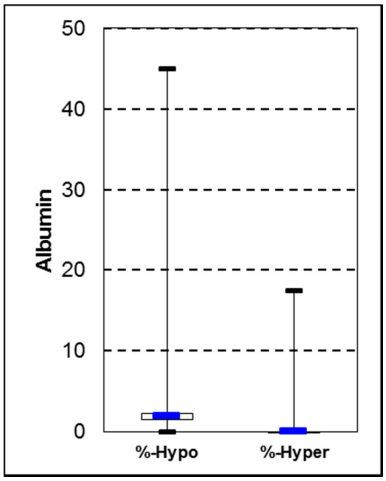
Just like in the Percentiler, you will be able to compare your long-term flagging rate with the overall and peer group median (= black dotted line in the graphs).

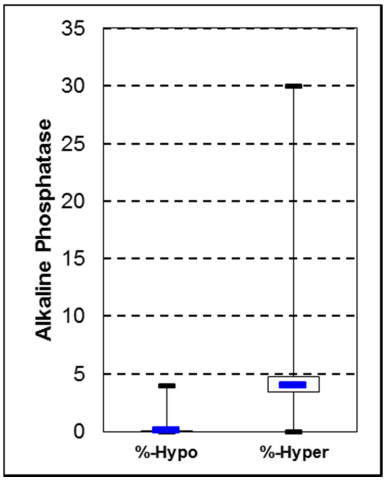


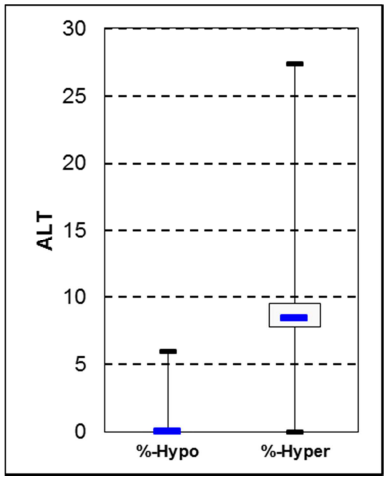
Comparison with the overall and/or peer group median, however, has limited value because different laboratories apply different reference intervals. As a consequence the long-term flagging rates can lie at grossly different levels.

Long-term flagging rates of all instruments

To give an idea about the distribution of the different laboratories, the long-term flagging rates of all instruments are presented as box-and whisker plots with indication of the long-term median of the flagging rates in blue. The box represents instruments within the 25th to 75th percentile; the whiskers extend to the minimum and maximum results. Data was extracted from the Flagger from October and November.


Albumin
50
40
30
20
10
0
%-Hypo
%-Hyper


Alkaline Phosphatase
35
30
25
20
15
10
5
0
%-Hypo
%-Hyper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15
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5
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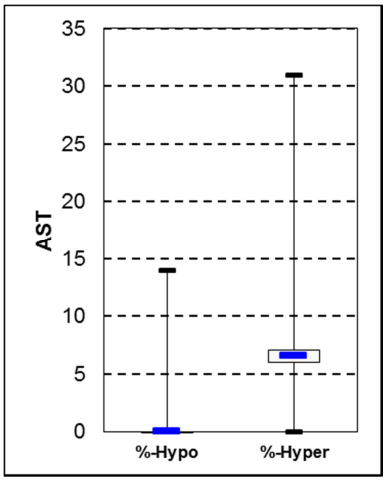
%-Hypo
%-Hyper


AST
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30
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15
10
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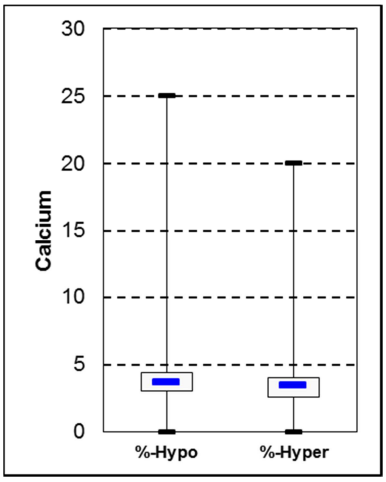
0
%-Hypo
%-Hyper


