表６－１　「生活習慣病のリスクを高める量を飲酒している者の割合の低減」に関する計算式

	１合未満	１合以上 ２合未満	２合以上 ３合未満	３合以上 ４合未満	４合以上 ５合未満	５合以上
毎日	1	②	$\boxed{3}$	$\boxed{4}$	$\boxed{5}$	$\boxed{6}$
週５－６日	7	⑧	$\boxed{9}$	$\boxed{10}$	$\boxed{11}$	$\boxed{12}$
週３－４日	13	⑭	⑮	$\boxed{16}$	$\boxed{17}$	$\boxed{18}$
週１－２日	19	20	21	㉒	㉓	$\boxed{24}$
月１－３日	25	26	27	28	29	$\boxed{30}$
やめた						
ほとんど飲まない						

男性：（３＋４＋５＋６＋９＋10＋11＋12＋16＋17＋18＋24＋30）／全回答者数
（四角で囲まれた数字の欄の人数の合計／全回答者数）
女性：（２＋３＋４＋５＋６＋８＋９＋10＋11＋12＋14＋15＋16＋17＋18＋22＋23＋24＋30）／全回答者
（丸と四角で囲まれた数字の欄の人数の合計／全回答者数）

表６－２　「生活習慣病のリスクを高める量を飲酒している者の割合の低減」に関する現状（男性，平成22年 [5]）

	１合未満	１合以上 ２合未満	２合以上 ３合未満	３合以上 ４合未満	４合以上 ５合未満	５合以上
毎日			264	90	30	28
週５－６日			74	9	5	7
週３－４日				13	10	2
週１－２日						14
月１－３日						16
やめた						
ほとんど飲まない						

（該当欄以外は空欄としている）

生活習慣病のリスクを高める量を飲酒している者の割合（男性，平成22年）
＝（264＋90＋30＋28＋74＋９＋５＋７＋13＋10＋２＋14＋16）／3668（全回答者数）
＝562／3668
＝15.3%

表６－３　「生活習慣病のリスクを高める量を飲酒している者の割合の低減」に関する現状（女性，平成22年 [5]）

	１合未満	１合以上 ２合未満	２合以上 ３合未満	３合以上 ４合未満	４合以上 ５合未満	５合以上
毎日		87	34	13	5	8
週５－６日		47	12	2	0	1
週３－４日		56	15	7	1	2
週１－２日				8	5	4
月１－３日						10
やめた						
ほとんど飲まない						

（該当欄以外は空欄としている）

生活習慣病のリスクを高める量を飲酒している者の割合（女性，平成22年）
＝（87＋34＋13＋５＋８＋47＋12＋２＋０＋１＋56＋15＋７＋１＋２＋８＋５＋４＋10）／4205（全回答者数）
＝317／4205
＝7.5%

表７「成人の喫煙率の減少（喫煙をやめたい人がやめる）」に関する生活習慣調査票の質問

問１　あなたは，これまでにたばこを吸ったことがありますか．
あてはまる番号を１つ選んで○印をつけて下さい．
1　合計100本以上，または６ヶ月以上吸っている（吸っていた）
2　吸っている（吸ったことはある）が合計100本未満で６ヶ月未満である
3　まったく吸ったことがない ――――→問３へ

問２　現在（この１ヶ月間），あなたはたばこを吸っていますか．
あてはまる番号を１つ選んで○印をつけて下さい．
1　毎日吸う
2　ときどき吸っている
3　今は（この１ヶ月間）吸っていない――→問３へ
（問２－１）たばこをやめたいと思いますか．
あてはまる番号を１つ選んで○印をつけて下さい．
1　やめたい
2　本数を減らしたい
3　やめたくない
4　わからない

（出典：平成22年国民健康・栄養調査 [5] を改変）

表８「日常生活で受動喫煙（家庭・職場・飲食店・行政機関・医療機関）の機会を有する者の割合の低下」に関する生活習慣調査票の質問

問１　あなたはこの１ヶ月間に，自分以外の人が吸っていたたばこの煙を吸う機会（受動喫煙）がありましたか．次のアからオの質問について，あてはまる番号を１つ選んで○印をつけて下さい．
※飲食店などに勤務していて，その職場で受動喫煙があった場合は，「イ　職場」欄に記入してください．

	1. ほぼ毎日	2. 週に数回程度	3. 週に１回程度	4. 月に１回程度	5. 全くなかった	6. 行かなかった
ア　家庭	1	2	3	4	5	
イ　職場	1	2	3	4	5	6
ウ　飲食店	1	2	3	4	5	6
エ　行政機関（市役所，町村役場，公民館など）	1	2	3	4	5	6
オ　医療機関	1	2	3	4	5	6

（出典：平成20年，平成22年国民健康・栄養調査 [5, 11] を改変）

別で約４割（37.6%）の喫煙率の減少が達成できるかどうかが重要である．

(5) 日常生活で受動喫煙の機会を有する者の割合の低下〔(5)⑤ (iv)〕

日常生活での受動喫煙について，家庭，職場，飲食店，行政機関，医療機関のそれぞれの場で，その機会を有する者の割合を減少させることが目標項目に挙げられた．国民健康・栄養調査では表８の質問にもとづき，家庭，飲食店（以上，平成22年国民健康・栄養調査），行政機関，医療機関（以上，平成20年国民健康・栄養調査）のデータが活用される．

