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ORIGINAL ARTICLE

National Survey on Internal Quality Control Practice for Lipid Parameters in Laboratories of China from 2014 to 2016

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SUMMARY

Background: **To investigate the situation of Internal Quality Control (IQC) practice for total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol from 2014 to 2016 in laboratories in China and provide improvement measurements.**
Methods: **A web-based External Quality Assessment (EQA) system was used to collect IQC data of lipid parameters in laboratories which continuously participated in the national EQA programs in China from 2014 to 2016. Pass rate of the coefficients of variation (CVs) of two level quality controls in four lipid parameters were calculated according to six quality specifications for precision to evaluate the current status of precision level of the four lipid parameters and their change over time in China.**
Results: **533, 512, 504, and 466 laboratories continuously reported the data of level one for total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol, and 212, 210, 208 and 198 laboratories reported the level two, respectively. The percentage of laboratories meeting the quality specification varied based on different criteria. Non-significant change can be found in the pass rate of CVs over time. The number of laboratories using a closed system increased over time, but still only accounted for a small proportion. There is no significant difference in the pass rate of CVs between closed and open systems.**
Conclusions: **Triglycerides currently have a fairly good performance in China. While the performance of laboratories on total cholesterol, HDL-cholesterol and LDL-cholesterol has yet to be improved.**
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INTRODUCTION

Lipid metabolism dysfunction may cause cardiovascular diseases, resulting in myocardial ischemia, infarct, and sudden death of patients clinically. High total cholesterol, high LDL-cholesterol and low HDL-cholesterol are risk factors of cardiovascular diseases [1]. Thus, correct blood lipid tests play an important role in the prevention, diagnosis, and treatment of relative diseases. Since Levey and Jennings introduced statistical process control to medical laboratories in 1950 [2], internal quality control (IQC) has continued to developed for over 60 years. The central role of IQC is to detect clini-

cally important errors in an analytical process [3]. With continuous improvement to the process, IQC had already become an important way for laboratories to ensure quality of laboratory testing. Quality control consists of two aspects: accuracy and precision. In this paper, we investigated the IQC practice of total cholesterol (TCHOL), triglycerides (TG), HDL-cholesterol (HDLC) and LDL-cholesterol (LDLC) from 2014 to 2016 and calculated the percentage meeting the six quality specifications for precision so as to have a general understanding of precision status in laboratories in China.

MATERIALS AND METHODS

Subjects

The official External Quality Assessment (EQA) provider in China, the National Center for Clinical Laboratories (NCCL), performed lipid EQA programs including TCHOL, TG, HDLC, and LDLC twice a year. Participating laboratories were informed about the survey and submitted data through the EQA network reporting system. Only laboratories which had participated continuously in the five EQA programs were included in the paper.

Study design

The IQC information of participating laboratories was collected via the EQA network reporting system developed by NCCL, including the CVs of IQC data under control in April 2014, July 2014, April 2015, July 2015, and April 2016 and corresponding information such as vendor of control material, mean of control material, standard deviation(s) of measurements for control material, principle of assay, instrument, reagent, and calibrator manufacturer. The submitted information and data were analyzed and compared against six imprecision criteria to calculate the percentages of laboratories meeting the quality specifications.

Analytical quality specifications for precision

CVs of IQC data under control of current month were compared against the six analytical quality specifications for precision to evaluate the IQC status of lipid parameters in China. Three levels of quality specifications for precision were derived from biological variation (BV), (i) desirable performance defined by $CV_A < 0.50CV_I$; (ii) optimum performance defined by $CV_A < 0.25CV_I$; and (iii) minimum performance defined by $CV_A < 0.75CV_I$ (where CV_A is the analytical precision and CV_I is the within-subject biological variation) [4]. Besides, 1/3 total analytical error (TEa) and 1/4 TEa based on the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88) proficiency testing criteria for acceptable analytical performance (except for LDLC) [5] and the imprecision requirement recommended by The National Cholesterol Education Program (NCEP) Working Group on Lipoprotein Measurement was employed as well [6]. The six quality specifications of precision of TCHOL, TG, HDLC, and LDLC were shown in Table 1.