Calcium
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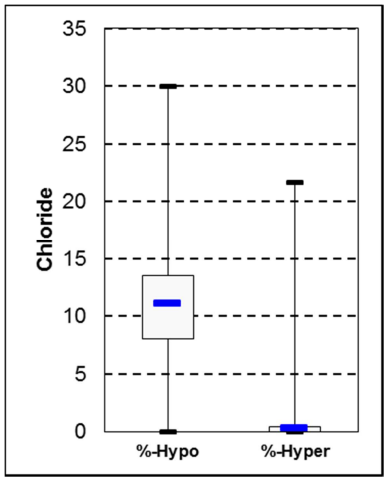
25
20
15
10
5
0
%-Hypo
%-Hyper


Chloride
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20
15
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5
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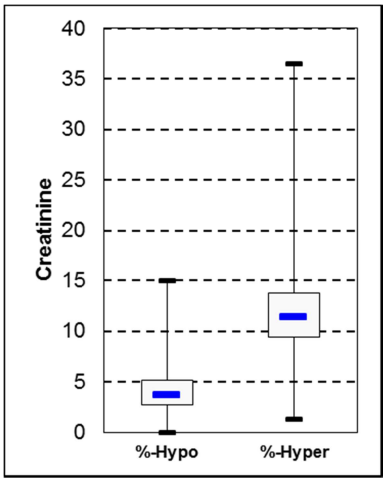
%-Hypo
%-Hyper


Creatinine
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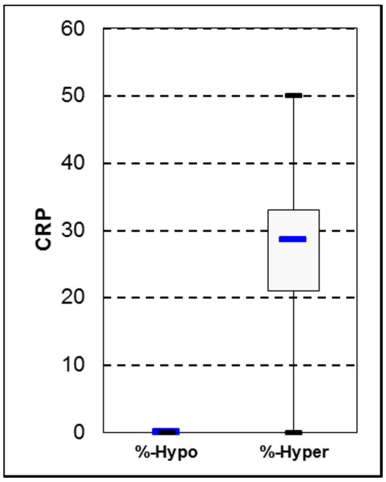
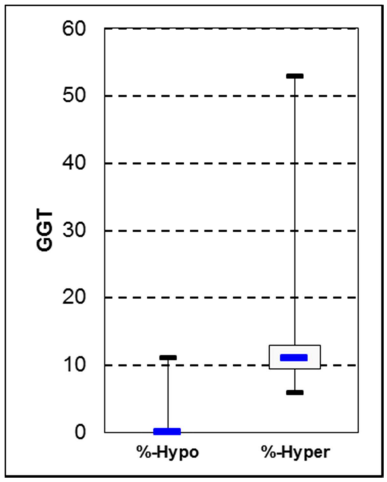
35
30
25
20
15
10
5
0
%-Hypo
%-Hyper