本目標項目での受動喫煙とは，現在習慣的に喫煙している者以外がたばこの煙を吸う機会のことであり，成人の男女総数のうち，その他の者（現在喫煙者以外）における回答をもとに現状は示されている．家庭における受動喫煙の現状は，「ほぼ毎日」と回答した者の割合10.7%である（「行かなかった」という選択肢は存在しない）．飲食店における受動喫煙の現状は，「行かなかった」と回答した者を除いて，「月に１回程度」以上（「全くなかった」以外）受動喫煙の機会があった者の割合50.1%である．行政機関と医療機関における受動喫煙の現状は，飲食店における受動喫煙の現状と同様，「行かなかった」と回答した者を除いて，「月に１回程度」以上（「全くなかった」以外）受動喫煙の機会があった者の割合で，それぞれ16.9%と13.3%である．

目標（平成34年度）は，家庭と飲食店については，現状値から，禁煙希望者がすべて禁煙した場合の割合（平成22年，37.6%）を減じた割合（家庭6.7%，飲食店31.3%）を半減させた値として，家庭３%，飲食店15%が設定された．行政機関と医療機関については，「受動喫煙の機会を有する者をなくす」という観点から，目標は０%とされた．

(6) 60歳代における咀嚼良好者の増加〔(5)⑥ (i)〕

高齢期においても，咀嚼機能をはじめとする口腔機能をできる限り維持するという重症化予防の観点から，60歳代における咀嚼良好者の増加が目標項目に掲げられた．現状（平成21年）は，表9の質問に「何でもかんで食べることができる」と回答した者の割合73.4%である．

目標（平成34年度）は，平成21年の50歳代の同割合（78.2%）を目指すという観点から，80%と設定された．

(7) 歯周病を有する者の減少「ア　20歳代における歯肉に炎症所見を有する者の割合の減少」〔(5)⑥ (ii)〕

歯肉に炎症所見を有する者については，表10の歯ぐきの状態に関する質問の「歯ぐきが腫れている」または「歯を磨いた時に血が出る」に「はい」と回答した者と定義し，その割合を減少させることが目標項目に挙げられた．20歳代のみ，国民健康・栄養調査のデータが用いられるのは，20歳代ではセルフチェックにより自己管理が重要であるという観点からである．

現状は，平成21年のデータで31.7%である．なお，「歯ぐきが腫れている」に「はい」と回答した者は9.6%（男性9.7%，女性9.6%)，「歯を磨いた時に血が出る」に「はい」と回答した者は27.9%（男性29.5%，女性26.5%）であり，両質問で「はい」と回答した者の割合は異なり，「歯を磨いた時に血が出る」については，女性より男性で「はい」と回答した者の割合が少し高かった．そのため，現状値の31.7%は，性別では男性33.4%，女性30.2%である．目標（平成34年度）は，平成16年と21年の比較もふまえて，25%と設定された．

(8) 過去1年間に歯科検診を受診した者の割合の増加（20歳以上）〔(5)⑥ (v)〕

過去1年間に歯科検診を受診した者については，表11の問1で質問することとし，20歳以上における割合を増加させることを目標項目とした．なお，健康日本21では，60歳（55～64歳）について同質問を用いた「6. 13　定期的な歯科検診の受診者の増加［過去1年間に受けた人の割合]」という目標項目があったが，過去1年間の歯科検診の受診の有無が必ずしも定期的な歯科検診の受診とはいえないことから，「過去1年間に歯科検診を受診した者の割合の増加」と改められている．

現状は，平成21年のデータで34.1%である．目標（平成34年度）は，平成11年から平成21年への変化をもとにした

表9 「60歳代における咀嚼良好者の増加」に関する生活習慣調査票の質問

問1　かんで食べる時の状態について，あてはまる番号を1つ選んで○印をつけて下さい．

1　何でもかんで食べることができる
2　一部かめない食べ物がある
3　かめない食べ物が多い
4　かんで食べることはできない

（出典：平成21年国民健康・栄養調査 [10] を改変）

表10 「20歳代における歯肉に炎症所見を有する者の割合の減少」に関する生活習慣調査票の質問

問1　あなたの歯ぐきの状態について，「はい」「いいえ」でお答え下さい．

ア　歯ぐきが腫れている	はい	いいえ
イ　歯を磨いた時に血が出る	はい	いいえ

（出典：平成21年国民健康・栄養調査 [10] を改変）

表11 「過去1年間に歯科検診を受診した者の割合の増加（20歳以上）」に関する生活習慣調査票

問1　あなたは，この1年間に歯科健康診査を受けましたか．

1　受けた　　2　受けていない

↓

問1－1　どこで受けましたか．あてはまる番号をすべて選んで○印をつけて下さい．

1　歯科診療所（病院）
2　市町村・保健所
3　職場
4　学校
5　その他

（出典：平成21年国民健康・栄養調査 [10] を改変）

推計から，65%に設定された．なお，問１－１は歯科健康診査を受ける場所を想起させるために重要であり，平成16年と21年で同一の選択肢が用いられていることから，今後も変更しないことが望まれる．

Ⅲ．おわりに

健康日本21（第二次）の目標設定における国民健康・栄養調査のデータの活用と今後のモニタリングの注意点について述べた．食塩摂取量の平均値や喫煙率は比較的国民になじみのある数値と思われるが，成人の男女総数での平均値が目標設定で用いられており，人口の高齢化や，性別・年齢による協力率の差異の影響を受けやすい．目標の評価のためには，性別に年齢調整した値や年齢階級別の値での変化も検討する必要がある．