Statistical analysis

The percentage of laboratories meeting the imprecision quality specifications was calculated using SPSS 12.0 and Microsoft Excel 2007 and shown in diagrams.

RESULTS

The number of laboratories which continuously participated in the five EQA programs for TCHOL, TG, HDLC, and LDLC of level one were 533, 512, 504 and 466. Of which, there were 212, 210, 208 and 198 laboratories reporting the results of level two, respectively. We did not define the range of measurement for each level, so there might be an overlap between the two levels.

There were no harmonized national control materials for TCHOL, TG, HDLC, and LDLC for daily IQC, and control materials among laboratories varied widely with respect to vendors.

Laboratories meeting the analytical quality specifications for precision

The percentage meeting the quality specification was varied based on different criteria. TG had a fairly good performance, and more than 90% of the laboratories (some of which even get to 100%) met the quality specification in both levels whichever the six criteria were employed. As for TCHOL, HDLC and LDLC, nearly 70% of the laboratories met the quality specification, but only a few laboratories could get to the imprecision requirement if the optimum allowable imprecision derived from BV was employed. Taking TCHOL for example, laboratories meeting the minimum quality specification accounted for over 90% in both levels, more than 80% of the laboratories met the desirable quality specification, while only about 30% of the laboratories met the optimum quality specification. In the continuous 5 programs, the pass rate had no significant change over time. The pass rate of lipid parameters based on different criteria was shown in Figure 1 and Figure 2.

Testing system

Instrument, reagent, and calibrator may have an effect on the results of precision. A system where the instrument, reagent, and calibrator are all from the same vendors was defined as a closed system in the study. The results showed that the reagent and calibrator used by each participating laboratory were all from the same producer. However, only some of them were matched with the instrument and consequently composed a closed system, while most of them did not. In the five programs, there were an increasing number of closed systems in all the four tests. Figure 3 showed the number of laboratories using closed systems over time.

Table 1. The 6 analytical quality specifications for precision of the 4 lipid parameters.

Item	Based on BV (%)			Based on CLIA'88 (%)		Based on NCEP (%)
	Minimum	Desirable	Optimum	1/3 TEa	1/4 TEa	NCEP
Total cholesterol	4.46	2.98	1.49	3.33	2.5	3
Triglyceride	14.93	9.95	4.98	8.33	6.25	5
HDL-cholesterol	5.48	3.65	1.83	10	7.5	4
LDL-cholesterol	5.85	3.9	1.95			4

Table 2. The percentage of closed systems and open systems meeting the NCEP criteria over time.

Analyte	Year	Closed system Roche	Closed system Beckman	Mean open systems	p-value
Total cholesterol	2014 04	75.96% (79/104)	90.48% (38/42)	82.01% (310/378)	0.110
	2014 07	75.70% (81/107)	92.86% (39/42)	85.29% (319/374)	0.015 *
	2015 04	82.61% (95/115)	87.50% (49/56)	83.43% (287/344)	0.701
	2015 07	86.21% (100/116)	94.83% (55/58)	86.09% (291/338)	0.176
	2016 04	86.44% (102/118)	88.71% (55/62)	87.38% (284/325)	0.909
Triglyceride	2014 04	95.24% (100/105)	94.29% (33/35)	91.99% (333/362)	0.494
	2014 07	95.37% (103/108)	91.89% (34/37)	90.17% (321/356)	0.238
	2015 04	93.91% (108/115)	90.20% (46/51)	91.41% (298/326)	0.629
	2015 07	95.69% (111/116)	96.23% (51/53)	93.77% (301/321)	0.623
	2016 04	98.31% (116/118)	91.23% (52/57)	94.16% (290/308)	0.096
HDL-cholesterol	2014 04	80.00% (76/95)	61.90% (13/21)	80.05% (305/381)	0.134
	2014 07	82.65% (81/98)	77.27% (17/22)	75.27% (283/376)	0.304
	2015 04	83.02% (88/106)	80.00% (28/35)	74.79% (261/349)	0.192
	2015 07	88.68% (94/106)	89.47% (34/38)	76.97% (264/343)	0.010 *
	2016 04	87.85% (94/107)	75.00% (30/40)	82.49% (278/337)	0.160
LDL-cholesterol	2014 04	84.88% (73/86)	80.00% (16/20)	81.64% (289/354)	0.754
	2014 07	87.78% (79/90)	75.00% (15/20)	81.38% (284/349)	0.247
	2015 04	84.54% (82/97)	87.10% (27/31)	84.36% (275/326)	0.922
	2015 07	91.84% (90/98)	85.29% (29/34)	84.38% (270/320)	0.174
	2016 04	90.00% (90/100)	82.86% (29/35)	84.39% (265/314)	0.343

