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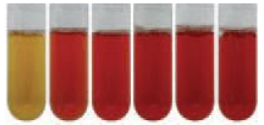
# Analytical interferences due to sample integrity Weqas Serum indices Programme – a 10 year journey

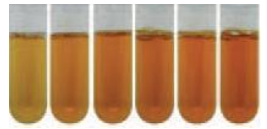
Annette Thomas

**Heamolysis** is the release of intracellular components from erythrocytes and other blood cells into the extra cellular fluid and can be caused by inappropriate or incorrect sample processing. Even if hemolysis is not visible there may still be discharge of cellular contents into the serum/plasma. At haemoglobin concentrations exceeding 300 mg/l (18.8 mmol/l), haemolysis is visible to the eye by the red colour of the plasma. Haemolyzed samples are a rather frequent occurrence in laboratory practice, with a prevalence as high as 3.3% and accounting for nearly 60% of rejected samples.



**Lipaemia** is turbidity of the sample due to the presence of triglyceride. It can be detected visually if the concentration of triglycerides in patient samples is over 300 mg/dl (3.4 mmol/L). Lipaemic samples cannot be avoided as increased concentration of lipids is often secondary to other disease states such as: diabetes mellitus, ethanol use, chronic renal failure and pancreatitis etc.

**Icterus** is the term given to elevated concentrations of bilirubin. Such elevations can be found in a variety of conditions including acute and chronic liver disease, biliary cirrhosis, alcoholism or as a physiological response to many drugs. The visual recognition of hyperbilirubinemia is often not sufficiently sensitive. Because of the high absorbance of bilirubin within the range 340 to 500 nm and the high background, the linearity range of the method can become a limiting factor for spectrophotometric analyses at these wavelengths.



# Pre-analytical errors due to sample interferences: A WEQAS study to monitor the effectiveness of serum indices and Bilirubin interference.

In late 2010 users of the Weqas Serum Chemistry programme were provided with challenging samples containing either bilirubin, haemoglobin or triglyceride. The aim of the studies were to assess:

- the ability of the analysers Haemolytic / Icteric / Lipaemic (HIL) indices test to identify the presence of these potential interference.
- how laboratories deal with results where indices suggest that interferences are present in the sample.
- the interference effects of these parameters on the respective methods in routine use.

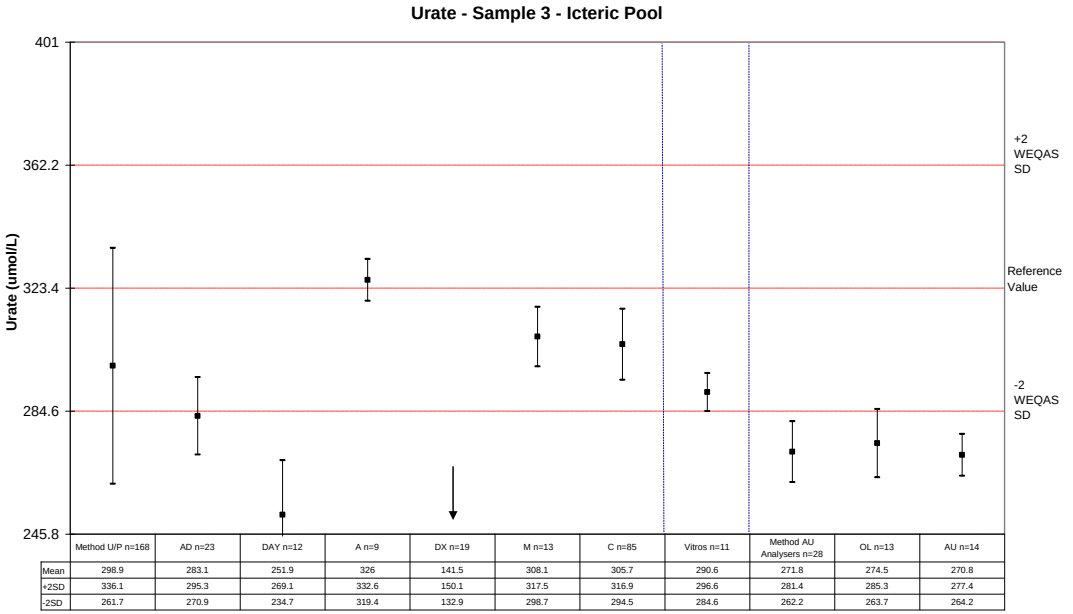
Samples were spiked with conjugated and unconjugated bilirubin to provide total bilirubin covering a range of 60- 500 µmol/L, Intralipid to a triglyceride range of 3 to 12.6 mmol/L and whole blood to provide a haemoglobin range of 0.4 to 3g/L. Two matched pools were distributed, one containing the interferant and the other the base serum.

In 2020, a separate stand alone serum indices programme was launched. Over 200 users now report results with the majority using semi-quantitative methods.