一方，「日常生活における歩数の増加」や「運動習慣者の割合の増加」では，データの特徴をもとに，性別に20～64歳と65歳以上の目標を示しており，非常にわかりやすい目標設定がなされている．ただ，このような年齢群での平均値は，以前の国民健康・栄養調査報告書では示されておらず，健康日本21（第二次）の現状値を示すため，平成22年の報告書で新たに再掲の集計値が示されている．このように新たに平成22年報告書で再掲値が示された目標項目には，他に「高血圧の改善」，「脂質異常症の減少」，「低栄養傾向（BMI 20以下）の高齢者の割合の増加の抑制」がある．また，「脂質異常症の減少」の「LDLコレステロール160mg/dl以上の者の割合」，「生活習慣病のリスクを高める量を飲酒している者の割合の低減」，歯周病を有する者の減少の「ア　20歳代における歯肉に炎症所見を有する者の割合の減少」については，現状値を平成22年報告書から得ることができないという課題が残されている．

今後，調査の協力率を低下させない方策を講じるとともに，毎年の国民健康・栄養調査報告書で健康日本21（第二次）の目標項目の数値を継続的に示すことを通じて，国民健康・栄養調査が経時的に比較可能で十分な精度を持つ調査としての役割を果たすことを期待したい．

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Original Article

Revised System to Evaluate Measurement of Blood Chemistry Data From the Japanese National Health and Nutrition Survey and Prefectural Health and Nutrition Surveys

Masakazu Nakamura[1], Masahiko Kiyama[2], Akihiko Kitamura[2], Yoshinori Ishikawa[2], Shinichi Sato[3], Hiroyuki Noda[4,5], and Nobuo Yoshiike[6]

[1]National Cerebral and Cardiovascular Center, Department of Preventive Cardiology, CDC/CRMLN Lipid Reference Laboratory, Suita, Osaka, Japan
[2]Osaka Center for Cancer and Cardiovascular Disease Prevention, Osaka, Japan
[3]Chiba Prefectural Institute of Public Health, Chiba, Japan
[4]Public Health, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan
[5]Cancer Control and Health Promotion Division, Health Service Bureau, Ministry of Health, Labour, and Welfare, Tokyo, Japan
[6]Aomori University of Health and Welfare, Aomori, Japan

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ABSTRACT

Background: We developed a monitoring system that uses total errors (TEs) to evaluate measurement of blood chemistry data from the National Health and Nutrition Survey (NHNS) and Prefectural Health and Nutrition Surveys (PHNS).

Methods: Blood chemistry data from the NHNS and PHNS were analyzed by SRL, Inc., a commercial laboratory in Tokyo, Japan. Using accuracy and precision from external and internal quality controls, TEs were calculated for 14 blood chemistry items during the period 1999–2010. The acceptable range was defined as less than the upper 80% confidence limit for the median, the unacceptable range as more than twice the cut-off value of the acceptable range, and the borderline range as the interval between the acceptable and unacceptable ranges.

Results: The TE upper limit for the acceptable and borderline ranges was 5.7% for total cholesterol (mg/dL), 9.9% for high-density lipoprotein cholesterol (mg/dL), 10.0% for low-density lipoprotein cholesterol (mg/dL), 10.4% for triglycerides (mg/dL), 6.6% for total protein (g/dL), 7.6% for albumin (g/dL), 10.8% for creatinine (mg/dL), 6.5% for glucose (mg/dL), 9.7% for γ-glutamyl transpeptidase (U/L), 7.7% for uric acid (mg/dL), 8.7% for urea nitrogen (mg/dL), 9.2% for aspartate aminotransferase (U/L), 9.5% for alanine aminotransferase (U/L), and 6.5% for hemoglobin A1c (%).

Conclusions: This monitoring system was established to assist health professionals in evaluating the continuity and comparability of NHNS and PHNS blood chemistry data among survey years and areas and to prevent biased or incorrect conclusions.

Key words: monitoring system; accuracy; precision; total error

INTRODUCTION

In November every year, the Japanese Ministry of Health, Labour, and Welfare conducts the National Health and Nutrition Survey (NHNS) in 300 unit areas. In addition, some local governments conduct an independent Prefectural Health and Nutrition Survey (PHNS) of extended samples, according to the procedures used for the NHNS. All blood samples collected in the NHNS, and some blood samples obtained in the PHNS, are analyzed by SRL Inc., a commercial laboratory in Tokyo, Japan, and measurements are performed using the same analytic system.

All measurement is subject to error. Errors are not always constant and can differ by survey year depending on variations in many factors, including the principles underlying the method, analytic instruments, reagents, calibrator, medical technologist, and other laboratory conditions.[1,2] Even if the external and internal quality controls used at SRL are sound, measurement errors are inevitable.

The monitoring system described in this study outlines principles that can be used by physicians and other health professionals who are interested in the continuity and comparability among survey years, or in the statistical results for components of physical examinations, in the

Address for correspondence. Masakazu Nakamura, National Cerebral and Cardiovascular Center, Department of Preventive Cardiology, CDC/CRMLN Lipid Reference Laboratory, 5-7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan (e-mail: nakamura.masakazu.hp@mail.ncvc.go.jp).

annual NHNS and PHNS reports. Using these principles, they can determine by themselves if the results after 2011 can be used, should be used with care, or cannot be recommended for use according to the newly established TE criteria, which are based on external and internal quality controls at SRL during the 12-year period 1999–2010. The criteria for TEs were developed for use in monitoring during 2011–2015 but not for evaluating past data. Because the results of the analysis of collected data are open to the public but information on analytic errors is not, we hoped to prevent researchers from reaching biased or incorrect conclusions in their evaluations.

In 2008, we reported tentative monitoring principles that could be used to compare blood chemistry data obtained by the NHNS.[3] However, after 2008, more PHNS data became available, to allow for evaluation of local plans in Health Japan 21. In addition, the number of blood chemistry items in the NHNS varies and has tended to increase. Finally, the Metabolic Syndrome-Focused Health Checkups Program[4] in Japan began throughout the country in 2008. Due to these developments, we decided to revise the 2008 monitoring system.

