労災疾病臨床研究事業費補助金

健康診断結果の経年変化に視点をおいた望ましい健診結果の活用と事後措置のあり方に関する研究

令和元年度　総括･分担研究報告書

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目次

Ⅰ．総括研究報告書

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研究代表者　立道　昌幸　　東海大学医学部基盤診療学衛生学公衆衛生学　教授

研究要旨

本研究は、H29 から H31 年までの 3 カ年計画にて本年度は、最終年度にあたる。本研究は、現行実施されている健康診断を如何に有効活用するかを目的に、その基礎的エビデンスの構築と、望まれる利用方法、評価方法を提案することを目指している。求められているアウトカムとすると、①定期健診における胸部 XP 検査の有用性に資するエビデンスの提示　②健康診断結果のメガデータを用いた、経年変化、加齢、肥満との関連に視点を置いた年齢毎の正常値の概念の提唱、その正常値に影響する因子の抽出、③健康診断結果を用いた、糖尿病、脳、心血管疾患のリスクモデルを提案し、保健指導すべき高リスク者の選定とともに、低リスク者における健診項目の省略基準の方法とそのエビデンスの構築、④望まれる事後措置のあり方の提唱と評価分析、という以上の 4 つの課題において、ほぼ計画通り結果を得た。

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A. 研究目的

職域における法定の定期健康診断については、検査項目、検査間隔の問題を始め健診実施の意義、エビデンスの検討など根源的問題について、H28 年度までの労災疾病臨床研究補助金;大久保班で討議された。その結果をもとに、労働安全衛生法に基づく定期健康診断のあり方検討会等での議論をへて、H30 年以降も現行の健康診断の実施を行われた。今回の改正では、血糖値を必須としたこと、省略基準は医師が個別に対応することとされた。いずれにしても、法定健康診断を否定的なとらえ方ではなく、

現行の健康診断を如何に有意義に活用していく方法を提示することが必要である。

本年度の目的は、この点を留意し、最終年度としてまとめを行った。一つは、議論の多い胸部 XP 検査におけるがん検診に関する低線量 CT の国際動向、国内研究からの提言を考えた。

二つ目は、年齢、BMI 毎の正常値、基準値を現行で利用されている基準値に当てはめ、既存の政府データと所見率の比較を行い、また、許容値の設定を試みた。年齢階層における正常値、基準値を設けることによって、その正常値を逸脱する生活習慣や労働因子の抽出を試み、保健指導による是正を考えていく。

三つ目は、現行の健康診断結果から有病率の上昇が危惧されている糖尿病、心血管イベント等のリスクスコアーを作成し、高リスク群を精度よく抽出して、保健指導につなげるスキームを作成すること。

そして四つ目には、望まれる事後措置について効果検証を行うこと、さらには、事後措置の指標を作成して、その効果を検証すること、以上 4 つを通じて、現行の健康診断の有効利用法を広く提示することを目的としている。

B. 方法

① 同一施設における 2009-2018 年の胸部レントゲン（XP）検査と低線量 CT（LDCT）検診を実施した場合の、結核、肺がん以外の疾患の発見率を集計し比較した。又、National Lung Screening Trial の 2011 年結果発表に基づき重喫煙者については 55 歳-74 歳の低線量 CT が推奨された。それ以降の世界、及び日本の低線量 CT に関する文献調査を実施した。

②については、平成 28 年度までの労災疾病臨床研究（大久保班研究）で構築されたデータベース（以下、健診 DB）を用い、法定健康診断項目の記述統計的解析を行った。

さらに、JECOH 研究のデータを用い、異常値が出る因子として、通勤手段や日常業務の活動性が重要であるか検討した。

③については、JECOH 研究データを用い、心血管発症におけるリスクモデル作成して、その妥当性を検証した。

④については、事後措置の指標として Crude coverage（CC） Effectiveness coverage(EC)の有用性を明らかにした。

（倫理面での配慮）

本研究遂行に当たっては、各研究機関における倫理委員会の承認のもと実施している。基本的には個人情報を取り扱っていないため、情報漏洩等による被害については推定されない。

C. 研究結果

① 胸部 XP の有用性に関する検討

最終年度である本年度は、同一施設内にて、2009-2018 年の胸部レントゲン（XP）検査と低線量 CT 検診を実施した場合の、結核、肺がん以外の疾患の発見率を集計し比較した。この結果、胸腺腫瘍、縦隔腫瘍については 20-40 倍 CT での発見率が上回っており、胸部 XP の検出の限界であった。また、気腫性のう胞についても CT での発見率が 10 倍以上高かった。さらに、気腫性のう胞について CT 画像を見せながらの禁煙指導により、禁煙率が上昇した。低線量 CT には喫煙者に、COPD のリスクを認知させ、禁煙行動を促するよい介入になりうることが示された。

これまでの結果からは、低線量 CT の有効利用を考える必要があるため、大規模 RCT（低線量 CT vs. 胸部 XP）の NLST の結果以降の国内外の研究動向を文献的に検討した。

② 職域定期健康診断の検査値と加齢および BMI 値との関連に関する検討

平成２９年度および３０年度の結果を踏まえ、職域定期健康診断の有所見にかかる検討として、性別・年齢階級および BMI 階級に注目し、現在汎用されている基準に基づく有所見率の横断的検討と、検査値等の縦断的データによる経年推移に基づく新たな予防介入の必要性について検討を行った。横断的検討では、事業場の健康診断集団集計結果との比較が可能でその後の健康管理施策の検討に資する性別年齢階級別有所見率を算出した。

縦断的検討では、特に若年層において検査値変動が大きい項目があることが示され、また BMI 階級の変動がなくとも経年的な検査値変動があること、特に肥満群ではその変動値が大きいこと、肥満改善群では肥満未変化群に比して検査値の有意な改善があり、特に若年層での改善幅が大きいことが示された。以上のことより、特に特定健康診査の対象外である 40 歳未満の若年層において、肥満群からの改善のみならず肥満群への移行の予防を目的とした介入の必要性が高いと考えられた。その結果に基づき、40 歳未満の若年層に対する介入ポイントとしての新たな基準値（許容値）を提案した。

糖尿病予防に喫煙や運動、適正体重の維持といった健康的な生活習慣が関わることはよく知られており、これらを実践するほどより健康効果が得られると期待されている。しかしながら、日常環境下において健康的な生活習慣の経時的な推移と糖尿病発症について検証した報告はない。職域多施設研究（J-ECOH スタディ）のサブコホート（1 社）の縦断データを用いて、3 年間の生活習慣パターンを同定したうえで、糖尿病発症との関連を検証した。全体的に健康的な習慣であるほど、糖尿病発症リスクは低く、さらに健康的な生活習慣に変わるとリスクが低下することも示唆された。

③ 糖尿病及び心血管疾患のリスク予測に関する研究

職域多施設研究（J-ECOH スタディ）で収集された 2011 年度の定期健康診断データおよび 2019 年 3 月までの心血管疾患の発症登録データを用いて、5 年間の発症リスクを予測するスコアを作成した。統計的検討の結果、年齢、喫煙、収縮期血圧、HDL コレステロール、LDL コレステロール、糖尿病が予測変数として選ばれた。これらの β 値を 10 倍し、四捨五入して、各変数カテゴリーのスコアとした。各スコアを合計することでリスクスコアが得られる。時間依存型ＲＯＣ分析により予測精度を評価したところ、0.8 と同程度の予測精度が得られた。本研究によって、勤労者向けの精度のよい心血管疾患リスクスコアが開発された。

④ 一般健康診断の事後措置のあり方に関する指標の開発について

産業保健専門職（産業医、保健師等）が健診事後措置に関与することにより、対象者が医療機関に受診し、かつ、治療による疾患のコントロールが良好となるか否かについて、Effectiveness coverage(EC)の指標を用いて検討した。53,720 名で検討した結果、専属の産業保健スタッフがいる事業所で EC が高血圧と糖尿病は有意に高く（高血圧 aOR 1.41: 95%CI 1.20-1.66、糖尿病　aOR 1.53: 95%CI 1.17-2.00)、一方で脂質異常症は有意な差を認めなかった。（脂質異常症　aOR 1.11: 95%CI 0.92-1.34）であった。

D. 考察

① 胸部 XP と低線量 CT の他の所見の比較

胸部 XP と低線量 CT の他の所見の比較を行った。縦隔病変については、明らかに CT での発見率が高かった。ただし、その罹患率は低いため、胸部 XP の健診実施項目としての課題で

あるとは考えにくい。但し、1%の頻度で検出される喫煙者における気腫性変化についてはCT の方が描出しやすい点で、さらには、この画像を用いた禁煙指導をすると、より効果が認められたことから、低線量 CT を適切に導入することが労働者の利益になると考えられた。

文献検討では低線量 CT については、被ばくの問題、偽陽性の問題、過剰診断の問題、診断時の侵襲性があるが、これに対して多くの研究がなされて、解決されてきている。偽陽性、過剰診断の問題は、結節のマネージメントの問題となっているが、体積や倍加時間の測定などで解決できる可能性示唆されている。肺がん死亡は、職域でも重点課題であるため、低線量 CT については、職域での肺癌検診としても、現在 on going で進められている JECS study の結果に基づき、任意型として職域のがん検診にどのように組み入れるかについて今後の重要な課題になると思われる。

② 職域定期健康診断の検査値と加齢および BMI 値との関連に関する検討

職域定期健康診断の有所見の検討に際して、性別・年齢階級と合わせて BMI 階級に注目し、現在汎用されている基準に基づく有所見率の横断的検討と、検査値等の経年推移に着目した縦断的検討による新たな予防介入の必要性について検討を行った。横断的検討では、事業場の健康診断集団集計結果との比較に基づく健康管理施策の検討に資する、性別年齢階級別有所見率を算出した。また、過去の研究結果との比較において、検査値の平均値・有所見率に改善があることが示唆された。また、現在の有所見の概念では受診勧奨値と保健指導勧奨値との混用が見られ、必要な保健指導が受けられていない者および過度に保健指導の対象となっている者がいる可能性が示唆された。縦断的検討では、特に若年層において検査値変動が大きい項目があることが示され、また BMI 階級の変動がなくとも経年的な検査値変動があること、特に肥満群ではその変動値が大きいことが示された。以上のことより、特に特定健康診査の対象外である 40 歳未満の若年層において、肥満群からの改善のみならず肥満群への移行の予防を目的とした介入の必要性が高いと考えられた。その結果に基づき、40 歳未満の若年層に対する介入ポイントとしての新たな基準値（許容値）を提案した。

③ 糖尿病及び心血管疾患のリスク予測に関する研究

昨年度の糖尿病のリスクスコアにつづき、脳心血管系イベントのリスクスコアの作成が完成し、その検証まで終了している。このスコアは非常に精度が高いことが明らかにされたことにより、このスコアを用いて、より効果的な保健指導へと結びつけることができることが示唆された。さらには、これらのリスクスコアは、健診結果をそのまま返却するよりも、疾病の発症リスクとして従業員や事業主にも理解しやすく、保健指導のツールとしても利用可能性を検討する価値があると思われた。

④ 一般健康診断の事後措置のあり方に関する指標の開発について

所属する事業場に産業医や産業看護職といった産業保健スタッフが常勤し、日常的に産業保健サービスを提供していることが、高血圧の Crude coverage (CC)が有意に良好な効果を及ぼしていた。また、高血圧および糖尿病の Effectiveness coverage (EC)に有意に良好な効果を及ぼしていた。高血圧と糖尿病においては、産業保健スタッフが受診勧奨の取り組みを行っていること、また、保健指導等の機会を含め受療後もフォローアップを行うことにより、疾患のコントロールも良好となっていることが考えられる。脂質については、CC、EC ともに有意に良好な効果を認めなかった。

特に生活習慣に関連する疾患に対して、産業

保健スタッフが本人の疾患に対する理解を高めながら介入を行うことが有効であり、また、その効果を Crude coverage (CC) や Effectiveness coverage (EC)のベンチマークを活用しながら評価すること提唱できた。

E. 結論

胸部 XP の健診での役割を明らかにした。結核検診として、肺がん検診の一定の役割があること、そして他の疾患の発見については、頻度が低いことから有用性評価の対象にはなりにくいことを示した。年齢階層別における正常値、変化率を求めることにより健康リスクが予想されること、さらに、現行の健康診断項目においても精度よく糖尿病のリスクや脳心血管系イベントのリスクが評価できることが示された。また、これらの検討は、事後措置の観点では、要保健指導レベルを明確にすることによって、より効率的な事後措置につなげられる可能性が示唆された。また、これらのリスク予測値は、36-39 歳の血液検査値の省略あるいは実施の根拠として提示できるものと考えた。

さらに、今回、事後措置の評価指標として、CC、EC の有用性を検討したことで、今後の産業保健の効果分析、評価を可能とした。

F. 研究危険情報

なし

G. 研究発表

1. 論文発表

1) Hu H, Mizoue T, et al. Low serum creatinine and risk of diabetes: The Japan Epidemiology Collaboration on Occupational Health Study. J Diabetes Investig. 2019;10(5):1209-1214.
2) Xiang M, Mizoue T, et al. Association between anthropometric indices of obesity and risk of cardiovascular disease in Japanese men. J Occup Health. 2020;62(1):E12098.
3) Hu H, Mizoue T, et al. Trajectories of body mass index and waist circumference before the onset of diabetes among people with prediabetes. Clin Nutr (印刷中)
4) Hashiguchi K, Nagata T, Mori K, Nagata M, Fujino Y, Ito M. Occupational health services improve effective coverage for hypertension and diabetes mellitus at Japanese companies. JUOEH. 2019: 41(3):271-282.

2. 学会発表

桑原恵介, 中川徹, 山本修一郎, 本多融, 林剛司, 溝上哲也. 通勤手段の変化と内臓脂肪の変化-5 年間の観察研究の結果から-. 第 29 回日本疫学会学術総会. 2019 年 2 月 2 日

橋口 克頼, 永田 智久, 森 晃爾, 永田 昌子, 伊藤 正人. 産業保健スタッフによる介入が生活習慣病とその合併症の発症および医療費に与える影響. 第 36 回産業医科大学学会. 北九州. 2018 年 10 月

永田智久, 橋口克頼, 森晃爾, 永田昌子, 藤野善久, 伊藤正人. 産業保健サービスは企業における高血圧および糖尿病の Effective Coverage を向上させる. 2019 年度日本産業衛生学会九州地方会学会. 福岡. 2019 年 7 月.

山本健也、黒田玲子、大久保靖司. 職域一般健康診断結果の経年変動にかかる検討：第 92 回日本産業衛生学会（2019 年 5 月 23 日）

立道昌幸：職域でのがん検診を考える。
第 92 回日本産業衛生学会　名古屋（2019 年 5
月 24 日）

H. 知的財産権の出願・登録状況
なし

Ⅱ．分担研究報告書

労災疾病臨床研究事業費補助金
分担研究報告書

1．胸部 XP 有用性評価に関する研究

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研究要旨
最終年度である本年度は、同一施設内にて、2009-2018 年の胸部レントゲン（XP）検査と低線量 CT 検診を実施した場合の、結核、肺がん以外の疾患の発見率を集計し比較した。この結果、胸腺腫瘍、縦隔腫瘍については 20-40 倍 CT での発見率が上回っており、胸部 XP の検出の限界であった。また、気腫性のう胞についても発見率が 10 倍以上高かった。さらに、気腫性のう胞について CT 画像を見せながらの禁煙指導により、禁煙率が上昇した。低線量 CT には喫煙者に、COPD のリスクを認知させ、禁煙行動を促するよい介入になりうることが示された。これまでの結果からは、低線量 CT の有効利用を考える必要があるため、最終年度として、大規模 RCT（低線量 CT vs.胸部 XP）の NLST の結果以降の国内外の研究動向を文献的に検討した。

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A. 研究目的

H29,H30 年は、肺結核、肺がんの発見率ついて検証した。本年度は、胸部レントゲン検査（胸部 XP）と低線量 CT（LDCT）検診における結核、肺がん以外の疾患の発見率の比較を行った。

LDCT 検診を考える場合、現時点でのエビデンスは、重喫煙者（30 箱・年）を対象とした大規模 RCT の NLST 研究の結果により肺がんの死亡率減少効果が 20%認められたことが根拠と考えられ、アメリカの USPSTF は、低線量 CT 検診について推奨する方向性を示した。そのため、NLST 研究以降の諸外国から発表された RCT の結果、国内外の文献を検討して、低線量 CT の有用性、限界を明らかにして、有効利用するために考察を加えて提案することを目的とした。

B.　研究方法

1）胸部 XP と LDCT による結核、肺がん以外の発見率の検討

2009 年より 2018 年まで日立健康管理センタで定期健康診断を受診した総計 252452 人、LDCT 検診を受診した 51651 人の肺結核、肺がん疑い症例の発見率を含め、他の疾患の発見率の比較を行った。

2) LDCT に、NLST 以降の国内外の文献的考察を実施した。

（倫理面での配慮）

本研究においては人体から採取された資料は用いない。本研究で収集する各種データは、既存資料からの集計値のみを用いるため、原則として「人を対象とする医学系研究に関する倫理指針」の適用とはならない。本調査には、いずれも個人情報は含んでおらず、個人情報漏洩の可能性はない。

C&D. 結果と考察

1）胸部 XP と LDCT 検査の有所率、発見率の割合　(2009-2018）と発見率の比＝LDCT での発見率/胸部 XP での発見率の比を表 1 に示した。

胸腺腫瘍、縦隔腫瘍、気腫性のう胞については、それぞれ、発見率は、43.5、22.0, 12.4 倍と顕著に LDCT での発見率が高かった。解剖学的位置関係からすると縦隔は心陰影と重なるため、当然の結果であると考えられた。ただし、胸腺腫瘍、縦隔腫瘍の発見率は、それぞれお 0.4、1.0（対 10 万人）と低かった。

気腫性のう胞については、COPD への進行を予防するため喫煙者への禁煙へのモチベーションになるかどうかを検討した結果、図 1 に示すように禁煙率の上昇を認めた。気腫性のう胞は、受検者の 1%程度の高い発見率であり、COPD は喫煙者にとって重要な疾患であるため、この気腫性のう胞の状態を示すことによって本人にリスクを認知させるために、有用であると考えられた。