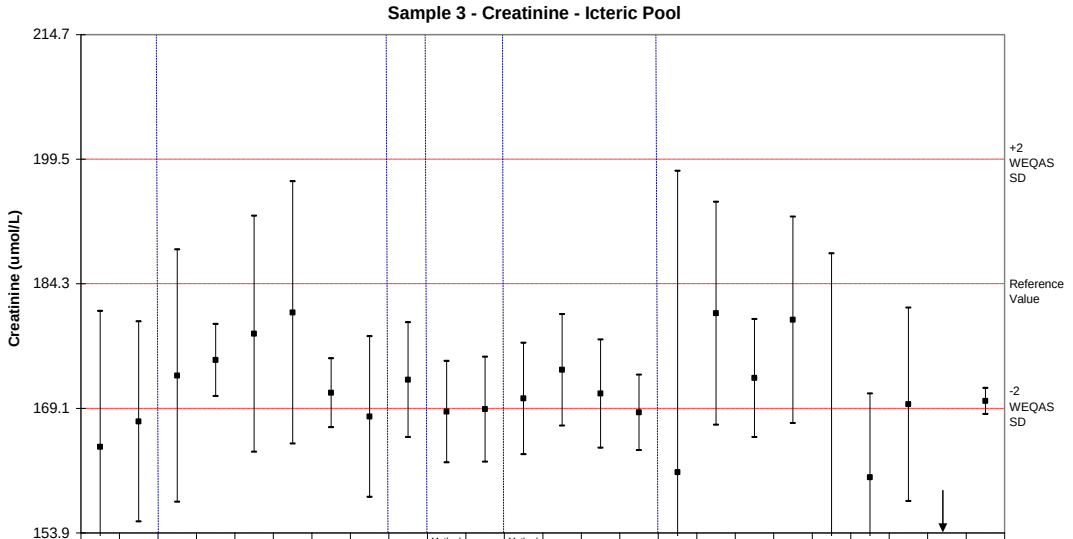
| | IQN | | IQQ | | IQT | | IQW | | IQZ | |
|---|---|---|---|---|---|---|---|---|---|---|
| | H | | I | | L | | I | | L | |
| Quant Mean | 0.3g/L | | 52 umol/L | | 6.3 mmol/L | | 347 umol/l | | 3.6 mmol/L | |
| Analyser | Results | No. | Results | No. | Results | No. | Results | No. | Results | No. |
| Interpretation | + | | + | | +++ | | +++ | | ++ | |
| Advia | Neg/- (0-0.22) | 12 | Neg, - | 1 | Neg,- | | Neg,- | 2 | Neg,- | |
| | + (0.23-1.0) | 1 | + | 26 | + | | + | | + | |
| | ++ (1.1-2.33) | | ++ | | ++ | | ++ | 6 | ++ | 29 |
| | +++ (2.34-3.78) | | +++ | | +++ | 27 | +++ | 22 | +++ | |
| | ++++ (3.79 ->) | | ++++ | | ++++ | | ++++ | | ++++ | 1 |
| % correct | | 8% | | 96% | | 100% | | 73% | | 97% |
| Interpretation | +/0.5-0.99 | | + | | ++++ | | +++ | | +++ | |
| Beckman AU | Neg/-/<0.5 | | Neg, - | 29 | Neg,- | 2 | Neg,- | | Neg,- | |
| | +/0.5-0.99 | 24 | + | 12 | + | | + | | + | |
| | ++/1.00-1.99 | | ++ | | ++ | | ++ | | ++ | 1 |
| | +++/2.00-2.99 | | +++ | | +++ | | +++ | 47 | +++ | 25 |
| | ++++/3.00-5.00 | | ++++ | | ++++ | 23 | ++++ | 1 | ++++ | 9 |
| | +++++/>5.00 | | +++++ | | +++++ | 17 | +++++ | | +++++ | |
| % correct | | 100% | | 29% | | 55% | | 98% | | 71% |
| Interpretation | 1 – 2/0.0-0.75 | | 2-4 | | 9-10 | | 11-17 | | 6 - 8 | |
| Beckman DX | Neg/0 | | Neg, 0-1 | | Neg, 0-1 | | Neg, 0-1 | | Neg, 0-1 | |
| | 1 – 2 (0.0-0.75) | 3 | 2-4 | 5 | 2 | | 2-4 | | 2 | |
| | 3 – 4 (0.75-1.50) | | 5-10 | | 3-5 | | 5-10 | | 3 - 5 | 1 |
| | 5 – 6 (1.50-2.25) | | 11-17 | | 6-8 | | 11-17 | 5 | 6 - 8 | 4 |
| | 7 – 8 (2.25-2.75) | | 18-20 | | 9-10 | 5 | 18-20 | | 9- 10 | |
| | 9 – 10 (2.75-3.50) | | | | | | | | | |
| % correct | | 100% | | 100% | | 100% | | 100% | | 80% |
| Interpretation | | | + | | +++ | | +++ | | +++ | |
| Piccolo | Neg/- | | Neg/- | 5 | Neg,- | | Neg,- | | Neg,- | |
| | + | | + | | + | | + | | + | |
| | ++ | | ++ | | ++ | | ++ | | ++ | |
| | +++ | | +++ | | +++ | 4 | +++ | 3 | +++ | 6 |
| | | | ++++ | | ++++ | | ++++ | | ++++ | |
| % correct | | | | 0% | | 100% | | 100% | | 100% |

# Assay Interferences

The early studies showed that for the icteric samples, method interferences were observed for creatinine, glucose, phosphate, protein and urate. For the lipaemic samples, interferences were observed for glucose, magnesium and urate, whilst for the haemolysed sample, potassium, creatinine, phosphate, magnesium, AST, ALT, CK, ALP, GGT, iron, TIBC, transferrin saturation were affected.




| | Method U/P n=168 | AD n=23 | DAY n=12 | A n=9 | DX n=19 | M n=13 | C n=85 | Vitros n=11 | Method AU Analysers n=28 | OL n=13 | AU n=14 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mean | 298.9 | 283.1 | 251.9 | 326 | 141.5 | 308.1 | 305.7 | 290.6 | 271.8 | 274.5 | 270.8 |
| +2SD | 336.1 | 295.3 | 269.1 | 332.6 | 150.1 | 317.5 | 316.9 | 296.6 | 281.4 | 285.3 | 277.4 |
| -2SD | 261.7 | 270.9 | 234.7 | 319.4 | 132.9 | 298.7 | 294.5 | 284.6 | 262.2 | 263.7 | 264.2 |




| | Method JR n=4 | C n=4 | Method KJ n=53 | AD n=3 | OL n=10 | AU n=10 | A n=7 | C n=25 | Method Vit n=4 | Method VIDMS n=9 | VI n=8 | Method Enz n=53 | AD n=12 | M n=7 | C n=32 | Method JI n=120 | AD n=18 | OL n=5 | AU n=7 | DX n=26 | C n=34 | M n=14 | DAY n=13 | A n=3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mean | 164.4 | 167.5 | 173.1 | 175.0 | 178.2 | 180.8 | 171.0 | 168.1 | 172.6 | 168.7 | 169.0 | 170.3 | 173.8 | 170.9 | 168.6 | 161.3 | 180.7 | 172.8 | 179.9 | 153.0 | 160.7 | 169.6 | 128.7 | 170 |
| +2SD | 181 | 179.7 | 188.5 | 179.4 | 192.6 | 196.8 | 175.2 | 177.9 | 179.6 | 174.9 | 175.4 | 177.1 | 180.6 | 177.5 | 173.2 | 198.1 | 194.3 | 180 | 192.5 | 188 | 170.9 | 181.4 | 142.1 | 171.6 |
| -2SD | 147.8 | 155.3 | 157.7 | 170.6 | 163.8 | 164.8 | 166.8 | 158.3 | 165.6 | 162.5 | 162.6 | 163.5 | 167 | 164.3 | 164 | 124.5 | 167.1 | 165.6 | 167.3 | 118 | 150.5 | 157.8 | 115.3 | 168.4 |

CLIN. CHEM. 32/3, 470–475 (1986)

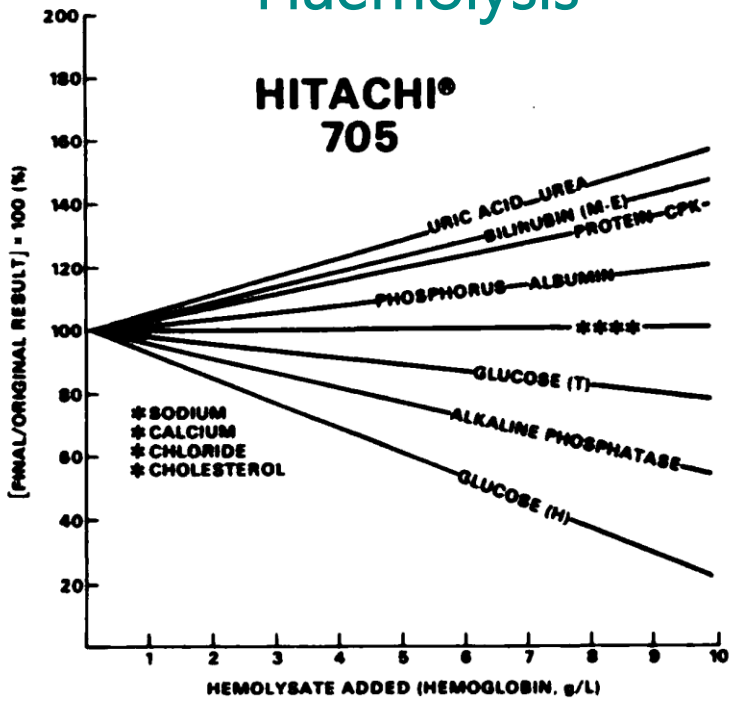
# Identiying Assay Interferences – the Glick interforographs.