* **- significance difference for different systems ($p < 0.05$).**

The main vendors of the closed systems in the lipid parameters are Roche, Beckman, and others (including Abbott, Siemens, Hitachi, and homemade system). We analyzed the percentage of closed systems and open systems meeting the imprecision criteria based on NCEP over time, which was shown in Table 2.

DISCUSSION

The conference on Strategies to Set Global Quality Specifications in Laboratory Medicine was held by the International Union of Pure and Applied Chemistry (IUPAC), the International Federation of Clinical Chemistry (IFCC), and the World Health Organization

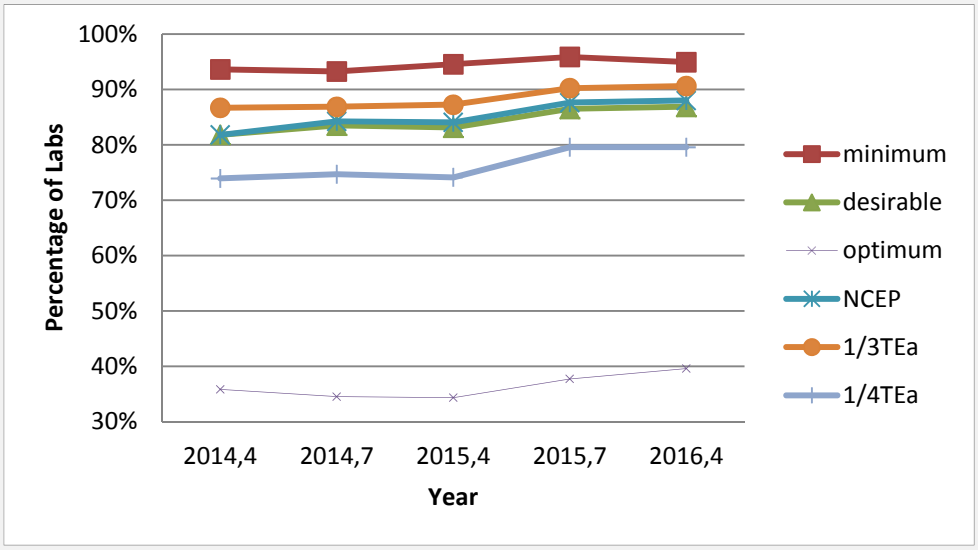

Figure 1A. Percentage of laboratories meeting different imprecision criteria of total cholesterol in level 1.