2）NLST 発表以降の国内、国際研究動向

2011 年大規模 RCT 研究である NLST 研究の結果から 20％の死亡率減少効果、NNS（Number Need Screening）は 303 と報告されて以降 (1)、直近のヨーロッパでの NLST に次ぐ規模の RCT ある NELSON の最終結果の発表(2020 年 1 月)(2)まで 7 つの RCT の結果が発表されている。NLST と NELSON 以外の小規模の RCT では、有意な死亡率減少効果は認められていない。しかし、これらは、研究規模や質の問題を考慮して、pooled 解析した場合には、有意に死亡率減少効果を認めている (3)。ただし、胸部 XP との比較は、NLST のみであった（表 1)。

LDCT 検診の社会実装には課題は 2 つあり、一つは、NLST は重喫煙者（30pack･year 以上）の高リスク群を対象にしており、USPSTF も低線量 CT 検診の対象者を同様としている。しかしながら、実際該当者の 2-4％程度しか LDCT の受診はされておらず、LDCT 検診が社会的に実装されているとは言い難い（4)。

もう一つは検診対象の問題である。LUSI の結果では、女性（非喫煙）の死亡率減少効果が認められている。低線量 CT の効果については、肺がんの高リスク群、人種でも差があると考えられており、日本人での報告は、2011 年以降では 2 報認められた。Nawa らの報告(5)では、死亡率減少効果を、Kakinuma らの報告（6)では、肺がん検出率の報告であるが、女性や低リスク群を含めた死亡率減少効果や発見率が高いため、これらの群も低線量 CT 検診に含めるべきと推奨している。もともと日本人の肺がんと欧米とは、人種差の影響が大きいと考えられる。IA 期の発見率は、NLST（46.8％）や NELSEN (40.0%) の報告 (1-2) とも異なり、日本での報告では、LDCT で発見される 85%以上と高く、90%以上が腺癌であった（5-6)。昨年の本研究でも、IA 期は 100%であり、95%は腺癌である結果と同様である。欧米の報告より早期腺癌の比率が高いのが特徴であることを考えれば、低喫煙、女性の対象も考慮する必要がある。

Kakinuma の報告では、喫煙者と非喫煙者での予後は、喫煙者では有意に低い。また、LDCTで発見された肺がんでは、NLST クライテリアに該当する重喫煙の割合は、49.6%であるため、重喫煙のみを肺がん検診にリクルートした場合は、半分は該当しないことになる。
このリサーチクレスチョンに答えるべく、日本人での RCT 研究は、JECS study として 2012 年より 10 年計画で進められており、初回と 5 年後(6 年目)に CT 検診をうける計画であり、その結果が待たれる（7)。

一方で、LDCT では常に被ばく、偽陽性と過剰診断、診断時の侵襲検査の課題がある。

3）被ばくの課題
LDCT により 108 の肺がんを見つける毎に 1 つのがん罹患が発生する（8)。20 年間毎年 LDCT 受検すると女性では 0.22%、男性では 0.12%の発がんリスクが上がると試算されているが (9)、このリスクは、肺がんで死亡するリスクである女性 5.9%や喫煙者の 15%に比して相当低いと考えられている（10)。

4）偽陽性の課題
NLST では、初回 CT 検診で 27%が陽性になっている。NLST では、4mm 大の結節を閾値としたことからと考えられており、現在 Lung Nodule Management の改訂により、日本では肺がん CT 学会のガイドラインの 6mm としたことにより、偽陽性率は改善されているが、感度とのトレードオフの関係となる。また、NELSON 研究ではこの解決方法として、LDCT で検出される結節に対して体積測定をもって判断し、偽陽性率を 1.2%とした。偽陽性率の報告は、他の研究で様々であり、DANTE 22.9%、DLCST 7.9%、MILD 0.8% (11)、であり結節陰影の取り扱いを如何に標準化するかによる。

5）過剰診断の課題
NLST では、LDCT で発見された肺がんの 18%は過剰診断であると指摘されている。様々なモデルでは初回 CT 検診には 10%に過剰診断が含まれる可能性があることが報告されている（12)。NELSON では、倍加時間（VDT）をもって判断することで、その改善を図っている。上述の LDCT 検診の対象を非、低喫煙者、女性を含める場合には、日本では、女性に多く発見される肺腺がんの過剰診断の問題が最大の課題となるため、肺がん CT 学会のガイドラインの結節のフォローアップに関するエビデンスの集積、さらには、新しい診断方法であるリキッドバイオプシー、遺伝子診断等の新技術を用いたエビデンスの集積が待たれるところである。

6）侵襲的診断とその医療過誤
最終診断は、肺針生検、気管支鏡検査が必要となるが、これらの侵襲的検査は、NLST では受検者の 1.4%肺針生検、3.8%の気管支鏡検査、NELSON ではそれぞれ、0.2%、3.2%に実施された。肺針生検等の侵襲的手技による重篤な副作用は、NLST で 12%、DANTE で 29%、DLCST で 38%、NELSON で 10.7%と報告されている（11)。

E. 結論

胸部 XP と LDCT の他の所見の比較を行った。縦隔病変については、明らかに CT での発見率が高かった。ただし、その罹患率は低いため、胸部 XP の健診実施項目としての課題であるとは考えにくい。但し、1%の頻度で検出される喫煙者における気腫性変化についても CT の方が描出しやすい点で、さらには、この画像を用いた禁煙指導をすると、より効果が認められたことから、LDCT を適切に導入する

ことが労働者の利益になると考えられた。

LDCT については、被ばくの問題、偽陽性の問題、過剰診断の問題、診断時の侵襲性があるが、これに対して多くの研究がなされて、解決されてきている。過剰診断の問題は、結節のマネージメントの問題となっているが、倍加時間の測定などで解決できる可能性示唆されている。肺がん死亡は、職域でも重点課題であるため、職域での肺癌検診としても、JECS study の結果に基づき、LDCT については、任意型として職域のがん検診にどのように組み入れるかについて今後の重要な課題になると思われる。

引用文献

1) Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395–409.

2) H.J. de Koning, C.M. van der Aalst, P.A. de Jong, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med 2020;382:503-13. DOI: 10.1056/NEJMoa1911793

3) Kai-Lin Huang1,2, Shih-Yuan Wang. Effects of low-dose computed tomography on lung cancer screening: a systematic review, meta-analysis, and trial sequential analysis. BMC Pulmonary Medicine 2019:19:126

4) Doria-Rose VP, White MC, Klabunde CN, Nadel MR, Richards TB, McNeel TS, et al. Use of lung cancer screening tests in the United States: results from the 2010 National Health Interview Survey. Canc Epidemiol Biomarkers Prev 2012;21:1049e59

5) Nawa T, Fukui K, Nakayama T, Sagawa M, Nakagawa T, Ichimura H, Mizoue T. A population-based cohort study to evaluate the effectiveness of lung cancer screening using low-dose CT in Hitachi city, Japan. Jpn J Clin Oncol. 2019 Feb 1;49(2):130-136

6) Kakinuma R, Muramatsu Y, Asamura H, Watanabe SI, Kusumoto M, Tsuchida T, Kaneko M, Tsuta K, Maeshima AM, Ishii G, Nagai K, Yamaji T, Matsuda T, Moriyama N. Low-dose CT lung cancer screening in never-smokers and smokers: results of an eight-year observational study. Transl Lung Cancer Res. 2020 Feb;9(1):10-22

7) Sagawa M, Nakayama T, Tanaka M, Sakuma T, Sobue T; JECS Study Group. A randomized controlled trial on the efficacy of thoracic CT screening for lung cancer in non-smokers and smokers of <30 pack-years aged 50-64 years (JECS study): research design. Jpn J Clin Oncol. 2012 Dec;42(12):1219-21

8) Rampinelli C, De Marco P, Origgi D, et al. Exposure to low dose computed tomography for lung cancer screening and risk of cancer: secondary analysis of trial data and risk-benefit analysis . BMJ 2017. ; 356 : j347

9) United States Food and Drug Administration . What are the Radiation Risks from CT? https://www.fda.gov/RadiationEmittingProducts/RadiationEmittingProductsandProcedures/MedicalImaging/MedicalX-Rays/ucm115329.htm. Updated December 5, 2017. Accessed April 17, 2019

10) Brennan P, Crispo A, Zaridze D, et al. . High cumulative risk of lung cancer death among smokers and nonsmokers in Central and Eastern Europe . Am J Epidemiol 2006. ; 164

(12): 1233 – 1241
11) O'Dowd EL1, Baldwin DR1. Lung cancer screening-low dose CT for lung cancer screening: recent trial results and next steps. Br J Radiol. 2018 Oct;91(1090):20170460
12) de Koning HJ, Meza R, Plevritis SK, et al. . Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force . Ann Intern Med 2014：160 (5): 311 – 320

F. 研究危険情報
なし

G. 研究発表
1. 論文発表
なし
2. 学会発表
なし

H. 知的財産権の出願・登録状況
なし

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表1　単純X線検査（胸部XP)と低線量CT（LDCT)検査の有所見割合　（2009-2018）

	胸部XP		LDCT		
	人数(人)	割合(%)	人数(人)	割合(%)	Ratio＝LDCT/胸部XP
肺結核の疑い	18	0.007%	13	0.025%	3.6
肺野異常陰影(肺がん疑い)	527	0.209%	220	0.426%	2.0
甲状腺・縦隔の異常	97	0.038%	69	0.134%	3.5
びまん性肺野陰影	254	0.101%	119	0.230%	2.3
肺門の異常陰影	35	0.014%	26	0.050%	3.6
甲状腺腫	15	0.006%	15	0.029%	4.9
甲状腺癌	1	0.0004%	2	0.004%	9.8
サルコイドーシス	4	0.002%	ND		
胸腺腫瘍	1	0.0004%	9	0.017%	43.5
縦隔腫瘍	2	0.001%	9	0.017%	22.0
気腫性のう胞	2512	0.995%	6376	12.344%	12.4
総受診者数	252,452		51,651		

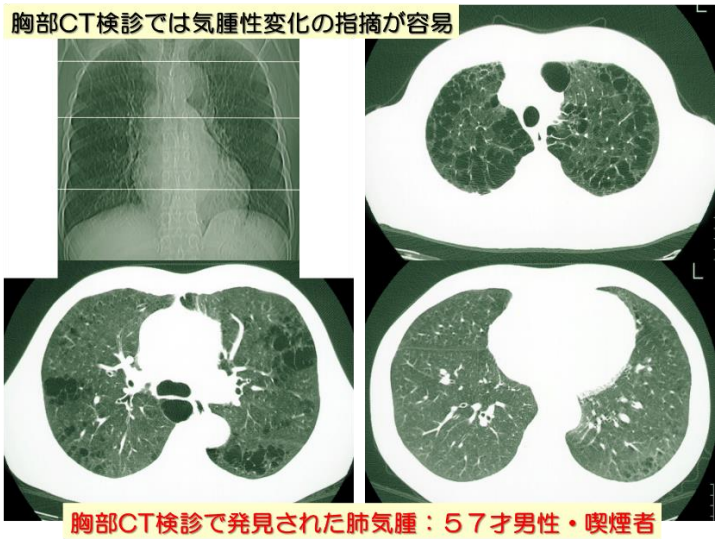
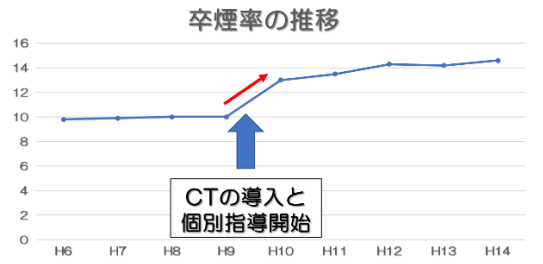


図 1



※（肺気腫所見を認めた者に対して医師による個別指導）
- ＣＴ画像の提示
- 肺気腫の病態説明
- 禁煙指導および禁煙外来への誘導

表2　NLST以降のRCT結果

NO	Name	発行年	LDCT Vs.	国	n	年齢	男性（%）	現喫煙	Pack-year	肺がん死亡率RR	全死因	副作用
	NLST	2011	CXR	USA	53454	61	59	48.2	48	0.85 (0.75-0.96)	0.94 (0.88-1.00)	1.30 (0.84-2.04)
1	MILD	2012	No screening	Italy	4099	66.3	66.3	77.5	39	0.73 (0.47-1.12)	0.94 (0.73-1.20)	NR
2	DANTE	2015	No screening	Italy	2472	64	100	56.9	45	1.01 (0.70-1.444)	0.96 (0.79-1.16)	NR
3	DLCST	2015	No screening	Denma	4104	57.9	55.2	76.1	36.4	1.05 (0.66-1.60)	1.01 (0.82-1.25)	LDCT; 4/49
4	LUSI	2015	No screening	Germar	4052	58	64.7	61.9	36	0.72 (0.45-1.16)	NR	NR
										Female 0.31 (0.10-094)		
5	ITALUNG	2017	No screening	Italy	3206	60.9	64.6	64.8	40	0.71 (0.48-1.04)	0.84 (0.69-1.03)	NR
6	Yang	2018	No screening	China	6717	59.8	46.8	21.5	12.8	0.18 (0.01-3.72)	NR	NR
7	NELSON	2020	No screening	Netherl	13195	58	83.6	55.4	38	0.76 (0.61-0.94)	1.01 (0.92-1.11)	NR

Hung et la BMC pulumonary Medicine 2019 19: 126 より改変

労災疾病臨床研究事業費補助金
分担研究報告書

2-1．職域定期健康診断の検査所見と加齢および BMI 値との関連に関する検討

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研究要旨
平成２９年度および３０年度の結果を踏まえ、職域定期健康診断の有所見にかかる検討として、性別・年齢階級および BMI 階級に注目し、現在汎用されている基準に基づく有所見率の横断的検討と、検査値等の縦断的データによる経年推移に基づく新たな予防介入の必要性について検討を行った。横断的検討では、事業場の健康診断集団集計結果との比較が可能でその後の健康管理施策の検討に資する性別年齢階級別有所見率を算出した。また、過去の研究との比較において、検査値の平均値・有所見率に改善傾向があることが示された。また、現在の有所見の概念では受診勧奨値と保健指導勧奨値との混用が見られ、必要な保健指導が受けられていない者および過度に保健指導の対象となっている者がいる可能性が示唆された。縦断的検討では、特に若年層において検査値変動が大きい項目があることが示され、また BMI 階級の変動がなくとも経年的な検査値変動があること、特に肥満群ではその変動値が大きいこと、肥満改善群では肥満未変化群に比して検査値の有意な改善があり、特に若年層での改善幅が大きいことが示された。以上のことより、特に特定健康診査の対象外である 40 歳未満の若年層において、肥満群からの改善のみならず肥満群への移行の予防を目的とした介入の必要性が高いと考えられた。その結果に基づき、40 歳未満の若年層に対する介入ポイントとしての新たな基準値（許容値）を提案した。

A. 研究目的

本研究の目的は、健康診断データの年齢階級および BMI 値階級による変動を検討し、これらの階級による「基準値（基準範囲）」のあり方のための基礎資料を作成することである。令和元年度は平成 30 年度までの研究結果を踏まえ、以下の点について検討を行った。

ア） 現在汎用されている基準値による性別年齢階級別有所見率の算出

イ） 検査値の個人間変動に着目した、検査値の経年推移

ウ） 上記 2 条件に基づく新たな基準範囲の考え方の提案

エ） BMI 値の改善が健康診断項目に与える影響に関する検討

B. 研究方法

平成 28 年度までの労災疾病臨床研究（大久保班研究）で構築されたデータベースに新たに 1 機関から健診データの追加

提供がされたDBを用い、以下の１）については最も受診者数の多い年度である2013年度を用いた断面的な解析を行った。また２）以降については、期間中に６回の健康診断受診結果がある者を対象として縦断的検討を行った。

１）　現在の基準値に基づく性別年齢階級別有所見率の算出

労働安全衛生法において労働基準監督署への提出が義務付けられている定期健康診断結果報告については、その判断が事業場間で一律ではないため、異なる有所見の定義に基づく集計結果が混在しており、事業場の健康診断集団分析結果との対比が困難であることが以前より指摘されている。従って、事業場における適正な健康状態の相対的評価とそれに基づく効率的・効果的な健康管理施策立案の判断材料に資する資料を作成することを目的に、一元的な基準範囲に基づく有所見率を性別年齢階級別に算出した。有所見率算出のためのカットオフ値は、特定健康診査・特定保健指導事業における「標準的な健診・保健指導プログラム【平成30年度版】」にて定められている以下のカットオフ値として、受診勧奨値（収縮期血圧（以下、SBP）>=140mmHg、拡張期血圧（以下、DBP）>=90mmHg、血色素量（以下、Hb）<=12.0g/dl（男性）・Hb<=11.0g/dl（女性）、アスパラギン酸アミノトランスフェラーゼ（以下、ASTまたはGOT）>=51U/l、アラニンアミノトランスフェラーゼ（以下、ALTまたはGPT）>=51U/l、γグルタミルトランスペプチダーゼ（以下、γ-GTまたはGGT）>=101U/l、中性脂肪（以下、TG）>=300mg/dl、低比重リポたんぱく質（以下、LDLC）>=140mg/dl、高比重リポたんぱく質（以下、HDLC）<=34mg/dl、空腹時血糖値(以下、BS)126mg/dl、糖化ヘモグロビンA1c（以下、HbA1c）>=6.5%)、および指導勧奨値（SBP>=130mmHg、DBP>=85mmHg、Hb>=13.0g/dl（男性）・同>=12.0g/dl（女性）、AST>=31U/l、ALT>=31U/l、GGT>=51U/l、TG>=150mg/dl、LDLC>=120mg/dl、HDLC <=39mg/dl、BS>=100mg/dl、HbA1c>= 5.6 %）をそれぞれ用い、その他の項目（赤血球数、以下RBC）は受診勧奨値をRBC<= 360×10^4個/ml（男性）・RBC <=300×10^4個/ml（女性）、指導勧奨値を RBC<=400×10^4個/ml（男性）・RBC<=360×10^4個/ml（女性）とした。また、定性的な検査方法である聴力検査および尿定性検査については、それぞれ「異常あり」および「（１＋）以上」を有所見とした。なお、横断的分析の対象とした2013年度においては、前年度の2012年度の厚生労働省通達（平成24年10月15日 基発697号）において「一般的な血中グルコースの量の検査によるほか、糖化ヘモグロビンA1c（HbA１c）の検査によることも差し支えない」とされたことから、糖質検査結果の解析では「血糖値検査のみ実施した者」「HbA1c 検査のみ実施した者」「両検査を実施した者」をそれぞれ解析対象とした。検査カテゴリは「血圧検査：SBPおよびDBP」、「貧血検査：RBCおよびHb」、「肝機能検査：AST、ALTおよびGGT」、「脂質検査：LDLC、HDLC、TG」とし、各検査項目のどれか一つでも基準値を逸脱した場合を「有所見」としてカウントした。