Weqas

Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation

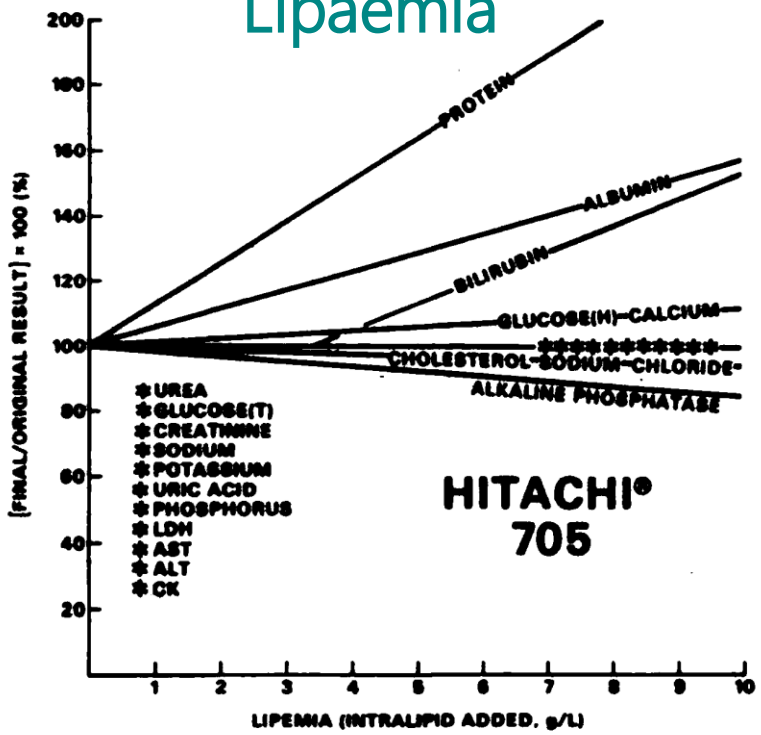
Melvin R. Glick, Kenneth W. Ryder, and Sheila A. Jackson