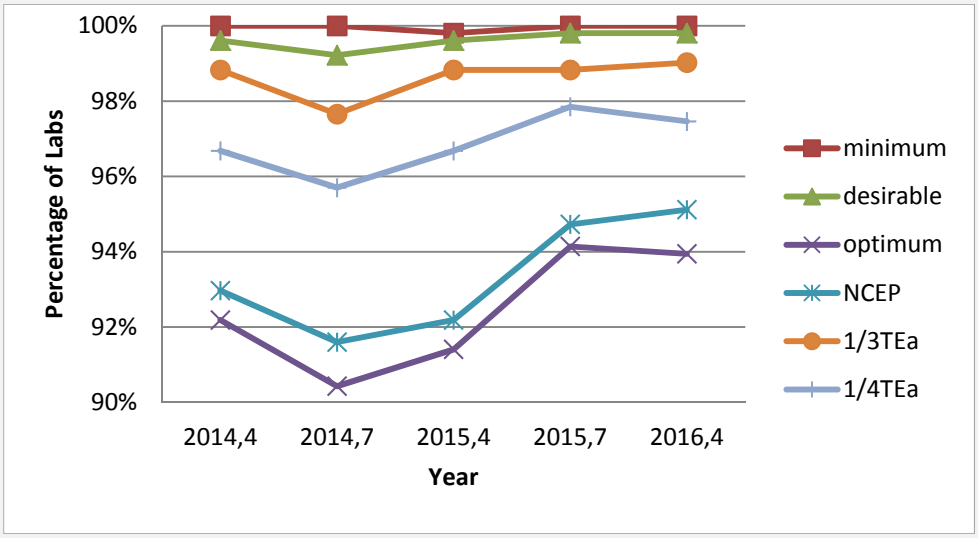

Figure 1B. Percentage of laboratories meeting different imprecision criteria of triglyceride in level 1.

(WHO) in Stockholm in 1999. The conference reached a consensus that a hierarchy model of quality specifications should be used; a model higher in the hierarchy should be preferred over a lower one [7]. In descending order, the hierarchy of quality specifications was based on: (i) clinical outcome; (ii) BV; (iii) published professional recommendations; (iv) regulatory bodies and EQA schemes; and (v) current state of the art [7].

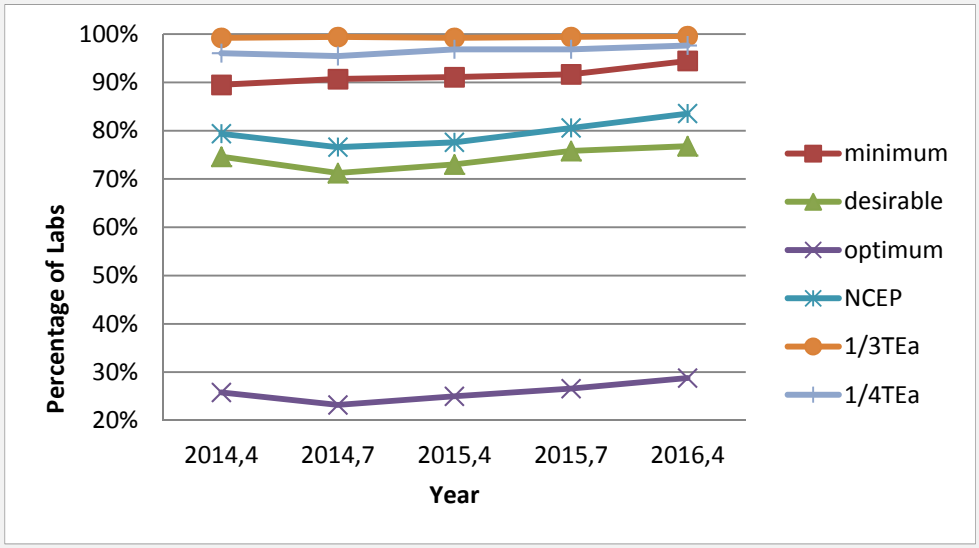

Figure 1C. Percentage of laboratories meeting different imprecision criteria of HDL-cholesterol in level 1.