METHODS

Blood chemistry items

In this study, 14 blood chemistry items (method, unit of measure at SRL) were evaluated: total cholesterol (TC) (enzymatic, mg/dL), high-density lipoprotein cholesterol (HDL-C) (homogeneous, mg/dL), low-density lipoprotein cholesterol (LDL-C) (homogeneous, mg/dL), triglycerides (enzymatic, mg/dL), total protein (Biuret, g/dL), albumin (bromcresol green, g/dL), creatinine (enzymatic, mg/dL), glucose (enzymatic, mg/dL), γ-glutamyl transpeptidase (γ-GT, γ-GTP) (Japanese Committee for Clinical Laboratory Standards [JSCC] recommended method, U/L), uric acid (enzymatic, mg/dL), urea nitrogen (enzymatic, mg/dL), aspartate aminotransferase (AST, GOT) (JSCC recommended, U/L), alanine aminotransferase (ALT, GPT) (JSCC recommended, U/L), and hemoglobin A1c (HbA1c) (latex agglutination-turbidimetric immunoassay [LA], %).

External and internal quality control

SRL participates in the External Quality Assessment of Clinical Laboratories (EQACL) program of the Japan Medical Association (JMA)[5] and the Lipid Standardization Program of the US Centers for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network (CDC/CRMLN). SRL also has an internal quality control system that uses 2 concentrations of quality-control materials.

Accuracy

Regarding accuracy (%bias) in Table 2, the evaluation method described in the 2010 annual report on EQACL by the JMA[5] was as follows: (1) values that deviate by 3 SDs or more from the center are removed, the mean and SD are obtained according to the measurement method used by the laboratories that participated in the survey, and the coefficient of variation (CV) is calculated according to the measurement method; (2) measurement methods are arranged in order of increasing CV; (3) measurement methods with a high rank in at least 80% of laboratories are selected; (4) the mean of data from laboratories using the measurement methods selected in the previous step is calculated, 1-way analysis of variance is used to calculate intra-method variation (expressed as SD), and a common CV is obtained; and (5) the common CV is corrected for the report unit width and a corrected common CV is obtained. Using both the adjusted mean obtained from this iterative truncation method and measurement values obtained by SRL, %bias according to samples was calculated and the mean of multiple %bias (accuracy) was calculated as an index of systematic error.[6]

Precision

Regarding precision (CV%) in Table 2, SD described in the EQACL represents dispersion in all participants, not the precision of measurement by SRL. Therefore, we were given data on the assayed values for 2 concentrations of internal quality control sera that were collected during a 1-month period, including values in November every year, randomly sampled 1 measurement value/day ($n = 1$) for 20 days, after which we calculated CV from the mean value and SD as an index of random error.[7]

Total error and relevant criteria

Subsequently, TE was calculated from accuracy and precision. Regarding total error (%) in Table 2, the equation used was "accuracy (absolute value of %bias) + precision ($1.96 \times CV$)", which is used by the US National Cholesterol Education Program (NCEP) and the Lipid Standardization Program by CDC/CRMLN.[6] The acceptable range of TE for each blood chemistry item was defined as less than the upper 80% confidence limit for the median of the 12-year period, as calculated by the nonparametric Bootstrap method (BC_a method).[8–10] Bootstrap method analyses were conducted using SAS, version 13 (SAS Institute, Inc., Cary, NC, USA). The unacceptable range was defined as more than twice the cut-off value of the acceptable range, based on evaluation criteria adopted by the US College of American Pathologists (CAP).[11] The interval between the acceptable and unacceptable ranges was classified as the borderline range. Thus, using these TE criteria, we have created a 3-level assessment of test performance.

Use in evaluating performance in 2011

We collected the results of EQACL evaluations and SRL internal quality control data in 2011 and attempted to evaluate SRL test performance in 2011 using the proposed TE criteria.

Table 1. Annual changes in numbers of assayed samples and blood chemistry items in the National Health and Nutrition Survey in Japan

Analyte	Year												*Application in 2011*
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	
No. of assayed samples	5492	5743	5592	5413	5327	3921	3877	4319	4020	4517	4300	3930	*3515*
Total cholesterol	○	○	○	○	○	○	○	○	○	○	○	○	○
HDL cholesterol	○	○	○	○	○	○	○	○	○	○	○	○	○
LDL cholesterol	—	—	—	—	—	—	—	—	○	○	○	○	○
Triglycerides	○	○	○	○	○	○	○	○	○	○	○	○	○
Total protein	○	○	○	○	○	○	○	○	○	○	○	○	○
Albumin	—	—	—	—	○	○	○	○	○	○	○	○	○
Creatinine	—	○	—	—	—	—	—	—	—	○	○	○	○
Glucose	○	○	○	○	○	○	○	○	○	○	○	○	○
γ-GT (γ-GTP)	—	○	—	—	—	—	—	—	—	—	—	○	○
Uric acid	—	○	—	—	—	—	—	—	—	—	—	○	○
Urea nitrogen	—	○	—	—	—	—	—	—	—	—	—	—	—
AST (GOT)	—	—	—	—	—	—	—	—	—	—	—	○	○
ALT (GPT)	—	—	—	—	—	—	—	—	—	—	—	○	○
HbA1c	—	—	—	○	○	○	○	○	○	○	○	○	○

White circles show blood chemistry items assayed in the corresponding year.
Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; γ-GT (γ-GTP), γ-glutamyl transpeptidase; AST (GOT), aspartate aminotransferase; ALT (GPT), alanine aminotransferase; HbA1c, hemoglobin A1c.