## Haemolysis



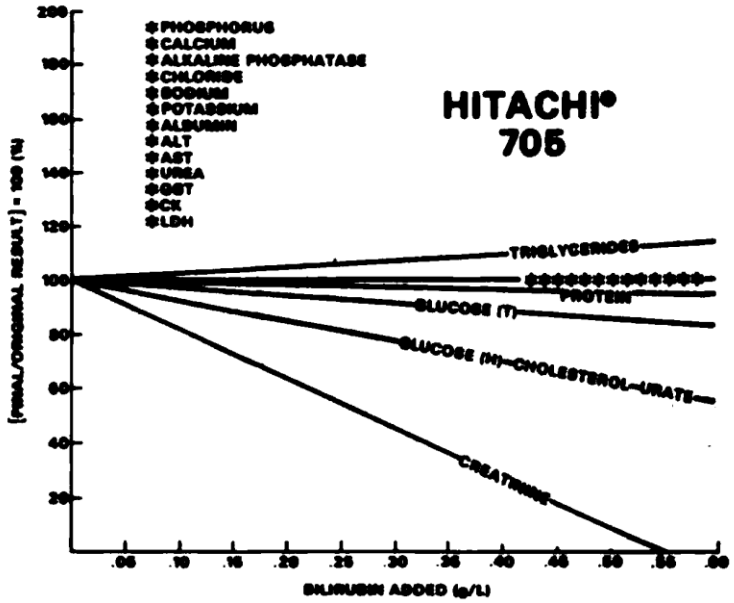

Pos effects on: UA,Urea, Bili, TP, CK, Alb, P.
Neg effects on:Glu, ALP

## Lipaemia



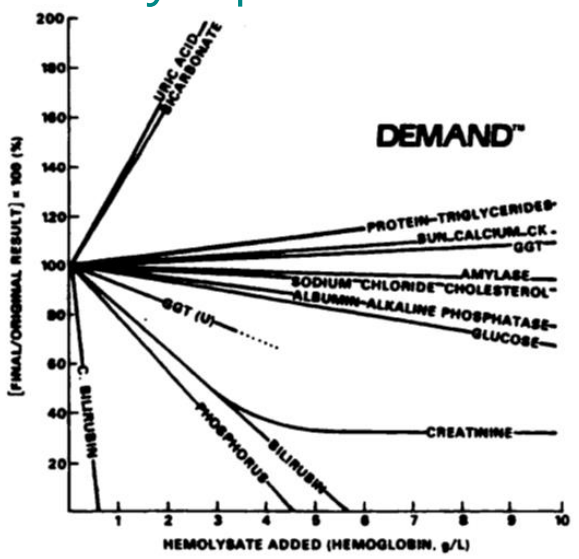

TP, Alb,Bili,Glu,Ca
Na,Cl,Chol,ALP

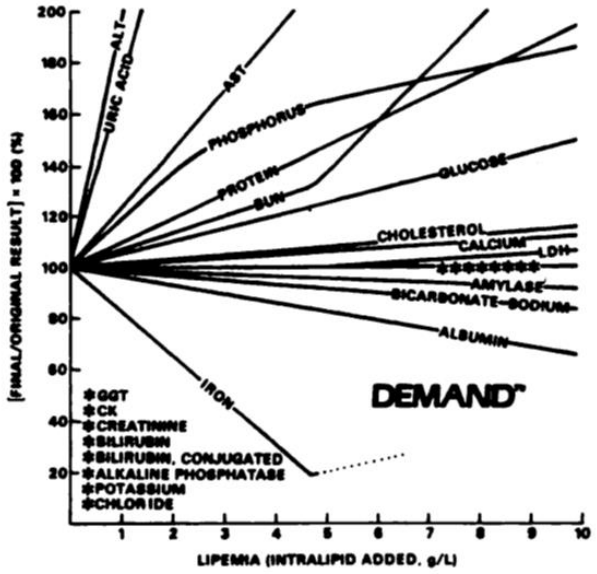
## Icterus

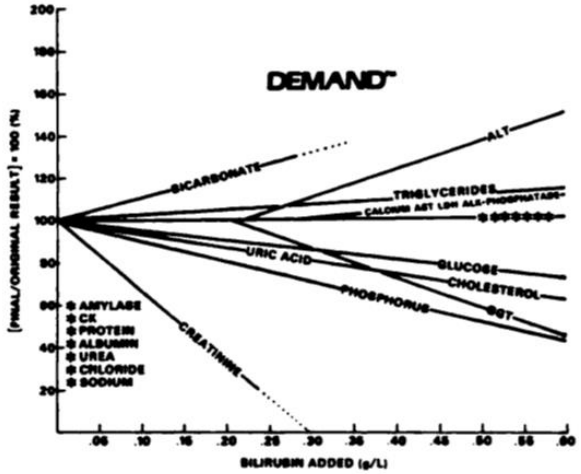



Trig
TP, Glu, Chol, UA, Creat

