DR TOM HARTLEY : HOBART LIPID SYMPOSIUM : SEPT 2005

ARE MY LIPIDS FALLING ?

"An Review of the Accuracies of Cholesterol and Triglyceride Measurements Made by Australian Pathology Labs".

Why is this an issue for all of you ?

- Because from the time of diagnosis, patients with lipid disorders are going to face years of blood testing and the associated concern that 'Are things moving in the right direction ?'.
- Researchers in this area have embarked on ambitious long term studies of lipids in various populations.

Consciously or unconsciously all players are relying upon their labs to provide accurate and precise results over very extended periods of time.

So how are the labs fairing in this task ?

There are 563 NATA Accredited Pathology Labs in Australia.

All these labs are obliged to participate in External Quality Assurance Programmes – these involve the regular circulation of panels of 'unknown' samples around all the participating labs followed up by extensive statistical reports to the participants.

The major provider of External Quality Assurance Programmes in Australia is the RCPA.

Participants get a wealth of statistical data from which I have been able to sketch the following 'accuracy performance profiles'.

Printed
Aug 31 10:06:02 2004

Prepared by:
RCPA-AACB Chemical Pathology QAP Group

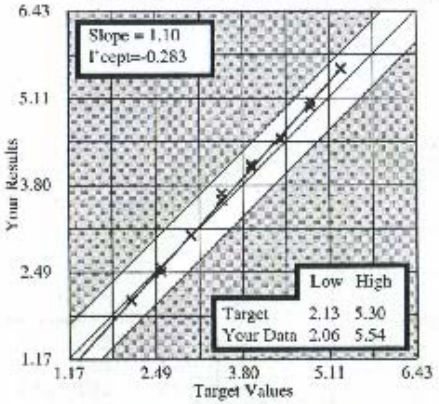
CHOLESTEROL (mmol/L)

Laboratory Number 142

DATA RECEIVED FOR CYCLE 66

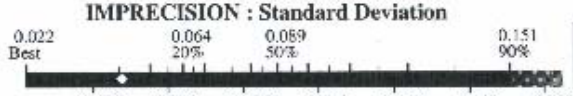
Spec.	Method	Target	Result
66-01	C 25G 052 C	3.03	3.03
66-02		4.39	4.48
66-03	C 25G 052 C	2.58	2.48
66-04		4.84	4.97
66-05	C 25G 052 C	3.49	3.57
66-06		3.94	4.06
66-07	C 25G 052 C	2.13	2.06
66-08		5.30	5.55
66-09	C 25G 052 C	4.84	5.04
66-10		3.94	4.10
66-11	C 25G 052 C	2.13	2.05
66-12		4.39	4.51
66-13	C 25G 052 C	3.49	3.67
66-14		2.58	2.54
66-15	C 25G 052 C	5.30	5.54
66-16		3.03	3.04

No results outside the allowable limits of performance.