Criteria for CDC/CRMLN lipid standardization

To evaluate lipid measurement, the following NCEP criteria were used: TC—accuracy within 3% of target value for CDC/CRMLN reference measurement procedure, precision as CV of 3% or less, and TE of 9% or less; HDL-C—accuracy within 5% of target value, precision as CV 4% or less, and TE of 13% or less; LDL-C—accuracy within 4% of target value, precision as CV of 4% or less, and TE of 12% or less.[12]

Implementation survey for PHNS

In 2007, our study group surveyed prefectural governments regarding implementation of their PHNS, including dietary intake surveys and blood examination, and collected additional data on the number of blood samples they entrusted to SRL for analysis in 2011.[13]

RESULTS

Table 1 shows annual changes in blood chemistry items measured and number of analyzed NHNS samples assayed at SRL during 1999–2010. Items measured every year since 1999 were TC, HDL-C, triglycerides, total protein, and glucose. LDL-C, albumin, creatinine, and HbA1c were recently added to these 5 items. Other items, such as γ-GT (γ-GTP), uric acid, urea nitrogen, AST (GOT), and ALT (GPT), have been measured infrequently. The average number of assayed samples in the NHNS was 4704 during 1999–2010.

Table 2 shows measurement performance at SRL, based on the EQACL of the JMA. On the basis of these calculations, criteria for acceptable, borderline, and unacceptable ranges were established, as shown in the column labeled Proposed TE Criteria.[10] The upper limit of TE in the new acceptable and borderline ranges for each item was 5.7% for TC, 9.9% for HDL-C, 10.0% for LDL-C, 10.4% for triglycerides, 6.6% for total protein, 7.6% for albumin, 10.8% for creatinine, 6.5% for glucose, 9.7% for γ-GT (γ-GTP), 7.7% for uric acid, 8.7% for urea nitrogen, 9.2% for AST (GOT), 9.5% for ALT (GPT), and 6.5% for HbA_{1C}. Concerning the acceptable TE range, 50% of the evaluation limits (1 side) of the CAP evaluation criteria, which are widely used worldwide, was adopted and is shown as a reference in the column labeled CAP TE in Table 2.[11] TE criteria for HbA_1c were not established in the CAP survey. Although the acceptable range for γ-GT (γ-GTP) is expressed as SD in the CAP evaluation criteria, 7.5% was used as the corresponding value.

A 2007 implementation survey showed that 25 (53.2%) of the 47 prefectures in Japan independently performed blood examinations. Blood examinations were entrusted to SRL by 21 of the 25 prefectures and to a local laboratory by the other 4. A total of 15 096 samples from the 21 prefectures were analyzed by SRL. This number was 3.2 times the mean sample number (4704) of the NHNS (Table 1). Additionally, according to the 2011 survey, 20 (42.6%) of the 47 prefectures performed blood examinations.

Blood examinations were entrusted to SRL by 15 of the 20 prefectures and to a local laboratory by the other 5. A total of 7063 samples from the 15 prefectures were analyzed by SRL. This number was 1.5 times the average sample number of the NHNS (Table 1). The survey of the current situation in each prefecture was not conducted systematically, and measurement items are different for each prefecture.

In 2011, urea nitrogen was not assayed in the NHNS or PHNS; thus, there was a total of 13 items. When TE was calculated for each SRL item in 2011 to establish proposed TE

Table 2. SRL performance based on JMA external quality assessment and SRL internal quality control system (unit, %)