# Olympus AU 500

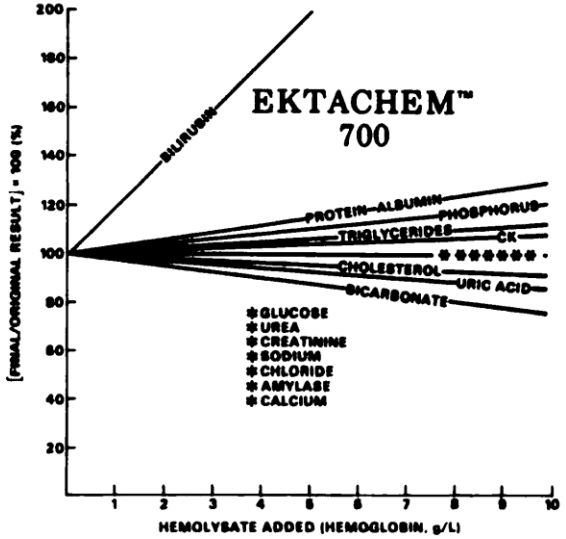


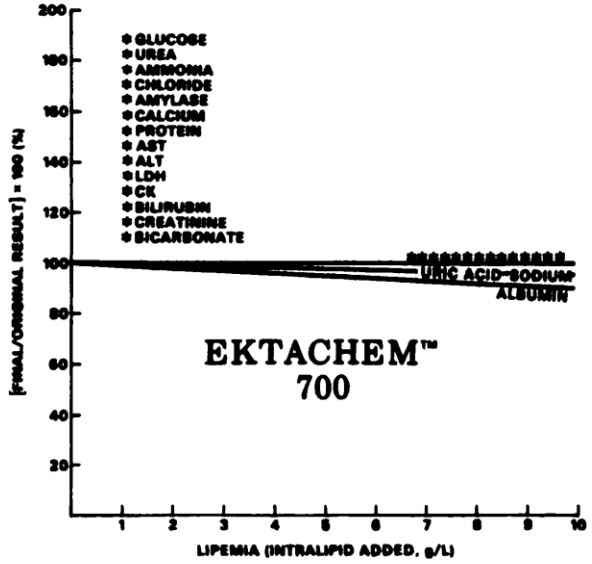



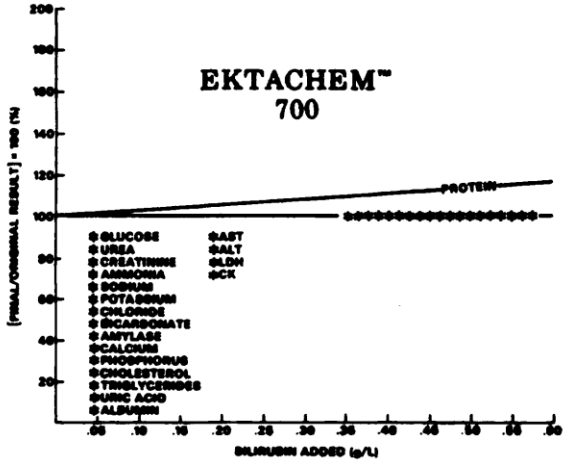




Large interference effects

# Vitros dry slide technology



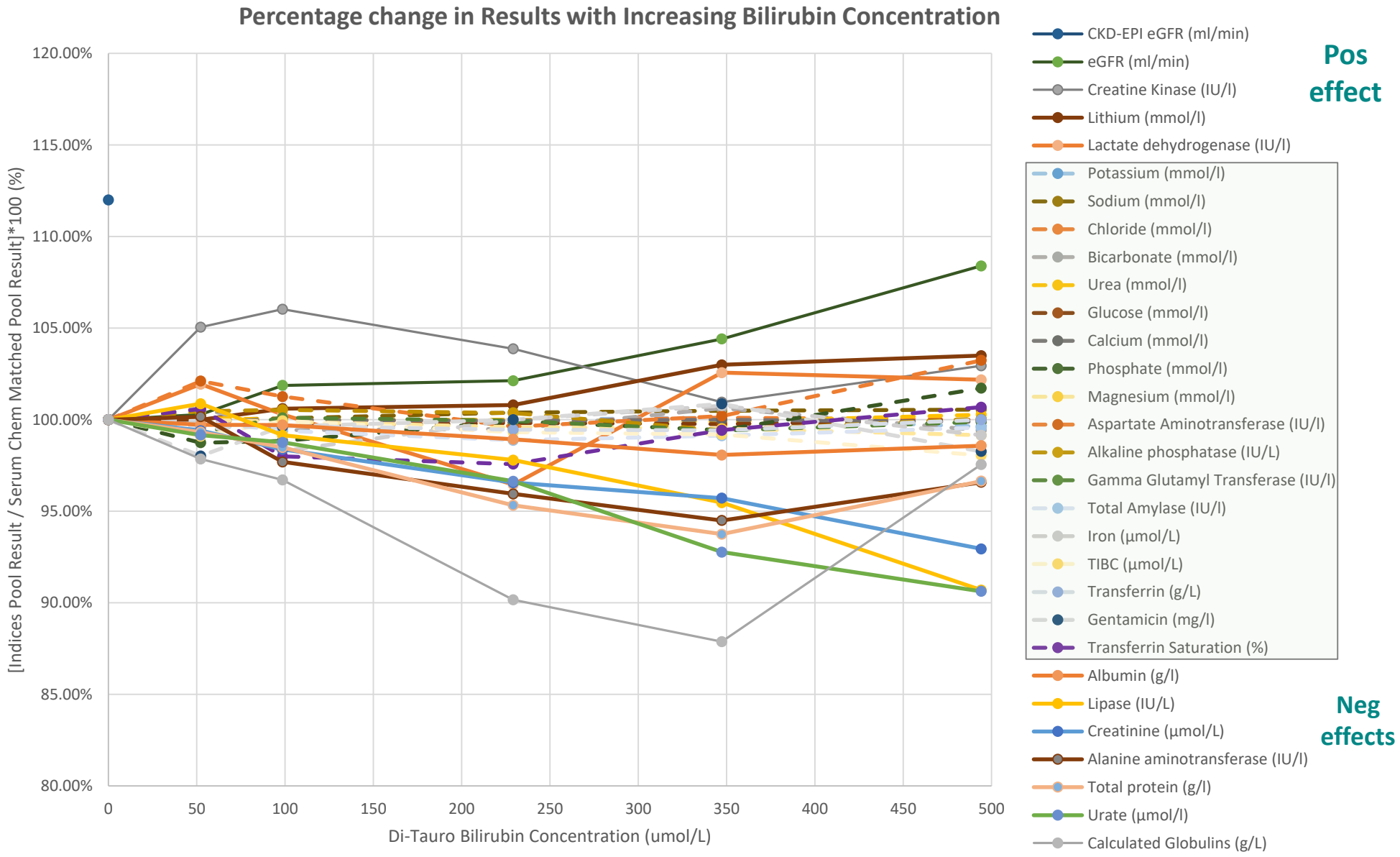




Minimal effects

# Where are we now, 36 years later?

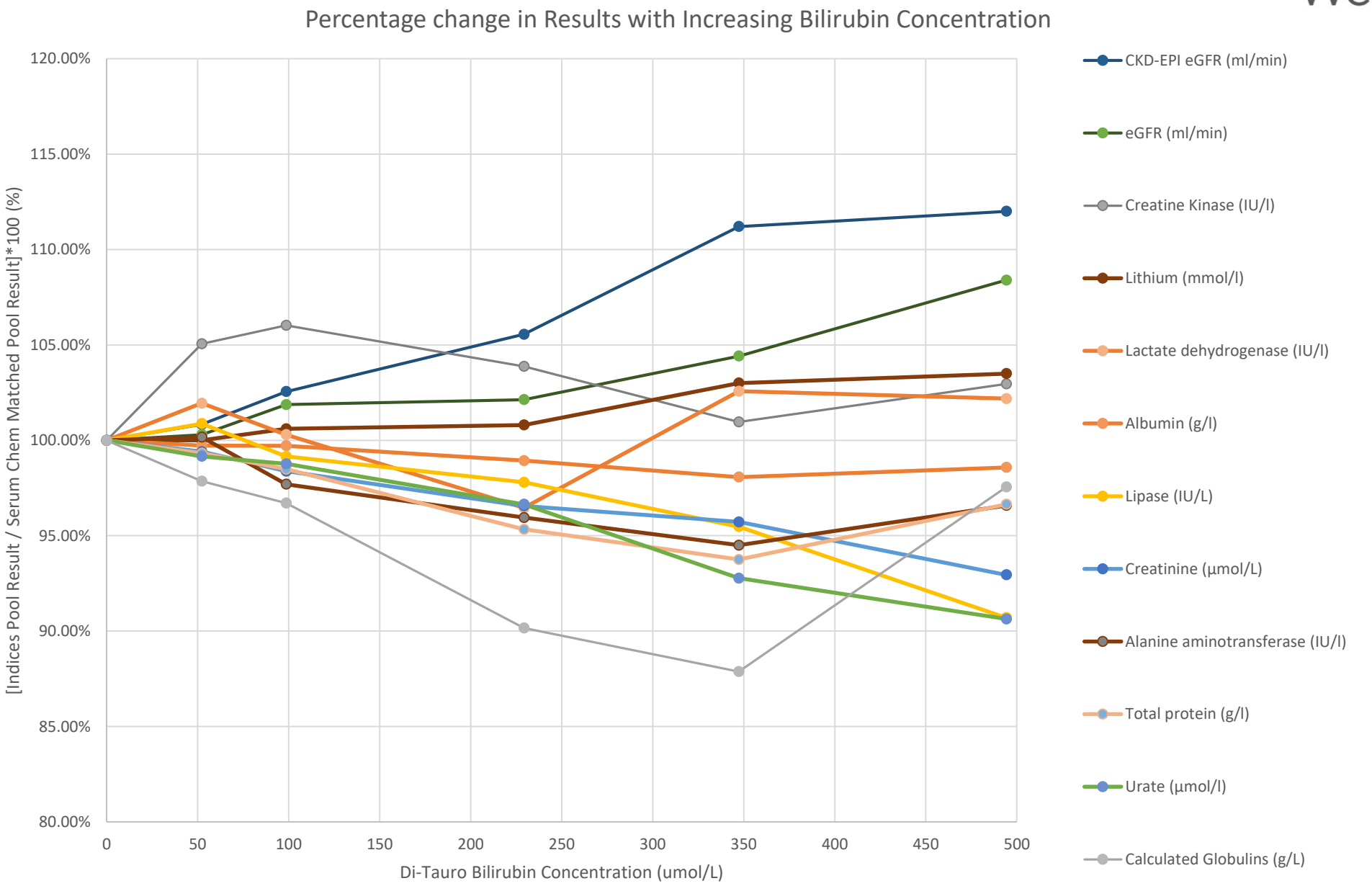