また、平成12年度に実施された職域健康診断結果に基づく調査研究「平成12年度労働安全衛生に関する調査研究　健康診断の有効的活用に関する評価調査研究

（研究代表者　大久保利晃）」で用いられた集計結果のうち対象者数の多い1998年度受診者の集計結果を用い、検査値の平均値および有所見率の比較を行った。

2）個人検査値の経年変化にかかる検討

平成29年度までに実施した、集団としての代表値を用いた経年変化にかかる検討に引き続き、検査値の個人変動にかかる代表値による縦断的検討を行った。途中5年間計6回の健診において労働安全衛生法での法定検査項目を全て受診した従業員を対象とし、5年間の検査値の推移を検査項目別に解析した。またこの内、前後5年間でBMI値が次の値で定義される階級（やせ群：BMI18.5未満、基準内群：18.5以上25未満、肥満群：BMI25以上）の中で推移し他の階級への移動がなかった者を、それぞれ「やせ未変化群」「基準内未変化群」「肥満未変化群」と定義し、その群における検査値の変動を分析した。なお、対象集団の選定において、高血圧・高脂血症・糖尿病の加療中の者は分析から除外した。

3）許容値の提案

これまでの研究結果より若年層への介入の重要性が示唆されることから、40歳未満の年代におけるカットオフ値の見直しにかかる検討を行った。「基準内未変化群」を標準集団とし、その経年推移を生理的変動とみなして、特定保健指導の対象となる40歳を起点に、表1の受診勧奨値および保健指導勧奨値から変化量の累積値を逆算する方法にて、30歳および35歳における検査結果許容値を算出した。

4）肥満未変化群と肥満改善群の性別年齢階級別個人検査値の経年推移（5年間）の比較

体重減少が検査値変動にもたらす効果について、5年間の前後の健康診断でBMIが25以上のままの群（肥満未変化群）と5年後に基準内に改善した群（肥満改善群）との個人検査値変動の差を検討した。両群の検査値の差について一般線形モデルにより時間と肥満の変動との交互作用について性別年齢階級別に解析を行った。

なお当調査は、平成28年度までの労災疾病臨床研究（大久保班研究）でのデータ収集の手順をもとに、データ提供機関において個人情報が特定されない方法で匿名化された情報の利用について、平成29年度内に改めて各機関に説明および同意を得て実施した。上記の倫理上の配慮については平成29年11月2日開催の東京大学倫理審査専門委員会において了承されている（審査番号17-187）。

C.　研究結果

（ア）現在の基準値に基づく性別年齢階級別有所見率の算出および過去の結果との比較

i）有所見率の算出

調査対象とした2013年度の分析対象者数は669,120人（男性450,153人、女性218,859人）であり、糖質検査の対象者については空腹時血糖のみの者は750,892人（男性500,541人、女性250,351人）、HbA1cのみの者は896,970人（男性593,526人、女性303,444人）であった。全年代での性別有所見率を表1および図1・2、性別年齢階級別有初見率を表2および図3・4に示す。性別有所見率では特に血液検査項目において男女の差が大きいことが明らかとなった。また、性別年齢階級別肥満者の割合（BMI>=25）を図5に示す。いずれの結果も年齢階級の上昇と共に有所見率の増加傾向を見るが、男性にお

いて肥満の割合･肝機能検査および脂質検査では 40 歳代をピークとして以降は減少傾向が認められた。

労働基準局による定期健康診断実施報告との対比では、多くの検査項目では当調査の有所見率が定期健康診断実施報告よりも低い傾向であり、当調査結果の方が高かったのは血圧検査および聴力検査(共に受診勧奨値）であった。

ii）過去の結果との比較

過去の研究との比較結果を表 3（平均値の比較）および表 4（有所見率の比較）に示す。この比較において、比較対象である 1998 年度には法定健康診断項目に LDLC および HbA1c が設定されていないことより、当該項目は比較していない。また、この比較においては、当調査の有所見率は比較対象の研究で用いられた有所見の基準（SBP>=160 mmHg、DBP>=95mmHg、RBC< 400 および>=580×10^4 個/ml（男性）・RBC <360 および>=520×10^4 個/ml（女性）、Hb<= 13.0 および>=17.6g/dl（男性）・Hb<=12.0g/dl および>=15.5g/dl（女性）、AST>=40U/l、ALT>= 40U/l、GGT>=80U/l、TG>=150mg/dl、HDL <40mg/dl、BS>=100mg/dl)に基づき算出した。また、TG/AST/ALT/GGT については比較対照研究報告書における表記が算術平均値であったことから、比較に際しては幾何平均ではなく算術平均値及び標準偏差値で実施した。

平均値の比較の結果、若年層の女性の Hb およびその他一部の項目では性別・年齢階級を除き、有意な変化が認められた。そのうち、BMI では軽度の増加傾向を認め、また GGT は検査値の増加が見られるが、その他の多くは検査値の改善傾向を示すものであった。

有所見率の比較では統計的検定は出来ないが、30 歳代後半から 50 歳代後半男性の BMI、30 歳代から 40 歳代前半の男性の SBP、30 歳代から 50 歳代後半男性および 30 歳代から 40 歳代前半女性 DBP、20 歳代後半から 50 歳代後半男性の AST(GOT)および ALT(GPT)で有所見率の増加傾向が見られたが、多くの項目では有所見率の改善傾向が認められた。

(イ)個人検査値の経年変化にかかる検討

解析対象人数は 109,853 人（男性 77.652 人、女性 32,201 人）であった。全対象者の個人検査値の経年推移について、性別年齢階級別に算出した結果を表 5 および図 5 に示す。また、初回および 6 回目の間の BMI 階級の変動を表 6 に示す。前後 5 年間で BMI 階級の変動が見られなかった割合は、「やせ群」のうち男性 64.1%・女性 72.1%、「基準内群」のうち男性 89.2%、女性 88.0%、「肥満群」のうち男性 82.7%・女性 83.8%であった。

これらの「未変化群」における、1 回目および 6 回目の間の検査値の変動を表 7 および図 6 に示す。以下のような傾向が認められた。

① SBP は全年代では男女ともに年齢階級の上昇と共に変化量は 60 歳代に向かって漸増傾向であるが、「やせ未変化群」では 50 代男性の変化が大きく、また「肥満未変化群」では 30 歳代から 40 歳代前半の女性での増加量が大きい。

② DBP は男女ともに 40 歳代をピークにそれまでの年代で漸増傾向であるが、「肥満未変化群」では増加量が他の群よりも大きく、また同群では 30

歳代から 40 歳代前半の男女双方での増加量が大きい。

③ AST(GOT) ・ ALT(GPT) ・ GGT(γGTP)は「基準内未変化群」「肥満未変化群」の双方において、20 歳代男性の増加量が大きい。

④ HDLC は「肥満未変化群」の 20 歳代から 30 歳代の男性女性双方での低下量が大きい。

⑤ LDLC および TG は、「基準内未変化群」「肥満未変化群」の双方において、20 歳代から 30 歳代での変化量が大きく、特に男性では両群での変化量は概ね同程度。

⑥ HbA1c は「肥満未変化群」の全年代に於いて男女共に増加量が多い傾向。

⑦ BMI 値について、「やせ未変化群」では増加傾向は殆ど見られないが、「肥満未変化群」では若年僧を中心に変化量が大きい傾向。

(ウ)許容値の提案

許容値の算出過程を表 8 に、またその結果によるカットオフ値とこの基準による 30-34 歳および 35-39 歳の年齢階級における有所見率を表 9-1 および 9-2 に示す。受診勧奨値および指導勧奨値では血圧検査・LDL・GGT 検査にて現在の汎用基準に照らした場合と比して 1.2-2.3 倍の対象者が抽出され、また指導勧奨値では HbA1c で現行基準よりも多い対象者抽出がされた。

なお、貧血検査については基準内群の若年僧での変動が大きくないことより検討対象とせず、また糖質検査については、検査値の安定が良いという点から血糖値ではなく HbA 1 c の値で提案した。

(エ)肥満未変化群と肥満改善群の性別年齢階級別個人検査値の経年推移（5 年間）の比較

結果を表 10 に示す。殆どの年代で Mauchly の球面性の仮説が成立しなかったため、Huynh-Feldt の自由度に換算をして被験者内効果の検定を行った。RBC・Hb 以外の殆どの検査項目で、肥満改善群での検査結果の改善傾向が認められ、男性の 40 歳代から 60 歳代を中心に、太字斜体の項目で両群の変化の差が認められた。RBC・Hb では肥満改善群での変化値の有意な低下を認めた。また、SBP・AST・ALT・GGT・HDL・LDL については、若年層の方が改善幅が大きいことが明らかとなった。

D. 考察

健康診断の有所見率については、これまで労働基準局により集計される定期健康診断実施報告によるもののほか、各健康診断機関がそれぞれの機関ごとの受診者に基づく有所見率を公表したもの、複数の健診機関により構成される協議会等により公表されるもの、また 40 歳以上の従業員については特定健康診断・特定保健指導にかかる事業の結果として公表されるもの等が存在するが、特定健康診断・特定保健指導にかかるもの以外については判定基準が一律ではない事、性別年齢階級が不明であるものが多い事、労働者以外の受診者が含まれている事、および地域性が限定されている事等の課題があり、事業場での集団集計結果との比較に資する精度が保たれているとは言い難い状況であった。特定健康診断・特定保健指導にかかるものについては、40 歳未満の者の年齢階級別有所見率がわからないという課題があった。本研究では、過去 20 年間の労働安全衛生関係の調査研究で算出されてい

なかった職域定期健康診断の有所見率、特に性別年齢階級別有所見率について、大規模データを用いて且つ一元的な有所見基準に基づき、事業場での集団集計結果との比較に資する有所見率を算出した。これにより、事業場の現在の健康状態の相対的位置付けが可能となり、今後の事業場の健康管理・健康増進施策を検討・決定する際での活用が期待される。

また、労働基準局による定期健康診断実施報告との対比において、当調査の結果は血圧検査および聴力検査について「受診勧奨」での有所見率の方が高く、その他の検査では低い傾向であった。また、「保健指導勧奨」での有所見率は全ての項目で高い結果となった。健康診断定期報告では「所見のあった者の人数」「医師指示人数」の提出を求めており、公開されている有所見率は前者の「所見のあった者の人数」の集計結果に該当する。今回の比較の結果からは、定期健康診断実施報告の有所見者の判断は当調査結果における「受診勧奨」の基準と近いと考えられるが、定期健康診断実施報告での血圧検査は全体的に過小評価傾向あると考えられ、またその他の血液検査については、保健指導基準よりも受診勧奨基準に近い値を示していることから、前述した、有所見の定義にかかる「受診勧奨基準」と「保健指導基準」の判断の混在の可能性に鑑みると、保健指導が必要である有所見者に対して適切な予防的介入が実施されていない可能性、および不必要な集団に対する過剰な保健指導の実施がされている可能性があることが示唆された。なお、定期健康診断実施報告は 50 人以上の事業場にその提出を求めていることから、小規模事業場を含む当調査との母集団の違いを考慮する必要がある。

過去の定期健康診断にかかる調査結果の平均値・有所見率との比較からは、平均値については BMI や一部の年齢階級での検査結果では値の増加が見られるものの、その他の多くは検査値の改善傾向を示すものであった。また、有所見率については BMI・血圧検査の有所見率は上昇傾向であるが、その他の項目は低下傾向であった。このことは、「BMI の平均値や有所見率増加に伴い他の検査の平均値・有所見率も増加する」という仮定に反する結果であった。その背景として、両者の母集団属性が異なること、当調査の対象年度が特定健診・特定保健指導導入後のものであること、などが影響している可能性が考えられる。特に、薬物療法受療者を除外した集団である本研究集団において、BMI の増加傾向に対して血圧以外の血液検査結果が改善傾向であることは、栄養状態の改善等の体重以外の要因への介入効果であることも考えられ、今後引き続き背景要因にかかる検討が必要である。

なお、中性脂肪や肝機能検査等については値の分布が正規分布ではないが、今回の比較に於いては過去の集計結果に準じたため算術平均値を用いての比較であることに留意が必要である。

個人検査値の経年推移については、血圧検査は年齢階級の増加が男女ともに 40/50 歳代まで漸増傾向であるのに対して、肝機能検査・脂質検査では男女差があり、特に男性では 40 歳未満の年代での上昇幅が大きいことが示された。循環器疾患のリスクファクターである項目に於けるこうした傾向から、40 歳未満の特に男性に対しては、積極的な予防的介入が必要であることが示唆された。

また、個人検査値の経年推移について、BMI 階級により差があることが示された。

特に、BMI 階級内での変動がない群において、肥満未変化群における検査値の上昇幅が基準内未変化群よりも大きい検査項目があり、「肥満群はすでに検査値が上昇していることが多いため変動率は小さい」という仮説に対する反証であるとすると、体重の増減がなくとも高体重を維持すること自体がその後の健康リスクとなることが示唆された。

この結果を受け、経年推移の調査対象者のうち肥満群における「未変化群」と「BMI 改善群」との検査結果の経年推移の差について検証した結果、RBC・Hb 以外の殆どの検査項目で、肥満改善群での検査結果の改善傾向が認められ、またその多くで 40 歳未満の若年層の改善幅が中高年齢層よりも大きい結果であったことから、若年肥満群への BMI 改善介入がその後の検査値上昇を大幅に改善する可能性があることが示された。

これらの知見を基に、基準値にかかる新たな提案を実施した。基準値にかかる議論はかねてより、その検査値の分布における 95 パーセンタイル値等の基準範囲からの逸脱を用いる場合や、標的疾患の予防に資するエビデンスに基づく値を設定する等の議論がされているが、現在本邦では循環器疾患等予防の観点において、後者に基づく特定健康診査・特定保健指導が国策として行われていること、またこれらの対象 40 歳未満が含まれていない事に鑑み、また限りのある保健医療資源を有効に活用する観点から、40 歳の段階で特定保健指導等の該当者を削減することを念頭に置くこととし、標的疾患の予防に資するエビデンスに基づき設定されている特定健康診査・特定保健指導の受診勧奨値および保健指導勧奨値から 40 歳時点までの検査値の生理的変動を差し引く方法で、30 歳及び 35 歳での許容値を提案した。この許容値による有所見者の増加は、検査項目によるが現在の基準に基づき抽出される率の 1.0-2.4 倍の範囲となった。

なお、当調査のデータベースには治療情報や病歴情報等、ばく露条件に対するアウトカム指標となる情報が含まれていないこと、また観察期間は最長でも 6 年間である事から、今後これらの値による実際の疾患の発生にかかる検討による妥当性の検証が望まれる。

E．結論

職域定期健康診断の有所見の検討に際して、性別・年齢階級と合わせて BMI 階級に注目し、現在汎用されている基準に基づく有所見率の横断的検討と、検査値等の経年推移に着目した縦断的検討による新たな予防介入の必要性について検討を行った。横断的検討では、事業場の健康診断集団集計結果との比較に基づく健康管理施策の検討に資する、性別年齢階級別有所見率を算出した。また、過去の研究結果との比較において、検査値の平均値・有所見率に改善があることが示唆された。また、現在の有所見の概念では受診勧奨値と保健指導勧奨値との混用が見られ、必要な保健指導が受けられていない者および過度に保健指導の対象となっている者がいる可能性が示唆された。縦断的検討では、特に若年層において検査値変動が大きい項目があることが示され、また BMI 階級の変動がなくとも経年的な検査値変動があること、特に肥満群ではその変動値が大きいことが示された。以上のことより、特に特定健康診査の対象外である 40 歳未満の若年層において、肥満群からの改善のみならず肥満群への移行の予防を目的とした介入の必要性が高いと考えられた。その結果

に基づき、40 歳未満の若年層に対する介入ポイントとしての新たな基準値(許容値)を提案した。

F. 健康危険情報

特記事項なし

G. 研究発表

山本健也、黒田玲子、大久保靖司. 職域一般健康診断結果の経年変動にかかる検討：第 92 回日本産業衛生学会（2019 年 5 月 23 日）

H. 知的財産権の出願・登録状況

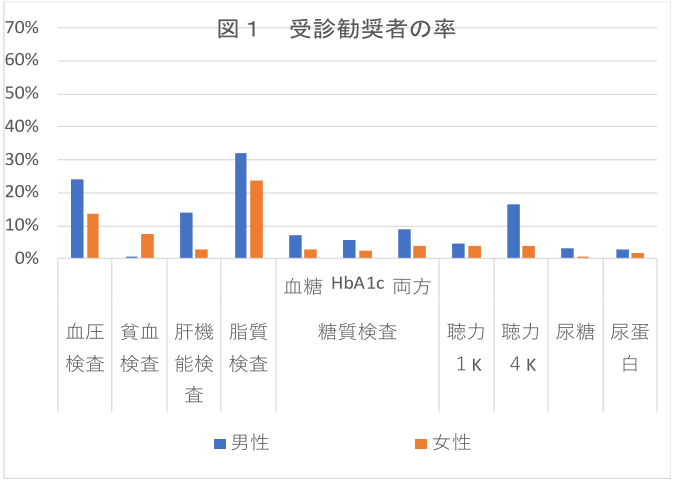
特記事項なし

図表中の検査項目の単位は以下の通り

SBP・DBP	：	mmHg
RBC	：	$\times 10^4$ 個/ml
Hb	：	g/dl
AST・ALT・GGT	：	U/l
TG・LDL・HDL・BS	：	mg/dl
HbA1c	：	6.5%

