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Reviewers' Summary Evaluations

Reviewer 1

This epidemiological investigation is a case-control study on the risk factors for sudden cardiac death (SCD) in 239 cases. Hypertension, diabetes mellitus, increased heart rate, and other traditional factors were associated with a higher risk for SCD.

The study provides previously unavailable data on victims of SCD among Japanese subjects living in Japan and contributes to a better picture of the risk factors for SCD around the world. Its major limitation is the absence of post-mortem examinations. This has two major consequences: the non-cardiac causes of sudden death cannot be identified and it is impossible to distinguish between sudden deaths due to a coronary or non-coronary cause.

Reviewer 2

The study was conducted before the introduction of public-access defibrillation and confirms a lower incidence of sudden death in Japan as compared to USA in the last 30 years. Unfortunately the lack of autopsy data, mainly in out of the hospital (37%) or non-witnessed deaths (45%), does not allow the distinction between coronary and non coronary death. Among all risk factors (non including family history for sudden death) the relevant role of ECG alterations, including LVH (high amplitude R waves in left anterior chest lead) and major ST-T abnormalities, is clearly shown by the independent association with a significant increase in the risk of sudden death.

千葉県における特定健康診査標準的質問表から得られる生活習慣とメタボリック症候群との関連性の検討

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目的　特定健診標準的質問項目のうち生活習慣に関する質問の回答と翌年の特定健診結果によるメタボリック症候群（MetS）罹患との関連性を検証した。

方法　千葉県内全54市町村国保から匿名化して提供を受けた平成20年度と21年度の特定健診連続受診者278,989人（男性111,524人，女性167,465人）の結果を用いた。標準的質問表のうち生活習慣に関する質問（10項目）は，運動「歩行速度が速い」，「運動習慣あり」，「身体活動あり」，食習慣「早食いである」，「夜食・間食あり」，「夕食後2時間以内に就寝」，「朝食抜き」，喫煙「習慣的な喫煙あり」，飲酒「毎日飲酒する」，睡眠「睡眠で休養十分」であり，平成20年度の回答で2値化し，「NO」に対する「YES」の年齢調整オッズ比を求めた。横断研究は，平成20年度にMetS群（MetS該当または予備群）とMetS非該当群との間で，縦断研究は，平成20年度MetS非該当者で平成21年度MetS予備群または該当群になった者をMetS罹患者と定義し，MetS罹患者と平成21年度も引き続きMetS非該当者との間で行った。また，MetS判定を従属変数として多変量ロジスティック回帰分析を行った。

結果　横断研究と同様に縦断研究でも，男性は「歩行速度が速い」（OR：0.88, 95％CI：0.83–0.93），「身体活動あり」（0.85, 0.80–0.90）が予防因子，「早食いである」（1.49, 1.40–1.59），「夜食・間食あり」（1.15, 1.05–1.27），「夕食後2時間以内に就寝」（1.15, 1.08–1.23），「毎日飲酒する」（1.08, 1.02–1.14）が危険因子となった。女性では「歩行速度が速い」（0.74, 0.70–0.78），「身体活動あり」（0.92, 0.87–0.98），「毎日飲酒する」（0.80, 0.71–0.90）が予防因子，「早食いである」（1.48, 1.39–1.58），「夜食・間食あり」（1.15, 1.05–1.26），「夕食後2時間以内に就寝」（1.19, 1.10–1.29），「朝食抜き」（1.21, 1.07–1.36）が危険因子となった。横断研究のみ有意であった項目は，予防因子として，男性の「運動習慣あり」，「習慣的な喫煙あり」，女性の「運動習慣あり」が，危険因子としては，男性の「朝食抜き」，「睡眠で休養十分」，女性の「睡眠で休養十分」が該当した。

結論　標準的質問項目で把握される不適切な運動習慣や食習慣がMetSの罹患につながることを示した結果であり，本質問表の有用性が示された。

Key words：メタボリック症候群，特定健康診査，国民健康保険，標準的質問項目，千葉県

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Ⅰ　緒　　言

現在の日本の状況は，40～74歳では，男性の2人に1人，女性の5人に1人が，メタボリック症候群（MetS）が強く疑われる者またはMetS予備群の者であり[1]，MetS予防対策は国民的課題であるとされている。このため，国は平成20年度より特定健康診査（特定健診）・特定保健指導を各医療保険者に義務付けした。千葉県では平成22年度より「特定健診・特定保健指導に係るデータ収集，評価・分析事業」を開始した。県内全54市町村国民健康保険加入者に対する特定健診データを収集し，分析することにより効果的なMetS予防施策を提言し，実施し，評価することを目標にしている。

生活習慣とMetSの関連を検討した先行研究[2]は多数みられるが，特定健診の標準的質問表の項目とMetSとの関連を網羅的に調査した報告は少ない。単一健保組合（対象人数3,879人）を対象とした先行研究[3]によると，男性は食べる速さと歩行速度，女性は食べる速さがMetSに関連していたことが示されている。そこで，本研究では千葉県内全54市町村国民健康保険加入者（対象人数278,989人）に対するデータを用いて，特定健診標準的質問表のうち生活習慣に関する質問とMetSとの関連性を検証した。

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Ⅱ　研究方法

県下全54市町村から，平成20年度以降の市町村国保の特定健康診査等の結果を千葉県へ提供することについて同意を得た。収集データは，国への法定報告の内容から必要な項目を抽出し，千葉県国民健康保険団体連合会（以下，国保連合会という。）を通して国に報告を行う市町村については国保連合会から，国保連合会を通さずに国に報告を提出する2市については，各市から電子的にデータの提供を受けた。

健診データの経年的な変化については，個人データを連結して分析するため，氏名等の個人情報をもとに連結可能匿名化IDを作製するプログラムを県で開発した[4]。このプログラムを，電子データを作製する国保連合会と2市に提供し，それぞれの機関において，個人識別情報をもとに連結可能匿名化IDを付与し，個人識別情報を削除した電子データの作成を依頼した。

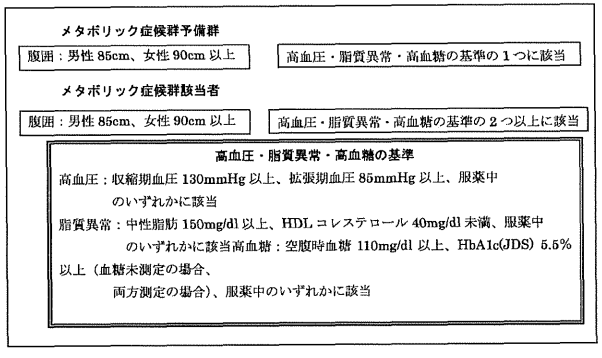
各市町村保険者から収集した特定健診データは，性，年齢，身体計測値（身長，体重，BMI，腹囲），理学的検査（身体診察所見），血圧，脂質検査（中性脂肪，HDLコレステロール，LDLコレステロール），血糖検査（空腹時血糖，ヘモグロビンA1c（JDS）（以下，HbA1cと記載）），標準的質問項目（22問）である[5]。

収集したデータ数は，平成20年度405,921人（男性166,648人，女性239,273人），平成21年度400,342人（男性164,833人，女性235,509人）であった。本研究では，このうち平成20年度と21年度に連続受診した278,989人（男性111,524人，女性167,465人）分を対象とした。

「標準的な健診・保健指導プログラム（確定版）」[6]に定められた基準（図1）をもとに判定を行った。血糖の判定に当たり，血糖とHbA1c測定を併用している場合は，HbA1cを優先して採用した。空腹時血糖値に関しては，本研究では採血が食後10時間以内か否かの確認はできていない。服薬情報は特定健診時の標準的質問項目を用いた。

各市町村により標準質問項目使用に差があるため，解析は連続受診者で下記の10項目すべてに回答した183,629人（男性73,698人，女性109,931人）を対象とした。標準的質問表のうち生活習慣に関する質問（10項目）は，運動「歩行速度が速い」，「運動習慣あり」，「身体活動あり」，食習慣「早食いである」，「夜食・間食あり」，「夕食後2時間以内に就寝」，「朝食抜き」，喫煙「習慣的に喫煙する」，飲酒「毎日飲酒する」，睡眠「睡眠で休養が十分」とした。平成20年度の回答で2値化し，男女別に，「NO」に対する「YES」の年齢階級別オッズ比とMantel-Haenszel推定値を求めた。横断研究は，平成20年度にMetS群（MetS該当または予備群）とMetS非該当群との間で，縦断研究は，平成20年度MetS非該当者で平成21年度MetS予備群または該当群になった者をMetS罹患者と定義し，MetS罹患者と平成21年度も引き続きMetS非該当者との間

図1　メタボリック症候群（MetS）判定基準



で行った。さらに，対象者をMetS群（1）と非該当（0）に分けて従属変数とし，生活習慣に関する質問10項目と年齢階級を独立変数として，男女別に多変量ロジスティック回帰分析（尤度比による変数減少法）を行った。独立変数の基準は生活習慣に関する質問ごとに「あり」と答えた人とした。年齢階級は，平成20年度の年齢で40～49歳，50～59歳，60～69歳，70～74歳の4群に分け，40～49歳を基準としてダミー変数化した。欠損値については，それぞれの項目において除外した。

統計解析にはIBM SPSS for Windows Ver. 16.0を使用した。

本研究は，千葉県衛生研究所疫学倫理審査委員会の承認を受けて行った（受付番号20）。

Ⅲ　研究結果

表1に性・年齢階級別にみた平成20年度21年度連続受診者数を，表2に，連続受診者の体重，BMI，腹囲，収縮期血圧，拡張期血圧，中性脂肪，HDLコレステロール，LDLコレステロール，空腹時血糖，HbA1cの平均，標準偏差を示した。空腹時血糖を除くすべての項目が有意に減少していたが，その減少幅はわずかであった。表3に平成20年度と平成21年度のMetS群の人数と割合を示した。女性は有意にMetS割合が減少していたが，減少幅はごくわずかであった。男性は有意差がなかった。