# Icterus Interferograph

Weqas Data from 2012 to 2019

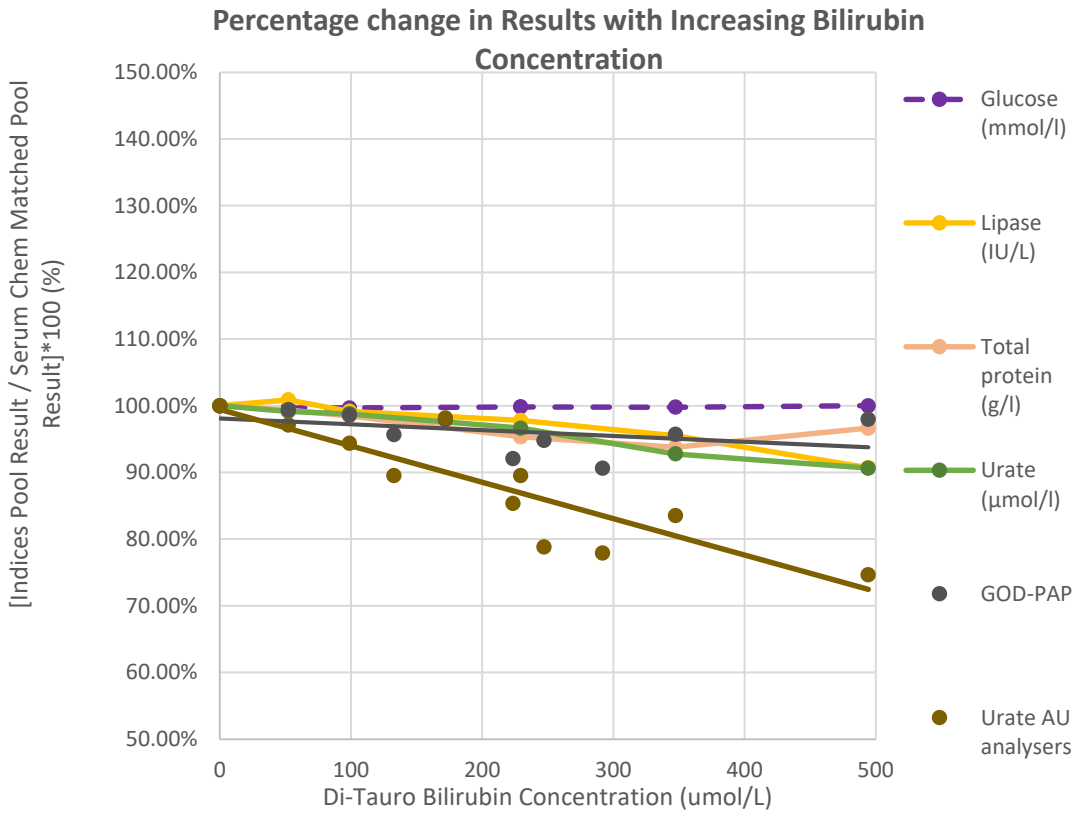


# Icterus Interferograph

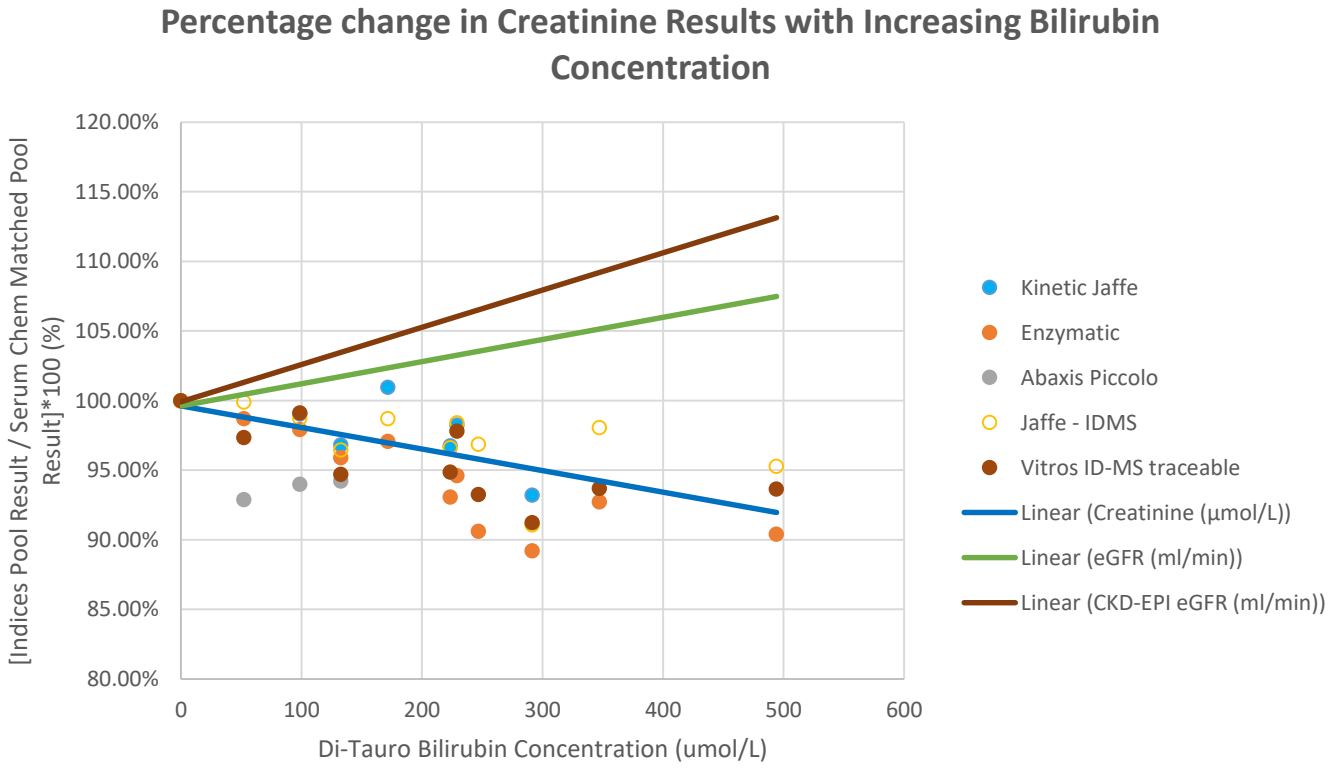
Weqas Data from 2012 to 2019



# Icterus Interferograph




Weqas Data from 2012 to 2019

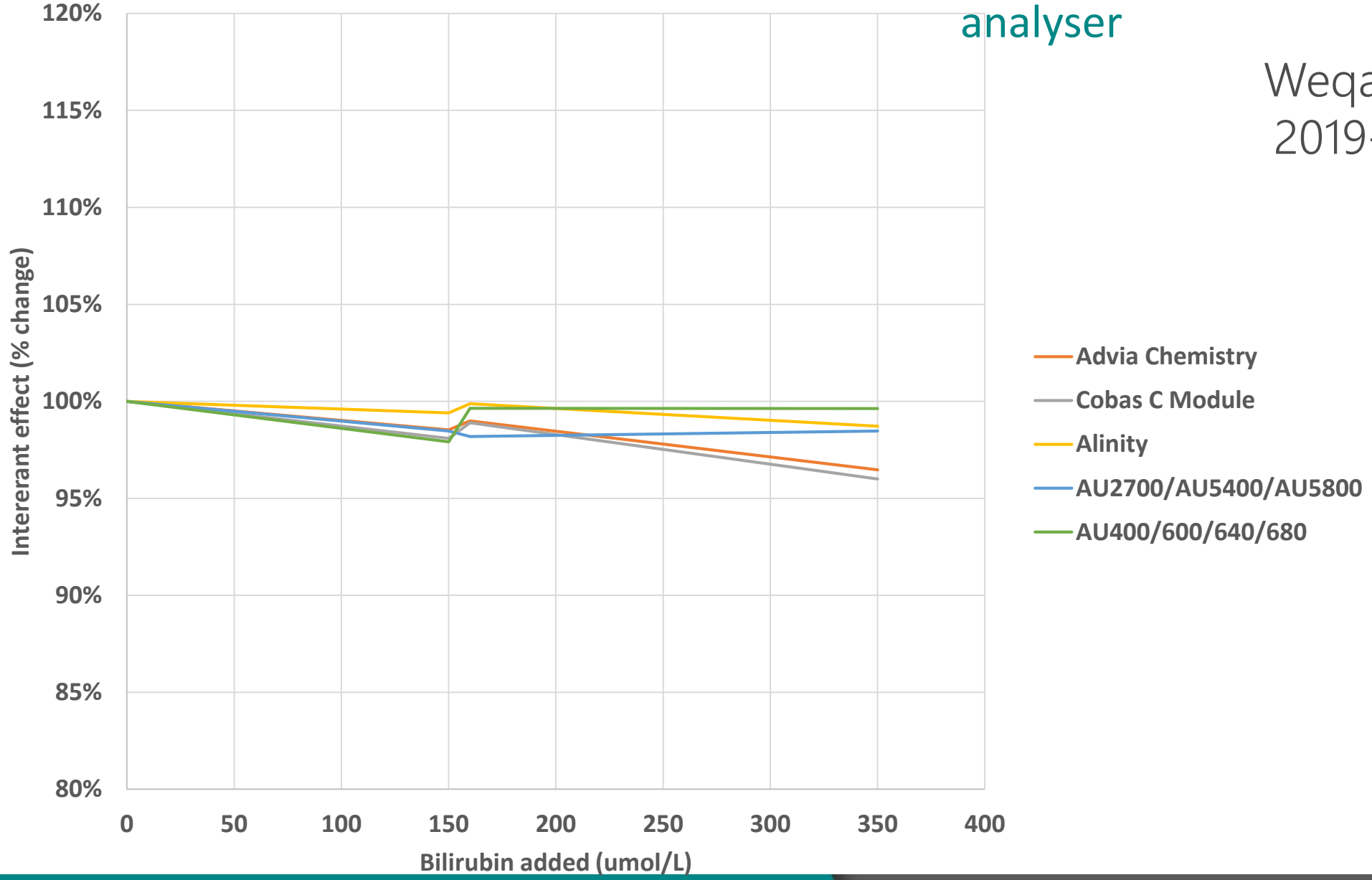


# Icterus Interferograph

## Interference effects for Urate by analyser

Weqas