表１　全年代の性別有所見率

		男性		女性		全体		参考
		n=450153		n=218859		n=669012		定期健康診断報告による有所見率
		受診勧奨	保健指導勧奨	受診勧奨	保健指導勧奨	受診勧奨	保健指導勧奨	
血圧検査		23.9%	41.4%	13.8%	24.5%	20.6%	35.9%	14.7%
貧血検査		0.8%	3.7%	7.4%	17.7%	3.0%	8.3%	7.5%
肝機能検査		14.0%	38.6%	2.9%	11.0%	10.4%	29.6%	14.8%
脂質検査		32.1%	62.3%	23.9%	47.8%	29.4%	57.6%	32.6%
糖質検査	血糖	7.1%	29.6%	3.0%	16.0%	5.7%	25.1%	10.2%
	HbA1c	5.7%	32.5%	2.5%	29.6%	4.6%	31.5%	
	両方	9.0%	44.5%	4.0%	35.7%	7.3%	41.6%	
聴力１K		4.5%		4.0%		4.3%		3.6%
聴力４K		16.4%		4.1%		12.4%		7.6%
尿糖		3.1%		0.8%		2.3%		2.5%
尿蛋白		2.8%		1.9%		2.5%		4.2%



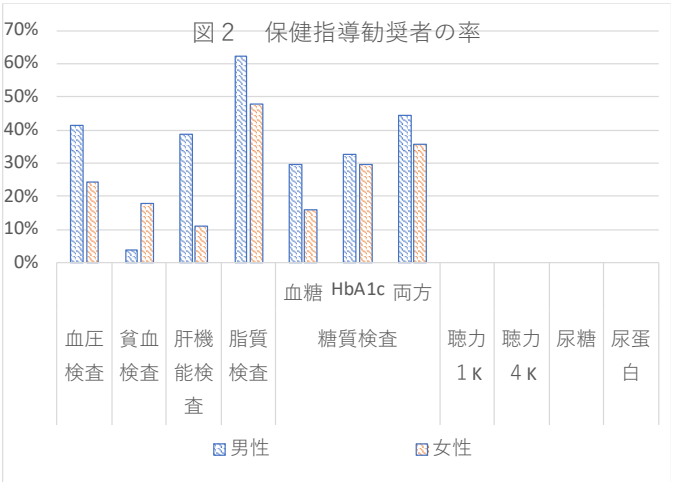
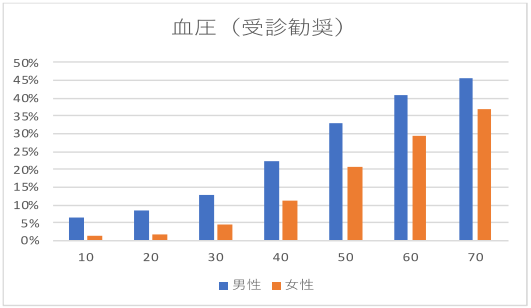


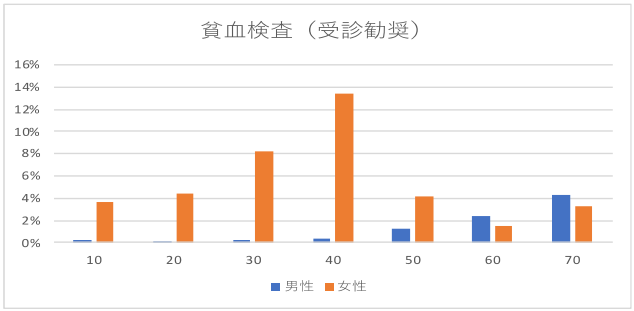
表２　性別年齢階級別有所見率

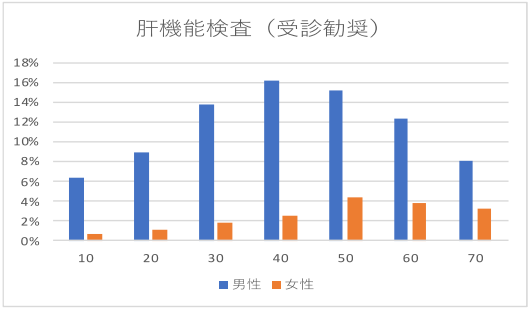
受診勧奨		男性							女性						
年代		10	20	30	40	50	60	70	10	20	30	40	50	60	70
n		3012	46354	98485	136406	99055	59067	7774	1308	25405	41413	67272	52936	27238	3287
血圧検査		6.3%	8.5%	13.0%	22.4%	33.0%	40.9%	45.5%	1.4%	1.7%	4.5%	11.4%	20.9%	29.2%	36.8%
貧血検査		0.3%	0.1%	0.2%	0.4%	1.2%	2.4%	4.3%	3.7%	4.4%	8.2%	13.4%	4.2%	1.5%	3.3%
肝機能検査		6.3%	8.9%	13.8%	16.2%	15.2%	12.3%	8.1%	0.8%	1.2%	1.9%	2.6%	4.5%	3.9%	3.3%
脂質検査		5.7%	14.0%	28.6%	37.8%	37.4%	32.2%	26.9%	5.5%	6.6%	11.3%	19.8%	38.5%	40.4%	36.1%
聴力１K		1.5%	1.1%	1.4%	2.3%	5.2%	13.2%	29.1%	1.5%	1.0%	1.5%	2.1%	4.8%	10.9%	27.8%
聴力４K		1.0%	1.3%	3.6%	9.2%	23.8%	47.8%	68.7%	0.7%	0.7%	1.1%	1.7%	4.6%	13.2%	33.3%
尿糖		0.3%	0.5%	1.1%	2.6%	4.7%	6.4%	6.9%	0.4%	0.3%	0.5%	0.7%	0.9%	1.3%	1.4%
尿蛋白		2.9%	1.9%	1.9%	2.5%	3.3%	4.2%	4.5%	4.1%	2.7%	1.9%	2.0%	1.5%	1.8%	2.0%
糖質検査	n	2353	50328	111059	144878	113854	67898	10171	1114	27503	48670	76978	59148	31475	5463
	血糖	0.9%	1.5%	2.6%	5.3%	10.7%	15.2%	15.3%	1.7%	1.5%	1.5%	2.0%	3.9%	6.3%	8.2%
	n	3869	61487	128496	170161	131796	83412	14305	1717	32858	54960	91627	73372	41457	7453
	HbA1c	0.2%	0.4%	1.5%	4.5%	8.9%	12.3%	13.4%	0.1%	0.2%	0.6%	1.5%	3.6%	6.4%	8.0%
	n	1638	35432	84485	116958	92336	54108	8663	759	18193	37295	62480	47197	25140	4739
	両方	0.7%	1.6%	3.2%	6.6%	13.2%	19.1%	19.6%	1.6%	1.8%	1.7%	2.5%	5.4%	9.2%	11.1%

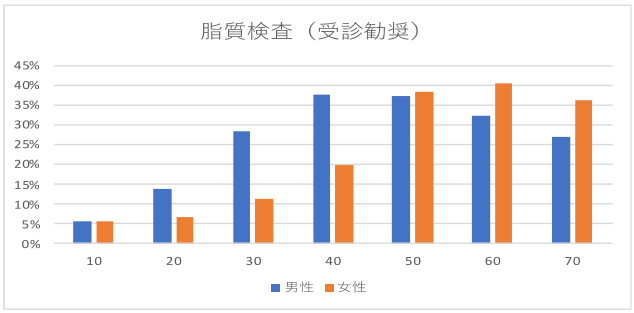
保健指導勧奨		男性							女性						
年代		10	20	30	40	50	60	70	10	20	30	40	50	60	70
血圧検査		20.8%	22.8%	28.1%	39.6%	52.5%	61.9%	65.9%	6.1%	5.3%	10.0%	21.4%	35.8%	47.2%	55.8%
貧血検査		0.9%	0.7%	1.1%	2.2%	5.3%	9.5%	16.8%	12.2%	13.9%	20.0%	25.9%	11.6%	9.7%	16.2%
肝機能検査		17.3%	23.5%	35.6%	42.9%	43.4%	39.2%	32.8%	3.5%	3.9%	6.5%	9.2%	16.8%	17.6%	16.8%
脂質検査		23.2%	37.3%	57.5%	68.5%	69.4%	66.1%	61.3%	20.8%	20.7%	30.0%	44.2%	67.1%	70.6%	67.6%
糖質検査	血糖	11.0%	11.8%	16.3%	26.2%	41.0%	50.4%	50.4%	9.6%	8.4%	8.1%	12.0%	21.1%	31.7%	34.9%
	HbA1c	6.1%	7.4%	17.0%	30.6%	44.7%	55.7%	61.6%	7.9%	7.3%	12.8%	23.1%	42.1%	56.6%	64.7%
	両方	14.3%	16.7%	26.6%	41.6%	58.3%	69.4%	73.1%	18.1%	14.2%	18.1%	28.6%	49.1%	63.8%	70.0%

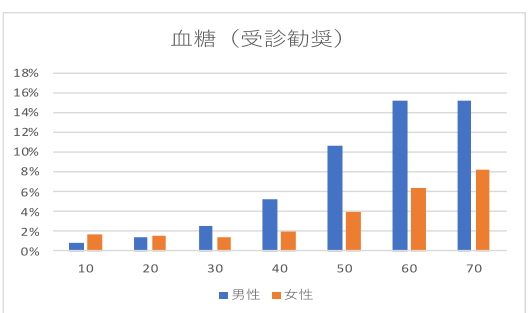
図３　受診勧奨対象者の性別年齢階級別有所見率











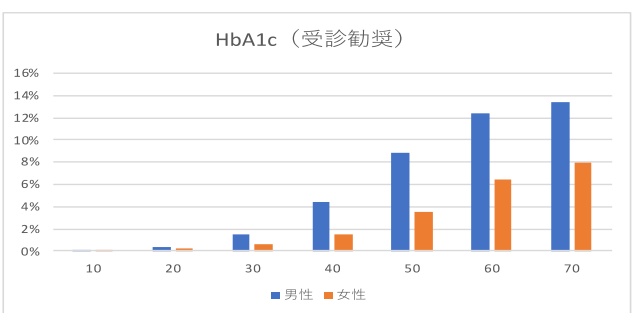
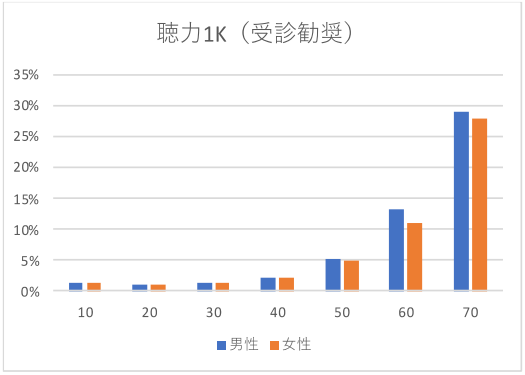
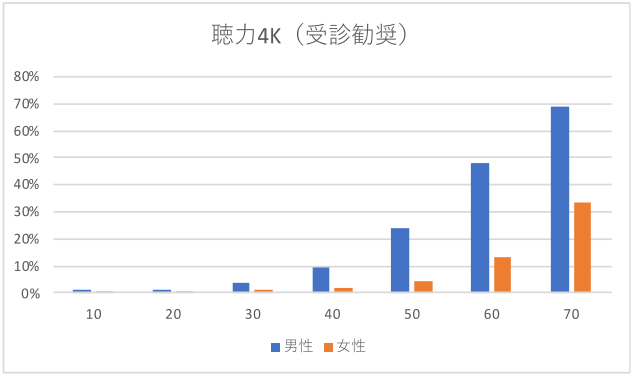
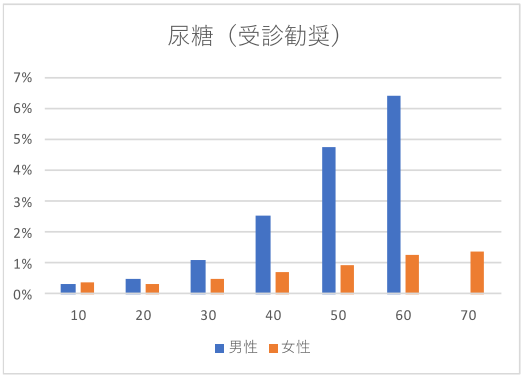


図３　続き







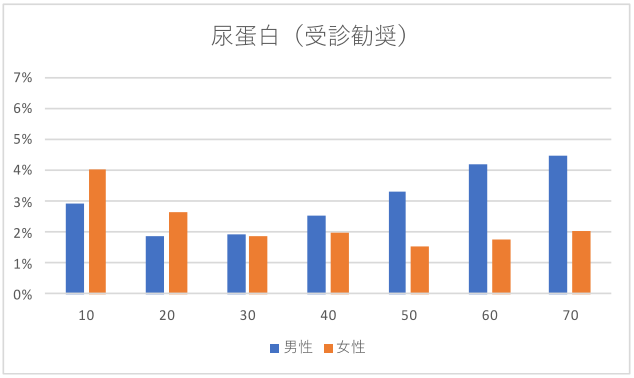
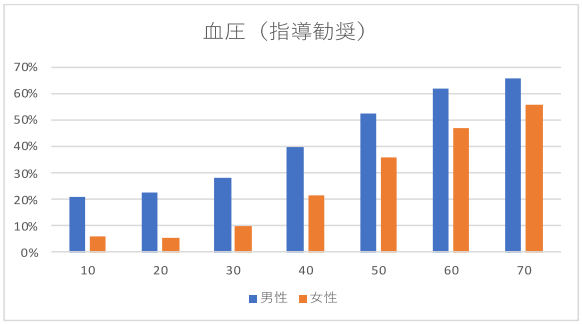
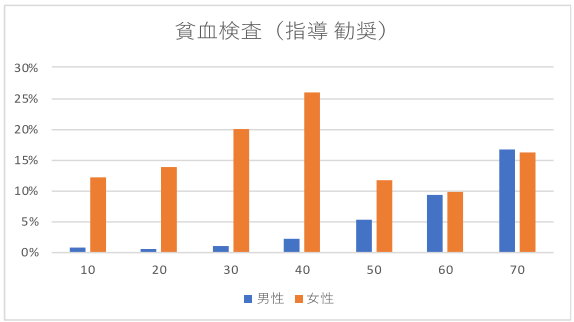
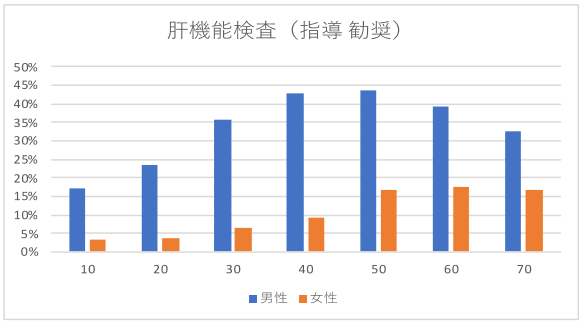
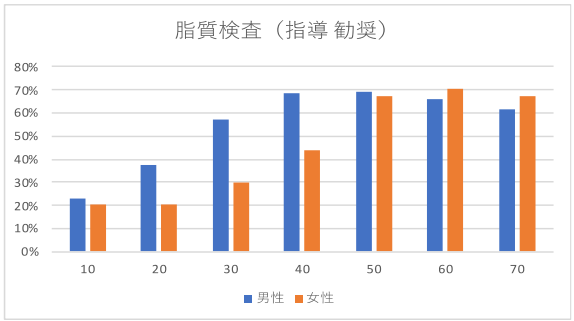