表4に性別にみた平成20年度の生活習慣に関する質問の回答状況を，表5に横断研究の結果を示した。

男女とも「歩行速度が速い」，「運動習慣あり」，「身体活動あり」が全年齢階級で予防因子となった。Mantel-Haenszel推定量を求めると男女とも「歩行速度が速い」，「運動習慣あり」，「身体活動あり」が予防因子となった。ロジスティック回帰分析の結果も同じであった。また，男性では「早食いである」，「夜食・間食あり」，「夕食後2時間以内に就寝」が全年齢階級で危険因子となった。女性では「早食いである」，「夜食・間食あり」，「朝食抜き」が全年齢階級で危険因子となった。Mantel-Haenszel推定量を求めると男女とも「早食いである」，「夜食・間食あり」，「夕食後2時間以内に就寝」，「朝食を抜く」が危険因子となった。ロジスティック回帰分析の結果も同じであった。「毎日飲酒する」は，男性は危険因子，女性は予防因子となった。「習慣的に喫煙する」は，男性が予防因子，女性がMantel-Haenszel推定量のみ危険因子となった。「睡眠で休養が十分」は男性がロジスティック回帰分析のみ危険因子となったが，女性はMantel-Haenszel推定量が予防因子，ロジスティック回帰分析が危険因子となった。

表6に平成20年度にMetS非該当者の生活習慣に関する質問の回答状況を，表7に縦断研究の結果を男女別に示した。

「歩行速度が速い」が女性のみ全年齢階級で予防因子となった。Mantel-Haenszel推定量を求めると男女とも「歩行速度が速い」，「身体活動あり」，「運動習慣あり」が予防因子となった。ロジスティック回帰分析では「歩行速度が速い」「身体活動あり」のみ予防因子となった。また，「早食いである」が男女とも，「夕食後2時間以内に就寝」が女性のみ全年齢階級で危険因子となった。Mantel-Haenszel推定量を求めると「早食いである」，「夜食・間食あり」，「夕食後2時間以内に就寝」は男女とも，「朝食を抜く」は女性でのみ危険因子となった。ロジスティック回帰分析の結果も同じであった。「毎日飲酒する」は，男性では危険因子，女性では予防因子となった。「睡眠で休養が十分」は統計的有意差が認められなかった「習慣的に喫煙する」は女性のみMantel-Haenszel推定量で危険因子となったが，ロジスティック回帰分析では有意ではなかった。

表1　性・年齢階級別にみた平成20年度21年度連続受診者数

	40～49歳	50～59歳	60～69歳	70～74歳[a]	合　計
男性	7,215	12,154	59,440	32,715	111,524
女性	8,909	24,140	96,513	37,903	167,465
合計	16,124	36,294	155,953	70,618	278,989

年齢は平成20年度の年齢で表示
a：H20年度に74歳の人は翌年対象外になるので，人数には含まれていない

表3　メタボリック症候群（MetS）と判定された人数

	MetS該当群またはMetS予備群と判定された人数（割合）*		P値 a)とb)の比較 χ^2乗検定
	平成20年度[a)]	平成21年度[b)]	
男性	43,967(41.5%)	43,482(41.0%)	0.363
女性	24,943(15.8%)	24,476(15.5%)	0.022

*：割合は判定不能者を除いて計算している

表2　平成20年度21年度連続受診者の検査成績

項　目	人　数	平均±SD		変化量[a]	P値
		H20	H21		
体重（kg）	278,989	57.24±10.27	57.05±10.27	−0.19	$P<0.001^b$
BMI（kg/m^2）	278,912	22.90±3.19	22.86±3.18	−0.04	$P<0.001^b$
腹囲（cm）	278,806	82.88±8.99	82.81±8.96	−0.06	$P<0.001^b$
収縮期血圧（mmHg）	278,968	129.9±17.1	129.2±16.9	−0.7	$P<0.001^b$
拡張期血圧（mmHg）	278,923	76.8±10.6	76.1±10.3	−0.7	$P<0.001^b$
中性脂肪（mg/dL）	278,961	119.9±77.2	117.6±74.3	−2.3	$P<0.001^c$
HDLコレステロール（mg/dL）	278,965	63.8±16.7	63.2±16.4	−0.6	$P<0.001^b$
LDLコレステロール（mg/dL）	278,892	126.8±30.2	125.4±29.8	−1.4	$P<0.001^b$
空腹時血糖（mg/dL）	141,235	96.5±18.0	96.5±17.9	0.0	0.221^b
HbA1c（JDS）(%)	222,950	5.353±0.634	5.348±0.625	−0.005	$P<0.001^b$

a：H21の検査値−H20の検査値
b：対応あるt検定
c：対応のあるwilcoxonの符号付き順位検定

表4　性別にみた平成20年度における標準的質問表の回答状況とメタボリック症候群（MetS）判定

生活習慣		あてはまる人の数	MetS群 あてはまる人の数と割合	MetS非該当 あてはまる人の数と割合
同年齢同性と比較して歩行速度が速い	男	40,708	16,207(51.9%)	24,501(57.7%)
	女	57,342	7,561(42.2%)	49,781(54.1%)
1年以上週2回30分以上の運動習慣あり	男	35,551	14,422(46.2%)	21,129(49.8%)
	女	44,797	6,719(37.5%)	38,006(41.3%)
1日1時間以上歩行と同等の身体活動あり	男	41,772	16,582(53.1%)	25,190(59.3%)
	女	58,162	8,772(48.9%)	49,390(53.7%)
睡眠で休養が十分とれている	男	60,648	25,805(82.6%)	34,843(82.1%)
	女	82,177	13,422(74.9%)	68,755(74.7%)
人と比較して早食いである	男	21,128	10,736(34.4%)	10,392(24.5%)
	女	25,430	5,754(32.1%)	19,676(21.4%)
週3回以上夜食・間食あり	男	6,566	3,073(9.8%)	3,493(8.2%)
	女	11,466	2,188(12.2%)	9,278(10.1%)
週3回以上夕食後2時間以内に就寝	男	18,040	8,261(26.4%)	9,779(23.0%)
	女	15,055	3,049(17.0%)	12,006(13.0%)
週3回以上朝食を抜く	男	5,998	2,678(8.6%)	3,320(7.8%)
	女	6,524	1,168(6.5%)	5,356(5.8%)
毎日飲酒する	男	34,256	14,979(48.0%)	19,277(45.4%)
	女	8,607	1,163(6.5%)	7,444(8.1%)
現在，たばこを習慣的に吸っている	男	19,019	7,837(25.1%)	11,182(26.3%)
	女	6,183	951(5.3%)	5,232(5.7%)
有効人数（全て回答した人）	男	73,698	31,238	42,460
	女	109,931	17,922	92,009

表5　年齢階級別オッズ比（横断研究）

性別	生活習慣	40～49歳			50～59歳			60～69歳			70～74歳			Mantel-Haenszel 推定量			Logistic regression[a]		
		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間	
			下限	上限		下限	上限		下限	上限		下限	上限		下限	上限		下限	上限
男	歩行速度速い	0.87	0.77	0.97	0.85	0.78	0.93	0.77	0.74	0.80	0.78	0.74	0.83	0.79	0.76	0.81	0.79	0.77	0.82
	運動習慣あり	0.75	0.65	0.85	0.88	0.80	0.97	0.82	0.79	0.85	0.89	0.85	0.94	0.84	0.82	0.87	0.95	0.92	0.98
	身体活動あり	0.71	0.63	0.80	0.73	0.67	0.80	0.75	0.72	0.78	0.81	0.77	0.86	0.76	0.74	0.78	0.80	0.78	0.83
	睡眠で休養十分	0.91	0.80	1.03	1.03	0.93	1.13	0.98	0.93	1.04	1.15	1.07	1.25	1.02	0.98	1.06	1.11	1.07	1.16
	早食いである	1.81	1.60	2.04	1.80	1.64	1.98	1.59	1.52	1.66	1.64	1.54	1.75	1.64	1.59	1.66	1.67	1.61	1.72
	夜食・間食あり	1.37	1.18	1.59	1.29	1.13	1.47	1.26	1.17	1.36	1.12	1.01	1.25	1.25	1.18	1.31	1.18	1.12	1.25
	夕食後2時間以内就寝	1.16	1.03	1.31	1.22	1.11	1.34	1.24	1.18	1.30	1.19	1.12	1.27	1.22	1.18	1.26	1.16	1.12	1.20
	朝食抜き	1.08	0.95	1.24	1.19	1.05	1.34	1.18	1.09	1.28	1.13	0.99	1.29	1.16	1.10	1.22	1.08	1.02	1.14
	毎日飲酒	0.88	0.78	0.99	1.03	0.94	1.13	1.11	1.07	1.15	1.19	1.13	1.26	1.11	1.08	1.14	1.13	1.09	1.16
	習慣的な喫煙あり	1.03	0.91	1.16	0.94	0.86	1.03	0.96	0.92	1.01	0.92	0.86	0.99	0.96	0.92	0.99	0.92	0.89	0.95
女	歩行速度速い	0.55	0.45	0.68	0.58	0.53	0.64	0.60	0.57	0.63	0.60	0.57	0.64	0.60	0.58	0.62	0.61	0.59	0.63
	運動習慣あり	0.71	0.53	0.94	0.84	0.75	0.93	0.78	0.75	0.82	0.79	0.74	0.84	0.79	0.76	0.82	0.91	0.87	0.94
	身体活動あり	0.62	0.50	0.77	0.75	0.68	0.82	0.80	0.76	0.83	0.78	0.73	0.83	0.78	0.76	0.81	0.90	0.87	0.93
	睡眠で休養十分	0.87	0.72	1.07	0.90	0.81	0.99	0.97	0.92	1.01	0.98	0.91	1.06	0.96	0.92	0.99	1.07	1.03	1.11
	早食いである	2.02	1.65	2.47	1.81	1.64	2.01	1.84	1.76	1.93	1.68	1.56	1.80	1.80	1.74	1.86	1.84	1.78	1.91
	夜食・間食あり	1.34	1.06	1.69	1.48	1.31	1.67	1.33	1.24	1.42	1.39	1.24	1.54	1.37	1.30	1.44	1.19	1.13	1.26
	夕食後2時間以内就寝	1.06	0.84	1.35	1.59	1.42	1.79	1.44	1.35	1.53	1.31	1.20	1.42	1.40	1.34	1.47	1.31	1.26	1.38
	朝食抜き	1.02	0.78	1.33	1.20	1.02	1.40	1.30	1.19	1.43	1.45	1.25	1.67	1.29	1.21	1.38	1.15	1.07	1.23
	毎日飲酒	0.75	0.55	1.01	0.75	0.63	0.88	0.88	0.81	0.95	0.94	0.82	1.08	0.86	0.81	0.92	0.86	0.80	0.92
	習慣的な喫煙あり	1.07	0.83	1.37	0.99	0.84	1.16	1.13	1.02	1.25	1.19	1.01	1.40	1.11	1.03	1.19			