Allowable Limits of Performance
±0.50 up to 10.00; ±5% > 10.00 mmol/L

IMPRECISION : Standard Deviation

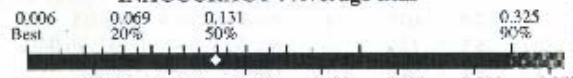


Your SD ◆ 0.048 Last Cycle 45%

IMPRECISION : Coefficient of Variation

Your CV ◆ 1.3 Last Cycle 42%

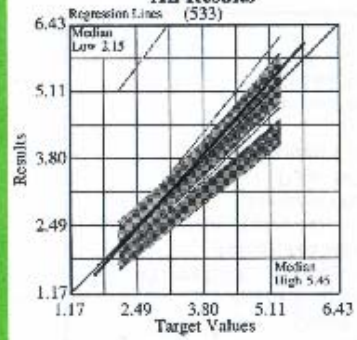
INACCURACY : Average Bias

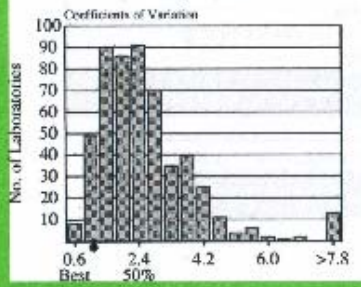


Your Bias ◆ 0.131 Last Cycle 54%

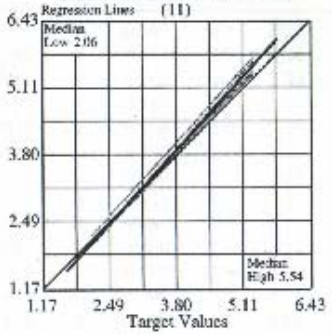
REVIEW OF YOUR METHOD CLASSIFICATION

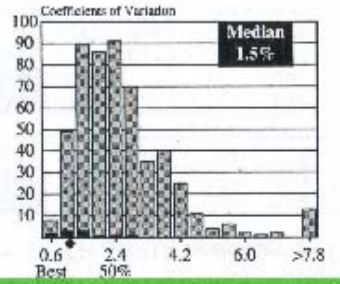
All Results



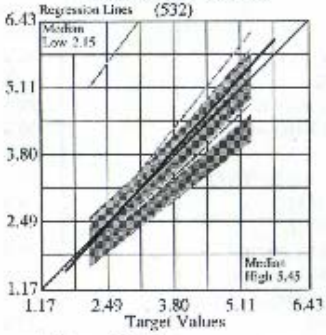


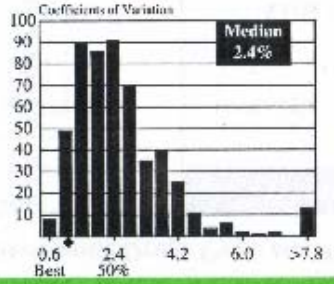
Your Method C 25G 052



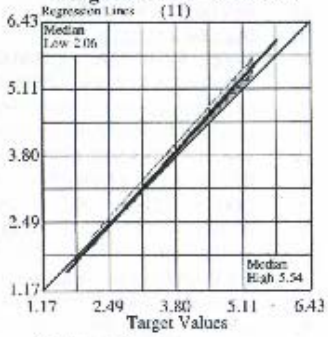


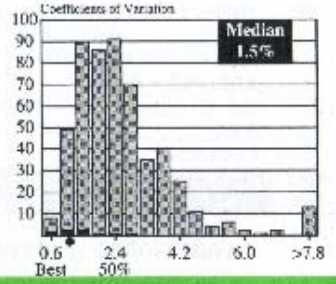
Cholesterol Oxidase/ Peroxidase



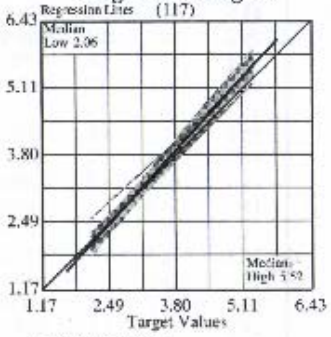


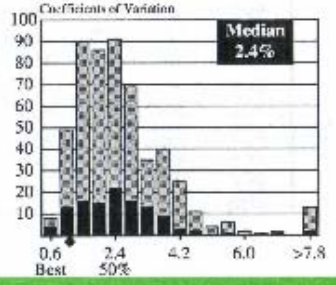
Ortho Clinical Diagnostics VITROS 950





Ortho-Clinical Diagnostics Reagent





General Chemistry & Therapeutic Drugs Cycle 66 : 3 May - 9 August 2004

ANALYTICAL PRINCIPLE	No. Labs	S.D.	CV	Low 2.13	High 5.30
Cholesterol Oxidase/ Peroxidase	532	0.089	2.4	2.15	5.45

REAGENT	No. Labs	S.D.	CV	Low 2.13	High 5.30
Abbott	6	0.052	1.3	2.21	5.38
Roche Diagnostics (BM)	187	0.085	2.2	2.20	5.52
Randox	1	0.084	2.3	2.11	5.22
Bayer Diagnostics	5	0.084	2.3	2.09	5.21
Roche Diagnostics	93	0.088	2.4	2.17	5.40
Ortho-Clinical Diagnostics	117	0.092	2.4	2.06	5.52
Integrated Sciences	21	0.090	2.4	2.19	5.44
Thermoelectron (Trace Scientific)	4	0.095	2.5	2.17	5.43
Olympus Optical	7	0.105	2.7	2.23	5.47
Dade Behring	47	0.080	2.7	1.81	4.35
Beckman Coulter	35	0.102	2.9	2.03	5.10
DiaSys	5	0.115	3.0	2.21	5.56
Pointe Scientific	1	0.149	3.6	2.43	5.74
Kyowa Medex	1	0.167	4.3	2.20	5.51
Biomerieux	1	0.213	5.2	2.35	5.78
Human	1	0.192	5.4	2.05	5.07

CALIBRATOR	No. Labs	S.D.	CV	Low 2.13	High 5.30
Own Preparation	1	0.084	2.2	2.19	5.45
Commercial/liquid stable serum	49	0.086	2.4	2.06	5.14
Commercial/lyophilised serum	474	0.089	2.4	2.15	5.47
Commercial/aqueous	4	0.114	3.2	2.07	5.39
Commercial/frozen serum	1	0.140	3.5	2.39	5.64

INSTRUMENT	No. Labs	S.D.	CV	Low 2.13	High 5.30
Kone Ultra	1	0.022	0.6	2.18	5.41
Abbott ARCHITECT c8000	2	0.052	1.3	2.24	5.34
Ortho Clinical Diagnostics VITROS 950	11	0.057	1.5	2.06	5.54
Abbott AEROSET	4	0.065	1.7	2.16	5.38
Bayer Diagnostics ADVIA 1650	3	0.069	1.9	2.07	5.20
Roche Diagnostics Hitachi 912	21	0.082	2.0	2.22	5.54
Roche Diagnostics Hitachi Modular	60	0.080	2.1	2.20	5.54
Roche Diagnostics Hitachi 917	56	0.082	2.2	2.19	5.47
Roche Diagnostics Cobas Integra 400/400+	38	0.084	2.2	2.16	5.39
Bayer Diagnostics RA1000/2000/500/XT	1	0.084	2.3	2.11	5.22
Dade Behring Dimension 380/SMS/ES	1	0.068	2.3	1.71	4.22
Dade Behring Dimension Xpand	8	0.072	2.3	1.83	4.32
Olympus AU2700/AU5421/AU5432	9	0.092	2.5	2.16	5.44
Ortho Clinical Diagnostics VITROS 250	105	0.093	2.5	2.06	5.52
Roche Diagnostics Hitachi 911	17	0.096	2.5	2.20	5.62
Roche Diagnostics Cobas Integra 700/800	55	0.094	2.5	2.17	5.40
Roche Diagnostics Hitachi 902 / 904	22	0.101	2.6	2.21	5.56
Beckman Coulter LX20/LX40	16	0.090	2.6	2.01	5.09
Dimension XL/RXL/RXL MAX	24	0.083	2.7	1.83	4.40
VITROS 700/750	1	0.107	2.8	2.07	5.56
Olympus AU600/640	16	0.109	2.8	2.22	5.51
Dade Behring Dimension AR	14	0.086	2.8	1.75	4.24
Olympus AU400	10	0.115	3.0	2.22	5.44
Beckman Coulter Synchron CX5	12	0.109	3.1	2.05	5.08
Roche Diagnostics Hitachi 747	9	0.120	3.1	2.16	5.47
Bayer Diagnostics Opera	1	0.131	3.4	2.23	5.45
Bayer Diagnostics Express Plus 560	1	0.129	3.5	2.22	5.27
Olympus AU800	1	0.136	3.6	2.15	5.30
Beckman Coulter Synchron CX7/CX9	7	0.127	3.6	2.03	5.12
Mira/Mira S/Mira Plus	1	0.160	4.2	2.11	5.51
Biomerieux Multiparametric ALIZE	1	0.213	5.2	2.35	5.78
Roche Diagnostics Hitachi 717	2	0.286	6.8	2.20	5.81

General Chemistry & Therapeutic Drugs Cycle 66 : 3 May - 9 August 2004

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Cholesterol : There is one analytical technique, 14 reagent systems and 5 types of calibrators.