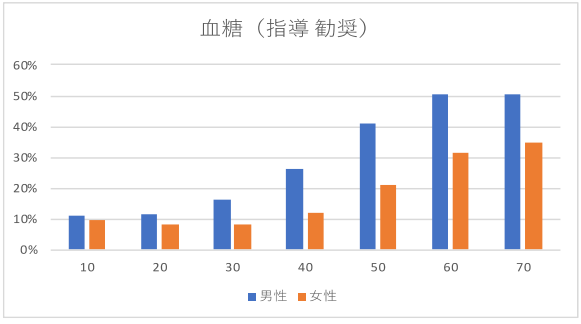
図４　保健指導勧奨対象者の性別年齢階級別有所見率











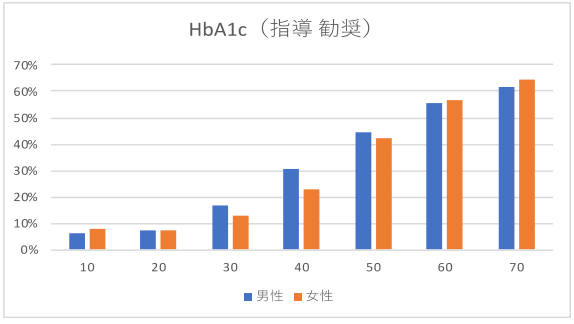
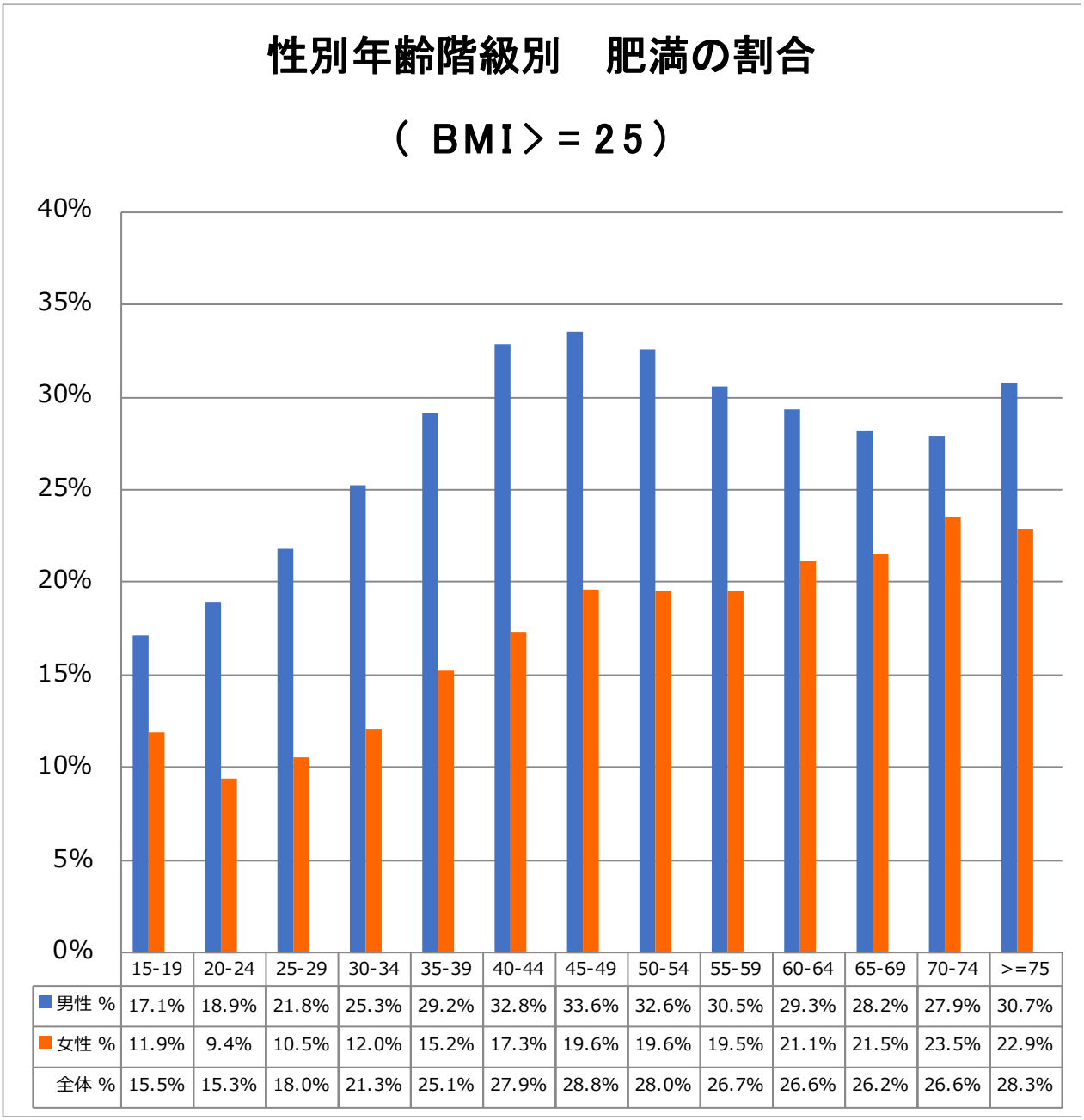


図５　性別年齢階級別肥満の割合



	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	>=75
男性 %	17.1%	18.9%	21.8%	25.3%	29.2%	32.8%	33.6%	32.6%	30.5%	29.3%	28.2%	27.9%	30.7%
女性 %	11.9%	9.4%	10.5%	12.0%	15.2%	17.3%	19.6%	19.6%	19.5%	21.1%	21.5%	23.5%	22.9%
全体 %	15.5%	15.3%	18.0%	21.3%	25.1%	27.9%	28.8%	28.0%	26.7%	26.6%	26.2%	26.6%	28.3%

表３　職域定期健康診断項目の定量的検査結果　過去の研究との平均値の比較

		令和元年度研究（2013年度受診）						平成12年度研究（1998年度受診）						T検定											
		M			F			M			F			M						F					
		n	M	SD	n	M	SD	n	M	SD	n	M	SD	平均値の差	s2	t	自由度	p		平均値の差	s2	t	自由度	p	
BMI	15-19	3014	22.1	3.80	1308	21.3	3.34	4263	21.7	3.58	2558	21.1	3.35	0.45	13.47	5.15	7275	0.00000	**	0.20	11.20	1.77	3865	0.07655	
	20-24	17324	22.3	3.88	10870	20.9	3.40	22542	22.2	3.48	14996	20.7	3.22	0.17	13.37	4.68	39864	0.00000	**	0.16	10.87	3.80	25865	0.00015	**
	25-29	29030	22.8	3.88	14535	21.0	3.63	28895	23.0	3.66	13759	20.9	3.50	−0.20	14.24	6.23	57923	0.00000	**	0.09	12.73	2.20	28293	0.02760	*
	30-34	37444	23.2	3.84	15892	21.2	3.72	25307	23.5	3.59	8383	21.4	3.73	−0.28	13.99	9.15	62749	0.00000	**	−0.23	13.87	4.57	24274	0.00000	**
	35-39	61047	23.7	3.83	25522	21.6	3.94	24914	23.6	3.37	9027	21.8	3.52	0.03	13.72	1.01	85959	0.31120		−0.19	14.73	3.99	34548	0.00007	**
	40-44	74194	24.0	3.81	34986	22.0	3.98	25079	23.6	3.19	12818	22.3	3.37	0.37	13.44	13.88	99271	0.00000	**	−0.36	14.63	9.03	47803	0.00000	**
	45-49	62216	24.0	3.64	32289	22.3	3.90	32582	23.6	3.05	19077	22.7	3.29	0.46	11.87	19.40	94796	0.00000	**	−0.49	13.55	14.47	51365	0.00000	**
	50-54	52441	23.9	3.44	28122	22.2	3.75	26959	23.5	2.95	16167	22.9	3.23	0.40	10.77	16.19	79398	0.00000	**	−0.71	12.75	20.01	44288	0.00000	**
	55-59	46620	23.7	3.25	24815	22.3	3.63	22535	23.5	2.91	12065	23.1	3.23	0.17	9.87	6.76	69153	0.00000	**	−0.83	12.30	21.33	36879	0.00000	**
	60-64	40886	23.5	3.07	19664	22.5	3.56	9837	23.7	2.89	4066	23.6	3.30	−0.20	9.22	5.98	50721	0.00000	**	−1.07	12.37	17.71	23729	0.00000	**
	65-69	18184	23.5	3.00	7574	22.6	3.40	4379	23.6	2.90	1147	23.6	3.32	−0.14	8.88	2.83	22561	0.00468	**	−0.93	11.50	8.69	8720	0.00000	**
	70−	6138	23.5	2.92	2580	22.7	3.44	1325	23.4	2.93	313	23.2	3.31	0.12	8.52	1.33	7461	0.18198		−0.45	11.73	2.21	2892	0.02740	*
	75−	1647	23.5	3.06	713	22.6	3.39																		
sBP	15-19	3014	119.2	13.29	1308	109.3	11.74	4263	118.9	12.33	2558	111.1	10.84	0.34	162.22	1.12	7275	0.26202		−1.85	124.34	4.88	3865	0.00000	**
	20-24	17324	120.1	13.66	10870	108.1	11.65	22558	121.6	11.99	15013	111.7	10.81	−1.55	162.40	12.04	39880	0.00000	**	−3.53	124.74	25.10	25882	0.00000	**
	25-29	29030	120.0	13.66	14535	107.5	12.28	31054	123.2	12.27	14190	112.7	11.29	−3.24	167.93	30.63	60082	0.00000	**	−5.20	139.28	37.34	28724	0.00000	**
	30-34	37444	121.0	14.63	15892	108.6	13.29	27510	124.2	12.67	8607	114.7	12.44	−3.16	191.32	28.77	64952	0.00000	**	−6.06	168.99	34.83	24498	0.00000	**
	35-39	61047	122.0	15.51	25522	110.9	14.89	26535	124.8	13.59	9153	117.4	13.85	−2.86	223.52	26.02	87580	0.00000	**	−6.49	213.80	36.43	34674	0.00000	**
	40-44	74194	124.4	16.72	34986	114.6	16.48	25245	126.5	15.21	12837	120.4	15.46	−2.07	267.24	17.38	99437	0.00000	**	−5.81	262.94	34.72	47822	0.00000	**
	45-49	62216	126.7	17.71	32289	118.8	18.45	32622	129.3	16.54	19081	125.0	17.48	−2.58	299.86	21.80	94836	0.00000	**	−6.21	327.39	37.59	51369	0.00000	**
	50-54	52441	129.2	18.67	28122	122.1	19.39	26985	132.4	18.06	16169	129.3	18.54	−3.23	341.06	23.35	79424	0.00000	**	−7.16	364.25	38.01	44290	0.00000	**
	55-59	46620	132.3	19.46	24815	125.6	20.13	22579	134.9	17.78	12068	131.8	19.12	−2.56	358.25	16.68	69197	0.00000	**	−6.28	392.14	28.58	36882	0.00000	**
	60-64	40886	135.2	19.90	19664	128.9	20.08	9843	139.2	17.44	4067	135.7	18.09	−3.99	378.16	18.28	50727	0.00000	**	−6.80	390.19	19.98	23730	0.00000	**
	65-69	18184	137.4	20.13	7574	131.2	20.10	4379	141.8	17.92	1147	138.2	17.95	−4.43	388.93	13.34	22561	0.00000	**	−7.01	393.08	11.16	8720	0.00000	**
	70−	6138	138.3	20.39	2580	133.8	20.56	1325	142.9	17.91	313	141.6	17.69	−4.56	398.83	7.54	7461	0.00000	**	−7.83	410.76	6.45	2892	0.00000	**
	75−	1647	138.8	19.68	713	135.0	19.76																		
dBP	15-19	3014	65.7	9.26	1308	63.9	9.21	4263	67.8	9.05	2558	64.9	8.41	−2.11	83.52	9.70	7275	0.00000	**	−0.99	75.50	3.35	3865	0.00081	**
	20-24	17324	67.7	9.42	10870	64.3	8.91	22558	70.2	9.06	15013	65.3	8.55	−2.51	84.97	26.95	39880	0.00000	**	−1.00	75.73	9.12	25882	0.00000	**
	25-29	29030	69.3	9.73	14535	64.7	9.36	31054	72.6	9.30	14190	66.9	8.86	−3.27	90.48	42.11	60082	0.00000	**	−2.20	83.14	20.45	28724	0.00000	**
	30-34	37444	71.6	10.62	15892	66.0	10.12	27510	75.0	9.76	8607	68.8	9.41	−3.44	105.37	42.20	64952	0.00000	**	−2.86	97.54	21.64	24498	0.00000	**
	35-39	61047	74.0	11.43	25522	67.7	11.07	26535	77.1	10.34	9153	70.7	10.19	−3.11	123.47	38.06	87580	0.00000	**	−3.03	117.53	22.94	34674	0.00000	**
	40-44	74194	76.9	12.25	34986	69.9	11.72	25245	79.1	11.11	12837	72.6	10.76	−2.24	143.34	25.68	99437	0.00000	**	−2.66	131.63	22.47	47822	0.00000	**
	45-49	62216	79.2	12.64	32289	72.3	12.35	32620	81.1	11.41	19081	75.3	11.52	−1.93	149.53	23.09	94834	0.00000	**	−2.97	145.13	27.00	51369	0.00000	**
	50-54	52441	80.8	12.52	28122	74.0	12.38	26985	82.6	11.33	16169	77.7	11.59	−1.82	147.17	20.02	79424	0.00000	**	−3.74	146.29	31.33	44290	0.00000	**
	55-59	46620	81.3	12.17	24815	75.2	12.06	22579	82.9	10.83	12068	78.7	11.60	−1.58	138.09	16.58	69197	0.00000	**	−3.55	141.90	26.85	36882	0.00000	**
	60-64	40886	80.8	11.84	19664	75.5	11.71	9843	83.6	10.46	4067	79.8	10.91	−2.82	134.23	21.68	50727	0.00000	**	−4.31	134.08	21.61	23730	0.00000	**
	65-69	18184	79.6	11.59	7574	74.9	11.45	4379	83.1	10.34	1147	79.8	10.70	−3.52	129.05	18.41	22561	0.00000	**	−4.90	128.94	13.62	8720	0.00000	**
	70−	6138	77.1	11.45	2580	73.8	11.53	1325	82.2	10.51	313	79.5	10.59	−5.03	127.50	14.71	7461	0.00000	**	−5.71	130.78	8.34	2892	0.00000	**
	75−	1647	75.0	11.46	713	73.1	10.67																		
RBC	15-19	3014	514.5	32.17	1308	450.4	31.56	1466	510.7	32.27	474	442.0	31.54	3.85	1037.14	3.76	4478	0.00017	**	8.48	995.56	5.01	1781	0.00000	**
	20-24	17324	511.8	32.55	10870	447.6	31.78	4914	504.5	33.54	2894	437.5	31.91	7.39	1074.05	13.95	22236	0.00000	**	10.08	1011.63	15.15	13763	0.00000	**
	25-29	29030	506.6	32.97	14535	443.5	32.12	7518	501.1	34.20	3296	434.1	32.67	5.51	1104.27	12.82	36546	0.00000	**	9.34	1038.04	15.03	17830	0.00000	**
	30-34	37444	503.5	33.86	15892	441.5	32.55	10393	500.4	35.88	2989	435.7	32.98	3.05	1177.08	8.02	47835	0.00000	**	5.80	1063.76	8.91	18880	0.00000	**
	35-39	61047	499.7	34.83	25522	440.1	33.76	15644	496.1	37.10	4274	433.1	33.99	3.67	1246.43	11.59	76689	0.00000	**	7.06	1142.24	12.64	29795	0.00000	**
	40-44	74194	494.8	36.38	34986	439.2	34.24	23585	487.9	38.10	12450	429.5	34.08	6.92	1354.41	25.14	97777	0.00000	**	9.69	1169.43	27.15	47435	0.00000	**
	45-49	62216	489.3	37.72	32289	440.2	35.42	29692	482.6	39.40	18493	432.1	35.34	6.73	1464.66	24.91	91906	0.00000	**	8.17	1252.41	25.05	50781	0.00000	**
	50-54	52441	482.6	39.37	28122	444.6	35.23	24118	478.5	40.80	15735	437.9	35.29	4.08	1586.25	13.16	76557	0.00000	**	6.68	1242.61	19.02	43856	0.00000	**
	55-59	46620	475.3	40.25	24815	443.4	34.47	20086	472.6	41.24	11746	436.7	35.13	2.67	1644.52	7.81	66704	0.00000	**	6.73	1202.92	17.32	36560	0.00000	**
	60-64	40886	469.5	40.70	19664	439.0	33.96	9170	464.5	41.24	3940	432.2	35.39	4.97	1664.41	10.54	50054	0.00000	**	6.87	1169.75	11.50	23603	0.00000	**
	65-69	18184	464.4	42.03	7574	436.5	34.65	4131	459.5	41.49	1107	428.0	36.68	4.89	1758.20	6.76	22313	0.00000	**	8.46	1218.97	7.53	8680	0.00000	**
	70−	6138	456.6	41.06	2580	430.9	35.34	1267	451.6	42.22	303	424.3	37.82	5.07	1702.41	3.98	7403	0.00007	**	6.63	1268.17	3.07	2882	0.00219	**
	75−	1647	446.9	42.60	713	421.9	39.22																		
Hb	15-19	3014	15.4	0.96	1308	13.1	1.10	1466	15.3	0.94	474	13.1	1.13	0.12	0.91	4.09	4478	0.00004	**	0.03	1.22	0.48	1781	0.63300	
	20-24	17324	15.5	0.93	10870	13.1	1.08	4914	15.4	0.91	2894	13.1	1.05	0.05	0.85	3.67	22236	0.00024	**	0.02	1.15	0.86	13763	0.39016	
	25-29	29030	15.4	0.92	14535	13.0	1.09	7517	15.4	0.91	3295	13.1	1.06	−0.06	0.85	4.78	36545	0.00000	**	−0.03	1.17	1.65	17829	0.09875	
	30-34	37444	15.3	0.95	15892	12.9	1.18	10391	15.4	0.97	2988	13.0	1.20	−0.12	0.92	11.34	47833	0.00000	**	−0.03	1.39	1.09	18879	0.27659	
	35-39	61047	15.3	0.98	25522	12.8	1.31	15644	15.4	1.00	4274	12.8	1.38	−0.11	0.97	12.12	76689	0.00000	**	−0.01	1.75	0.42	29795	0.67414	
	40-44	74194	15.2	1.02	34986	12.7	1.47	23585	15.3	1.05	12450	12.6	1.52	−0.03	1.06	3.33	97777	0.00087	**	0.11	2.21	7.08	47435	0.00000	**
	45-49	62216	15.2	1.07	32289	12.7	1.59	29692	15.2	1.09	18494	12.6	1.59	−0.01	1.15	1.15	91906	0.25058		0.05	2.51	3.28	50782	0.00103	**
	50-54	52441	15.1	1.12	28122	13.1	1.34	24118	15.1	1.14	15735	13.1	1.29	−0.05	1.27	5.25	76557	0.00000	**	0.05	1.74	3.88	43856	0.00011	**
	55-59	46620	14.9	1.17	24815	13.4	0.99	20086	15.0	1.17	11746	13.3	0.98	−0.07	1.37	7.05	66704	0.00000	**	0.10	0.98	8.77	36560	0.00000	**
	60-64	40886	14.7	1.20	19664	13.3	0.98	9170	14.7	1.19	3940	13.2	1.00	0.00	1.44	0.09	50054	0.92532		0.08	0.97	4.65	23603	0.00000	**
	65-69	18184	14.6	1.24	7574	13.2	0.99	4131	14.6	1.22	1107	13.1	1.04	0.02	1.53	0.80	22313	0.42201		0.15	0.99	4.63	8680	0.00000	**
	70−	6138	14.3	1.24	2580	13.1	1.01	1267	14.3	1.26	303	13.0	1.08	0.03	1.55	0.67	7403	0.50581		0.12	1.03	1.91	2882	0.05675	
	75−	1647	14.0	1.30	713	12.8	1.16																		
TG	15-19	3014	87.3	56.60	1308	67.8	38.85	1422	80.5	55.95	428	68.2	33.26	6.76	3179.88	3.73	4434	0.00020	**	−0.43	1409.88	0.21	1735	0.83709	
	20-24	17324	96.0	72.35	10870	67.2	38.52	4726	107.5	79.67	2624	71.1	45.70	−11.47	5473.23	9.45	22048	0.00000	**	−3.86	1601.16	4.44	13493	0.00001	**
	25-29	29030	106.3	83.94	14535	69.2	45.85	7385	126.9	89.42	3017	72.9	51.11	−20.63	7238.71	18.60	36413	0.00000	**	−3.70	2190.10	3.95	17551	0.00008	**
	30-34	37444	120.9	102.54	15892	72.6	46.30	10412	145.9	115.58	2873	77.8	47.67	−24.99	11133.73	21.38	47854	0.00000	**	−5.21	2163.00	5.53	18764	0.00000	**
	35-39	61047	129.7	114.80	25522	75.4	49.51	16122	154.3	131.84	4276	82.1	56.34	−24.51	14056.67	23.35	77167	0.00000	**	−6.65	2554.88	7.96	29797	0.00000	**
	40-44	74194	141.2	127.08	34986	80.1	54.86	24098	157.9	129.05	12471	84.9	53.83	−16.69	16273.03	17.65	98290	0.00000	**	−4.75	2980.12	8.34	47456	0.00000	**
	45-49	62216	147.1	134.64	32289	86.9	58.64	30788	154.6	119.77	18555	91.2	60.36	−7.54	16875.96	8.33	93002	0.00000	**	−4.25	3513.27	7.78	50843	0.00000	**
	50-54	52441	147.3	125.60	28122	96.1	62.99	25256	149.1	116.70	15811	99.9	64.10	−1.81	15073.71	1.92	77695	0.05426		−3.83	4018.83	6.08	43932	0.00000	**
	55-59	46620	143.0	114.74	24815	104.1	67.58	21103	143.4	109.70	11806	107.5	66.72	−0.32	12812.16	0.34	67721	0.73330		−3.31	4529.46	4.40	36620	0.00001	**
	60-64	40886	138.2	107.93	19664	108.3	66.98	9400	140.2	93.75	3959	117.7	70.50	−2.02	11113.98	1.68	50284	0.09392		−9.43	4566.96	8.01	23622	0.00000	**
	65-69	18184	134.3	92.94	7574	111.3	65.61	4188	131.9	87.63	1115	121.0	68.82	2.43	8458.53	1.54	22370	0.12320		−9.69	4359.78	4.58	8688	0.00000	**
	70−	6138	127.0	80.38	2580	112.2	62.61	1276	128.7	84.72	306	129.8	78.46	−1.67	6583.94	0.67	7412	0.50356		−17.55	4156.37	4.50	2885	0.00001	**
	75−	1647	121.1	79.00	713	110.0	64.67																		