a：多変量ロジスティック回帰分析（尤度比による変数減少法）

表6　平成20年度の生活習慣に関する質問の回答と21年度のメタボリック症候群（MetS）罹患（縦断研究）

生活習慣		あてはまる人			あてはまらない人		
		有効N数	罹患数[a]	%	有効N数	罹患数[a]	%
同年齢同性と比較して歩行速度が速い	男	24,501	3,233	13.2	17,959	2,647	14.7
	女	49,781	2,466	5.0	42,228	2,702	6.4
1年以上週2回30分以上の運動習慣あり	男	21,129	2,848	13.5	21,331	3,032	14.2
	女	38,006	2,142	5.6	54,003	3,026	5.6
1日1時間以上歩行と同等の身体活動あり	男	25,190	3,274	13.0	17,270	2,606	15.1
	女	49,390	2,653	5.4	42,619	2,515	5.9
睡眠で休養が十分とれている	男	34,843	4,795	13.8	7,617	1,085	14.2
	女	68,755	3,860	5.6	23,254	1,308	5.6
人と比較して早食いである	男	10,392	1,882	17.5	32,068	4,058	12.7
	女	19,676	1,421	7.2	72,333	3,747	5.2
週3回以上夜食・間食あり	男	3,493	553	15.8	38,967	5,327	13.7
	女	9,278	578	6.3	82,731	8,691	5.5
週3回以上夕食後2時間以内に就寝	男	9,779	1,513	15.5	32,681	4,367	13.4
	女	12,006	786	6.5	80,003	4,382	5.5
週3回以上朝食を抜く	男	3,320	479	14.4	39,140	5,401	13.8
	女	5,356	334	6.2	86,653	4,834	5.6
毎日飲酒する	男	19,277	2,766	14.3	23,183	3,114	13.4
	女	7,444	322	4.3	84,565	4,846	5.7
現在，習慣的にたばこを吸っている	男	11,182	1,518	13.6	31,278	4,362	13.9
	女	5,232	284	5.4	86,777	4,884	5.6

a：H20年にMetS非該当であった人がH21年にMetS該当またはMetS予備群になった人

Ⅳ　考　　察

本研究は，千葉県内の全54市町村国民健康保険加入者の特定健診データのうち平成20年度21年度連続受診者278,989人の連結データを使用して行われた。このような網羅的かつ大量のデータセットを用いて，質問項目を検証した研究はこれが初めてである。

健康づくりのための運動指針[7]によると，通常歩行（平地67 m/分）が3メッツに対して速歩（平地95～100 m/分）は4メッツとなり，歩行速度が上がると運動強度が増すことが分かっている。また，運動に関する質問項目の回答によって，比較的健康な一般成人の身体活動状況をある程度推定することができると報告[8]されている。これらのことから，運動に関する質問項目にあてはまる人はあてはまらない人に比べて日常の身体活動量が多いと推定されて採用されている項目である。「歩行速度が速い」「身体活動あり」の項目は，本研究によりMetS判定だけでなくMetS罹患への寄与が統計的に示されたことから，これらの運動に関する質問項目は特定健診に用いる有用性があると考える。「運動習慣あり」もMetS判定への寄与が統計的に示されたことから，特定健診に用いることが望ましい。

平成9年国民栄養調査[9]によると，肥満者は普通体重の者に比べ，夕食以後に間食をすることが多い。また，食べる速さと肥満度（BMI）には関連がみられるという報告[10～12]がある。これらのことから，食習慣とMetSは関連が深いことが推定されて採用されている項目である。男性の「朝食抜き」回答を除き，本研究によりMetS判定だけでなくMetS罹患への寄与が統計的に示されたことから，これらの食習慣に関する質問項目は特定健診に用いる妥当性があると考える。男性の「朝食抜き」回答もMetS判定への寄与が統計的に示されたことから，特定健診に用いることが望ましい。

先行研究によると，飲酒や喫煙はそれぞれMetSの危険因子であり，毎日飲酒している喫煙者ではMetS罹患率が高いとの報告がある[13]。また，睡眠不足や睡眠障害によって肥満になることが報告[14,15]

表7　年齢階級別オッズ比（縦断研究）

性別	生活習慣	40～49歳			50～59歳			60～69歳			70～74歳			Mantel-Haenszel 推定量			Logistic regression[a]		
		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間		オッズ比	95%信頼区間	
			下限	上限		下限	上限		下限	上限		下限	上限		下限	上限		下限	上限
男	歩行速度速い	0.89	0.71	1.10	0.85	0.72	1.00	0.86	0.80	0.93	0.91	0.82	1.01	0.88	0.83	0.93	0.88	0.83	0.93
	運動習慣あり	0.88	0.69	1.13	0.84	0.70	1.01	0.96	0.89	1.03	0.92	0.83	1.02	0.93	0.88	0.99			
	身体活動あり	0.83	0.67	1.04	0.83	0.70	0.98	0.88	0.81	0.95	0.75	0.68	0.84	0.83	0.79	0.88	0.85	0.80	0.90
	睡眠で休養十分	1.00	0.79	1.27	0.85	0.71	1.02	0.95	0.86	1.05	1.02	0.88	1.18	0.95	0.89	1.02			
	早食いである	1.75	1.40	2.19	1.59	1.34	1.89	1.47	1.35	1.59	1.39	1.23	1.57	1.48	1.39	1.57	1.49	1.40	1.59
	夜食・間食あり	1.11	0.83	1.49	1.00	0.78	1.29	1.37	1.20	1.56	1.05	0.85	1.29	1.20	1.09	1.32	1.15	1.05	1.27
	夕食後2時間以内就寝	1.20	0.95	1.50	1.40	1.18	1.66	1.25	1.14	1.36	1.01	0.89	1.15	1.20	1.12	1.27	1.15	1.08	1.23
	朝食抜き	1.08	0.84	1.39	1.16	0.93	1.45	1.08	0.93	1.26	0.99	0.76	1.28	1.08	0.98	1.20			
	毎日飲酒	0.86	0.69	1.08	1.11	0.94	1.31	1.10	1.02	1.18	1.08	0.97	1.20	1.08	1.02	1.14	1.08	1.02	1.14
	習慣的な喫煙あり	1.07	0.86	1.33	1.14	0.96	1.34	0.97	0.89	1.06	0.87	0.76	1.00	0.98	0.92	1.04			
女	歩行速度速い	0.52	0.36	0.76	0.69	0.58	0.81	0.76	0.71	0.82	0.72	0.65	0.80	0.74	0.70	0.78	0.74	0.70	0.78
	運動習慣あり	0.72	0.44	1.17	0.95	0.79	1.14	0.91	0.84	0.98	0.95	0.86	1.06	0.92	0.87	0.98			
	身体活動あり	0.72	0.50	1.03	0.87	0.74	1.03	0.87	0.81	0.94	0.83	0.75	0.93	0.86	0.81	0.91	0.92	0.87	0.98
	睡眠で休養十分	0.87	0.61	1.23	0.97	0.81	1.15	0.93	0.85	1.01	0.99	0.88	1.13	0.95	0.89	1.01			
	早食いである	1.61	1.12	2.31	1.42	1.19	1.71	1.54	1.42	1.67	1.33	1.17	1.51	1.47	1.38	1.57	1.48	1.39	1.58
	夜食・間食あり	1.33	0.88	1.99	1.15	0.92	1.44	1.29	1.15	1.45	1.27	1.05	1.54	1.27	1.16	1.38	1.15	1.05	1.26
	夕食後2時間以内就寝	1.49	1.01	2.18	1.43	1.16	1.77	1.28	1.15	1.42	1.08	0.93	1.25	1.24	1.15	1.34	1.19	1.10	1.29
	朝食抜き	1.55	1.02	2.35	1.16	0.88	1.52	1.27	1.09	1.49	1.39	1.08	1.79	1.29	1.15	1.45	1.21	1.07	1.36
	毎日飲酒	0.66	0.38	1.15	1.09	0.84	1.41	0.71	0.60	0.83	0.94	0.74	1.20	0.81	0.72	0.91	0.80	0.71	0.90
	習慣的な喫煙あり	1.17	0.76	1.79	1.19	0.91	1.56	1.00	0.84	1.20	1.50	1.15	1.95	1.14	1.01	1.30			

a：多変量ロジスティック回帰分析（尤度比による変数減少法）

されている。しかしながら，MetS 罹患との関連は示されていない。本研究においては「毎日飲酒する」が男性では危険因子，女性では予防因子となった。睡眠・喫煙に関する質問項目の MetS 罹患への寄与は認められなかった。睡眠・喫煙に関する回答の2値化によって関連を認め難くなった可能性もあるが，MetS 罹患との関係性を示すためにはより長期にわたる追跡調査が必要であるのかも知れない。今後，長期にわたる追跡調査や設問方法の工夫を検討して行くべき課題と考える。また，女性の「毎日飲酒する」ことが MetS 罹患に対して予防因子であることについても詳細な分析が必要と考える。