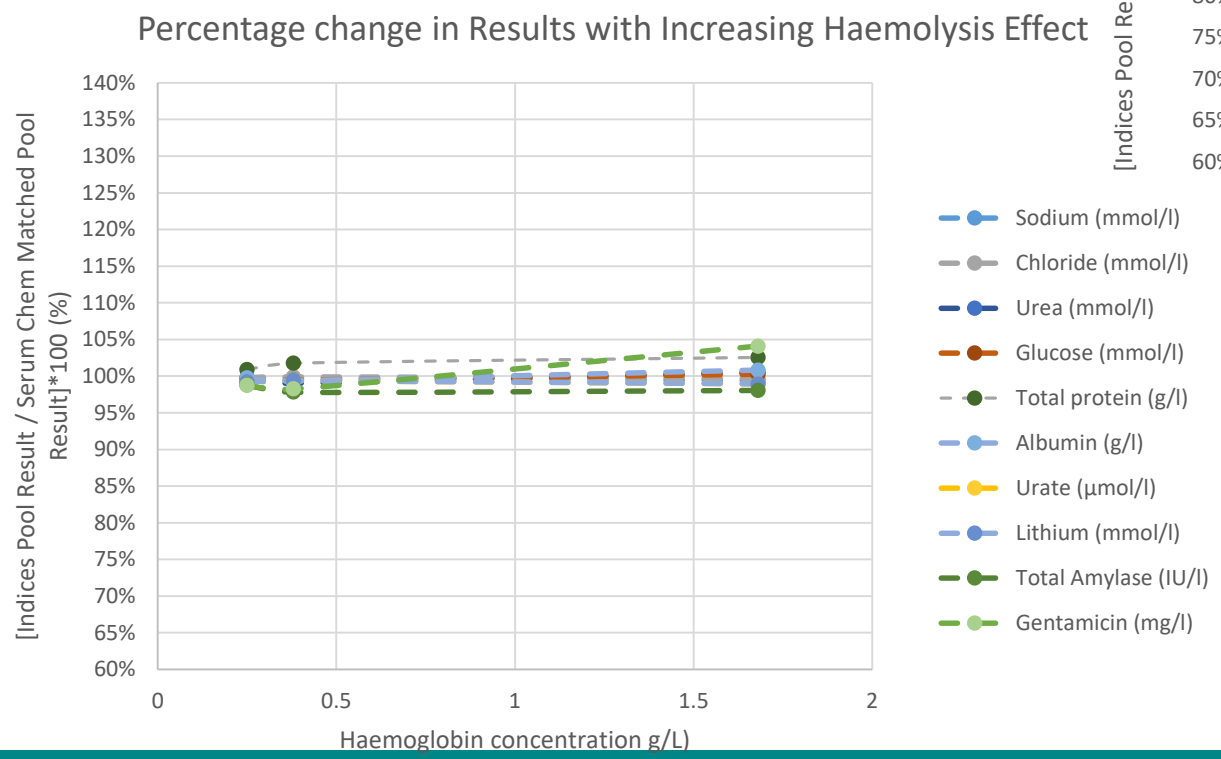
Weqas Data
2019- 2022

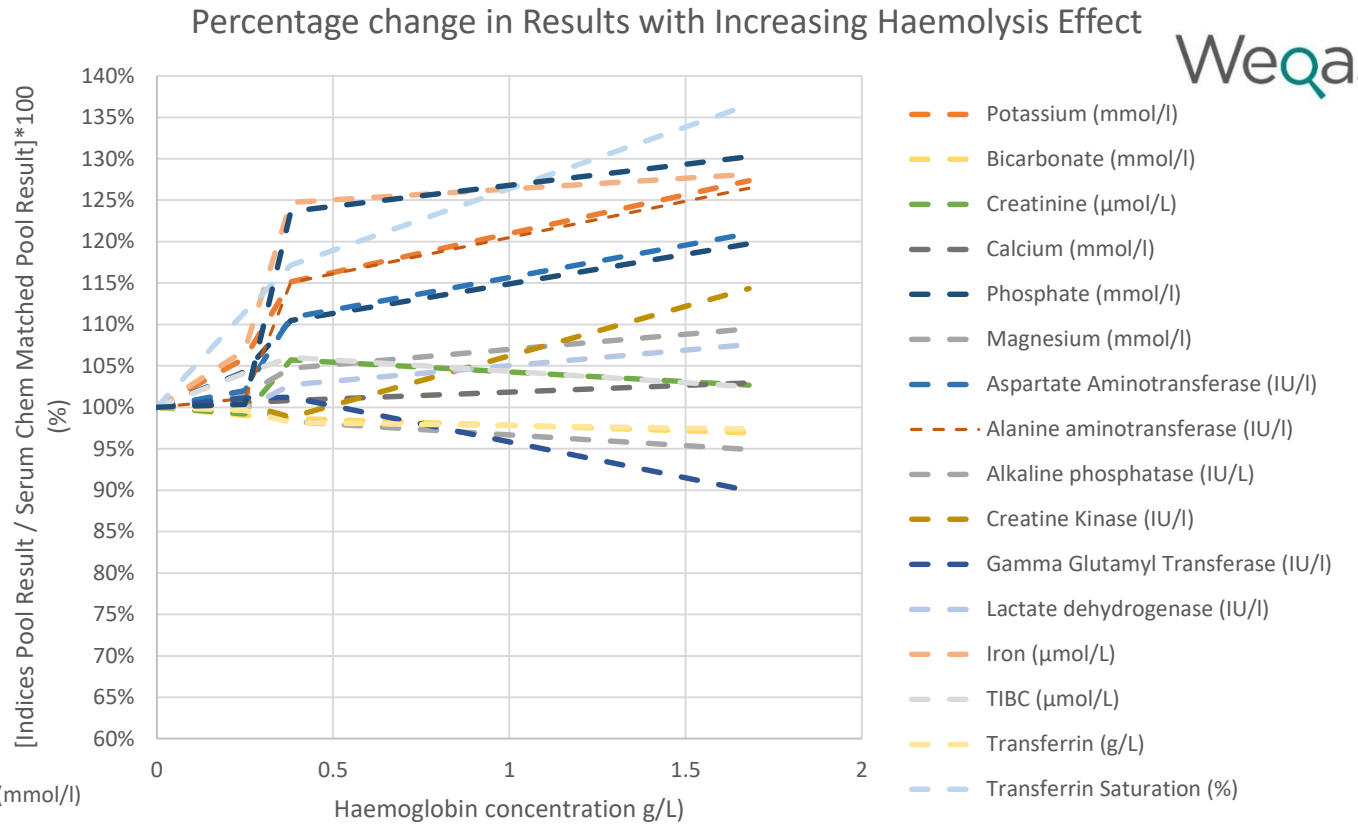


# Haemolysis Interferograph

Weqas Data from 2012 to 2018

## Analytes where little or no effect observed

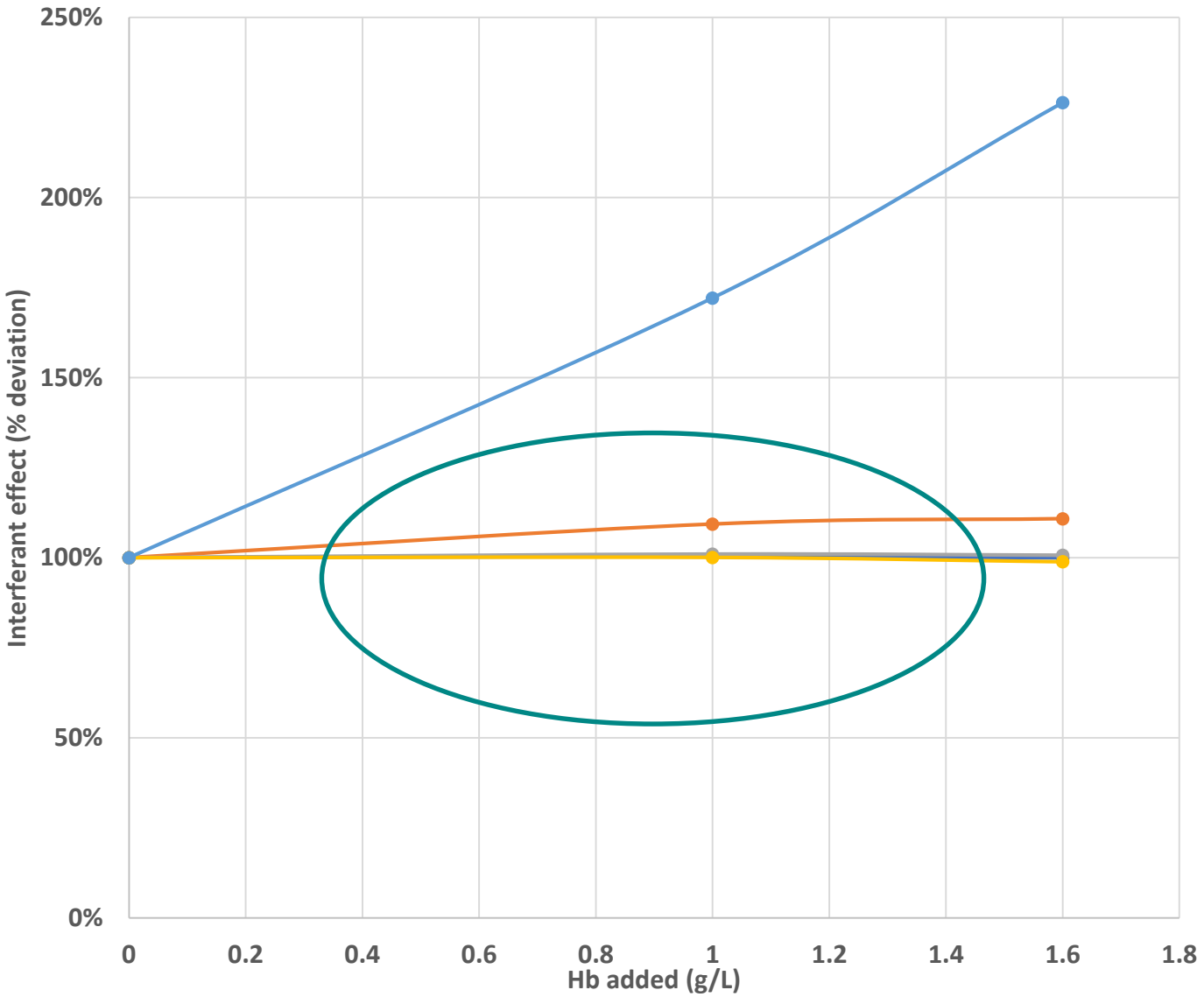


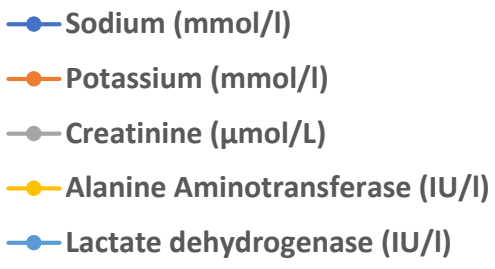




Greatest influence

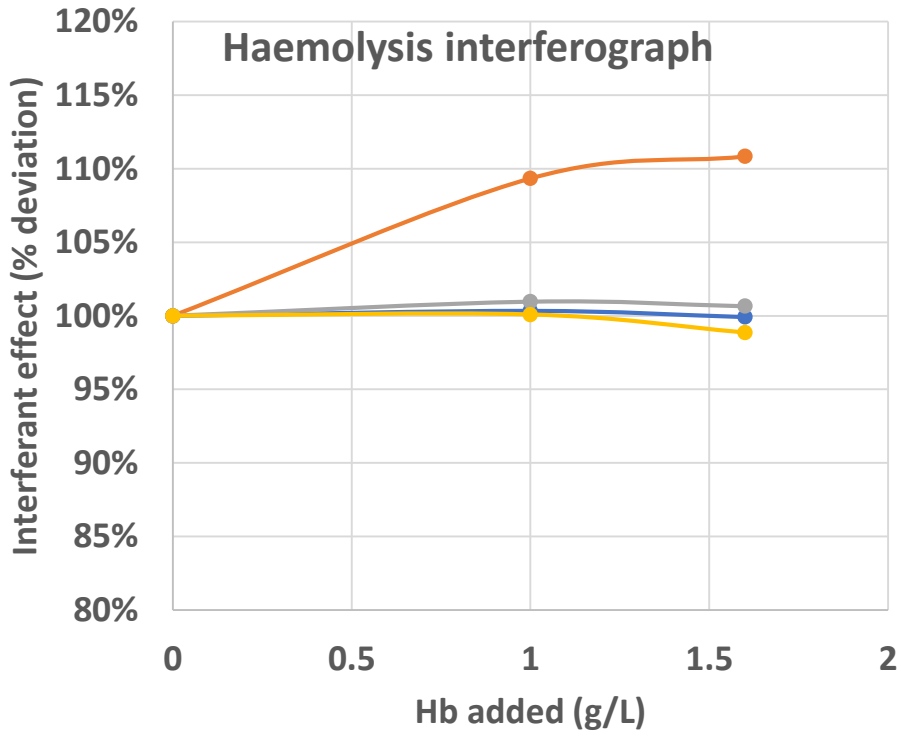
| | Analytes affected by Interferant | |
|---|---|---|
| Pos (RBC) | Positive | Negative |
| Iron | Lipase, ALT | GGT |
| K | CK | ALP |
| AST, P | Mg, LDH | Transferrin |
| | Creat, TiBC | |

# Haemolysis Interferograph




Weqas Data 2019- 2022



# Lipaemia Interferograph

Weqas Data from
2012 to 2019

## Analytes where little or no effect observed