		令和元年度研究 (2013年度受診)						平成12年度研究 (1998年度受診)						T検定									
		M			F			M			F			M					F				
		n	M	SD	n	M	SD	n	M	SD	n	M	SD	平均値の差	s2	t	自由度	p	平均値の差	s2	t	自由度	p
HDL	15-19	3014	56.7	11.39	1308	66.8	13.28	868	53.5	11.22	133	61.3	13.80	3.14	128.91	7.17	3880	0.00000 **	5.49	177.72	4.53	1440	0.00001 **
	20-24	17324	57.6	12.45	10870	68.8	14.03	1601	55.4	12.67	876	65.7	14.32	2.24	155.41	6.87	18923	0.00000 **	3.08	197.35	6.25	11745	0.00000 **
	25-29	29030	57.4	13.06	14535	69.3	14.24	3185	54.7	13.45	1276	66.7	14.75	2.79	171.63	11.40	32213	0.00000 **	2.53	203.89	6.06	15810	0.00000 **
	30-34	37444	57.0	13.80	15892	69.6	14.91	5940	53.4	13.75	1541	66.4	14.75	3.58	190.32	18.59	43382	0.00000 **	3.23	222.00	8.12	17432	0.00000 **
	35-39	61047	57.3	14.54	25522	69.8	15.31	11706	53.5	14.09	2812	66.2	15.06	3.83	209.29	26.22	72751	0.00000 **	3.60	233.52	11.85	28333	0.00000 **
	40-44	74194	57.5	14.99	34986	70.1	15.94	16602	54.3	14.71	8320	66.0	15.30	3.15	223.20	24.59	90794	0.00000 **	4.06	250.30	21.05	43305	0.00000 **
	45-49	62216	58.0	15.37	32289	71.0	16.59	20746	54.5	15.21	12571	66.8	15.78	3.46	235.10	28.12	82960	0.00000 **	4.15	267.94	24.11	44859	0.00000 **
	50-54	52441	58.7	15.75	28122	72.7	17.42	17561	55.3	15.47	11116	66.8	16.15	3.39	245.83	24.83	70000	0.00000 **	5.90	291.43	30.83	39237	0.00000 **
	55-59	46620	59.3	16.13	24815	71.8	17.39	14264	56.1	15.59	8264	65.9	16.02	3.15	256.17	20.55	60882	0.00000 **	5.91	291.06	27.27	33078	0.00000 **
	60-64	40886	59.1	15.98	19664	70.0	16.99	4698	55.1	15.79	2156	64.4	16.16	3.91	254.70	15.91	45582	0.00000 **	5.61	285.92	14.61	21819	0.00000 **
	65-69	18184	58.7	15.65	7574	68.2	16.67	1753	56.0	16.03	506	64.1	17.49	2.71	246.04	6.91	19935	0.00000 **	4.12	279.61	5.37	8079	0.00000 **
	70-	6138	57.7	15.29	2580	66.3	15.76	507	54.7	14.46	129	61.2	14.19	2.96	231.81	4.21	6643	0.00003 **	5.07	246.09	3.58	2708	0.00035 **
	75-	1647	56.6	15.00	713	65.1	15.94																
GOT	15-19	3014	21.6	14.69	1308	17.3	4.37	1452	20.4	10.04	433	17.0	6.69	1.19	178.40	2.79	4464	0.00531 **	0.34	25.47	1.22	1740	0.22450
	20-24	17324	21.5	9.69	10870	17.4	5.91	5058	21.3	11.85	2783	16.8	5.51	0.21	104.45	1.29	22380	0.19858	0.68	34.01	5.49	13652	0.00000 **
	25-29	29030	22.0	10.16	14535	17.6	6.72	7788	23.0	11.98	3157	17.3	5.79	-0.95	111.67	7.04	36816	0.00000 **	0.25	43.04	1.94	17691	0.05231
	30-34	37444	22.9	10.96	15892	17.9	6.69	10653	25.0	13.68	2943	18.0	7.25	-2.16	134.98	16.93	48095	0.00000 **	-0.11	45.96	0.81	18834	0.41881
	35-39	61047	23.5	11.58	25522	18.1	7.48	16157	25.8	15.46	4292	18.5	15.46	-2.26	156.13	20.44	77202	0.00000 **	-0.34	82.35	2.27	29813	0.02315 *
	40-44	74194	24.1	15.53	34986	18.6	7.94	24108	26.1	20.20	12491	18.8	10.22	-1.99	282.08	15.98	98300	0.00000 **	-0.17	73.98	1.90	47476	0.05794
	45-49	62216	24.4	21.03	32289	19.5	9.94	30795	26.3	19.29	18577	19.9	8.61	-1.86	419.03	13.04	93009	0.00000 **	-0.47	89.77	5.39	50865	0.00000 **
	50-54	52441	24.7	14.60	28122	21.4	10.59	25258	26.7	17.78	15819	22.0	9.90	-1.99	246.59	16.55	77697	0.00000 **	-0.60	107.04	5.84	43940	0.00000 **
	55-59	46620	24.9	14.22	24815	22.8	9.44	21103	27.5	19.36	11808	23.9	11.43	-2.52	255.91	18.99	67721	0.00000 **	-1.10	102.53	9.72	36622	0.00000 **
	60-64	40886	25.2	21.04	19664	23.0	11.33	9404	27.3	19.86	3961	24.4	9.85	-2.11	433.59	8.86	50288	0.00000 **	-1.32	123.02	6.83	23624	0.00000 **
	65-69	18184	25.2	12.88	7574	23.6	12.98	4193	27.5	19.91	1115	24.7	9.81	-2.30	209.14	9.28	22375	0.00000 **	-1.10	159.22	2.72	8688	0.00659 **
	70-	6138	25.2	10.17	2580	23.8	8.50	1276	26.5	13.41	306	24.8	9.89	-1.34	116.62	4.03	7412	0.00006 **	-1.00	75.00	1.91	2885	0.05625
	75-	1647	25.1	11.34	713	24.4	8.80																
GPT	15-19	3014	22.5	24.79	1308	12.9	7.68	1452	22.0	23.83	433	13.5	11.69	0.59	599.37	0.75	4464	0.45065	-0.62	78.28	1.26	1740	0.20643
	20-24	17324	24.1	22.24	10870	13.4	9.60	5058	25.5	26.59	2783	13.8	11.48	-1.36	542.51	3.65	22380	0.00026 **	-0.41	100.30	1.93	13652	0.05399
	25-29	29030	26.0	23.30	14535	13.8	10.51	7788	30.6	27.26	3157	14.6	11.29	-4.54	585.31	14.71	36816	0.00000 **	-0.77	113.51	3.68	17691	0.00023 **
	30-34	37444	28.2	24.09	15892	14.5	10.38	10653	34.3	29.43	2943	15.3	11.64	-6.13	643.74	22.00	48095	0.00000 **	-0.72	112.03	3.39	18834	0.00070 **
	35-39	61047	29.3	22.96	25522	15.1	11.83	16157	34.3	29.40	4292	16.1	21.49	-5.02	597.76	23.21	77202	0.00000 **	-0.94	186.28	4.17	29813	0.00003 **
	40-44	74194	29.4	22.13	34986	15.7	12.08	24108	32.3	32.98	12491	15.9	13.09	-2.84	636.24	15.19	98300	0.00000 **	-0.23	152.53	1.79	47476	0.07399
	45-49	62216	28.6	21.44	32289	16.5	12.00	30795	30.4	26.00	18577	17.1	11.41	-1.78	531.18	11.08	93009	0.00000 **	-0.58	139.00	5.34	50865	0.00000 **
	50-54	52441	27.2	18.76	28122	18.8	13.06	25258	29.0	22.97	15819	19.5	14.13	-1.88	409.10	12.14	77697	0.00000 **	-0.71	181.05	5.31	43940	0.00000 **
	55-59	46620	25.6	17.74	24815	20.1	12.72	21103	27.7	21.36	11808	21.0	15.16	-2.13	358.84	13.55	67721	0.00000 **	-0.91	183.73	6.01	36622	0.00000 **
	60-64	40886	24.4	17.41	19664	19.9	14.25	9404	26.1	21.31	3961	21.3	13.78	-1.61	331.32	7.73	50288	0.00000 **	-1.39	200.76	5.63	23624	0.00000 **
	65-69	18184	23.4	17.94	7574	19.9	14.28	4193	25.0	26.16	1115	20.6	11.85	-1.56	389.61	4.61	22375	0.00000 **	-0.66	195.88	1.47	8688	0.14155
	70-	6138	22.0	12.04	2580	19.5	11.71	1276	22.5	17.09	306	19.8	12.30	-0.52	170.19	1.30	7412	0.19517	-0.33	138.58	0.46	2885	0.64294
	75-	1647	20.7	17.50	713	18.3	9.69																
GGT	15-19	3014	21.9	13.51	1308	15.1	7.46	1422	20.2	12.29	429	12.2	7.59	1.72	172.47	4.06	4434	0.00005 **	2.85	56.19	6.84	1736	0.00000 **
	20-24	17324	25.8	20.57	10870	15.9	8.80	4770	20.6	18.42	2669	11.7	7.54	5.21	405.00	15.83	22092	0.00000 **	4.13	73.34	22.32	13538	0.00000 **
	25-29	29030	29.9	27.40	14535	16.8	19.44	7451	27.4	27.59	3078	12.5	9.98	2.55	752.85	7.16	36479	0.00000 **	4.28	329.43	11.88	17612	0.00000 **
	30-34	37444	36.2	37.26	15892	18.2	15.91	10448	38.6	45.57	2989	14.6	14.29	-2.42	1538.36	5.57	47890	0.00000 **	3.63	245.30	11.62	18880	0.00000 **
	35-39	61047	42.3	49.72	25522	19.7	19.02	16129	45.4	56.17	4276	15.4	14.54	-3.12	2614.98	6.89	77174	0.00000 **	4.34	340.17	14.23	29797	0.00000 **
	40-44	74194	48.4	60.05	34986	21.4	23.16	24070	47.8	56.68	12469	16.1	22.25	0.61	3509.60	1.39	98262	0.16455	5.27	525.63	22.04	47454	0.00000 **
	45-49	62216	53.2	66.40	32289	23.2	29.67	30764	50.7	62.62	18557	17.8	23.17	2.55	4247.78	5.62	92978	0.00000 **	5.47	754.78	21.60	50845	0.00000 **
	50-54	52441	56.0	73.75	28122	27.1	32.74	25198	52.2	67.99	15812	20.3	25.85	3.75	5173.84	6.80	77637	0.00000 **	6.78	926.50	22.40	43933	0.00000 **
	55-59	46620	55.5	73.03	24815	29.3	33.37	21057	53.1	74.13	11804	21.8	24.99	2.40	5383.32	3.95	67675	0.00008 **	7.52	955.96	21.74	36618	0.00000 **
	60-64	40886	52.8	71.15	19664	28.1	30.48	9401	43.5	61.49	3961	20.3	20.25	9.34	4822.72	11.76	50285	0.00000 **	7.78	842.10	15.40	23624	0.00000 **
	65-69	18184	48.8	59.43	7574	26.8	26.52	4192	37.0	51.43	1115	20.1	25.31	11.77	3365.90	11.84	22374	0.00000 **	6.69	695.23	7.91	8688	0.00000 **
	70-	6138	44.0	52.42	2580	26.0	22.82	1276	30.3	30.43	306	19.6	40.43	13.66	2434.23	9.00	7412	0.00000 **	6.39	638.59	4.18	2885	0.00003 **
	75-	1647	37.7	36.59	713	23.0	19.48																
BS	15-19	1620	88.1	11.59	701	88.9	17.53	880	89.8	12.74	151	89.8	16.00	-1.7	144.13	3.34	2498	0.00085 **	-0.92	298.13	0.59	851	0.55274
	20-24	10922	88.8	15.27	6817	87.2	11.59	1691	90.4	12.61	984	88.7	15.83	-1.61	223.13	4.12	12611	0.00004 **	-1.55	149.00	3.72	7800	0.00020 **
	25-29	17603	89.2	13.01	9086	86.4	11.55	3247	92.9	16.60	1429	89.0	13.47	-3.74	185.85	14.36	20848	0.00000 **	-2.64	139.99	7.84	10514	0.00000 **
	30-34	22295	91.0	15.08	10399	86.7	12.29	6124	95.2	18.55	1696	90.6	15.25	-4.17	252.48	18.19	28417	0.00000 **	-3.84	162.41	11.51	12094	0.00000 **
	35-39	42186	92.9	17.86	18312	87.8	11.86	11740	97.5	23.35	2784	91.9	14.74	-4.65	368.09	23.23	53924	0.00000 **	-4.08	150.66	16.34	21095	0.00000 **
	40-44	49525	95.4	20.94	23267	89.5	14.14	16443	100.2	24.94	7829	93.2	17.18	-4.78	484.29	24.13	65966	0.00000 **	-3.65	223.97	18.67	31095	0.00000 **
	45-49	41967	98.5	24.61	20618	91.0	15.22	20922	104.5	30.73	11743	95.5	20.77	-6.05	718.16	26.68	62887	0.00000 **	-4.45	304.07	22.07	32360	0.00000 **
	50-54	35574	101.7	26.35	17352	92.9	17.62	17873	108.1	35.10	10532	98.7	21.58	-6.42	874.23	23.68	53445	0.00000 **	-5.81	369.14	24.48	27883	0.00000 **
	55-59	30232	104.7	28.33	14535	95.3	18.93	14612	109.1	34.05	7959	99.6	23.15	-4.33	918.93	14.18	44842	0.00000 **	-4.29	421.27	14.99	22493	0.00000 **
	60-64	25105	106.8	29.48	10763	97.8	20.52	4781	113.3	39.94	2097	103.0	28.14	-6.49	985.32	13.10	29884	0.00000 **	-5.20	481.58	9.93	12859	0.00000 **
	65-69	9624	108.8	30.64	3905	98.9	22.21	1764	113.0	38.24	494	102.6	26.69	-4.18	1019.71	5.05	11386	0.00000 **	-3.67	517.69	3.38	4398	0.00074 **
	70-	3045	107.6	27.38	1397	98.5	19.83	509	115.3	39.53	124	104.2	26.07	-7.72	865.70	5.48	3552	0.00000 **	-5.73	416.31	3.00	1520	0.00277 **
	75-	818	106.8	25.60	413	98.1	20.12																