本研究において，生活習慣に関する質問のうち運動に関係する質問（3項目）と食習慣に関する質問（4項目）と MetS との関連を，横断研究だけでなく縦断研究（MetS 罹患率）によっても統計的に示すことができた。このことは本研究が初めてである。なお，平成25年4月に改訂された「標準的な健診・保健指導プログラム（改訂版）」[16]において，標準的な質問項目に関する先行研究が示されているが，本研究の結果とも矛盾していない。

特定健診の標準的質問項目の利用は，MetS 判定に必要な服薬に関することや喫煙に関することを除き，保険者に任されている。よって，MetS 予防対策のために標準的質問表を積極的に利用することを提案したい。なぜならば，特定保健指導実施率が14.7%（平成20年，千葉県内市町村国保全体）[17]と低迷しているため，特定保健指導による MetS 改善効果[5]が，各年度の横断結果に反映されてこないと考えられるからである。特定健診受診時に，本研究の結果をもとに不適切な生活習慣と MetS との関連を示し，MetS 非該当者が MetS にならないための情報提供として役立てることが MetS 者の改善に重要と考える。検診受診時に情報提供することは，MetS 群で特定保健指導不参加者に対しても情報提供できる点が有利であり，被保険者全体への情報提供にも有利であろう。

本研究の限界として，国民健康保険加入者のデータセットであるため男女とも40～59歳にかけての比率が人口構成に比べてかなり少ないことがあげられる。ただし，性・年齢階級別に階層化した Mantel-Haenszel 推定値や，年齢階級別にダミー化した独立変数を使用した多変量ロジスティック回帰分析を用いたので，影響は限定的であると考える。また，本研究に用いた質問項目のうち，喫煙に関する質問は必須であるが，その他の項目は保険者つまり市町村毎に対応バイアスがかかっている可能性が考えられる。この点は，本研究の成果を市町村にフィードバックして採用市町村を増やし，再解析することにより検証したい。

データ欠損による選択バイアスが考えられるが，特定健診は市町村において行われているものであるため，確認することは困難である。また，質問票が自記式であることによる影響が考えられるが，先行研究[8]において標準的質問項目を用いた運動量の推定が行われていることから，限定的であると言える。さらに，採血が食後であることの可能性とそれに伴う血糖や中性脂肪への影響が考えられるが，国から特定健診の方法が示されている[6]ことから，極めて限定的なものと思われる。本研究では主に，生活習慣を MetS の有病と罹患から予測的妥当性の観点で調査したものであり，他の食事調査法や運動量の評価など併存的妥当性は含まない。

V　結　　語

標準的質問項目で把握される不適切な運動習慣や食習慣が MetS の罹患につながることを示した成績であり，特定健診において MetS と関連性の高い質問項目と考えられた。質問の採否は各保険者に任されていることから，積極的に標準的質問項目を活用し，MetS 予防対策に利用することが望まれる。

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文　　献

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Exploring the link between standard lifestyle questionnaires administered during specific medical check-ups and incidence of metabolic syndrome in Chiba Prefecture

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Key words: metabolic syndrome, specific medical check-ups, health insurance, standard lifestyle questionnaires, Chiba Prefecture

Objectives The aim of this study was to clarify the relationship between standard lifestyle questionnaires and the development of metabolic syndrome (MetS).

Methods We analyzed the data on 278,989 people (111,524 males and 167,465 females) living in Chiba Prefecture who underwent consecutive medical check-ups in 2008 and 2009. The standard lifestyle questionnaire administered during the check-ups consisted of 10 items, including three on exercise behaviors, four on dietary behaviors, and one each on drinking, smoking, and sleeping behaviors. An individual was assigned to the "developing MetS" category if there was no diagnosis of MetS in 2008, followed by a diagnosis of MetS or pre-MetS in 2009. We calculated the odds ratios for developing MetS adjusted for gender and age. Developing MetS was the dependent factor in a multiple logistic regression analysis used to examine its relationship to responses on the lifestyle questionnaire.

Results In men, the odds of developing MetS were significantly lower for participants who exercised regularly ("walking fast," OR=0.88, 95% CI [0.83–0.93]; and "higher physical activity," 0.85, [0.80–0.90]), but were significantly higher for those who engaged in _ dietary behaviors and drinking ("eating fast," 1.49, [1.40–1.59]; "having a habit of eating late-night snacks," 1.15, [1.05–1.27]; "having a late night meal," 1.15, [1.08–1.23]; and "drinking every night," 1.08, [1.02–1.14]). In women, the odds of developing MetS were significantly lower for subjects who reported engaging in regular exercise and drinking ("walking fast," 0.74, [0.70–0.78]; "higher physical activity," 0.92, [0.87–0.98]; and "drinking every night," 0.80, [0.71–0.90]), but were significantly higher for those who had such dietary behaviors as "eating fast" (1.48, [1.39–1.58]), "having a habit of eating late-night snacks" (1.15, [1.05–1.26]), "having a late night meal" (1.19, [1.10–1.29]), and "not having breakfast" (1.21, [1.07–1.36]).

Conclusion These results show that poor dietary or exercise habits as determined by the standard lifestyle questionnaire were associated with the development of MetS.

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High-density Lipoprotein Subclasses and Risk of Stroke and its Subtypes in Japanese Population

The Circulatory Risk in Communities Study

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Background and Purpose—High-density lipoprotein (HDL) cholesterol is an established protective factor for ischemic stroke. However, the contribution of HDL subclasses to stroke risk and its subtypes is uncertain.

Methods—A prospective nested case–control study of 40- to 85-year-old Japanese was undertaken using frozen serum samples collected from 5280 men and 7524 women. They participated in cardiovascular risk surveys from 1985 to 1999 (1 community) and 1989 to 1998 (2 communities) under Circulatory Risk in Communities Study. HDL cholesterol subclasses were classified by high-performance liquid chromatography into 3 subgroups: S-HDL (very small or small HDL), M-HDL (medium HDL), and L-HDL (large or very large HDL) cholesterol. One control subject per case was matched by sex, age, community, serum storage year, and fasting status.

Results—In 2005, we identified 241 strokes (155 ischemic and 86 hemorrhagic). S-HDL and M-HDL cholesterol levels were inversely associated with total stroke risk, ischemic stroke, specifically lacunar infarction, and hemorrhagic stroke. After adjustment for cardiovascular risk factors, these associations remained statistically significant. Multivariable conditional odds ratios (95% confidence interval) for 1 SD (0.12 mmol/L) increment of S-HDL cholesterol levels were 0.34 (0.23–0.52) for total stroke, 0.38 (0.23–0.63) for ischemic stroke, 0.33 (0.18–0.61) for lacunar infarction, 0.30 (0.14–0.65) for hemorrhagic stroke, and 0.30 (0.12–0.77) for intraparenchymal hemorrhage. The respective multivariable odds ratios for 1SD (0.10 mmol/L) increment of M-HDL cholesterol levels were 0.56 (0.41–0.75), 0.63 (0.45–0.88), 0.59 (0.40–0.87), 0.41 (0.21–0.80), and 0.38 (0.16–0.90). No associations were found between L-HDL cholesterol levels and risk of total stroke and its subtypes.

Conclusions—Small- to medium-sized HDL, not large HDL, cholesterol levels were inversely associated with total stroke risk. **(*Stroke*. 2013;44:327-333.)**

Key Words: high-density lipoprotein cholesterol ■ Japanese ■ nested case-control study ■ particle size ■ stroke

High-density lipoprotein (HDL) particles are heterogeneous in structure, having differential effect on their antiatherogenic properties.[1] Small, dense HDL particles display higher cholesterol efflux capacity,[2] potent protection for low-density lipoprotein (LDL) oxidation[3,4], and possess stronger anti-inflammatory properties than large HDL particles.[5]

Lipoprotein subclasses were quantified by gradient gel electrophoresis and nuclear magnetic resonance methods, the findings on the associations of HDL subclasses and cardiovascular disease have been inconsistent. Case–control studies using the gradient gel electrophoresis method reported that small HDL particles were inversely associated with the progression of coronary atherosclerosis[6] and risk of coronary heart disease,[7,8] and other studies showed opposite trends with prevalence of carotid atherosclerosis[9] and ischemic stroke risk.[10] In addition, studies using nuclear magnetic resonance observed that only large HDL particles, not small HDL or medium HDL particles, were inversely associated with risk of cardiovascular disease,[11] whereas another study with the nuclear magnetic resonance method showed that larger HDL particles were inversely associated, and smaller HDL particles were positively associated with the prevalence of coronary artery disease.[12]

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High-performance liquid chromatography (HPLC) with gel permeation columns is an alternative method for classifying and quantifying lipoproteins according to particle sizes.[13] This method can provide cholesterol levels of major lipoproteins and their subclasses using a small amount of serum or plasma and measure simultaneously cholesterol levels in each lipoprotein fraction and lipoprotein particle size distribution. The HPLC defines 5 HDL subclasses based on HDL particle diameter size, which is similar to gradient gel electrophoresis and nuclear magnetic resonance methods.[13,14] Advantages of the HPLC method include its direct cholesterol determination in HDL and HDL subclasses within 16 minutes by using a small amount of plasma (<10 μL).[13,15]

In the present study, a prospective nested case–control study of men and women was conducted in 3 Japanese communities of the Circulatory Risk in Communities Study (CIRCS) using stored serum samples. We applied the HPLC method to assess HDL subclasses and to seek their associations with risk of stroke and its subtypes.