HDL : There are seven analytical techniques, 18 reagent systems and 3 types of calibrator

Triglycerides : There are seven analytical techniques, 16 reagent systems and 4 types of calibrators

General Chemistry & Therapeutic Drugs Cycle 66 : 3 May - 9 August 2004

Cholesterol : There are 32 different analytical instruments

HDL : There are 27 different analytical instruments

Triglycerides : There are 28 different analytical instruments

INSTRUMENT	No. Labs	S.D.	CV	Low 2.13	High 5.30
Kone Ultra	1	0.022	0.6	2.18	5.41
Abbott ARCHITECT c8000	2	0.052	1.3	2.24	5.34
Ortho Clinical Diagnostics VITROS 950	11	0.057	1.5	2.06	5.54
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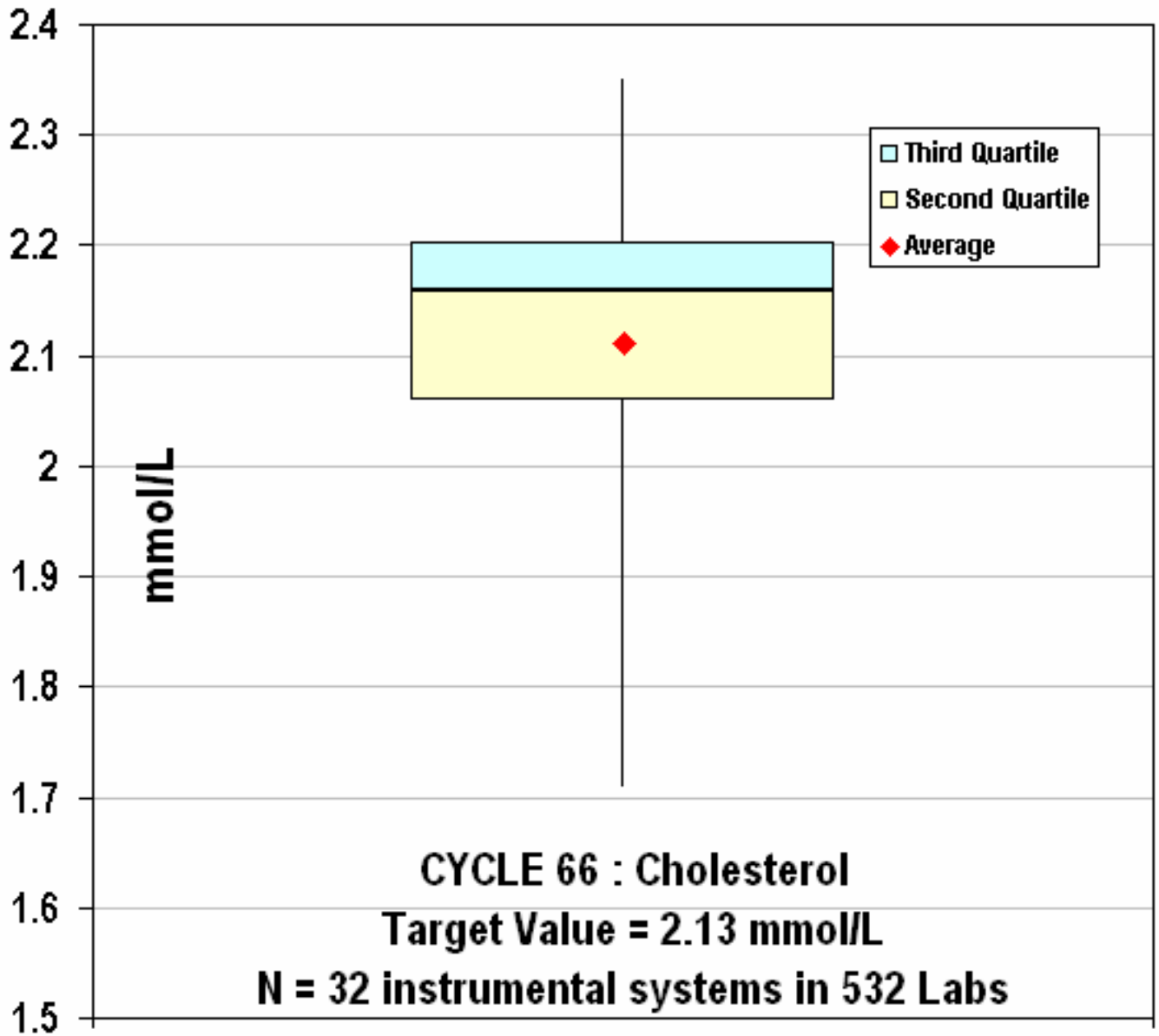
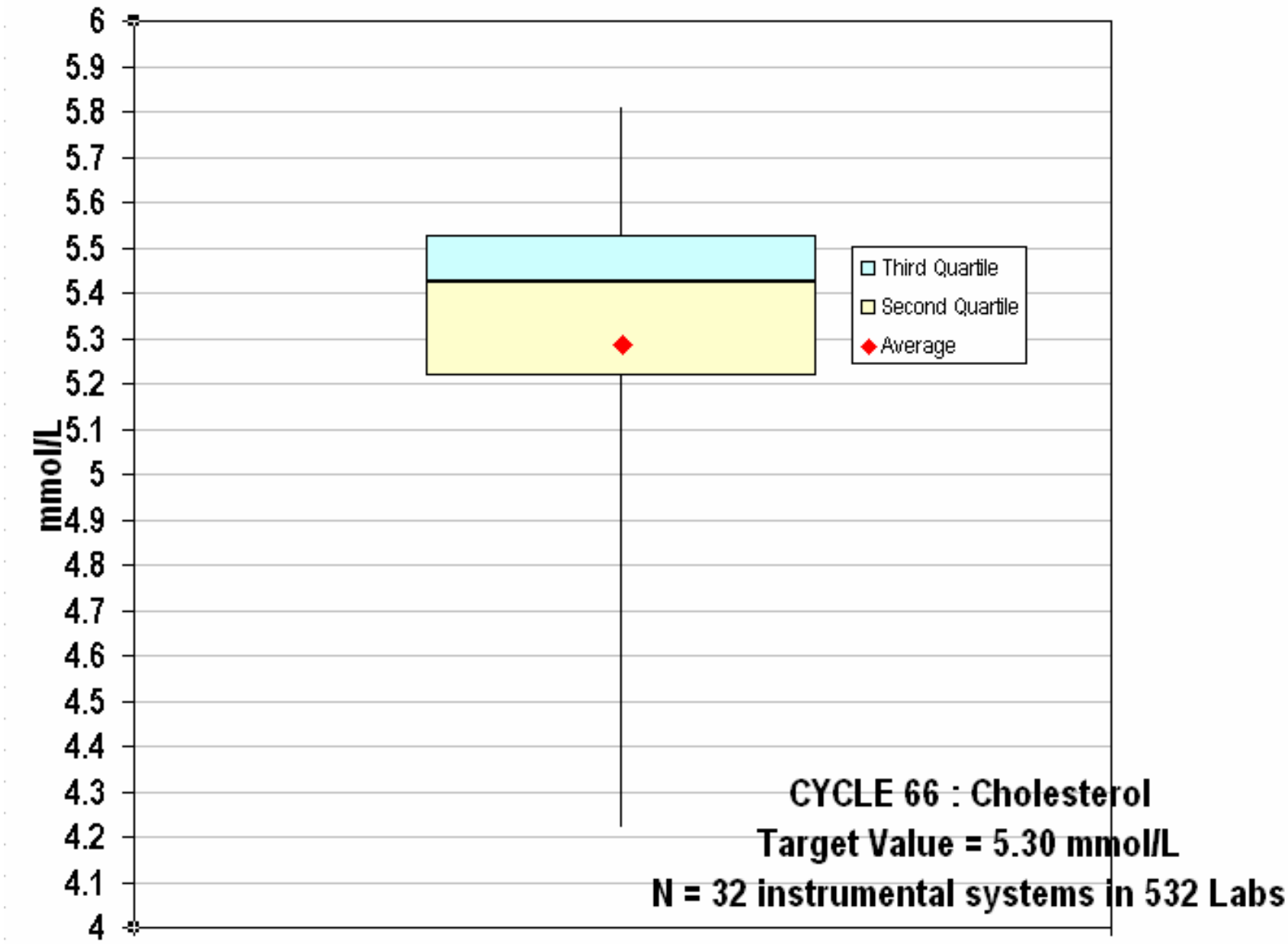
My Geoffrey Robertson Hypothetical……. If my doctor sends my blood samples to every Aust Lab in the EQAP then