＊1998 年度の検査では LDLC および HbA1c の検査項目は法定項目ではないため比較対象外。

表４　職域定期健康診断項目の定量的検査結果　過去の研究との有所見率の比較

		令和元年度研究		H12年度研究	
調査対象年度		2013		1998	
性別		M	F	M	F
BMI	15-19	11.6	6.7	9.7	6.8
>=26.4	20-24	13.0	6.1	10.5	5.3
	25-29	14.6	7.3	15.2	7.2
	30-34	16.6	8.4	18.1	9.8
	35-39	19.1	10.6	18.2	9.9
	40-44	21.7	12.0	17.4	11.5
	45-49	21.7	13.2	16.7	12.8
	50-54	20.4	12.8	15.5	13.6
	55-59	18.1	12.6	15.2	14.9
	60-64	16.4	13.2	17.0	19.1
	65-69	15.3	13.0	16.4	18.4
	70-	14.8	14.4	14.9	15.3
	75-	16.3	12.8		
sBP	15-19	0.4	0.1	0.2	0.1
>=160	20-24	0.8	0.1	0.5	0.0
	25-29	0.9	0.2	0.7	0.2
	30-34	1.4	0.4	1.0	0.5
	35-39	2.1	0.9	1.6	1.0
	40-44	3.4	1.7	2.8	2.2
	45-49	4.8	3.4	4.6	4.3
	50-54	6.7	4.6	6.7	6.3
	55-59	9.0	6.2	8.5	8.2
	60-64	11.5	7.5	11.1	9.0
	65-69	13.6	8.9	13.9	11.7
	70-	14.3	11.4	16.3	14.7
	75-	14.5	11.8		
dBP	15-19	0.3	0.3	0.2	0.2
>=95	20-24	0.7	0.3	0.6	0.1
	25-29	1.4	0.6	1.2	0.4
	30-34	2.8	1.1	2.4	1.0
	35-39	4.9	2.1	4.5	1.8
	40-44	8.3	3.5	7.7	2.9
	45-49	11.5	5.2	10.6	5.3
	50-54	13.6	6.1	12.6	7.2
	55-59	13.5	6.2	12.0	7.9
	60-64	12.1	5.8	12.7	7.5
	65-69	9.6	4.7	11.4	7.6
	70-	6.9	4.6	9.4	5.1
	75-	4.9	2.8		
RBC	15-19	2.0	2.4	1.7	1.1
M<400 & >=580	20-24	2.1	1.9	1.7	1.1
F<360 & >=520	25-29	1.7	1.8	1.3	1.7
	30-34	1.6	1.8	1.9	1.5
	35-39	1.6	2.1	2.1	1.9
	40-44	1.8	2.3	2.2	2.2
	45-49	2.0	2.7	2.6	2.6
	50-54	2.8	3.0	3.7	2.4
	55-59	3.7	2.4	4.3	2.4
	60-64	4.6	2.1	5.5	2.7
	65-69	6.2	2.1	7.2	3.2
	70-	7.8	3.0	10.3	4.6
	75-	12.8	5.2		

	令和元年度研究		H12年度研究	
	2013		1998	
	M	F	M	F
Hb	2.0	4.2	1.2	7.6
M<13.0 & >=17.6	1.8	4.2	1.4	5.0
F<11.40 & >=15.5	1.5	4.7	1.3	6.4
	1.8	6.4	2.3	9.0
	2.2	9.3	2.4	12.7
	2.6	12.7	3.0	16.8
	3.2	14.4	3.6	17.1
	4.1	7.9	4.4	8.5
	5.4	2.7	5.3	3.8
	7.1	2.6	6.7	4.2
	9.1	2.4	8.7	5.0
	11.8	3.3	12.2	6.9
	19.7	6.5		
TG	10.3	4.1	6.8	1.9
>=150	13.8	3.9	17.5	4.1
	17.8	4.5	26.9	4.9
	23.2	5.6	33.7	7.0
	26.2	6.4	36.3	8.1
	30.6	7.3	38.5	8.3
	32.9	9.5	37.4	10.4
	33.0	12.7	34.8	13.7
	31.7	15.7	32.8	17.2
	30.0	17.2	32.5	21.3
	29.4	18.8	29.1	23.4
	26.6	19.1	25.9	27.1
	23.7	16.4		
HDL	4.3	1.1	8.9	3.0
<40	4.8	0.8	8.0	1.6
	5.8	1.0	10.7	2.0
	7.4	1.0	13.6	2.3
	7.9	1.2	14.5	1.7
	8.2	1.2	13.7	2.3
	8.0	1.2	13.7	2.1
	7.6	1.0	13.1	2.5
	7.5	1.3	12.2	2.3
	7.5	1.4	14.0	3.1
	7.7	1.7	13.8	4.9
	8.7	2.1	11.8	5.4
	10.9	2.8		
GOT	3.3	0.7	1.7	0.7
>=40	3.6	0.7	2.5	0.4
	4.3	0.9	3.5	0.6
	4.8	1.1	5.0	0.8
	5.5	1.1	5.3	0.9
	5.9	1.4	5.4	0.9
	6.0	1.8	5.3	1.2
	6.3	2.5	5.7	1.7
	6.5	3.1	6.2	2.2
	6.1	2.9	5.8	2.7
	6.2	3.3	5.3	3.6
	5.5	3.1	4.4	2.6
	5.0	4.1		

	令和元年度研究		H12年度研究	
	2013		1998	
	M	F	M	F
GPT	9.4	1.3	8.7	2.5
>=40	11.2	1.5	12.8	1.8
	13.8	1.8	20.2	2.5
	16.6	2.3	26.6	2.9
	18.7	2.4	26.5	2.8
	18.7	2.7	23.0	2.7
	17.1	3.1	19.7	3.5
	14.4	4.6	17.1	5.1
	11.8	5.0	15.0	5.9
	9.7	4.4	11.6	5.9
	8.3	3.9	10.1	5.7
	6.4	3.9	7.2	5.6
	3.9	2.7		
GGT	1.0	0.1	0.6	0.2
>=80	2.1	0.2	1.5	0.2
	4.1	0.4	3.9	0.4
	7.1	0.9	9.2	0.9
	10.1	1.2	12.6	0.8
	12.9	1.7	14.2	1.1
	15.3	2.4	15.3	1.6
	16.4	3.7	15.8	2.3
	15.9	4.2	15.5	2.7
	14.5	3.5	10.9	2.1
	12.7	2.9	7.9	1.8
	10.0	2.6	5.5	1.0
	6.9	1.5		
BS	3.6	4.0	2.6	4.0
>=110	3.9	3.0	6.4	4.5
	4.0	2.9	7.9	3.1
	5.0	2.6	9.3	4.4
	5.9	2.8	11.1	5.8
	8.7	4.0	15.3	6.3
	12.7	5.0	21.3	9.0
	17.9	7.3	25.8	12.6
	23.2	10.4	28.3	15.0
	27.7	13.9	33.8	19.4
	31.3	15.8	34.4	19.8
	30.6	16.2	37.5	23.4
	30.8	14.3		

表５　性別年齢階級別　個人検査値の経年推移（5 年間）の平均値

性別	年代	n	検査値の変化の平均値																					
			SBP		DBP		RBC		Hb		GOT		GPT		GGT		HDLC		LDLC		TG		HbA1c		BMI	
			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
男性	15→19	301	-1.64	13.92	0.05	10.04	-2.59	23.61	0.07	0.79	0.92	9.58	2.18	20.91	4.90	16.84	0.04	8.81	5.50	19.28	11.80	94.58	0.01	0.21	0.32	2.16
	20→24	2937	0.53	12.91	1.78	9.52	-2.47	23.06	0.01	0.79	1.47	16.76	4.79	22.30	7.68	28.29	-1.10	8.84	7.59	19.52	14.87	81.37	0.05	0.32	0.72	1.78
	25→29	6623	0.92	12.78	2.18	9.49	-1.62	23.04	-0.01	0.76	1.44	11.61	3.00	23.35	7.31	32.85	-1.38	8.91	8.00	20.40	17.56	105.17	0.05	0.35	0.57	1.64
	30→34	9584	1.40	13.08	2.80	9.84	-1.03	22.53	0.03	0.76	0.65	11.88	0.75	22.91	6.16	41.17	-0.63	9.05	6.70	21.40	9.94	109.12	0.05	0.39	0.40	1.54
	35→39	13832	2.55	13.39	3.11	9.80	-1.81	22.65	0.02	0.75	0.48	12.07	-0.40	22.72	4.37	43.08	-0.40	9.22	5.03	21.85	7.57	111.70	0.05	0.40	0.26	1.48
	40→44	13113	3.37	14.14	3.34	10.16	-1.91	23.37	0.01	0.78	0.46	13.04	-0.72	18.82	2.59	51.77	-0.06	9.13	4.42	22.25	3.66	124.60	0.06	0.43	0.16	1.40
	45→49	10642	4.67	14.63	3.36	10.15	-1.92	23.95	-0.01	0.82	0.31	14.34	-1.19	18.57	-0.06	56.95	0.13	9.38	3.67	22.07	0.17	126.16	0.06	0.43	0.03	1.28
	50→54	9157	5.20	15.50	2.95	10.25	-1.64	24.22	-0.01	0.84	0.25	12.00	-1.46	15.41	-1.88	54.04	0.24	9.44	2.64	21.60	-3.21	110.48	0.07	0.40	-0.07	1.24
	55→59	7148	6.00	16.14	2.29	10.53	-1.39	24.67	-0.02	0.90	0.46	16.75	-0.73	15.06	-0.95	49.25	-0.02	9.09	2.60	21.45	-2.07	100.80	0.07	0.42	-0.09	1.14
	60→64	2959	5.62	17.21	1.69	10.41	-1.88	24.57	-0.05	0.86	0.15	12.55	-0.92	16.75	-2.09	44.42	0.02	9.33	1.82	21.11	-0.96	84.69	0.07	0.41	-0.15	1.16
	65→69	1071	4.42	16.92	0.35	9.94	-3.87	23.96	-0.13	0.80	0.47	7.63	-0.73	10.87	-3.81	27.37	-0.11	8.60	2.15	20.93	-2.71	72.07	0.07	0.45	-0.20	1.12
	70→74	224	3.65	17.21	-0.41	9.90	-6.30	22.36	-0.20	0.83	0.92	16.57	1.08	38.04	-2.82	21.56	-0.27	8.77	2.30	19.92	-12.08	61.62	0.03	0.36	-0.24	0.97
	75→79	61	2.33	16.42	-0.52	9.04	-6.87	25.90	-0.24	0.79	0.74	3.53	-0.15	5.16	-1.08	7.96	-0.34	6.88	3.36	19.14	-5.34	36.45	-0.05	0.28	-0.43	1.18
女性	15→19	129	-2.38	11.23	0.88	9.57	-2.66	26.03	0.06	1.07	-0.24	4.49	-0.23	9.02	0.86	4.67	1.32	10.09	-1.88	18.03	6.98	49.93	-0.04	0.29	-0.41	1.99
	20→24	1257	-1.14	11.79	1.03	9.31	-2.55	26.15	-0.08	1.05	0.25	7.77	0.65	12.54	0.84	15.97	-0.05	10.46	2.94	18.03	4.75	44.41	-0.02	0.23	0.11	1.72
	25→29	1978	0.58	11.72	1.58	9.15	-0.27	25.50	-0.08	0.96	0.23	8.06	0.75	13.46	1.41	10.35	-0.73	10.57	5.14	19.82	9.07	44.07	-0.03	0.30	0.40	1.72
	30→34	2466	1.99	12.67	2.23	9.78	1.88	24.75	-0.02	1.07	0.16	6.79	0.27	11.61	2.23	15.84	-0.68	10.33	5.49	20.22	6.69	48.83	-0.03	0.30	0.46	1.57
	35→39	4427	3.24	13.18	2.56	9.75	2.87	24.82	-0.04	1.23	0.62	7.70	0.73	11.43	2.31	19.43	-0.77	9.97	6.70	18.98	7.29	49.69	-0.01	0.34	0.46	1.52
	40→44	5994	4.77	14.00	3.09	9.71	4.59	25.94	0.08	1.48	0.98	9.38	1.03	12.19	2.86	23.08	0.12	9.68	8.66	19.83	7.74	55.26	0.01	0.35	0.34	1.42
	45→49	5731	4.58	14.63	3.26	9.89	9.55	25.95	0.55	1.59	2.09	9.51	2.39	12.14	4.51	23.11	1.01	9.95	13.49	21.40	11.73	54.01	0.04	0.31	0.10	1.34
	50→54	4900	4.12	15.69	2.38	9.85	5.37	24.73	0.52	1.42	1.42	8.81	1.32	11.52	3.32	20.96	-0.01	9.91	11.33	21.76	8.62	63.67	0.03	0.34	-0.08	1.27
	55→59	3595	5.33	15.89	1.87	9.83	1.52	20.75	0.12	0.82	0.70	19.18	0.31	20.64	1.35	36.81	-0.62	9.52	5.90	20.94	4.64	58.64	0.01	0.28	-0.02	1.25
	60→64	1229	5.01	16.14	0.81	9.33	1.79	20.84	0.07	0.73	0.29	8.76	-0.26	10.84	-0.03	15.26	-0.50	9.19	4.94	21.47	6.18	57.10	0.01	0.37	-0.12	1.27
	65→69	394	5.91	17.20	1.28	9.86	2.61	19.61	0.06	0.72	0.19	5.58	-0.21	7.46	-1.08	19.80	0.21	8.74	6.03	22.60	4.32	59.88	-0.05	0.28	-0.24	1.23
	70→74	79	3.54	19.20	-0.99	10.57	-1.23	20.07	0.01	0.69	-0.94	6.13	-0.90	6.79	-1.78	11.71	-0.34	10.56	6.29	21.05	3.65	68.81	-0.04	0.25	-0.11	1.36
	75→79	22	5.45	29.44	0.82	10.01	-11.90	32.19	-0.38	1.02	2.55	7.05	0.86	8.13	0.09	7.39	-0.14	9.75	-3.50	24.06	-3.64	55.46	-0.06	0.39	-0.24	1.20

図５　性別年齢階級別　個人検査値の経年推移（5 年間）の平均値

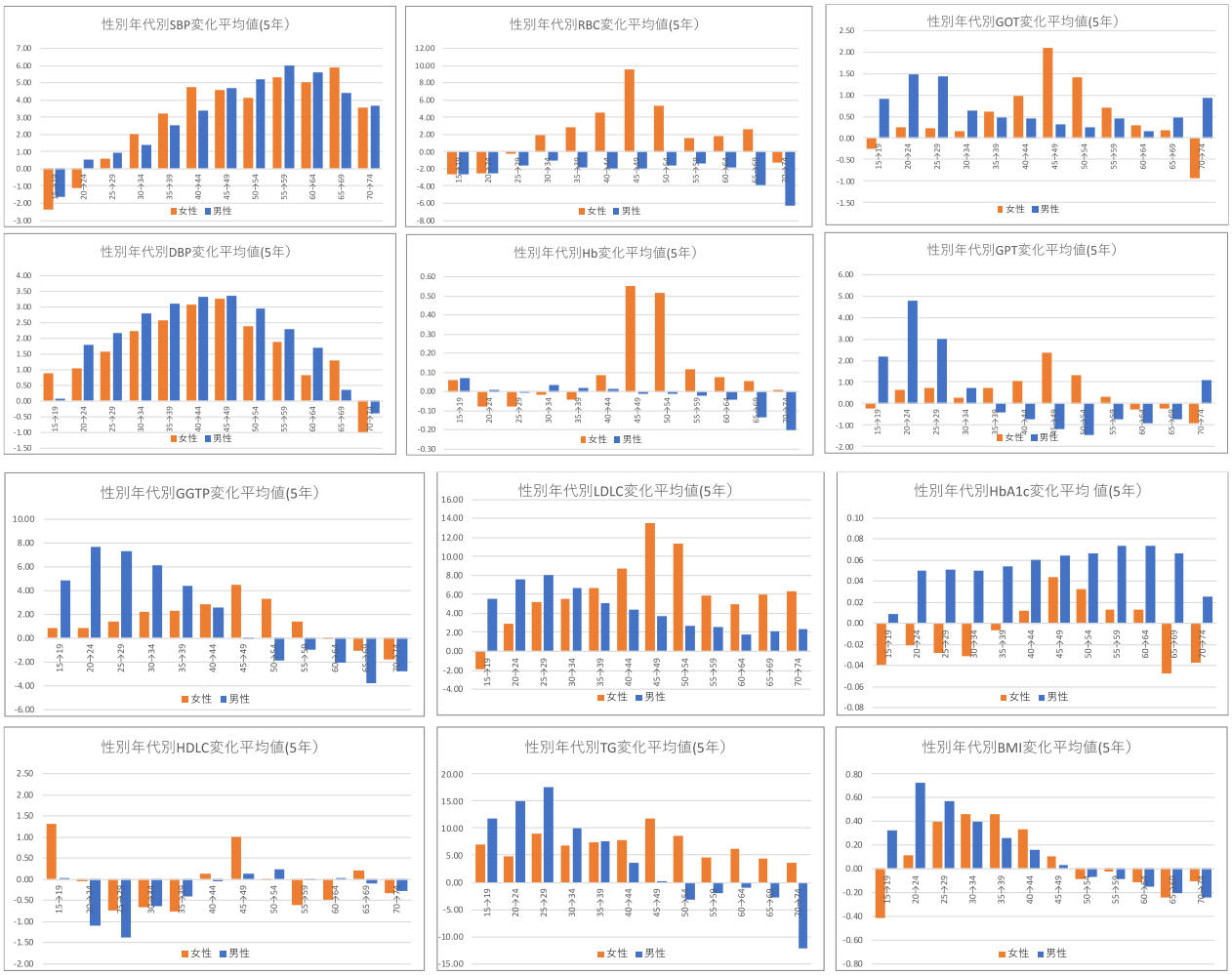


表６　１回目および６回目の間の BMI 階級の変化の割合

			6回目			
性別	BMI		＜18.5	＜25	＞＝25	小計
男性	1回目	＜18.5	64.1%	35.9%	0.0%	100.0%
		＜25	1.9%	89.2%	8.8%	100.0%
		＞＝25	0.0%	17.3%	82.7%	100.0%
		小計	4.2%	68.0%	27.7%	100.0%
女性		＜18.5	72.1%	27.9%	0.0%	100.0%
		＜25	5.6%	88.0%	6.4%	100.0%
		＞＝25	0.1%	16.1%	83.8%	100.0%
		小計	13.2%	69.6%	17.2%	100.0%