Methods

Surveyed Populations

The present study was an ancillary study of the CIRCS.[16] CIRCS is a dynamic cohort of Japanese men and women aged ≥30 years in 5 communities across Japan, overseen by a research team from the Osaka Medical Center for Health Science and Promotion, Osaka University and the University of Tsukuba. The surveyed populations comprised 13 314 men and women aged 40 to 85 years, who participated in cardiovascular risk surveys between 1985 and 2000 in a mideastern rural community (Kyowa; participants and census population for 40–85 years; n=6829 and n=8557, respectively) and between 1989 and 1998 in northeastern rural community (Ikawa; n=2570 and n=2981, respectively) and a southwest rural community (Noichi; n=3915 and n=7169, respectively). The participation rate in cardiovascular risk surveys among men and women aged 40 to 85 years was 80% in Kyowa, 86% in Ikawa, 55% in Noichi, and 71% for the total population. A 1.0- to 2.0-mL serum sample obtained from each participant was stored at −80°C for 1 to 20 years (median, 10.5 years). Participants with a history of stroke or coronary heart disease (n=510) were excluded from the analyses. The participants were followed up to determine the incidence of stroke occurring by the end of 2005. The Ethics Committee of Osaka University, The University of Tsukuba and the Osaka Medical Center for Health Science and Promotion approved this study.

Surveillance of Stroke and Classification of Stroke Subtypes

Susceptible cases of stroke were ascertained from national insurance claims, ambulance records, death certificates (cases with stroke as the underlying cause of death [International Classification of Diseases, 9th revision: 430–438] were selected), reports by local physicians, and reports by public health nurses and volunteers. To confirm the diagnosis of stroke, we called, visited, or invited the susceptible subjects to participate in annual cardiovascular risk surveys to obtain clinical histories. In addition, physicians obtained medical histories and reviewed medical records, including computed tomography/magnetic resonance imaging from local clinics and hospitals. In the case of deaths, histories were obtained from families, and medical records were reviewed.

The diagnosis of stroke was made according to the criteria of the National Survey of Stroke,[17] which requires a constellation of neurological deficits of sudden or rapid onset lasting ≥24 hours or until death. Strokes were classified as intraparenchymal hemorrhage, subarachnoid hemorrhage, or ischemic stroke (lacunar infarction, large-artery occlusive infarction, and embolic infarction) by computed tomography/magnetic resonance imaging using standardized criteria.[18] Strokes with negative findings on imaging studies and unclassified strokes were excluded. For each new case of stroke, 1 control subject was selected randomly from the participants with no incident stroke, matched for sex, age (±2 years), community, year of serum storage, and fasting status at serum collection (<8 and ≥8 hours).

Determination of HDL Particle Size

Nonfasting venous blood was collected in 7- to 10-mL plain tubes and allowed to stand for 30 minutes for serum separation. The serum samples were aliquoted immediately and placed on dry ice at survey sites and then stored at −80°C.

Serum lipoprotein analyses were performed by HPLC with gel permeation columns (LipoSEARCH; Skylight-Biotec, Inc., Akita, Japan).[15] By this method, HDL was classified by particle size into 5 subgroups: 13.5 to 15.0 nm (very large HDL), 12.1 nm (large HDL), 10.9 nm (medium HDL), 9.8 nm (small HDL), and 7.6 to 8.8 nm (very small HDL).[13] To simplify data analysis, we grouped these HDL subclasses as follows: S-HDL (very small or small HDL), M-HDL (medium HDL), and L-HDL (large or very large HDL).

Statistical Analysis

The odds ratios and 95% confidence intervals for total stroke and stroke subtype were estimated according to quartiles and 1SD increment of total HDL, S-HDL, M-HDL, and L-HDL cholesterol levels with conditional logistic regression models. Adjustment was made for hypertension status (normal, borderline, and hypertension), body mass index (kg/m^2), current alcohol intake (g/d), cigarette smoking status (never, ex-smoker, and current), cholesterol-lowering medication (yes/no), log-transformed triglycerides levels (mmol/L), and serum glucose category (normal, impaired glucose tolerance, and diabetes mellitus). SAS version 9.1.3 was used for the statistical analyses (2-tailed).

Results

Age-adjusted baseline characteristics of the controls according to quartiles of HDL subclasses are shown in Table 1. Body mass index was inversely associated with total HDL cholesterol and L-HDL, and the prevalence of current smokers was lower with the higher quartiles of L-HDL cholesterol levels. Total HDL cholesterol levels were positively associated with S-HDL, M-HDL, and L-HDL cholesterol levels, whereas triglycerides were inversely associated with total HDL cholesterol, S-HDL, M-HDL, and L-HDL cholesterol levels. Mean blood pressure, mean ethanol intake, and prevalence of hypertensive and glucose abnormality did not vary according to total HDL cholesterol, S-HDL, M-HDL, and L-HDL cholesterol levels. The prevalence of diabetes mellitus was lower with the higher quartiles of total HDL and L-HDL cholesterol levels.

During the follow-up period, we identified 241 incident strokes comprising 155 ischemic strokes (116 lacunar infarctions, 35 large-artery occlusive infarctions, and 11 embolic infarctions) and 86 hemorrhagic strokes (64 intraparenchymal hemorrhages and 22 subarachnoid hemorrhages).

Table 2 shows odd ratios and 95% confidence intervals for total stroke and stroke subtypes according to the quartiles and 1SD increment of total HDL, S-HDL, M-HDL, and L-HDL cholesterol levels. We did not show the results for large-artery occlusive infarction, embolic infarctions, and subarachnoid hemorrhage because of small incidence numbers. Total HDL cholesterol levels were inversely associated

Table 1. Age-adjusted Baseline Characteristics of Control Subjects According to Quartiles of High-density Lipoprotein Cholesterol Levels by High-density Lipoprotein Subclass

	Total HDL cholesterol, mg/dL					L-HDL, mg/dL					M-HDL, mg/dL					S-HDL, mg/dL				
	13.1–36.0	36.5–44.9	45.0–53.7	54.0–87.8	*P* for trend	5.1–12.1	12.1–17.1	17.1–24.2	24.3–51.6	*P* for trend	1.9–9.1	9.2–11.6	11.9–14.4	14.4–21.5	*P* for trend	3.9–11.7	11.7–14.6	14.7–17.9	17.9–39.6	*P* for trend
No. of controls	51	58	67	65		65	53	66	57		52	54	66	69		45	57	68	71	
Age, y	66	67	65	66	0.56	66	67	65	65	0.56	67	68	65	64	0.03	67	65	66	66	0.87
Men, %	55	52	47	51	0.74	57	50	44	54	0.58	47	51	57	48	0.78	40	56	56	49	0.61
Systolic BP, mm Hg	135	137	134	132	0.25	135	138	133	132	0.21	132	135	138	133	0.54	134	136	134	134	0.83
Diastolic BP, mm Hg	79	79	78	77	0.34	80	78	76	79	0.36	78	77	80	77	0.84	77	80	79	78	0.80
Hypertension, %	39	42	34	37	0.71	41	44	34	32	0.33	37	37	36	41	0.64	35	39	35	41	0.91
Body mass index, kg/m^2	23.9	23.8	23.0	22.8	0.03	24.2	24.0	23.3	21.6	<0.001	22.8	22.9	23.7	23.6	0.07	23.0	23.1	22.9	24.0	0.12
Ethanol intake, g/d	13.2	11.7	11.3	14.7	0.73	16.1	9.7	10.9	13.9	0.64	10.7	11.3	10.7	17.4	0.10	9.6	13.1	11.0	16.1	0.15
Current smokers, %	38	30	19	23	0.07	48	20	24	12	0.001	28	25	27	26	0.94	6	18	16	18	0.57
Cholesterol-lowering medication, %	4	3	5	0	0.23	5	6	2	0	0.96	2	2	5	3	0.78	2	2	4	3	0.85
Total HDL cholesterol, mmol/L	0.74	1.05	1.26	1.61	<0.001	0.90	1.05	1.32	1.51	<0.001	0.84	1.08	1.24	1.51	<0.001	0.85	1.15	1.25	1.38	<0.001
L-HDL, mmol/L	0.26	0.36	0.53	0.71	<0.002	0.23	0.37	0.52	0.81	<0.002	0.39	0.45	0.49	0.56	<0.002	0.43	0.52	0.50	0.44	0.91
M-HDL, mmol/L	0.20	0.30	0.33	0.41	<0.003	0.27	0.29	0.37	0.33	<0.003	0.18	0.26	0.34	0.44	<0.003	0.19	0.29	0.34	0.40	<0.001
S-HDL, mmol/L	0.29	0.39	0.40	0.48	<0.004	0.40	0.38	0.43	0.38	0.79	0.27	0.36	0.42	0.51	<0.004	0.23	0.34	0.41	0.54	<0.002
Triglycerides, mmol/L	1.77	1.52	1.13	1.00	<0.005	1.77	1.4	1.13	0.98	<0.001	1.47	1.40	1.29	1.10	0.001	1.50	1.31	1.23	1.21	0.02
Impaired glucose tolerance, %	12	12	14	9	0.64	14	12	14	7	0.97	9	11	15	11	0.32	16	9	12	12	0.87
Diabetes mellitus, %	14	7	5	6	0.04	11	10	5	5	0.04	12	5	9	5	0.23	9	7	9	6	0.84

Triglycerides are expressed as geometric mean

BP indicates blood pressure; HDL, high-density lipoprotein; L-HDL, large high-density lipoprotein; M-HDL, medium high-density lipoprotein; and S-HDL, small high-density lipoprotein.