What would the spread of results look like ?

How will he/she decide upon the answer my usual question …. "Are my lipids falling ?"

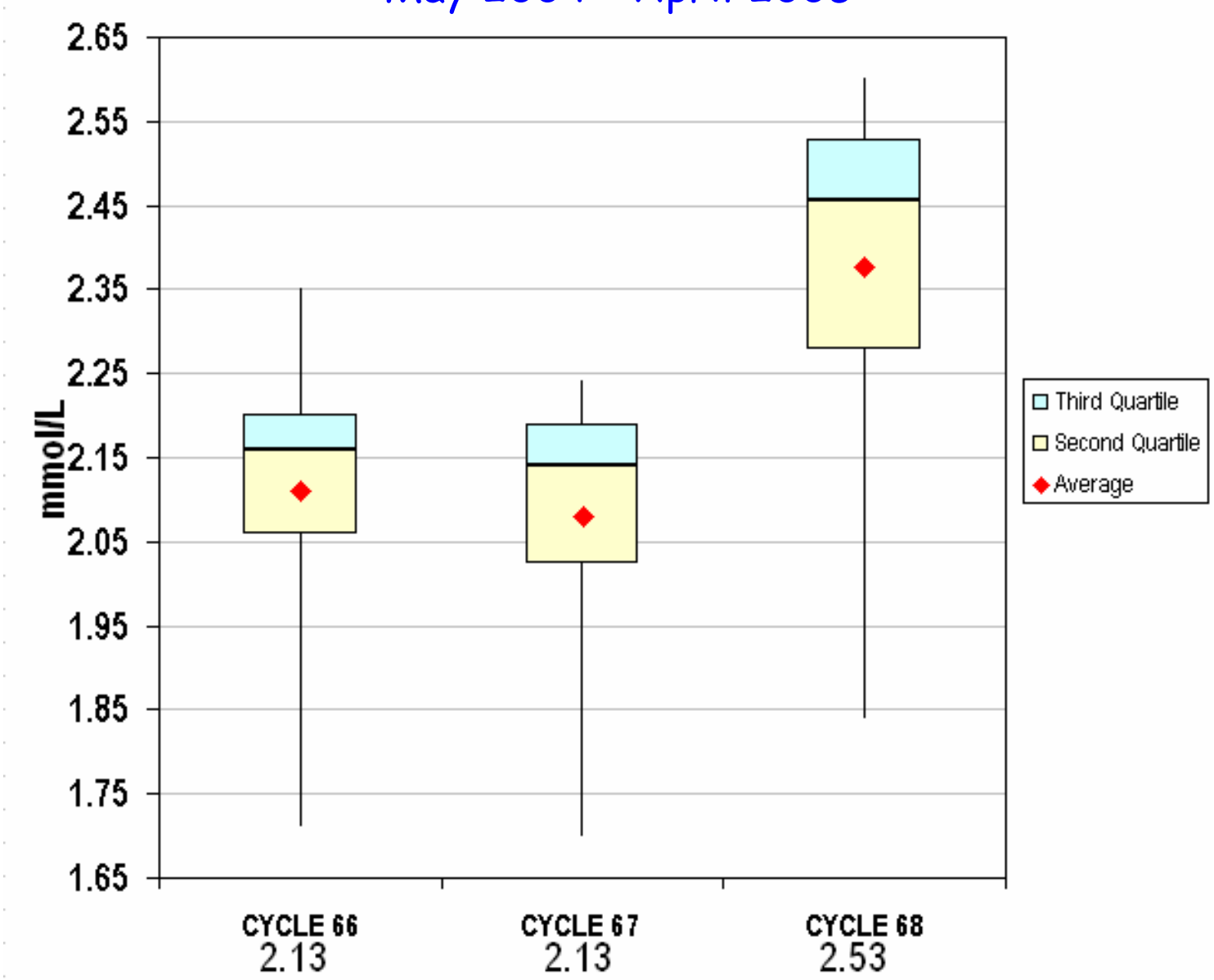
CHOLESTEROL							
CYCLE 66 : May - August 2004							
TARGET	INSTRUMENT		DIFFs	TARGET	INSTRUMENT		DIFFs
2.13	1.71		-0.42	5.3	4.22		-1.08
2.13	1.75		-0.38	5.3	4.24		-1.06
2.13	1.83		-0.3	5.3	4.32		-0.98
2.13	1.83		-0.3	5.3	4.4		-0.9
2.13	2.01		-0.12	5.3	5.08		-0.22
2.13	2.03		-0.1	5.3	5.09		-0.21
2.13	2.05		-0.08	5.3	5.12		-0.18
2.13	2.06		-0.07	5.3	5.2		-0.1
2.13	2.06		-0.07	5.3	5.22		-0.08
2.13	2.07		-0.06	5.3	5.27		-0.03
2.13	2.07		-0.06	5.3	5.3		0
2.13	2.11		-0.02	5.3	5.34		0.04
2.13	2.11		-0.02	5.3	5.38		0.08
2.13	2.15		0.02	5.3	5.39		0.09
2.13	2.16		0.03	5.3	5.4		0.1
2.13	2.16		0.03	5.3	5.41		0.11
2.13	2.16		0.03	5.3	5.44		0.14
2.13	2.16		0.03	5.3	5.44		0.14
2.13	2.17		0.04	5.3	5.45		0.15
2.13	2.18		0.05	5.3	5.47		0.17
2.13	2.19		0.06	5.3	5.47		0.17
2.13	2.2		0.07	5.3	5.51		0.21
2.13	2.2		0.07	5.3	5.51		0.21
2.13	2.2		0.07	5.3	5.52		0.22
2.13	2.21		0.08	5.3	5.54		0.24
2.13	2.22		0.09	5.3	5.54		0.24
2.13	2.22		0.09	5.3	5.54		0.24
2.13	2.22		0.09	5.3	5.56		0.26
2.13	2.22		0.09	5.3	5.56		0.26
2.13	2.23		0.1	5.3	5.62		0.32
2.13	2.24		0.11	5.3	5.78		0.48
2.13	2.35		0.22	5.3	5.81		0.51