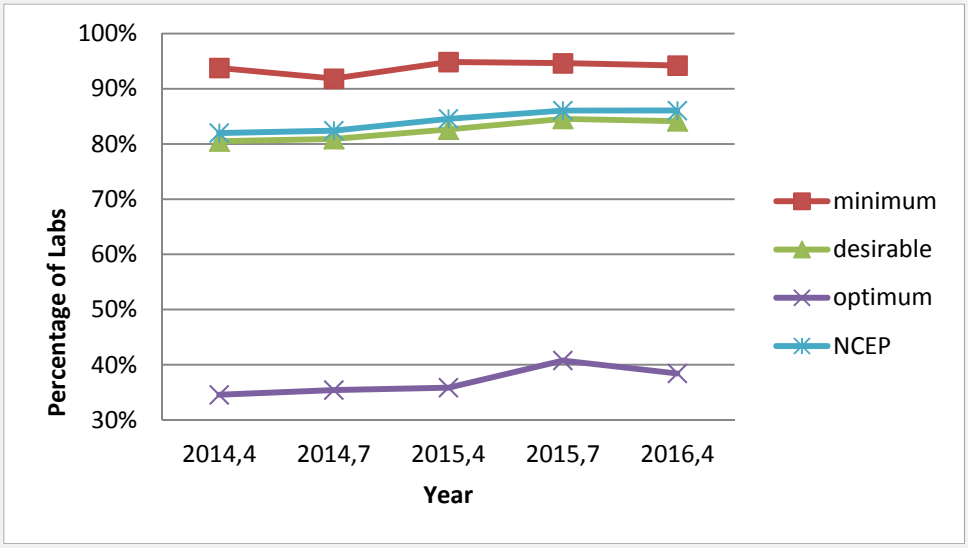

Figure 1D. Percentage of laboratories meeting different imprecision criteria of LDL-cholesterol in level 1.

According to the hierarchy system, CLIA'88 belongs to the fourth hierarchy, the recommendation of NCEP belongs to the third hierarchy, and the one derived from BV is the second hierarchy. In this study, the recommendation of NCEP is tighter than the minimum imprecision criteria and looser than the optimum criteria of all the 4 parameters. Here, we evaluated the CVs against the specification based on BV and criteria from CLIA'

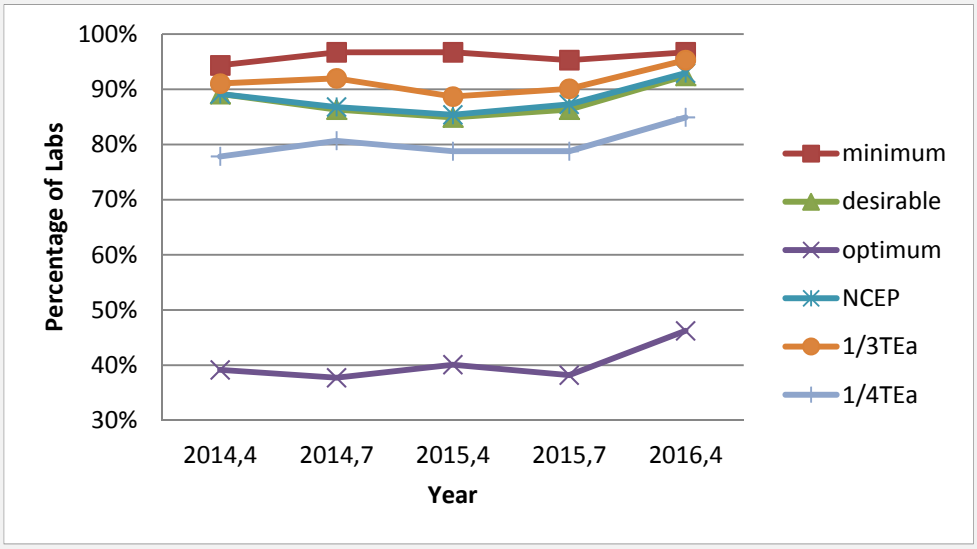

Figure 2A. Percentage of laboratories meeting different imprecision criteria of total cholesterol in level 2.

Figure 2B. Percentage of laboratories meeting different imprecision criteria of triglyceride in level 2.

88 and NCEP. Performance specifications based on within-subject BV and NCEP seem more reasonable for IQC imprecision evaluation. Currently there is no database on BV in Chinese population. The data about intra- and inter-individual biological CV we referred is provided by Ricos and updated by Westgard [8]. However, Zengjie et al. [9] investigated preanalytical and intra-individual BV of 19 biochemistry analytes. The study