Table 2. Odds Ratios (95% Confidence Interval) of Stroke and Subtypes According to High-density Lipoprotein Cholesterol Levels by High-density Lipoprotein Subclass

	Total HDL cholesterol					L-HDL quartiles				
	1	2	3	4	OR per 1 SD increment	1	2	3	4	OR per 1 SD increment
Total stroke										
No of cases	70	62	54	55		55	67	56	63	
No of controls	51	58	67	65		65	53	66	57	
Age-, sex-, and community-matched OR	1.00	0.67 (0.39–1.17)	0.46 (0.25–0.84)*	0.47 (0.26–0.88)*	0.85 (0.69–1.06)	1.00	1.54 (0.91–2.62)	1.04 (0.62–1.76)	1.38 (0.78–2.41)	1.09 (0.89–1.32)
Multivariable OR[a]	1.00	0.60 (0.33–1.10)	0.41 (0.21–0.81)*	0.40 (0.19–0.80)†	0.79 (0.61–1.02)	1.00	1.78 (1.00–3.16)	1.25 (0.70–2.23)	1.57 (0.81–3.05)	1.13 (0.89–1.44)
Ischemic stroke										
No of cases	49	43	28	35		38	42	37	38	
No of controls	38	39	39	39		44	38	40	33	
Age-, sex-, and community-matched OR	1.00	0.77 (0.41–1.44)	0.46 (0.22–0.96)*	0.57 (0.27–1.18)	0.89 (0.69–1.15)	1.00	1.30 (0.70–2.44)	1.11 (0.58–2.11)	1.40 (0.69–2.83)	1.11 (0.87–1.41)
Multivariable OR[a]	1.00	0.66 (0.33–1.35)	0.37 (0.15–0.87)*	0.47 (0.20–1.12)	0.85 (0.62–1.16)	1.00	1.70 (0.83–3.48)	1.35 (0.65–2.80)	1.80 (0.76–4.24)	1.19 (0.87–1.62)
Lacunar infarction										
No of cases	40	30	21	25		31	34	21	30	
No of controls	23	31	30	32		30	26	33	27	
Age-, sex-, and community-matched OR	1.00	0.50 (0.23–1.07)	0.29 (0.12–0.72)†	0.33 (0.14–0.79)*	0.82 (0.61–1.10)	1.00	1.25 (0.60–2.61)	0.58 (0.26–1.30)	1.00 (0.44–2.25)	1.02 (0.78–1.34)
Multivariable OR[a]	1.00	0.52 (0.22–1.21)	0.23 (0.08–0.67)†	0.27 (0.10–0.75)*	0.75 (0.53–1.06)	1.00	1.77 (0.75–4.16)	0.62 (0.24–1.60)	0.97 (0.35–2.69)	1.02 (0.72–1.44)
Hemorrhagic stroke										
No of cases	21	19	26	20		17	25	19	25	
No of controls	13	19	28	26		21	15	26	24	
Age-, sex-, and community-matched OR	1.00	0.46 (0.14–1.47)	0.39 (0.13–1.20)	0.30 (0.09–1.00)	0.75 (0.50–1.13)	1.00	2.24 (0.83–6.06)	1.00 (0.40–2.51)	1.46 (0.56–3.84)	1.04 (0.74–1.46)
Multivariable OR[a]	1.00	0.46 (0.13–1.64)	0.44 (0.12–1.62)	0.35 (0.09–1.35)	0.79 (0.49–1.29)	1.00	2.71 (0.83–8.84)	1.43 (0.45–4.56)	1.87 (0.57–6.13)	1.17 (0.76–1.80)
Intraparenchymal hemorrhage										
No of cases	13	18	17	16		12	18	16	18	
No of controls	9	14	21	20		17	10	17	20	
Age-, sex-, and community-matched OR	1.00	0.66 (0.15–2.99)	0.36 (0.08–1.57)	0.33 (0.07–1.52)	0.74 (0.45–1.22)	1.00	2.85 (0.86–9.47)	1.49 (0.49–4.54)	1.45 (0.44–4.81)	1.08 (0.72–1.62)
Multivariable OR[a]	1.00	0.80 (0.13–4.95)	0.52 (0.07–3.89)	0.32 (0.05–2.16)	0.68 (0.37–1.28)	1.00	4.06 (0.74–22.2)	3.71 (0.61–2.60)	1.60 (0.25–10.4)	1.06 (0.60–1.87)

BMI indicates body mass index; HDL, high-density lipoprotein; L-HDL, large high-density lipoprotein; M-HDL, medium high-density lipoprotein; OR, odds ratio; and S-HDL, small high-density lipoprotein.

*P<0.05, †P<0.01, ‡P<0.001.

[a]Adjusted for hypertension status BMI, current alcohol intake, cigarette smoking status, cholesterol-lowering medication, log-transformed triglyceride levels, serum glucose category, and matching for sex, age, community, year of serum stored, and fasting status.

with risk of total stroke and lacunar infarction but not of hemorrhagic stroke. S-HDL cholesterol levels were strongly and inversely associated with risk of total stroke, ischemic stroke, particularly lacunar infarction, and hemorrhagic stroke, specifically intraparenchymal hemorrhage. These associations remained statistically significant after further adjustment for cardiovascular risk factors. Moderate inverse associations were observed between M-HDL cholesterol levels and risk of total stroke and its subtypes. No associations were found between L-HDL cholesterol levels and risk of total stroke or its subtypes.

Discussion

The present study is the first study to show that higher cholesterol levels in small HDL and medium HDL particles were associated with lower risk of total stroke, either ischemic or hemorrhagic stroke even after adjustment for known cardiovascular risk factors and matching variables of age, sex, years of serum

M-HDL quartiles					S-HDL quartiles				
1	2	3	4	OR per 1 SD increment	1	2	3	4	OR per 1 SD increment
68	67	55	51		75	64	53	49	
52	54	66	69		45	57	68	71	
1.00	0.77 (0.42–1.39)	0.41 (0.21–0.80)†	0.35 (0.17–0.69)†	0.64 (0.49–0.83)‡	1.00	0.36 (0.18–0.73)†	0.14 (0.06–0.33)‡	0.08 (0.03–0.21) ‡	0.39 (0.27–0.57)‡
1.00	0.66 (0.34–1.28)	0.31 (0.15–0.64)†	0.23 (0.11–0.51)‡	0.56 (0.41–0.75)‡	1.00	0.37 (0.17–0.78)†	0.18 (0.06–0.34)‡	0.05 (0.02–0.15) ‡	0.34 (0.23–0.52) ‡
46	41	35	33		50	40	32	33	
37	33	41	44		31	36	42	46	
1.00	0.84 (0.41–1.73)	0.51 (0.24–1.10)	0.44 (0.12–0.97)*	0.72 (0.54–0.96)*	1.00	0.33 (0.13–0.85)*	0.14 (0.05–0.42)‡	0.09 (0.03–0.30) ‡	0.44 (0.28–0.69) ‡
1.00	0.72 (0.33–1.61)	0.39 (0.17–0.90)*	0.30 (0.12–0.76)*	0.63 (0.45–0.88)†	1.00	0.34 (0.13–0.89)*	0.14 (0.05–0.44)‡	0.07 (0.02–0.25)‡	0.38 (0.23–0.63)‡
33	32	26	25		36	30	26	24	
26	23	33	34		20	30	30	36	
1.00	0.92 (0.40–2.15)	0.45 (0.18–1.12)	0.40 (0.16–1.01)	0.68 (0.49–0.95)*	1.00	0.26 (0.09–0.79)*	0.13 (0.04–0.47)†	0.08 (0.02–0.31)‡	0.36 (0.21–0.63)‡
1.00	0.70 (0.27–1.80)	0.35 (0.13–0.94)*	0.30 (0.11–0.86)*	0.59 (0.40–0.87)†	1.00	0.29 (0.09–0.93)*	0.15 (0.04–0.57)†	0.07 (0.02–0.32)‡	0.33 (0.18–0.61)‡
22	26	20	18		25	24	21	16	
15	21	25	25		14	21	26	25	
1.00	0.58 (0.19–1.74)	0.21 (0.05–0.83)*	0.17 (0.04–0.72)*	0.43 (0.24–0.78)†	1.00	0.40 (0.14–1.13)	0.12 (0.03–0.52)†	0.04 (0.01–0.28)‡	0.30 (0.15–0.61)‡
1.00	0.30 (0.07–1.34)	0.11 (0.02–0.62)*	0.09 (0.02–0.53)†	0.41 (0.21–0.80)†	1.00	0.45 (0.13–1.54)	0.12 (0.02–0.66)*	0.02 (0.002–0.20)‡	0.30 (0.14–0.65)‡
14	23	17	10		17	21	16	10	
10	19	17	18		9	18	20	17	
1.00	0.64 (0.19–2.22)	0.31 (0.06–1.58)	0.14 (0.03–0.82)*	0.36 (0.17–0.75)†	1.00	0.42 (0.13–1.36)	0.15 (0.03–0.68)*	0.04 (0.005–0.35)†	0.29 (0.13–0.66)†
1.00	0.25 (0.04–1.72)	0.18 (0.02–1.60)	0.06 (0.005–0.62)*	0.38 (0.16–0.90)*	1.00	0.46 (0.11–2.00)	0.16 (0.03–1.02)	0.02 (0.001–0.29)†	0.30 (0.12–0.77)*

storage, fasting status, and community. There was no association between L-HDL cholesterol levels and risk of total stroke and its subtypes. Risk of total stroke was ≈90% lower among persons at the highest quartile of S-HDL cholesterol levels or M-HDL cholesterol levels than among those at the lowest quartile. S-HDL and M-HDL cholesterol levels were not associated with age, sex, blood pressure levels, body mass index, smoking, and diabetes mellitus. Taken together, higher cholesterol levels in S-HDL and M-HDL are suggested to reduce risk of stroke beyond the effects of other conventional risk factors. Small HDL and medium HDL cholesterol levels can be increased by increasing dietary intake of carbohydrate[19] and use of fenofibrate.[20] These nonpharmacological and pharmacological interventions may increase hepatic triglyceride lipase activity that promotes the conversion of large HDL particles into small HDL particles via cholesteryl ester transfer protein.[21,22]