2.4
2.3
2.2
2.1
2
1.9
1.8
1.7
1.6
1.5
mmol/L
Third Quartile
Second Quartile
Average
CYCLE 66 : Cholesterol
Target Value = 2.13 mmol/L
N = 32 instrumental systems in 532 Labs


6
5.9
5.8
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4
mmol/L
Third Quartile
Second Quartile
Average
CYCLE 66 : Cholesterol
Target Value = 5.30 mmol/L
N = 32 instrumental systems in 532 Labs

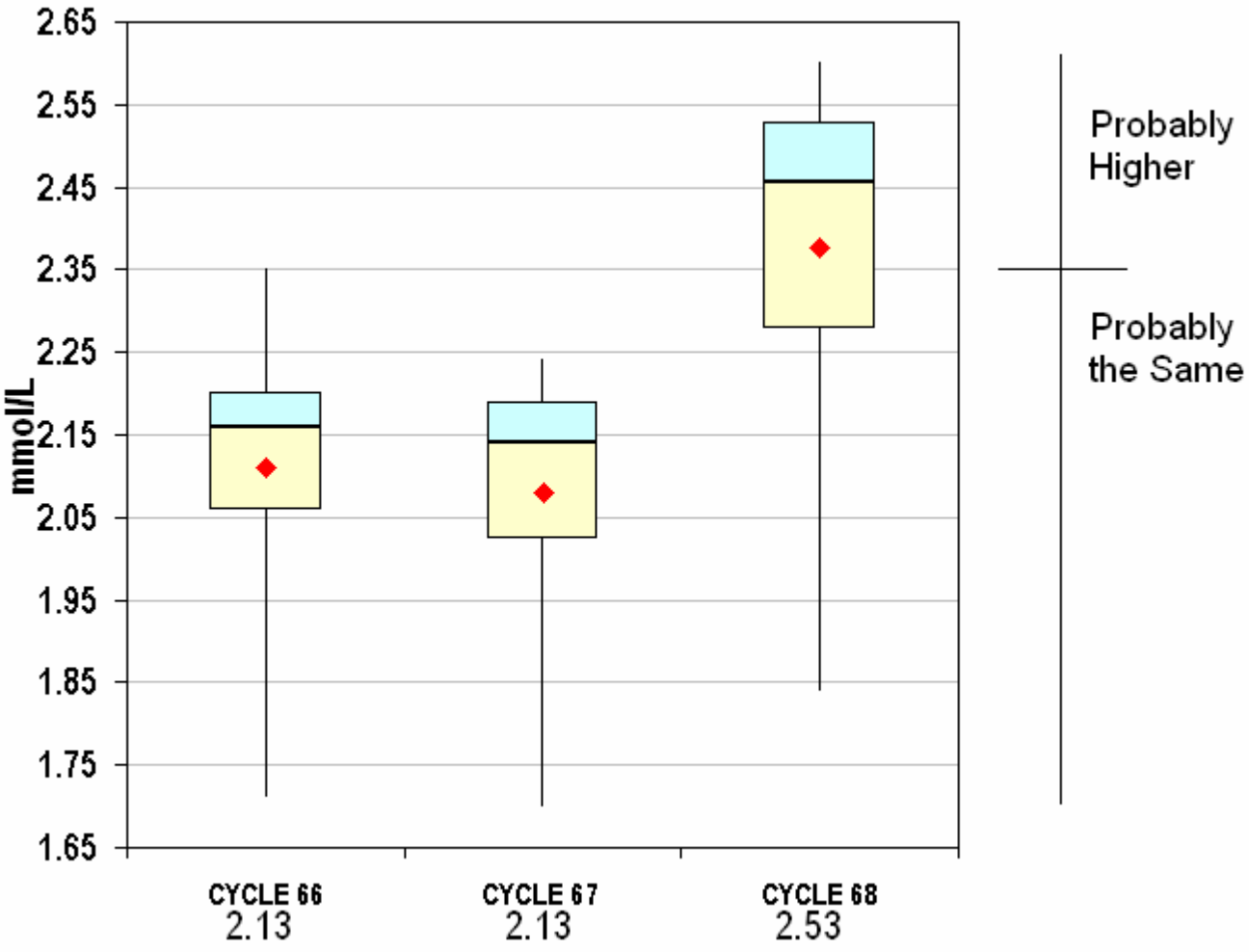
MY 'LOW' CHOLESTEROL MEASURED ON ALL INSTRUMENTS

May 2004 – April 2005



MY 'LOW' CHOLESTEROLS ALL AUSTRALIAN LABS

May 2004 – April 2005



The empirical scenario is that only those labs that used instruments that reported my cholesterol as being above 2.35 mmol/L in the third sample (Cycle 68 – target = 2.53) could state that

"No, your previously 'low' cholesterol has not fallen – it has risen !"