Analyte	Performance	Measurement performance by SRL during observation period													Proposed TE Criteria			*Application to new data*		(For reference) CAP TE Criteria
		Year												Median (LL, UL of 80% CL)	Acceptable	Borderline	Unacceptable	*Performance in 2011*	*Evaluation by proposed TE criteria in 2011*	
		1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010							
Total cholesterol	Accuracy (%bias)	0.19	−0.48	0.27	0.34	−0.15	−0.06	0.13	−0.82	−1.31	−1.45	−0.82	−0.66	−0.32 (−0.74, 0.04)				*0.19*		
	Precision (CV%)	1.7	1.6	1.3	1.1	1.6	1.0	1.2	1.0	0.7	0.8	0.7	0.7	1.1 (0.9, 1.3)				*0.8*		
	Total Error (%)	3.6	3.6	2.7	2.5	3.3	2.1	2.4	2.7	2.7	3.0	2.2	2.0	2.7 (2.5, 2.9)	<2.9	2.9–5.7	≥5.8	*1.8*	*acceptable*	5.0
HDL cholesterol	Accuracy (%bias)	−0.19	−1.57	−1.09	1.60	0.02	−0.33	0.70	1.29	−2.89	−0.90	−0.17	−0.68	−0.26 (−0.79, −0.08)				*−2.00*		
	Precision (CV%)	2.4	1.8	1.6	2.1	2.0	1.5	1.6	2.3	1.5	1.8	1.3	1.7	1.8 (1.6, 1.9)				*1.7*		
	Total Error (%)	4.9	5.1	4.2	5.7	4.0	3.2	3.8	5.7	5.8	4.4	2.7	4.0	4.3 (4.0, 5.0)	<5.0	5.0–9.9	≥10.0	*5.3*	*Borderline*	15.0
LDL cholesterol	Accuracy (%bias)	—	—	—	—	—	—	—	—	−0.39	1.95	−2.45	0.50	0.06 (−1.42, 1.23)				*0.63*		
	Precision (CV%)	—	—	—	—	—	—	—	—	1.2	2.0	0.9	1.4	1.3 (1.1, 1.7)				*1.1*		
	Total Error (%)	—	—	—	—	—	—	—	—	2.7	5.9	4.2	3.2	3.7 (3.0, 5.0)	<5.0	5.0–10.0	≥10.1	*2.8*	*acceptable*	15.0
Triglycerides	Accuracy (%bias)	1.91	−0.58	−1.34	0.37	1.56	−0.12	−0.36	0.00	−0.97	−1.10	−1.86	−1.67	−0.47 (−1.04, −0.06)				*−0.18*		
	Precision (CV%)	1.8	2.3	2.4	2.6	2.3	1.5	1.4	2.3	1.0	1.0	1.1	1.2	1.7 (1.3, 2.3)				*1.6*		
	Total Error (%)	5.5	5.2	6.1	5.5	6.2	3.0	3.1	4.6	2.9	3.1	4.0	4.0	4.3 (3.6, 5.3)	<5.3	5.3–10.4	≥10.5	*4.4*	*acceptable*	12.5
Total protein	Accuracy (%bias)	−0.27	−0.12	0.46	−0.24	−0.14	−0.28	0.19	−0.07	−0.39	1.59	−0.58	1.78	−0.13 (−0.26, 0.06)				*3.21*		
	Precision (CV%)	1.4	1.0	0.9	1.5	2.0	1.6	1.4	1.5	1.5	1.6	1.0	1.3	1.5 (1.4, 1.5)				*1.3*		
	Total Error (%)	3.0	2.1	2.2	3.2	4.1	3.4	2.9	3.0	3.3	4.7	2.5	4.3	3.1 (3.0, 3.4)	<3.4	3.4–6.6	≥6.7	*5.8*	*Borderline*	5.0
Albumin	Accuracy (%bias)	−2.43	−0.75	0.45	−1.12	0.64	0.12	−0.06	0.11	1.05	−0.28	−1.14	0.46	0.03 (−0.52, 0.29)				*5.19*		
	Precision (CV%)	1.7	1.3	2.0	1.8	1.9	1.2	1.6	1.1	0.9	1.2	1.0	1.2	1.3 (1.2, 1.6)				*1.0*		
	Total Error (%)	5.8	3.3	4.4	4.6	4.4	2.5	3.2	2.3	2.8	2.6	3.1	2.8	3.1 (2.8, 3.8)	<3.8	3.8–7.6	≥7.7	*7.1*	*Borderline*	5.0
Creatinine	Accuracy (%bias)	−2.24	1.93	−0.08	−0.34	0.15	0.19	−0.76	−0.55	−0.76	−1.25	−0.54	−4.18	−0.55 (−0.76, −0.21)				*−2.77*		
	Precision (CV%)	1.5	2.6	3.7	2.0	1.9	2.3	1.8	2.3	1.7	2.3	1.3	1.8	2.0 (1.8, 2.3)				*1.7*		
	Total Error (%)	5.1	7.1	7.2	4.3	3.9	4.8	4.3	5.0	4.1	5.8	3.1	7.7	4.9 (4.3, 5.5)	<5.5	5.5–10.8	≥10.9	*6.1*	*Borderline*	7.5
Glucose	Accuracy (%bias)	0.42	−0.58	−0.39	−0.31	0.17	−0.06	0.76	0.53	−0.83	−0.04	0.01	−0.74	−0.05 (−0.35, 0.09)				*−0.47*		
	Precision (CV%)	1.4	1.0	1.7	1.2	1.4	1.4	1.4	1.5	1.5	0.8	0.8	1.0	1.4 (0.8, 0.8)				*1.1*		
	Total Error (%)	3.1	2.5	3.7	2.7	3.0	2.7	3.5	3.5	3.8	1.6	1.6	2.7	2.9 (2.7, 3.3)	<3.3	3.3–6.5	≥6.6	*2.6*	*acceptable*	5.0
γ-GT (γ-GTP)	Accuracy (%bias)	0.74	−0.01	−0.24	0.82	0.37	−0.13	−0.48	−0.83	−1.50	0.45	−0.75	−1.04	−0.19 (−0.62, 0.18)				*−1.39*		
	Precision (CV%)	1.8	1.8	1.6	1.7	2.3	1.3	2.0	2.1	1.9	2.0	2.5	2.1	2.0 (1.8, 2.1)				*1.8*		
	Total Error (%)	4.2	3.5	3.4	4.2	4.8	2.7	4.4	5.0	5.2	4.4	5.7	5.2	4.4 (4.2, 4.9)	<4.9	4.9–9.7	≥9.8	*4.9*	*acceptable*	7.5
Uric acid	Accuracy (%bias)	0.21	−0.59	−0.43	0.25	−0.26	0.81	−0.44	0.88	−0.44	−0.56	0.31	1.26	−0.03 (−0.44, 0.28)				*1.11*		
	Precision (CV%)	2.1	2.1	1.4	1.5	1.4	1.4	1.8	1.5	1.6	1.1	1.3	1.6	1.5 (1.1, 1.1)				*1.1*		
	Total Error (%)	4.4	4.8	3.2	3.2	3.1	3.6	4.0	3.8	3.6	2.7	2.9	4.4	3.6 (3.2, 3.9)	<3.9	3.9–7.7	≥7.8	*3.3*	*acceptable*	8.5
Urea nitrogen	Accuracy (%bias)	−1.69	0.16	0.25	1.74	−0.17	0.75	−0.33	0.69	−2.86	—	—	1.58	0.21 (−0.25, 0.69)				*not assayed*		
	Precision (CV%)	1.3	1.2	1.2	1.7	1.8	1.1	1.9	1.4	1.5	—	—	1.5	1.5 (1.3, 1.6)				*not assayed*		
	Total Error (%)	4.3	2.6	2.7	5.1	3.7	3.0	4.1	3.4	5.8	—	—	4.5	3.9 (3.3, 4.4)	<4.4	4.4–8.7	≥8.8	*not assayed*		4.5
AST (GOT)	Accuracy (%bias)	3.03	−0.43	0.21	−0.07	1.37	0.59	−0.60	0.25	−1.25	0.51	0.71	0.64	0.38 (0.07, 0.62)				*−0.37*		
	Precision (CV%)	1.7	1.8	1.3	1.1	2.1	1.4	1.9	1.5	2.2	1.5	1.6	2.2	1.7 (1.5, 1.9)				*1.8*		
	Total Error (%)	6.3	4.0	2.7	2.3	5.5	3.4	4.4	3.3	5.6	3.5	3.8	5.0	3.9 (3.4, 4.6)	<4.6	4.6–9.2	≥9.3	*3.9*	*acceptable*	10.0
ALT (GPT)	Accuracy (%bias)	2.81	−0.22	0.38	−1.43	−0.08	1.48	1.06	−0.64	−1.47	0.95	0.88	0.37	0.38 (−0.15, 0.92)				*−1.12*		
	Precision (CV%)	1.4	1.7	1.4	1.4	2.3	1.5	2.3	2.2	2.2	1.6	1.8	2.2	1.8 (1.6, 2.2)				*2.3*		
	Total Error (%)	5.5	3.6	3.2	4.2	4.5	4.4	5.5	4.9	5.8	4.1	4.4	4.7	4.5 (4.3, 4.8)	<4.8	4.8–9.5	≥9.6	*5.6*	*Borderline*	10.0
HbA_1c	Accuracy (%bias)	—	—	−0.39	0.52	0.01	2.25	1.01	1.28	−0.34	−1.08	−0.14	−0.26	−0.07 (−0.30, 0.52)				*0.12*		
	Precision (CV%)	—	—	1.1	1.1	1.0	1.2	1.1	1.0	1.4	1.2	1.4	1.6	1.2 (1.1, 1.3)				*2.0*		
	Total Error (%)	—	—	2.5	2.7	2.0	4.6	3.2	3.2	3.1	3.4	2.9	3.4	3.1 (2.8, 3.3)	<3.3	3.3–6.5	≥6.6	*4.0*	*Borderline*	