Mechanisms for HDL subpopulation in protection against cardiovascular disease are complex and not fully understood. The ATP-binding cassette transporter A1 (ABCA1) mediates the efflux of cellular cholesterol and phospholipids to lipid-poor apolipoproteins.[23,24] Because smaller HDL particles contained phospholipid and more apoA-1 compared with large HDL particles, they have a larger capacity to remove cholesterol from membranes of peripheral cells, particularly macrophages and form cells.[2] Our result is in line with this mechanism, supporting those subjects with higher cholesterol levels in small HDL or medium HDL particle subclasses may protect against atherosclerosis and atherosclerotic cardiovascular disease. The inverse association between cholesterol levels in smaller HDL particles and risk of cardiovascular disease was observed in the Epic-Norfolk prospective population study,[8] Lopid Coronary Angiography Trial Study[6], and Caerphilly Study.[7] The ATP-binding cassette transporter G1 (ABCG1) stimulates the cholesterol efflux to larger HDL particles[25] because larger HDL particles are the preferred acceptor of ABCG1-mediated cholesterol efflux.[26] This may explain findings of a previous study that large HDL particles were inversely associated with risk of cardiovascular disease, including myocardial infarction and ischemic stroke in women.[11] ABCA1 mediates cholesterol and phospholipid efflux to lipid-poor apoA-I but not to mature HDL. ABCG1 mediates macrophage cholesterol efflux to mature HDL, which might explain mechanism of the relationship of HDL to atherosclerosis risk.[25] However, a study with mice suggested that both ABCA1 and ABCG1 contribute to macrophage reverse cholesterol transport. That study showed a greater decrease in macrophage reverse cholesterol transport from cells where both ABCA1 and ABCG1 expressions were knocked down than from ABCG1-knockdown cells.[27] Another study also indicated that ABCA1 may lipidate lipid-poor apoA-I to generate nascent HDL, which can then act as acceptor for ABCG1-mediated cholesterol efflux.[28]

The present study first showed that cholesterol levels in smaller HDL particles were inversely associated with risk of lacunar infarction. The mechanism for a protective effect of small HDL particles on lacunar infarction is unknown. Anti-inflammatory effects of smaller HDL particles[5,29] may reduce risk of lacunar infarction by inhibiting angionecrosis[30,31] or microatheroma formation[32] in cerebral vessels.

An inverse association was found between smaller HDL cholesterol levels and risk of hemorrhagic stroke, primarily intraparenchymal hemorrhage. One mechanism to explain the protective effect of smaller HDL particles might be their enriched apolipoprotein and enzymes with antioxidative activities.[4] Reduced LDL oxidation may contribute to inhibition of microatheroma formation in small cerebral vessels.[31,33,34]

The strength of the present study is the large number of strokes confirmed by imaging studies, which allowed investigation of the association between S-HDL, M-HDL, and L-HDL cholesterol levels and risk of total stroke and its subtypes. There are several limitations. First, we used frozen serum to estimate HDL cholesterol levels and did not examine long-term changes in HDL cholesterol levels in stored serum samples. A previous study on frozen storage (−70°C) of serum samples for up to 7 years showed no significant change in HDL cholesterol.[35] Second, the frozen serum samples used in the present study had been thawed once. However, a previous study reported that freezing and thawing of HDL have no effect on HDL particle size.[36]

In conclusion, the present study showed that cholesterol levels in small HDL and medium HDL particles were inversely associated with risks of total stroke, either ischemic or hemorrhagic stroke, whereas those in large HDL particles were not associated with risk of total stroke or any subtypes.

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Disclosure

None.

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High-density Lipoprotein Subclasses and Risk of Stroke and its Subtypes in Japanese Population: The Circulatory Risk in Communities Study

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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

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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 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.

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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 × 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: Year												Median (LL, UL of 80% CL)	Proposed TE Criteria			Application to new data		(For reference) CAP TE Criteria
		1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010		Acceptable	Borderline	Unacceptable	Performance in 2011	Evaluation by proposed TE criteria in 2011	
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%)									2.0	0.9	1.4	1.3	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	3.1	3.6	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, 4.6)	<4.8	4.8–9.5	≥9.6	*5.6*	*Borderline*	10.0
HbA1c	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	1.0	1.2	1.1	1.0	1.4	1.2	1.4	1.6	1.2	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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Conflicts of interest: None declared.

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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Review

Saturated Fat Intake and Cardiovascular Disease in Japanese Population

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The evidence for the impact of saturated fat intake on cardiovascular disease remains inconsistent. One reason for this inconsistency may be the large difference in the distribution of saturated fat intake between the East and West. In this review, we focus on the published literature on this topic among Japanese population. Three studies have examined the link between saturated fat intake and intraparenchymal hemorrhage, consistently showing an inverse association. However, the association for ischemic stroke is less clear, although it is generally inverse. As for myocardial infarction, the findings in Japanese studies are inconsistent, as are those of Western studies. The JPHC study, however, found a positive association, the first report in Asia. Taken together with the results of the JPHC and Western studies, a saturated fat intake of around 20 g/day (approximately 10% of total energy) may be optimal, which corresponds to 200 g of milk a day and 150 g of meat every other day.

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The amount of dietary intake of saturated fatty acids is an important determinant of the blood cholesterol level[1, 2]. Correspondingly, a high blood cholesterol level raises the risk of myocardial infarction[3]. Some studies, mainly from Western countries, have shown that high cholesterol levels are also associated with an increased risk of ischemic stroke[4]. The 'lower the better' cholesterol hypothesis was subsequently accepted and quickly spread nationwide in Japan, although the Seven Countries Study showed that the association between blood cholesterol and mortality from coronary heart disease is prominent only among populations with high blood cholesterol levels, such as in Northern Europe and the United States, and not among populations with low blood cholesterol levels, such as in Japan[5]. This hypothesis has also been applied to stroke, although the epidemiological evidence is lacking.

On the other hand, Yoshio Komachi, a pioneer Japanese cardiovascular epidemiologist, observed a far higher incidence of intraparenchymal hemorrhage in Akita, in northeastern Japan, where the population cholesterol levels were very low in the era of the 1960-70's, compared with that observed among Osaka residents, whose cholesterol levels were relatively high[6]. He observed that the lifestyles of the Akita people at that time were characterized by the consumption of traditional Japanese foods, including a large amount of rice and salt and a small amount of animal products, as well as heavy agricultural work. In general, among the traditional Akita farmers, lean, poor-looking middle-aged men suffered from stroke. Based on this observation, Komachi hypothesized that the association between the blood cholesterol level and cardiovascular disease may not be linear and that a very low cholesterol level also has an adverse effect on the incidence of stroke.

This hypothesis has long been under debate and became widely familiar in 1989 according to the results of a cohort study in Akita (presently a part of the Circulatory Risk in Communities Study, CIRCS)[7] and a cohort study in the United States (Multiple Risk Factor Intervention Trial, MRFIT)[4], which independently showed an inverse association between a low total cholesterol level and the risk of intraparenchymal hemorrhage. As a result of these reports, the National Heart, Lung and Blood Institute (NHLBI) held an international conference on low blood cholesterol in 1990 to review and discuss existing data on the U-shaped relationship between the total cholesterol level and cardiovascular disease collected from cohort studies worldwide[8]. Since then, the inverse association between the total or low-density lipoprotein (LDL) cholesterol levels and intraparenchymal hemorrhage has been repeatedly replicated in meta-analyses and cohort studies[3].

A similar hypothesis was recently tested with respect to the association between saturated fat intake and the risk of cardiovascular disease. Several studies have found a positive association between saturated fat intake and myocardial infarction, and the new Japanese guidelines recommend a dietary pattern involving <7% energy from saturated fat[9], although the positive association is not clear in meta-analyses[10, 11]. As for cerebral infarction, some studies have demonstrated an inverse association, while others have shown null associations[11]. In contrast, most studies have documented an inverse association between saturated fat intake and the risk of intraparenchymal hemorrhage[11].

However, considering that the range of saturated fat intake is significantly different between Western countries and Asia, it is inappropriate to directly apply the results of these meta-analyses to Japan, as they include many Western studies. Therefore, we focused on six cohort studies of Japanese population[12-17]. A summary of these studies is presented in **Table 1**.

In the CIRCS, the authors followed up 4,775 residents in Akita, Ibaraki, Osaka and Kochi for 14 years and found a strong inverse association between the level of saturated fat intake estimated according to the 24-hour dietary recall method and the risk of intraparenchymal hemorrhage[12]. In addition, the authors compared these results with those of the Nurses' Health Study (NHS)[18] and found a similar inverse association, although the range of saturated fat intake was far different between the two studies. That is, the median value of saturated fat intake in the highest category of the CIRCS was 17 g/day, while that in the lowest category of the NHS was 20 g/day, indicating the absence of overlap in the distribution of saturated fat intake between the two populations.

In the Shibata Study[13] and Life Span Study (LSS)[14], albeit statistically non-significant, an inverse

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Table 1. Summary of Japanese studies regarding saturated fat intake and cardiovascular disease

Study	Population	Events	Endpoint	Category	Median values of saturated fat in each category		Hazard ratio (95%CI) of highest vs lowest categories	Reference
					Lowest category (g/d)	Highest category (g/d)		
Intraparenchymal hemorrage								
CIRCS	4,775	67	Incidence	Quartiles	5	17	0.30 (0.12-0.71)	Iso H, et al., 2003[12].
JACC	58,453	224	Mortality	Quintiles	9	20	0.48 (0.27-0.85)	Yamagishi K, et al., 2010[15].
JPHC	81,931	894	Incidence	Quintiles	10	25	0.61 (0.43-0.86)	Yamagishi K, et al., 2013[16].
Ischemic stroke								
Shibata Study	2,283	75	Incidence	Quartiles	7	15	0.68 (0.21-2.26)	Seino F, et al., 1997[13].
LSS	3,731	60	Mortality	Tirtiles	7	21	0.58 (0.28-1.20)	Sauvaget C, et al., 2004[14].
JACC	58,453	321	Mortality	Quintiles	9	20	0.58 (0.37-0.90)	Yamagishi K, et al., 2010[15].
JPHC	81,931	1,939	Incidence	Quintiles	10	25	0.84 (0.67-1.06)	Yamagishi K, et al., 2013[16].
Myocardial infarction								
JACC	58,453	330	Mortality	Quintiles	9	20	0.85 (0.56-1.29)	Yamagishi K, et al., 2010[15].
JPHC	81,931	610	Incidence	Quintiles	10	25	1.39 (0.93-2.08)	Yamagishi K, et al., 2013[16].
NIPPON DATA90	7,819	72	Mortality	Quintiles	1.2-4.7 %E 1.4-5.2 %E	7.0-13.0 %E 7.7-13.8 %E	M 0.92 (0.73-1.16) F 1.34 (1.02-1.74)	Nakamura Y, et al. 2013[17].