CRP
60
50
40
30
20
10
0
%-Hypo
%-Hyper


GGT
60
50
40
30
20
10
0
%-Hypo
%-Hyper

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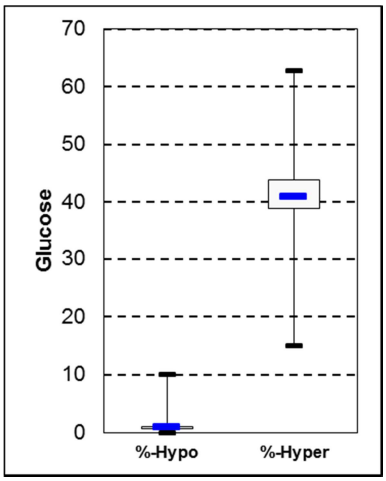
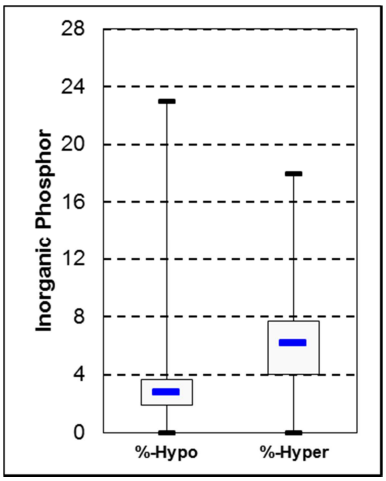
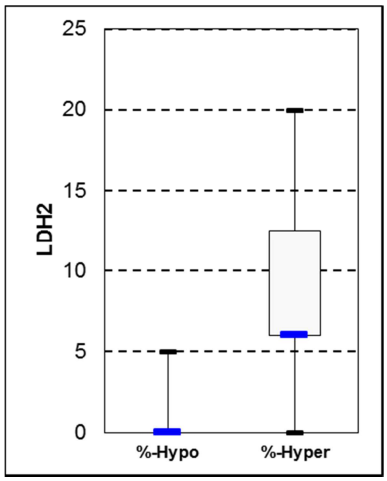
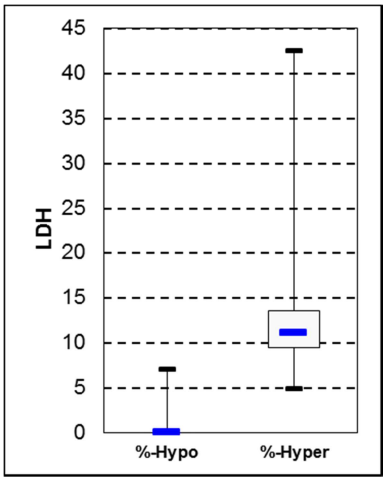
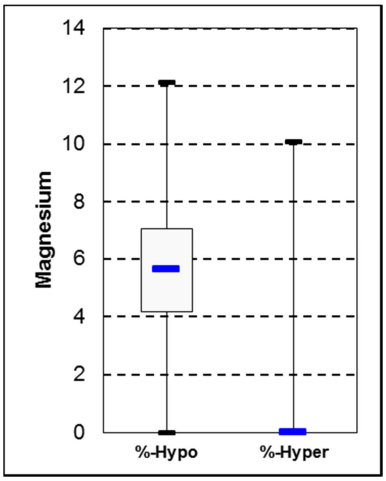
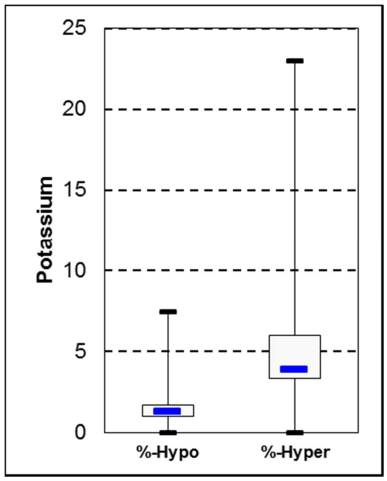