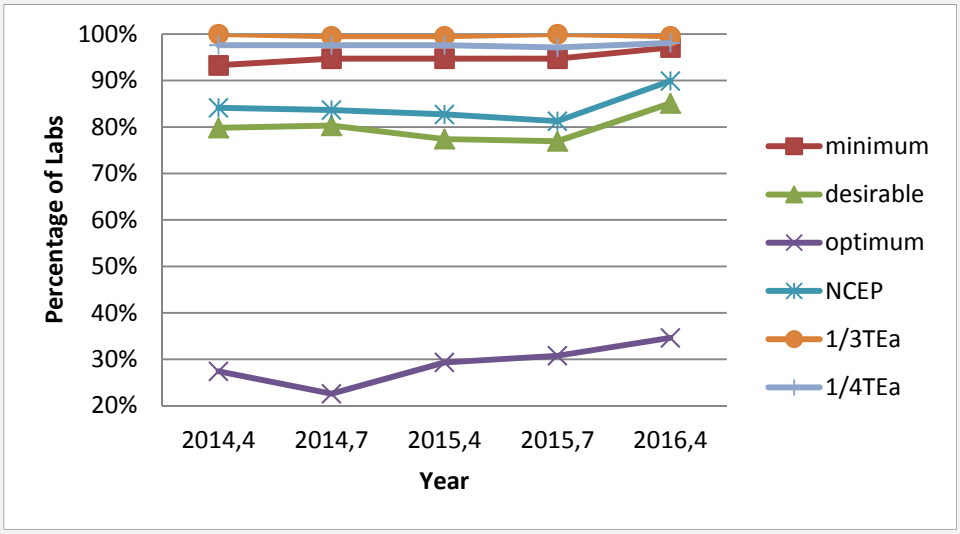

Figure 2C. Percentage of laboratories meeting different imprecision criteria of HDL-cholesterol in level 2.

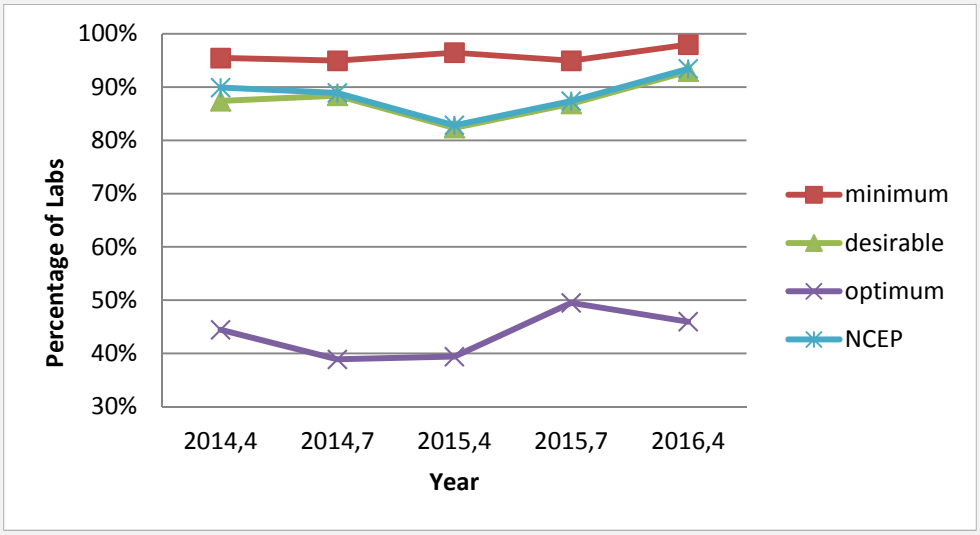

Figure 2D. Percentage of laboratories meeting different imprecision criteria of LDL-cholesterol in level 2.

showed that no obvious difference exists of BV data between Chinese and healthy population abroad. Our study investigated laboratories which continuously participated in the EQA program from 2014 to 2016 to evaluate the status of IQC in China. The results of our investigation suggested that TG had a fairly good performance. Nearly 100% of the participating laboratories met the minimum and desirable performance. Even though compared to the strictest one of optimum performance, there were still over 90% of the participant