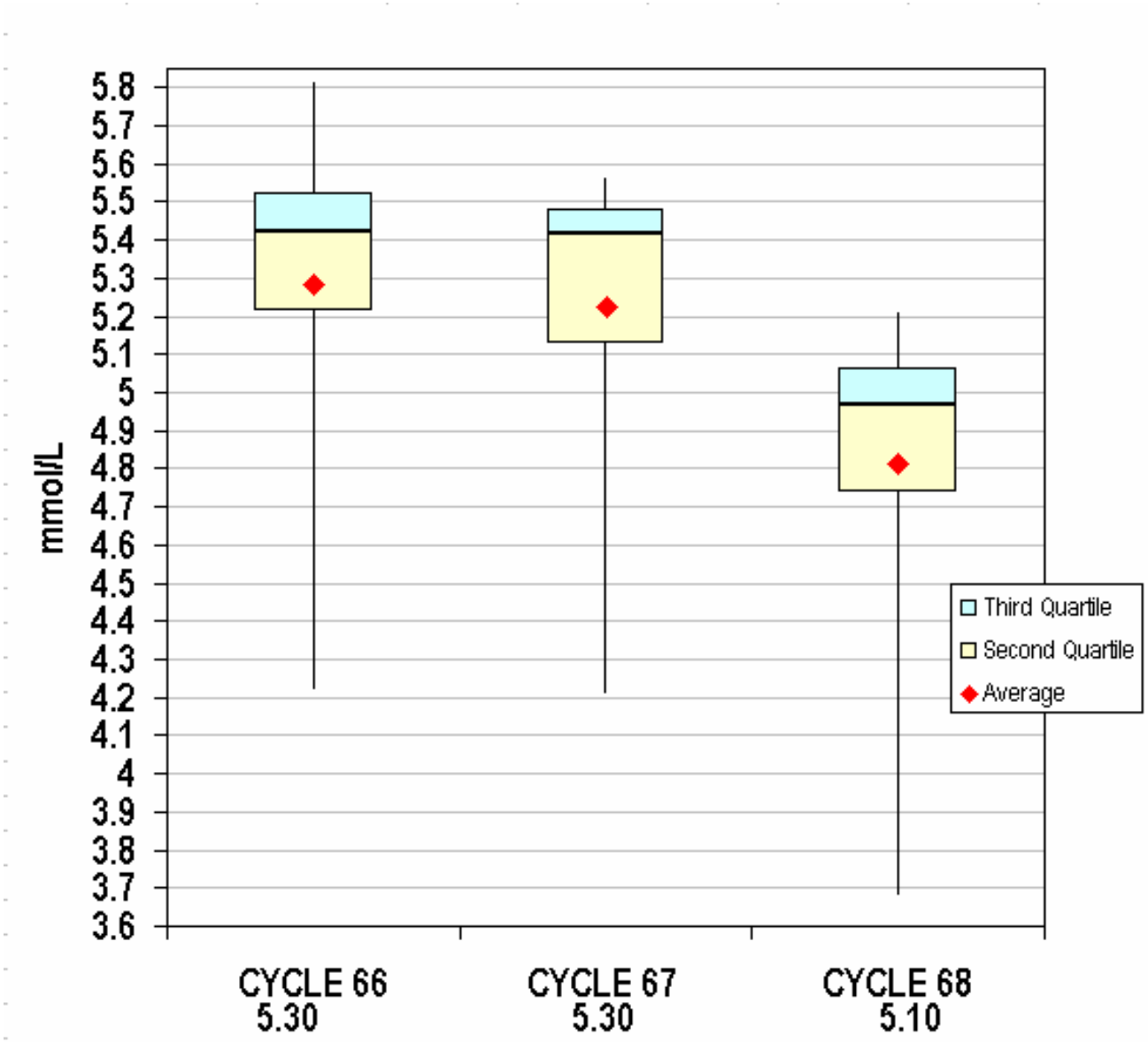
How many labs could say this ?

340 out of a total of 533 ……

equivalent to 64%

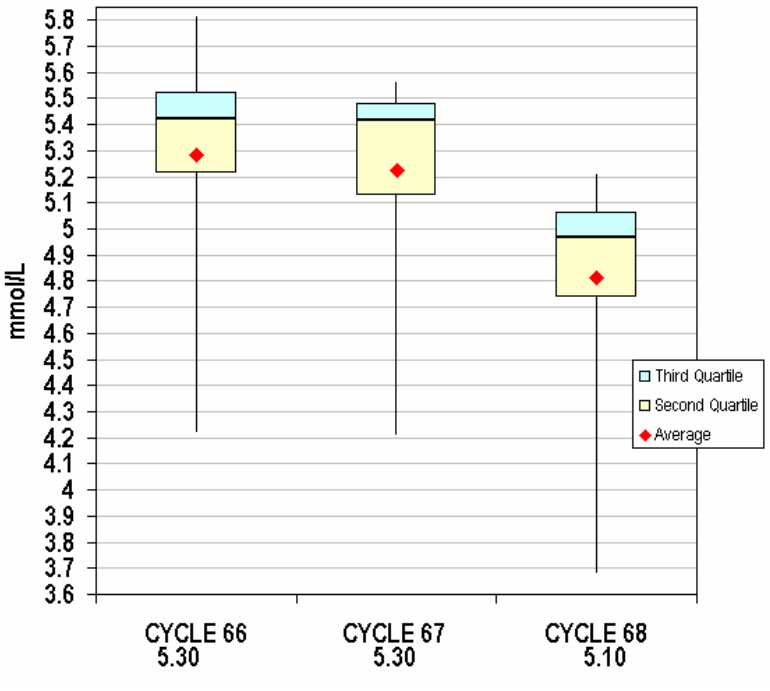
MY 'HIGH' CHOLESTEROLS MEASURED ON ALL INSTRUMENTS