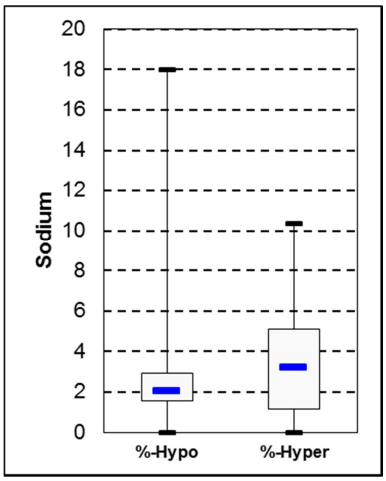


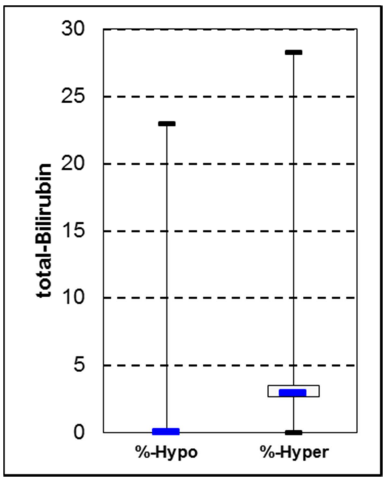


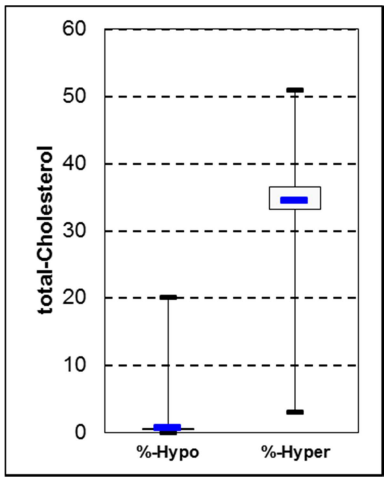


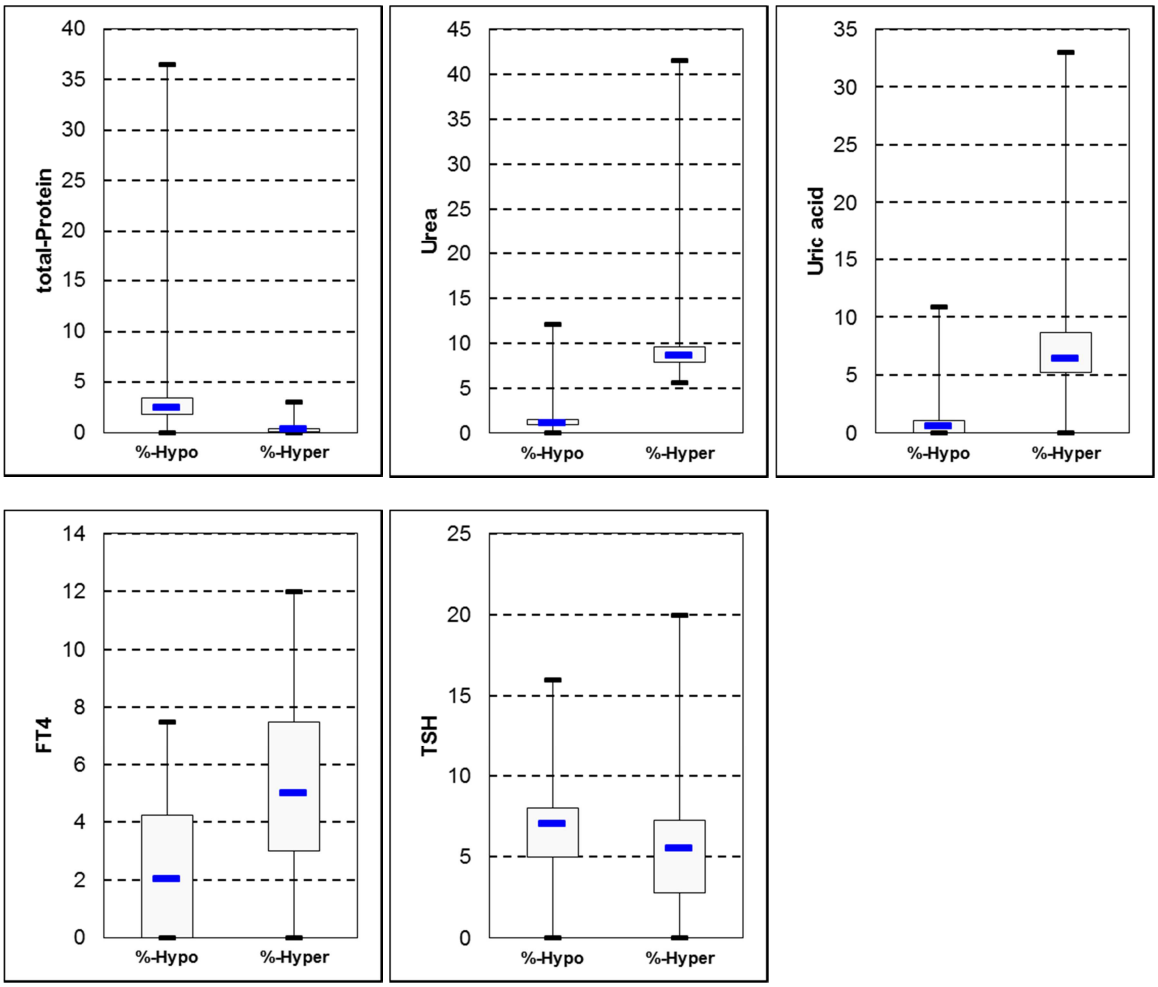








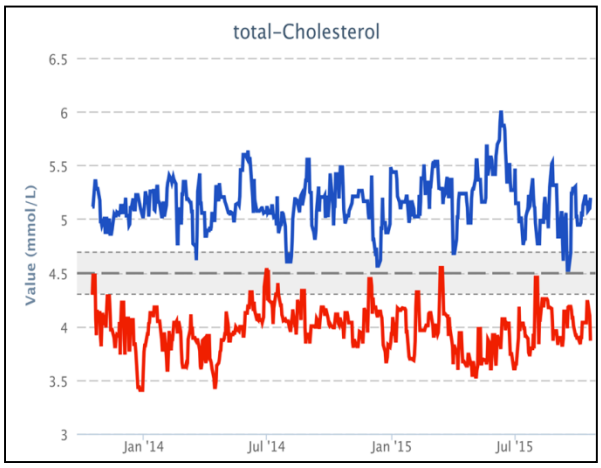




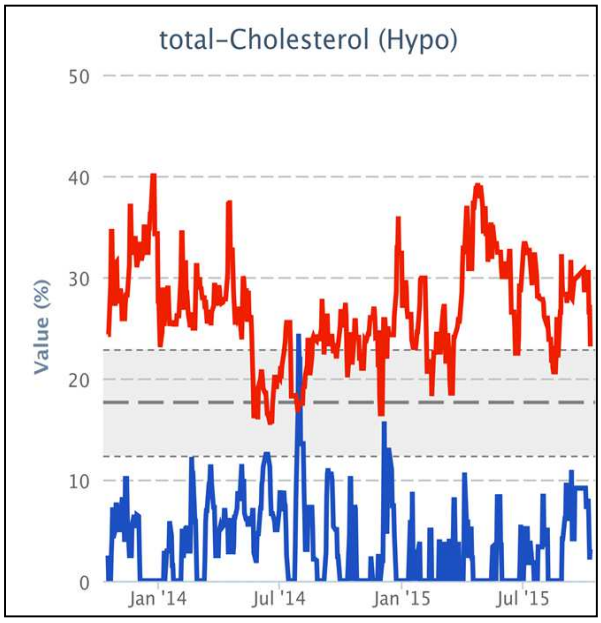
Some laboratories show long-term flagging rates that are significantly higher or lower than most instruments in the database. This can be caused by a population effect and/or by the use of atypical reference intervals.

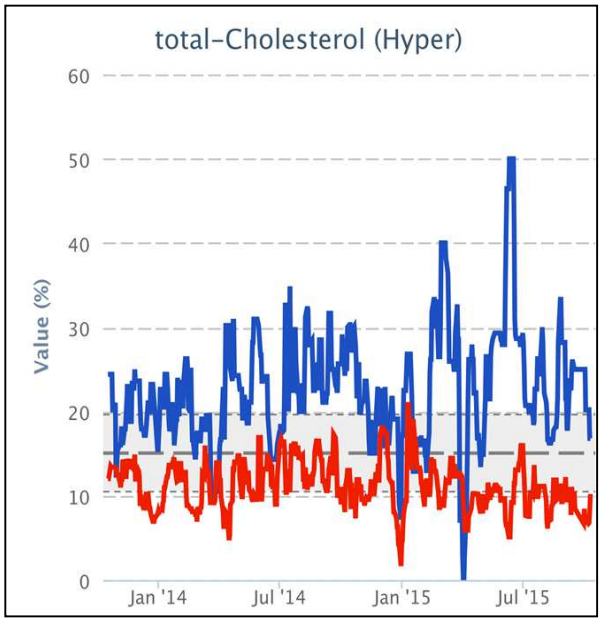