CI stands for confidence interval, %E for percent energy, M for male, F for female.

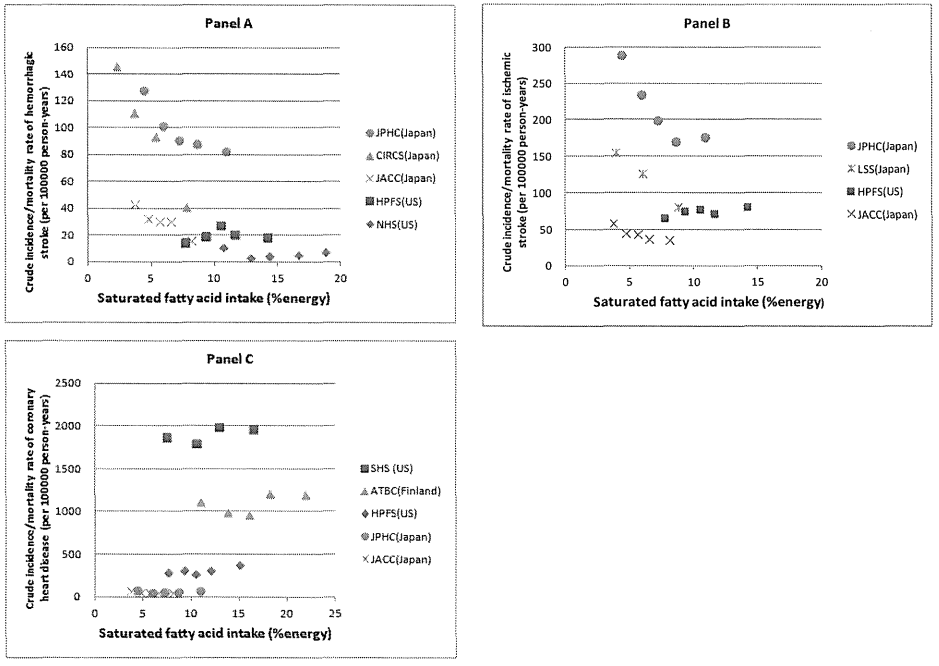

Fig 1. Comparison of the association between the proportion of saturated fat relative to the total energy intake and the crude incidence/mortality rates (per 100,000 person-years) of intraparenchymal hemorrhage (Panel A), ischemic stroke (Panel B) and coronary heart disease/myocardial infarction (Panel C)

NHS: Nurses' Health Study[18], ages 34-59, women only, US; HPFS: Health Professional Follow-up Study[19, 20], ages 40-75, men only, US; CIRCS: Circulatory Risk in Communities Study[12], ages 40-69, men:women=48:52, Japan; JPHC; Japan Public Health Center-based Prospective Study[16], ages 45-74, men:women=46:54, Japan; JACC; Japan Collaborative Cohort Study[15], ages 40-79, men:women=39:61, Japan; LSS: Life Span Study[14], ages 35-89, men:women=38:62, Japan; ATBC: Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study[22], ages 50-69, male smokers only, Finland; SHS: Strong Heart Study[21], ages 47-79, men:women=36:64, US. The JACC and LSS were mortality studies, the other studies were incidence studies. The ATBC was an intervention study for male smokers. Note that the characteristics of the study population (e.g., age range, gender proportion) varied in each study.

association was observed between saturated fat intake and the incidence or mortality of ischemic stroke. In the Japan Collaborative Cohort (JACC) Study, a strong inverse association was noted between saturated fat intake and mortality from both ischemic stroke and intraparenchymal hemorrhage[15].

In the Japan Public Health Center-based Prospective Study (JPHC Study), a large community-based cohort of 81,931 Japanese men and women, we found an inverse association between saturated fat intake and the risk of incident intraparenchymal hemorrhage and ischemic stroke; the hazard ratio [95% confidence interval] for the highest quintile (around 24.9 g/day) versus the lowest quintile (around 9.6 g/day) was 0.61 ([0.43-0.86], p for trend =0.005) for intraparenchymal hemorrhage and 0.84 ([0.67-1.06], p=0.08) for ischemic stroke[15]. These associations were more prominent for lesions in perforating artery areas (i.e., cases of deep intraparenchymal hemorrhage and lacunar infarction). In contrast, we found a positive association between saturated fat intake and myocardial infarction (hazard ratio [confidence interval]=1.39 [0.93-2.08] for the highest versus lowest quintiles, p for trend=0.046), the first epidemiological observation in Asia. A similar positive association was also identified among women in the NIPPON DATA90 study[17].

The distribution of saturated fat intake in the Japanese population is significantly lower than that observed in the US or European populations, and the profile of cardiovascular disease differs among these groups. The differential rates of stroke and myocardial infarction observed between Asian and Western countries may be explained partly (but not completely) by the difference in saturated fat intake. In the JPHC paper[16], we plotted the absolute amount of saturated fat intake and the crude incidence or mortality of intraparenchymal hemorrhage, ischemic stroke and coronary heart disease based on the published literature. In **Fig. 1** in the present paper, we plotted the proportion of saturated fat relative to the total energy intake instead of the absolute amount based on the published literature[12, 14-16, 18-22]. Consequently, there appears to be a threshold for saturated fat intake of around 7.5% to 10% of the total energy for the inverse relationship between saturated fat intake and the risk of stroke, especially with respect to intraparenchymal hemorrhage, consistent with that observed for the absolute amount of energy (15 to 20 g/day assuming a total energy intake of 1,800 kcal)[16]. As shown in the table, the distribution of saturated fat intake among Japanese is around 7 g (3.5% energy) to 20 g (10% energy). To date, the inverse association has only been confirmed in this distribution, and there is no evidence of a beneficial impact of a saturated fat intake of >20 g/day in Japan, a level above which the risk of myocardial infarction may begin to increase, taken together with the results of the JPHC and Western studies. These observations suggest that a saturated fat intake of around 20 g/day may be optimal, although this finding should be confirmed in meta-analyses. An example of 20 g of saturated fat is the consumption of 200 g of milk a day and 150 g of meat every other day.

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Conflicts of Interest

None declared.

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ヘルスコミュニケーション
小さなまちで健診・検診受診率を高める秘訣

Global Health Communications
蝦名　玲子　（えびなりょうこ）

本日のメニュー

1. ヘルスコミュニケーションとは
2. ヘルスコミュニケーション・ウィールを用いた検診受診率向上キャンペーン
3. 「健診・検診を受診するのが当然」な文化づくり
4. 演習

1.
ヘルスコミュニケーションとは

ヘルスコミュニケーション

- 定義：　人々に、健康上の関心事についての情報を提供し、重要な健康問題を公的な議題に取り上げ続けるための主要戦略のこと（WHO, 1996）

米国疾病管理センター（CDC）の ヘルスコミュニケーションの定義

- ヘルスコミュニケーションとは、個人やコミュニティの健康を高めるために、消費者研究をもとにメッセージや戦略を巧みにつくり伝達すること（1993年）

CDCのヘルスコミュニケーション・ウィール

1. 背景となる情報をレビューする
2. コミュニケーションをとるうえでの目標を設定する
3. 対象となる人を分析し、特徴ごとに細分化する
4. メッセージの概念を明確にし、事前調査をする
5. コミュニケーションチャンネルを選ぶ
6. メッセージやモノをつくり事前調査をする
7. プロモーション計画を開発する
8. 戦略を実践する
9. 効果を評価する
10. 改善するためにフィードバック

2. ヘルスコミュニケーション・ウィールを用いた検診受診率向上キャンペーン （宮崎県串間市）

1. 背景となる情報をレビューする 「そこに何があるのか？」

胃がん

- 全国、県と比較して、罹患率、死亡率ともに高い
- 検診受診率が8.3% (H17)

↓

- ヘルスコミュニケーションを駆使した健康教育
- 胃がん検診受診率の向上を目的としたヘルスキャンペーン

2. ヘルスコミュニケーションをとる上での目標を設定する「私たちは何を達成したいのか？」

- H18当時は、がん対策基本法もなく、判断基準がない
- 健康日本21の「10年間で受診者5割以上の増加を達成すること」を参考に

↓

- 目標：1年間で受診者5割以上の増加を達成する
- 胃がんバス検診受診者数（医療機関を除く）833人（H17）⇒1250人以上

3. 対象となる人たちを分析し特徴ごとに細分化する「誰に、伝えたいのか？」

- 串間市で胃がん検診受診者数が最も低く、リスクの高いのは誰なのか？
- 40代から60代男性（なんと、140人しか受けていない！）

4-1. メッセージの概念を明確にし事前調査をする「何を伝えたいのか？」

- 「何があれば、胃がん検診を受けようという気持ちになるのか」の答えを探る、40代から60代の男性約20名をインタビュー（フォーカス・グループ・インタビュー）

1. 未受診者
2. 毎年、バス検診を受診している人
3. 医療機関で受けている人

4-2. メッセージの概念を明確にし事前調査をする「何を伝えたいのか？」

- 「未受診者に一度でもいいから受診してもらう」という視点と、費用と時間の側面から検討

1. 待ち時間ゼロの電話予約体制
2. 具体的な値（値段、串間市の現状）を示したメッセージ
3. 胃がん体験者からのメッセージ
4. 家族からの勧め