May 2004 – April 2005



MY 'HIGH' CHOLESTEROLS ALL AUSTRALIAN LABS

May 2004 – April 2005



The high degree of overlap limits the comment to …

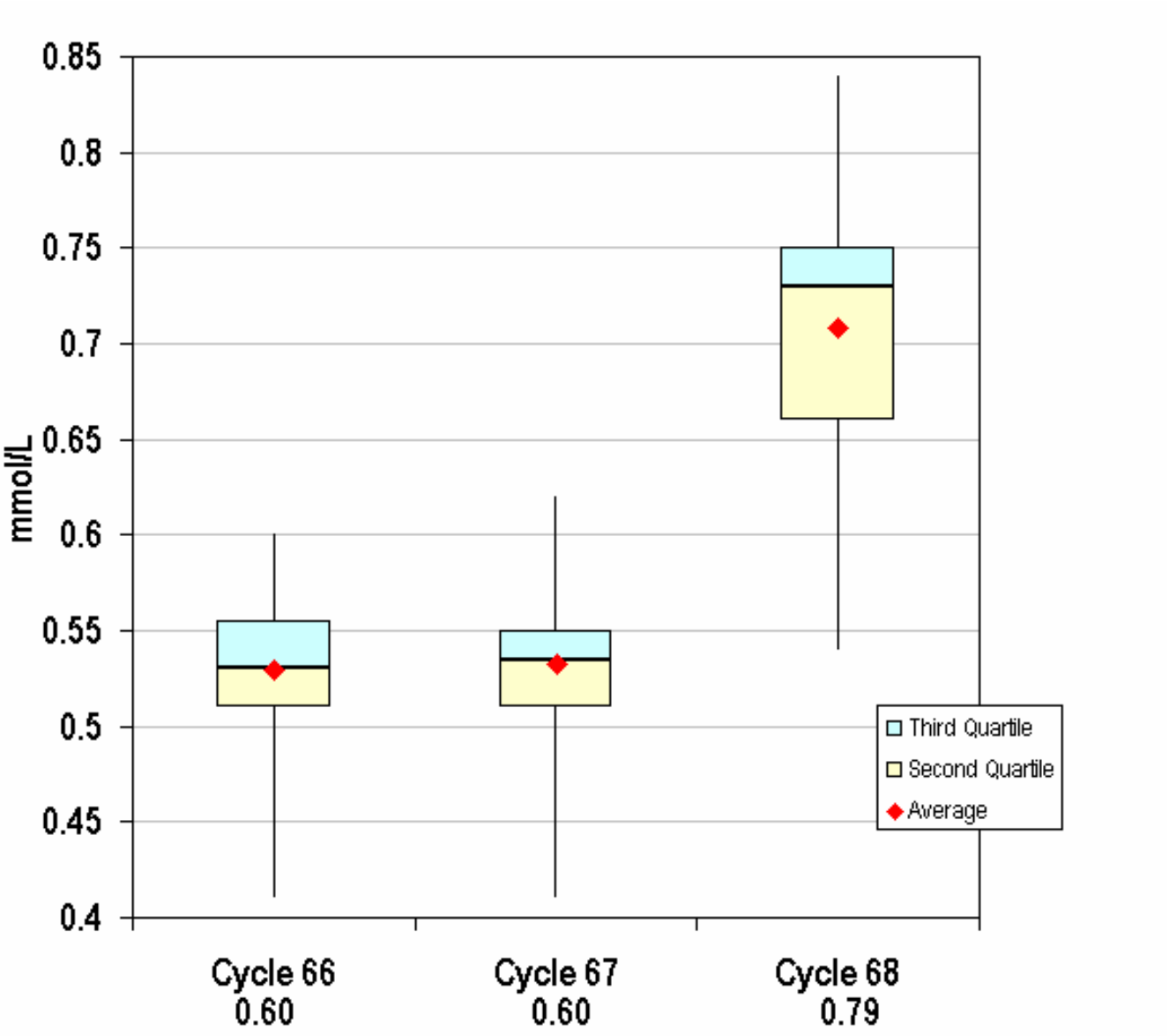
Labs using instruments in the second and third quartiles of Cycle 68 could confidently state that my lipids had fallen.

How many labs are in the second and third quartiles ?

338 out of a total of 533 labs ……
63%

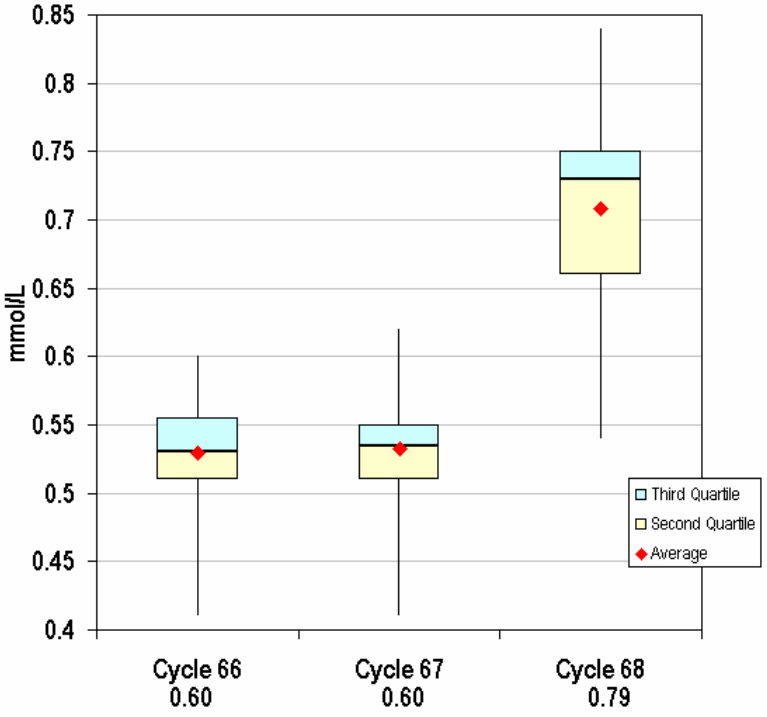
MY 'LOW' TRIGLYCERIDES MEASURED ON ALL INSTRUMENTS

May 2004 – April 2005



MY 'LOW' TRIGLYCERIDES ALL AUSTRALIAN LABS

May 2004 – April 2005



Empirically all those labs reporting a value of 0.65 mmol/L and above on the Cycle 68 sample could confidently say that my triglyceride levels had risen.

How many labs could say this ?