Examples

In principle the link between the Percentiler and Flagger tool is quite clear. When the values for the patient medians increase, the hypo-flagging rate will drop, and the hyper-flagging rate will increase and vice versa. In the example below, the Percentiler shows a bias between two instruments that measure total-cholesterol.

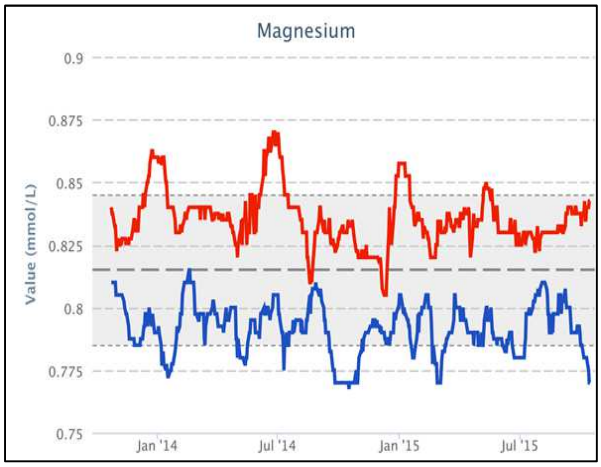


This bias is also visible in the low and high concentration ranges, resulting in a significant difference for both the hypo- and hyper-flagging rate.