Accuracy as an index of systematic error is expressed as %bias calculated based on JMA criteria.
Precision as an index of random error is expressed as CV calculated from SRL internal quality control data.
Total error is calculated as the sum of accuracy and precision, ie, absolute value of %bias + 1.96 × CV.
Abbreviations: JMA, Japan Medical Association; CAP, College of American Pathologists; TE, total error; LL, lower limit; UL, upper limit; CL, confidence limit; HDL, high-density lipoprotein; LDL, low-density lipoprotein; γ-GT (γ-GTP), γ-glutamyl transpeptidase; AST (GOT), aspartate aminotransferase; ALT (GPT), alanine aminotransferase; HbA1c, hemoglobin A1c.

Table 3. SRL performance based on CDC/CRMLN Lipid Standardization Program (unit, %)

Analyte	Performance	CDC Criteria	Year												Average	SD
			1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010		
Total cholesterol	Accuracy (%bias)	±3.0	0.00	−1.30	0.00	−0.90	0.30	−0.10	−0.90	−0.90	−0.90	−0.30	−0.50	0.10	−0.45	0.52
	Precision (CV%)	3.0	0.5	0.6	0.6	0.5	0.5	0.6	0.4	0.4	0.4	0.5	0.4	0.3	0.48	0.10
	Total Error (%)	9.0	1.0	2.5	1.2	1.9	1.3	1.4	1.7	1.7	1.7	1.3	1.3	0.8	1.48	0.45
HDL cholesterol	Accuracy (%bias)	±5.0	0.70	0.70	2.00	2.00	1.00	1.00	1.20	1.20	1.20	−1.00	0.00	0.00	0.83	0.85
	Precision (CV%)	4.0	1.0	1.0	1.3	1.3	1.7	1.7	1.1	1.1	1.1	1.0	0.7	0.7	1.14	0.32
	Total Error (%)	13.0	2.7	2.7	4.6	4.6	4.4	4.4	3.4	3.4	3.4	3.0	1.4	1.4	3.28	1.12
LDL cholesterol	Accuracy (%bias)	±4.0				−0.60	−0.60	−0.70	−0.70	0.30	0.30	1.70	−1.40	−1.40	−0.34	0.98
	Precision (CV%)	4.0				1.2	1.2	0.7	0.7	0.4	0.4	0.6	0.6	0.6	0.71	0.30
	Total Error (%)	12.0				3.0	3.0	2.1	2.1	1.1	1.1	2.9	2.6	2.6	2.28	0.75

Accuracy as an index of systematic error is expressed as %bias calculated based on CDC criteria.
Precision as an index of random error is expressed as CV calculated based on lipid standardization criteria of CDC.
Total error is calculated as the sum of accuracy and precision, ie, absolute value of %bias + 1.96 × CV.
Abbreviations: CDC, Centers for Disease Control and Prevention; CRMLN, Cholesterol Reference Method Laboratory Network; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

criteria, the evaluation was acceptable for 7 items (53.8%)—TC, LDL-C, triglycerides, glucose, γ-GT (γ-GTP), uric acid, and AST (GOT)—and borderline for 6 items (46.2%), namely, HDL-C, total protein, albumin, creatinine, ALT (GPT), and HbA_1c. No item was evaluated as unacceptable (Table 2).

Table 3 shows the measurement performance of SRL for TC, HDL-C, and LDL-C, based on the criteria of the Lipid Standardization Program by CDC/CRMLN. In each standardization year, performance satisfied the CDC/CRMLN criteria for clinical laboratories.