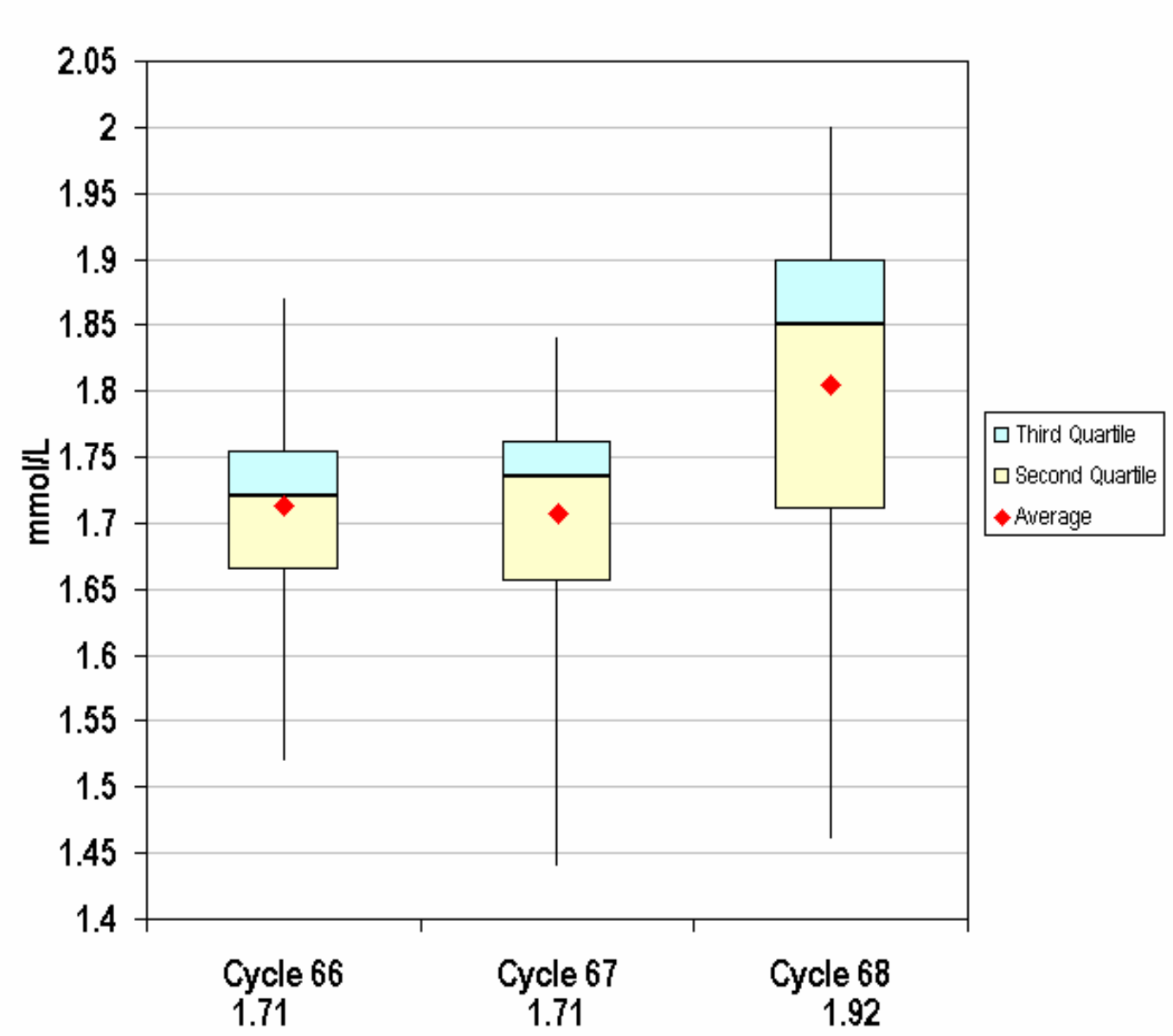
421 out of 528 ……80%

There seems to be a concensus that the target value was

Too high / Inaccurate …. ?

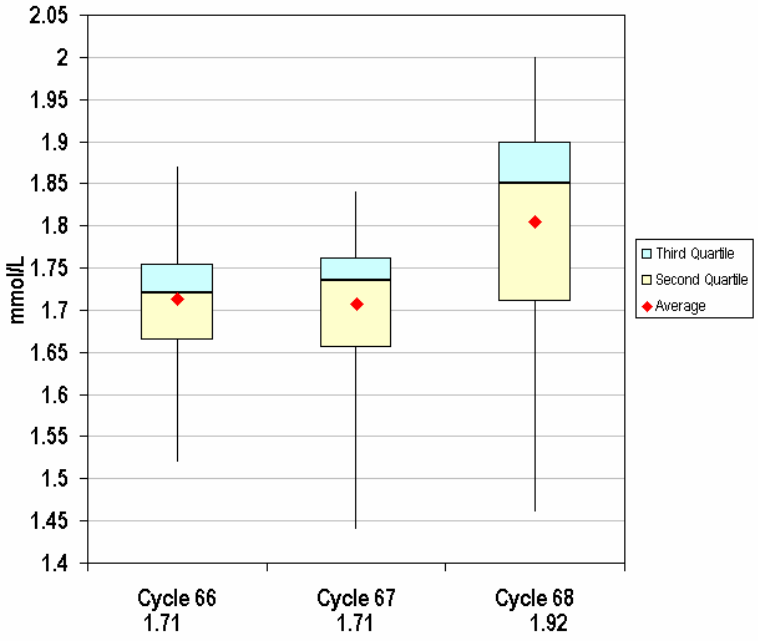
MY 'HIGH' TRIGLYCERIDES MEASURED ON ALL INSTRUMENTS

May 2004 – April 2005



'HIGH' TRIGLYCERIDES ALL AUSTRALIAN LABS

May 2004 – April 2005



Again the high degree of overlap leads to the empirical observation that only those labs using instruments that reported the Cycle 68 sample as 1.85 mmol/L and above could say that my triglycerides had risen.

How many labs are in this category ?

234 out of 528 ..... 44%

CHOLESTEROL : SUMMING UP

THE BEST CASE SCENARIO

Laboratories that used methods that fell into the second and third quartiles were probably the best performing labs

CHOLESTEROL : BEST CASE SCENARIO : THE DATA

TARGET mmol/L	2.13	2.53	5.30	5.10
ALL LABS' MEDIAN	2.15	2.46	5.42	4.97
INACCURACY	+0.02	-0.07	+0.12	-0.13
2nd QUARTILE	2.05	2.28	5.17	4.74
3rd QUARTILE	2.20	2.53	5.50	5.07
# OF LABS In 2nd & 3rd QUARTILES	666	233	509	337
% OF ALL LABS In 2nd & 3rd QUARTILES	63%	44%	48%	63%

CHOLESTEROL : SUMMING UP

THE BEST CASE SCENARIO

Laboratories that used methods that fell into the second and third quartiles were probably the best performing labs

They were able to report results consistent with the 'true' changes in my cholesterol concentrations.

The labs that fell within this 'acceptable' performance bracket for CHOLESTEROL comprised 44% to 63% of all participating labs.

These labs reported CHOLESTEROLS that were accurate to within -0.13 to + 0.12 mmol/L.

TRIGLYCERIDES : SUMMING UP

THE BEST CASE SCENARIO

Laboratories that used methods that fell into the second and third quartiles were probably the best performing labs

TRIGLYCERIDES : BEST CASE SCENARIO : THE DATA

TARGET mmol/L	0.60	0.79	1.71	1.92
ALL LABS' MEDIAN	0.53	0.73	1.73	1.85
INACCURACY	-0.07	-0.06	+0.02	-0.07
2nd QUARTILE	0.51	0.66	1.66	1.71
3rd QUARTILE	0.55	0.75	1.76	1.90
# OF LABS In 2nd & 3rd QUARTILES	875	368	752	229
% OF ALL LABS In 2nd & 3rd QUARTILES	83%	70%	72%	43%

TRIGLYCERIDES : SUMMING UP

THE BEST CASE SCENARIO

Laboratories that used methods that fell into the second and third quartiles were probably the best performing labs

They were able to report results consistent with the 'true' my triglyceride concentrations.

The labs that fell within this 'acceptable' performance bracket for TRIGLYCERIDE comprised 43% to 83% of all participating labs.

These labs reported TRIGLYCERIDES that were accurate to within – 0.07 to + 0.02 mmol/L.

CONCLUSIONS

TRIGLYCERIDE measurements are probably more reliable than CHOLESTEROL measurements.

There is a clear need for many Australian labs to substantially improve their accuracy of measurements of CHOLESTEROL. This can be achieved by

- The use of a single source of serum based calibrators.
- The discontinuation of the use of instruments that continually under perform in the QAP survey.