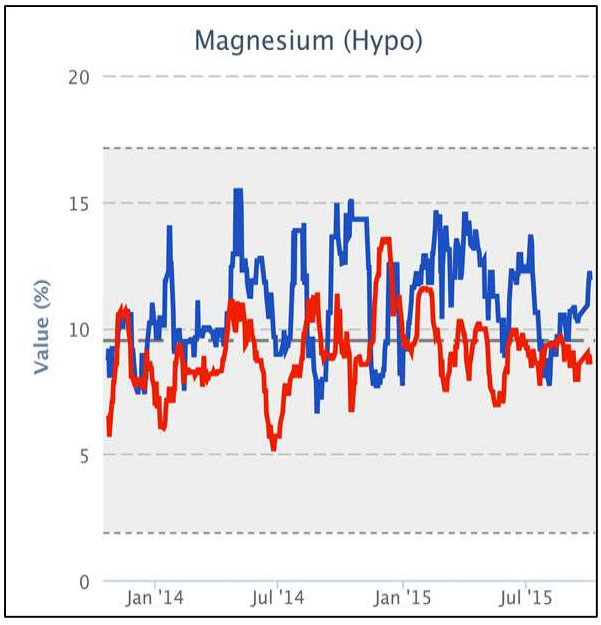


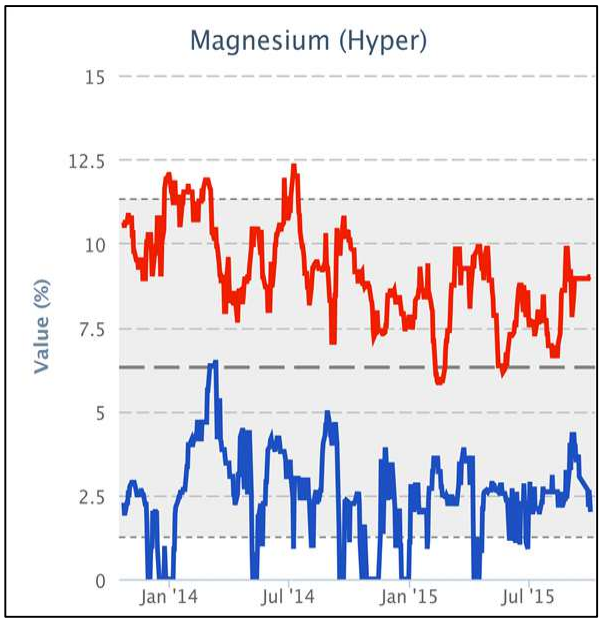


However, some exceptions can be found. Again, the Percentiler shows a bias between two instruments that measure magnesium.

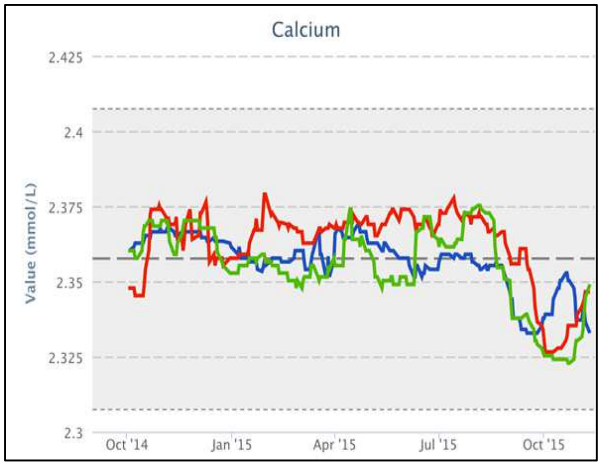


Also the hyper-flagging rate shows that bias observation. However, these instruments are more comparable at the low concentration range than at the median or high concentration. This observation can be explained by a difference in calibration at different concentration ranges.





In addition, when the population variation is low (or when the number of samples measured on a single instrument each day is high), it becomes possible to translate even small effects of an analytical shift on the flagging frequency. In the example below, the patient medians for calcium shift to values that are ~0.03 mmol/L lower.



By comparing the Percentiler graph with the Flagger graphs, this laboratory is able to translate the effect of their shift on the flagging frequency. The hypo-flagging rate increases from ~3% to ~4%, and the hyper-flagging rate decreases from ~5% to ~3%.