DISCUSSION

In standardization—the most advanced system of quality control assessment—target values are obtained by using globally accepted definitive or reference measurement procedures. However, in the EQACL, measurement values are collected from all participants and, after statistical analysis, adjusted mean values are obtained and used as an index of accuracy. A similar data processing method is used in external quality control assurance programs in Western countries.[14,15] This method statistically excludes extreme outliers and misreports, which improves the reliability of adjusted mean values as indices of accuracy. Such adjusted means do not represent physicochemical accuracy, as such, but are often used for practical purposes as consensus values in clinical surveys. Consensus values are often used as a substitute for accuracy when there is no established reference method, or when a reference method exists but is not used due to its complexity or technical difficulty. In this respect, we have no objection to the use of consensus values at many laboratories, such as those derived from approximately 3000 participants in the EQACL of the JMA.[5]

The sources of error in measured values include changes in: the underlying principles of the measurement method, analytic devices, sample status (fresh, frozen), reagents or reagent reactivity, calibrators and their value assignments, the skill of analytical technologists, and other laboratory conditions.[1,2,5,6] Measurement error can result in clinical examination-derived discontinuities with previously obtained results in surveys (such as retrospective case-control studies), which could markedly affect annual follow-up. In this study, we conducted detailed follow-up surveys of these factors to avoid discontinuities derived from clinical examinations. A disadvantage of using the mean value of an external quality assessment as an index of accuracy is that the method routinely used during each period has a direct influence on measurement values. For example, when an analytic method based on new measurement principles is developed and adopted at clinical laboratories, due to convenience and/or cost and time savings, changes in mean value are sometimes observed along with analytic errors.

Case 1: The routine analytic method for HDL-C changed from a precipitation method using polyanions and cations to a homogeneous method using detergent or surfactant. The new method has been adopted by many laboratories, and age-related changes in mean HDL-C values have been reported since the switch. In this former case, changes in mean HDL-C values were observed and, as a consequence, analytic errors change.[16–19]

Case 2: There has been increasing demand for more-precise creatinine analysis for people with diabetes mellitus and renal disorders, and the calibrator is changing from the old, water-soluble standard to a new serum-based reference material with high accuracy, as confirmed by gas chromatography/isotope dilution/mass spectrometry. Additionally, in many laboratories the creatinine method has changed from the classic Jaffe method to newly developed enzymatic methods. Changes in mean creatinine values have been observed with these new methods and, inevitably, analytic errors also change.[20,21]

The survey protocol agreed by the Ministry of Health, Labour, and Welfare in Japan and SRL stipulates that the same analytic system for the NHNS (BioMajesty 8060 device No. 1, JEOL Ltd.; installed in the SRL Medical Ultimate Quality Service [MUQS] Laboratory) should also be used for blood examinations that are independently entrusted by prefectures to SRL. This protocol allows PHNS and NHNS results to be monitored in the same manner and permits PHNS data to be added to NHNS. The sample numbers of the PHNS are generally larger than those of the NHNS. However, there are 2 limitations in the use of PHNS data: the measured items differ according to prefecture, and it is possible that the analytic laboratory was changed from SRL to a local laboratory or from a local laboratory to SRL. Therefore, before using PHNS results as additional data, the laboratory responsible for the results should be confirmed. In this study, only samples measured by SRL were included.

In this study, on the basis of quality control results, target TE values for the subsequent 5 years were determined. Specifically, the acceptable limit was defined as the upper 80% confidence limit of TE. TE values above this limit were considered to be in the borderline or unacceptable range, and a caution was issued. The probability of including borderline or unacceptable ranges using these target values remains at 10% even if performance remains equal to that during the previous 12-year period. Assuming annual improvements in performance, approximately 50% of TE values in the subsequent 5-year period are expected to be within the acceptable range. In quality control, there are no absolute criteria for quality, and quality is improved by daily efforts to repeatedly establish and meet criteria. Our monitoring system uses past data to establish target values for a subsequent 5-year period, and adjustments are made by revising target values at 5-year intervals. The system is thus compatible with the idea of quality control. The TE limit for the acceptable and borderline ranges was established for monitoring during 2011–2015, not for its application to past data. Application to the year 2011 (Table 2) confirms the suitability of the proposed TE criteria. When TE falls within the acceptable or borderline ranges, annual continuity and comparability of survey results can be regarded as satisfactory. However, when TE falls within the unacceptable range, measurement values should be used with caution.

Precision is an index of the reproducibility of measurement values obtained by a laboratory. In this study, since TE was calculated using an equation, CV was limited to a singlicate value ($n = 1$) in internal quality control sera for 20 days. CV was calculated from 2 types of commercially available internal quality control serum in SRL. However, if there was a difference of 10% or more in CV between the concentrations of internal quality control materials, the higher CV was used.[7]

In lipid standardization by CDC/CRMLN,[12] the accuracy, precision, and TE for SRL measurements of TC, HDL-C, and LDL-C met CDC criteria (Table 3) for clinical laboratory use. Therefore, concerning these 3 lipid items, all results in the NHNS and the results in some PHNS can be compared with results in Western countries. However, only results obtained during the previous 9-year period are available for LDL-C, and it is desirable to use these results as a reference.

In conclusion, we used TE criteria to develop a revised 3-level assessment of test performance and evaluated the continuity and comparability of 14 blood chemistry items assayed at SRL for the NHNS and PHNS in Japan. To further improve reliability, TE performance criteria should be updated every 5 years.

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ONLINE ONLY MATERIALS

The Japanese-language abstract for articles can be accessed by clicking on the tab labeled Supplementary materials at the journal website http://dx.doi.org/10.2188/jea.JE20120032.

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