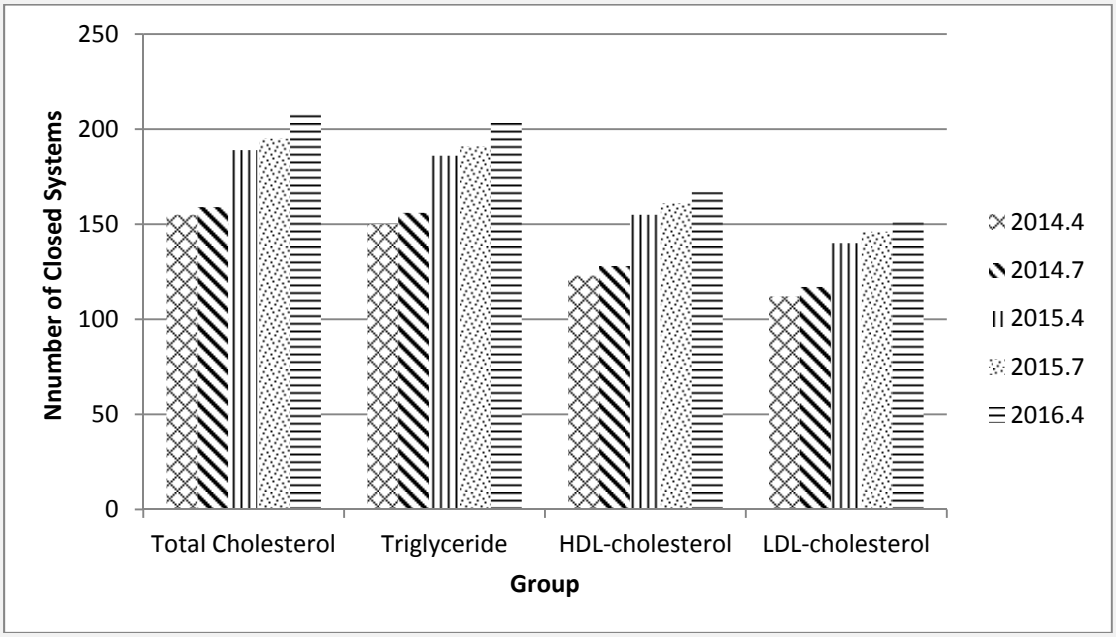

Figure 3. The number of laboratories using closed systems over time.

laboratories meeting the requirement, which demonstrated that the imprecision status of TG in participating laboratories was in a fair condition. Laboratories should keep up the good work. However, it was unsatisfactory to find that TCHOL, HDLC and LDLC did not perform so well. Only a small part of participating laboratories could reach the optimum performance, which showed that substantial effort was needed for TCHOL, HDLC, and LDLC measurement in laboratories in China. Besides, the results in the continuous five programs suggested that there was no obvious change of the imprecision level over time in the participating laboratories. Constituent levels of quality control materials should be chosen at medical decision concentrations and/or at critical method performance limits such as upper and lower linearity limits. Two or three different concentrations are often needed for each analyte [10]. CLSI C24-Ed4 noted that for most analyte-method combinations, a minimum of two levels (concentrations) of control materials is recommended. Where possible, analyte concentrations should be at clinically relevant levels to reflect values encountered in patient specimens [11]. Unfortunately, as the data showed, less than half of participating laboratories reported the data for level 2, TCHOL was 39.77%, TG was 41.02%, HDLC was 41.27%, and LDLC was 42.49%. Many laboratories actually only performed one level quality control, which was not enough to reflect the actual condition of IQC. We also analyzed the main testing systems of the four parameters used in China. Instrument, reagent, and calibrator may be factors influencing the precision of test results, but we surprisingly found that although there was an increasing number of laboratories using closed systems, most of laboratories in China did not use the closed systems. Among the closed systems used by participating laboratories, Roche had the biggest share, followed by Beckman. Abbott, Siemens, Hitachi, and in-house system only accounted for a small proportion. As is known to all there are many factors affecting the variation of test, the testing system is one of the important ones, but we surprisingly found that there were no significant differences among the closed systems and mean open systems (except for HDLC in July 2015). Even so, further study is still needed to make a much more exact conclusion.

CONCLUSION

All in all, carrying out IQC plays an important role for daily practice of clinical laboratories. Much more attention should be paid in the IQC practice of lipid parameters in laboratories in China so as to achieve better quality. Precision status within laboratories for each analyte is directly related to the quality of results. It is an effective way for clinical laboratories to improve test quality by monitoring the current CVs of IQC and comparing them against proper quality specification to evaluate if

the analysis system can meet quality requirements, monitor the performance of methods, and provide information on precision for mutual recognition of test results.

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Declaration of Interest:
The authors stated that there are no conflicts of interest regarding the publication of this article.

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