表 7 -1　BMI 階級未変化群別における性別年齢階級別個人検査値の経年推移（5 年間）の平均値（男性）

性別	年代	BMI階級	n	検査値の変化の平均値																					
				SBP		DBP		RBC		Hb		GOT		GPT		GGT		HDLC		LDLC		TG		HDA1c		BMI	
				M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
男性	15→19	やせ (BMI<18.5) 未変化群	16	-9.00	12.89	-4.31	9.60	-4.56	25.35	0.08	0.69	-0.38	3.30	2.44	4.73	1.56	2.28	-1.44	9.35	4.31	14.06	9.25	59.98	0.04	0.16	-0.08	0.61
		基準内 (BMI<25.0) 未変化群	173	-1.64	13.16	-0.12	8.82	-1.55	25.18	0.07	0.86	1.24	7.41	1.44	14.56	2.67	10.00	1.10	8.07	5.64	17.71	11.13	99.60	0.01	0.20	0.13	1.33
		肥満 (BMI) >=25.0未変化群	55	-3.16	15.08	2.20	12.57	-2.42	21.17	0.13	0.64	-1.25	16.40	-0.25	37.99	6.18	23.57	-1.89	8.25	2.22	22.77	11.13	98.75	0.00	0.25	0.49	3.10
	20→24	やせ (BMI) <18.5未変化群	164	0.36	12.08	0.65	8.98	-3.28	22.89	0.00	0.73	0.15	7.05	-0.21	6.88	1.89	10.81	2.41	8.09	3.12	16.60	-4.23	60.29	-0.01	0.20	-0.06	0.63
		基準内 (BMI) <25.0未変化群	1760	0.65	12.76	1.58	9.19	-2.92	22.80	-0.01	0.80	0.80	10.12	2.96	13.66	5.45	17.73	-0.63	8.73	7.59	18.57	10.47	71.32	0.03	0.27	0.54	1.26
		肥満 (BMI) >=25.0未変化群	535	-1.38	12.94	1.70	10.08	-0.68	22.89	0.06	0.72	3.51	16.84	9.02	37.84	13.83	50.82	-2.55	8.04	8.04	21.41	26.56	111.72	0.14	0.50	1.03	2.46
	25→29	やせ (BMI) <18.5未変化群	275	-0.51	11.33	0.36	8.68	-4.28	22.19	-0.16	1.00	0.29	5.50	1.07	8.51	2.09	10.53	0.40	9.52	5.10	16.18	3.19	44.40	0.01	0.22	0.04	0.62
		基準内 (BMI) <25.0未変化群	4062	0.87	12.35	1.94	9.12	-2.00	23.00	-0.02	0.75	1.36	10.80	2.92	19.25	6.81	33.03	-1.27	9.10	7.98	19.11	15.20	90.72	0.02	0.22	0.45	1.22
		肥満 (BMI) >=25.0未変化群	1273	0.88	14.29	3.19	10.36	-1.12	21.84	0.03	0.70	1.51	15.22	1.99	33.82	7.17	34.60	-1.50	7.35	6.45	22.85	21.04	145.40	0.15	0.65	0.68	2.05
	30→34	やせ (BMI) <18.5未変化群	269	0.43	12.49	2.57	9.17	0.74	24.53	0.10	0.95	0.90	9.09	0.53	10.60	4.54	22.79	1.75	9.99	5.39	16.18	-2.57	56.61	-0.01	0.22	0.01	0.61
		基準内 (BMI) <25.0未変化群	5733	1.31	12.60	2.54	9.41	-1.46	22.32	0.02	0.76	0.68	11.28	1.18	19.29	6.52	38.88	-0.52	9.39	7.25	20.26	11.51	94.08	0.01	0.25	0.33	1.15
		肥満 (BMI) >=25.0未変化群	2143	1.40	14.08	3.36	10.51	-0.67	21.11	0.05	0.71	0.04	13.47	-2.00	29.70	3.49	40.14	-0.78	7.34	4.74	22.94	1.57	135.56	0.15	0.58	0.49	1.82
	35→39	やせ (BMI) <18.5未変化群	333	1.22	11.64	1.87	8.72	-5.80	22.42	-0.08	0.74	0.12	7.72	0.53	7.69	3.48	25.05	0.52	9.77	3.93	18.57	-7.01	68.19	0.01	0.22	-0.04	0.59
		基準内 (BMI) <25.0未変化群	8155	1.99	12.84	2.65	9.37	-2.51	22.54	0.00	0.74	0.67	11.83	0.29	20.25	5.38	44.24	-0.37	9.68	5.68	20.99	7.57	103.17	0.02	0.27	0.18	1.16
		肥満 (BMI) >=25.0未変化群	3387	3.99	14.44	4.21	10.53	-0.11	21.74	0.07	0.73	-0.16	12.95	-2.71	27.68	1.39	38.59	-0.70	7.26	2.89	22.56	7.13	128.88	0.14	0.61	0.39	1.61
	40→44	やせ (BMI) <18.5未変化群	286	2.80	13.09	2.53	9.60	-3.25	24.83	0.01	1.00	1.81	10.41	0.51	8.16	5.70	61.32	-0.45	10.88	4.44	18.00	11.66	99.44	0.01	0.22	-0.03	0.65
		基準内 (BMI) <25.0未変化群	7864	3.03	13.59	3.11	9.85	-2.38	23.33	0.00	0.77	0.64	10.72	0.00	15.23	3.65	50.21	-0.09	9.32	5.18	21.45	5.16	109.89	0.03	0.32	0.11	1.12
		肥満 (BMI) >=25.0未変化群	3213	4.07	14.97	3.91	10.50	-0.53	21.75	0.06	0.74	-0.07	12.93	-2.89	23.49	-0.63	46.38	0.03	7.70	2.79	22.53	-3.13	143.57	0.14	0.61	0.25	1.47
	45→49	やせ (BMI) <18.5未変化群	275	3.69	14.43	2.16	10.44	-4.32	24.62	-0.11	0.82	-0.17	10.72	0.03	9.10	2.33	54.85	-1.07	11.26	3.45	18.77	15.31	106.16	0.02	0.22	-0.11	0.61
		基準内 (BMI) <25.0未変化群	6619	4.49	14.27	3.30	9.83	-2.10	23.95	-0.02	0.81	0.39	15.71	-0.88	17.52	0.22	62.06	0.09	9.70	4.25	21.42	3.21	122.31	0.03	0.31	0.03	1.05
		肥満 (BMI) >=25.0未変化群	2318	5.45	15.00	3.77	10.33	-0.74	22.41	0.04	0.78	0.12	11.91	-2.21	21.72	-0.47	45.09	-0.02	7.43	2.06	22.87	-9.74	128.03	0.14	0.57	0.13	1.33
	50→54	やせ (BMI) <18.5未変化群	269	5.11	15.22	2.19	9.28	-2.79	22.73	-0.03	0.79	-0.52	18.85	-0.65	11.09	8.83	100.04	0.60	11.35	3.26	19.61	5.12	70.75	0.01	0.24	-0.16	0.62
		基準内 (BMI) <25.0未変化群	5881	5.16	15.42	3.00	10.19	-1.85	24.47	-0.02	0.86	0.35	11.56	-1.01	12.67	-2.11	53.44	0.22	9.67	3.13	21.32	-2.09	105.13	0.05	0.31	-0.06	1.03
		肥満 (BMI) >=25.0未変化群	1797	5.74	15.78	3.10	10.47	0.39	21.70	0.06	0.75	0.18	11.57	-2.46	19.36	-2.23	45.14	0.12	7.39	1.34	21.43	-6.79	128.15	0.15	0.57	0.06	1.30
	55→59	やせ (BMI) <18.5未変化群	211	8.38	15.73	2.90	9.13	-1.27	24.38	-0.02	0.90	2.06	12.87	0.47	8.56	2.79	63.38	0.61	11.69	-0.09	18.78	7.25	95.63	0.05	0.23	-0.23	0.59
		基準内 (BMI) <25.0未変化群	4780	5.84	16.02	2.36	10.46	-1.63	24.81	-0.03	0.91	0.58	18.34	-0.49	15.40	0.07	48.34	-0.07	9.20	2.88	21.28	-1.98	97.50	0.06	0.37	-0.11	1.01
		肥満 (BMI) >=25.0未変化群	1250	7.05	15.82	2.28	10.67	-0.13	22.70	0.01	0.78	0.47	10.48	-1.13	14.66	-1.84	37.58	-0.05	7.46	2.25	21.67	-1.47	113.37	0.13	0.50	0.08	1.09
	60→64	やせ (BMI) <18.5未変化群	103	5.84	16.49	1.52	10.97	-0.46	31.59	0.04	1.06	0.57	9.46	-0.72	8.18	4.25	41.59	0.49	11.23	1.29	20.42	10.25	55.43	0.03	0.23	-0.27	0.72
		基準内 (BMI) <25.0未変化群	1960	5.86	16.93	1.86	10.20	-1.64	23.87	-0.03	0.81	0.18	11.67	-0.62	15.57	-1.71	44.65	-0.06	9.56	2.75	20.72	-1.12	86.69	0.06	0.38	-0.15	1.00
		肥満 (BMI) >=25.0未変化群	506	4.67	17.25	1.06	10.52	-2.64	22.38	-0.07	0.87	-0.78	17.13	-3.07	22.73	-5.58	39.05	-0.18	7.91	-0.76	21.44	-1.97	81.42	0.14	0.49	0.03	1.17
	65→69	やせ (BMI) <18.5未変化群	27	1.78	17.91	-1.52	8.85	-0.85	26.78	-0.03	1.02	-0.44	5.58	-2.26	7.07	-0.26	20.46	-0.93	8.33	-2.67	15.27	-8.22	39.48	0.09	0.23	-0.55	0.97
		基準内 (BMI) <25.0未変化群	730	4.79	16.98	0.29	9.85	-3.90	23.60	-0.15	0.77	0.58	7.68	-0.61	11.19	-3.94	25.17	-0.06	8.68	2.27	20.72	-2.75	70.64	0.04	0.34	-0.22	1.02
		肥満 (BMI) >=25.0未変化群	194	3.71	15.58	1.06	10.21	-2.41	21.58	-0.02	0.76	0.94	7.70	0.07	10.86	-1.18	31.78	0.03	7.55	1.81	21.39	-6.32	74.67	0.14	0.51	-0.02	0.94
	70→74	やせ (BMI) <18.5未変化群	6	-3.17	11.57	-4.50	14.07	-5.33	34.47	-0.35	0.87	1.67	3.50	2.17	7.03	6.67	22.42	-6.83	6.46	4.83	18.52	-1.83	35.21	0.14	0.32	-0.16	0.67
		基準内 (BMI) <25.0未変化群	150	3.95	17.72	-0.25	10.28	-7.49	20.22	-0.19	0.83	1.33	19.96	2.17	46.17	-1.56	13.64	-0.05	9.86	0.53	17.55	-9.61	60.20	0.04	0.36	-0.30	1.00
		肥満 (BMI) >=25.0未変化群	47	6.28	16.19	0.19	9.25	-2.16	20.86	-0.17	0.86	-0.72	4.98	-2.68	8.58	-9.96	38.36	-0.23	5.30	7.57	21.25	-12.04	46.36	0.03	0.33	-0.06	0.81
	75→79	やせ (BMI) <18.5未変化群	2	13.50	7.78	-5.50	7.78	-13.00	14.14	-0.45	0.21	3.50	2.12	-1.50	2.12	-3.50	2.12	-0.50	7.78	5.00	15.56	-11.50	14.85	-0.06	0.14	-0.75	1.16
		基準内 (BMI) <25.0未変化群	41	3.78	16.94	-0.05	8.83	-7.50	27.84	-0.25	0.87	1.15	3.21	0.83	4.42	-0.39	7.88	-1.15	6.52	3.88	15.04	-0.10	33.38	-0.04	0.30	-0.19	1.09
		肥満 (BMI) >=25.0未変化群	9	2.11	13.47	4.44	8.50	5.44	16.46	-0.06	0.61	-0.22	3.93	-1.44	5.83	-3.56	4.88	-1.78	5.09	10.22	21.14	5.78	36.13	-0.11	0.25	-0.23	0.65

表 7 -2　BMI 階級未変化群別における性別年齢階級別個人検査値の経年推移（5 年間）の平均値（女性）

性別	年代	BMI階級	n	検査値の変化の平均値																					
				SBP		DBP		RBC		Hb		GOT		GPT		GGT		HDLC		LDLC		TG		HbA1c		BMI	
				M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
女性	15→19	やせ（BMI<18.5）未変化群	24	-0.79	10.98	2.79	8.94	-1.00	26.58	0.31	1.27	-0.79	3.32	-0.08	4.12	-0.54	2.75	1.92	11.86	-3.38	21.03	12.13	64.82	-0.01	0.20	-0.03	0.92
		基準内（BMI<25.0）未変化群	65	-2.02	11.85	0.14	9.28	-3.61	25.89	0.11	1.03	0.14	3.53	0.55	6.05	1.28	4.27	1.91	10.13	0.35	18.30	1.46	43.13	-0.04	0.20	-0.64	1.39
		肥満（BMI）>=25.0未変化群	18	-0.94	10.17	4.22	11.31	-1.82	22.56	-0.03	0.78	-0.72	7.14	-1.39	16.93	0.22	7.03	-1.83	9.95	-4.89	14.28	19.44	62.71	-0.11	0.63	-0.07	3.41
	20→24	やせ（BMI）<18.5未変化群	181	-1.46	10.39	0.46	8.98	-3.66	24.57	-0.13	1.06	-0.42	3.97	-0.85	5.58	-0.02	5.68	1.08	9.14	2.51	14.88	-1.48	39.02	-0.02	0.21	-0.17	0.82
		基準内（BMI）<25.0未変化群	725	-1.34	11.54	1.06	8.73	-3.77	25.81	-0.11	1.05	-0.03	5.69	0.46	10.63	1.16	7.97	-0.11	11.07	1.82	17.58	3.95	40.59	-0.03	0.23	0.03	1.37
		肥満（BMI）>=25.0未変化群	111	-0.23	13.44	2.18	10.82	1.34	27.40	-0.04	1.12	1.55	19.15	2.30	28.47	-1.23	44.62	-0.92	7.98	5.50	21.04	16.79	60.18	0.06	0.26	0.78	2.57
	25→29	やせ（BMI）<18.5未変化群	246	1.48	11.04	2.06	8.37	-0.43	25.52	0.02	0.95	0.30	3.95	-0.13	4.96	0.57	4.80	-0.45	10.15	3.62	17.17	3.67	41.04	-0.03	0.22	0.09	0.68
		基準内（BMI）<25.0未変化群	1178	0.44	11.44	1.46	9.02	-0.74	25.21	-0.07	0.97	0.07	7.68	0.45	10.84	1.36	8.10	-0.45	10.32	5.29	18.55	7.63	38.81	-0.05	0.33	0.25	1.26
		肥満（BMI）>=25.0未変化群	200	2.08	13.63	3.00	9.88	3.79	21.68	-0.10	0.80	0.26	14.27	2.36	29.55	2.87	16.27	-1.72	8.87	4.47	20.68	17.06	50.60	0.07	0.30	0.94	2.38
	30→34	やせ（BMI）<18.5未変化群	302	0.49	11.27	0.60	8.62	-1.17	22.30	-0.12	1.02	0.32	5.08	0.18	6.46	1.82	13.42	0.02	10.09	5.22	16.47	3.26	30.12	-0.04	0.25	0.09	0.77
		基準内（BMI）<25.0未変化群	1426	1.23	12.19	1.87	9.41	1.25	25.34	-0.02	1.04	0.08	5.08	0.23	8.41	1.61	9.81	-0.29	10.43	5.37	19.78	4.77	41.94	-0.05	0.26	0.33	1.22
		肥満（BMI）>=25.0未変化群	311	5.74	15.13	4.15	11.86	3.77	21.89	-0.10	1.11	-0.29	11.41	-0.30	19.78	4.81	24.97	-2.01	9.09	3.55	23.12	12.82	66.21	0.07	0.45	0.79	1.99
	35→39	やせ（BMI）<18.5未変化群	447	3.09	12.56	2.59	9.37	2.16	23.79	-0.05	1.30	1.15	9.59	0.84	10.10	2.73	19.20	-0.41	10.12	5.20	16.21	4.38	37.80	-0.04	0.27	0.04	0.73
		基準内（BMI）<25.0未変化群	2711	2.66	12.67	2.24	9.36	2.73	24.95	-0.04	1.24	0.39	6.77	0.41	8.63	1.79	20.43	-0.74	9.94	6.57	18.43	7.22	45.74	-0.03	0.28	0.38	1.18
		肥満（BMI）>=25.0未変化群	544	5.44	15.06	3.59	11.05	4.34	24.10	-0.07	1.30	1.37	11.04	2.19	18.92	4.33	21.06	-1.13	9.01	5.48	20.96	9.03	67.18	0.11	0.53	0.81	1.98
	40→44	やせ（BMI）<18.5未変化群	513	3.15	12.59	2.35	8.96	2.91	25.93	0.11	1.45	0.75	5.78	0.41	8.40	1.63	14.24	1.24	10.35	6.88	16.71	4.96	35.76	-0.04	0.27	0.00	0.67
		基準内（BMI）<25.0未変化群	3792	4.59	13.61	3.07	9.51	4.63	25.60	0.10	1.44	1.01	8.54	0.93	10.53	2.66	23.51	0.22	9.62	9.02	19.00	7.82	54.39	0.00	0.28	0.31	1.10
		肥満（BMI）>=25.0未変化群	826	6.09	15.93	3.57	10.36	4.69	25.62	-0.08	1.48	0.75	15.15	1.11	19.45	3.85	21.42	-0.28	8.56	7.97	22.02	8.78	59.59	0.09	0.53	0.49	1.73
	45→49	やせ（BMI）<18.5未変化群	440	2.07	14.10	2.57	9.64	8.44	25.68	0.61	1.53	1.69	4.94	1.55	6.72	4.33	12.05	2.57	10.35	10.19	19.69	8.01	37.54	0.03	0.26	-0.20	0.70
		基準内（BMI）<25.0未変化群	3755	4.58	14.03	3.26	9.70	9.59	25.46	0.53	1.58	1.89	7.95	1.96	9.29	4.27	22.34	1.05	9.91	14.20	21.02	10.87	50.80	0.03	0.29	0.08	1.11
		肥満（BMI）>=25.0未変化群	741	5.82	16.16	3.60	10.57	11.49	26.90	0.62	1.69	2.74	8.81	4.42	14.50	4.99	26.17	-0.49	8.50	12.08	23.06	15.04	67.14	0.12	0.41	0.44	1.64
	50→54	やせ（BMI）<18.5未変化群	361	3.06	15.47	1.92	9.31	2.37	23.41	0.28	1.25	1.27	11.41	0.56	11.49	1.91	17.90	0.63	10.44	9.00	18.23	2.91	40.98	-0.01	0.22	-0.18	0.75
		基準内（BMI）<25.0未変化群	3211	3.86	15.32	2.19	9.57	5.42	23.63	0.51	1.37	1.16	7.45	1.15	9.73	3.41	16.68	-0.29	9.80	11.63	21.34	9.30	59.84	0.02	0.29	-0.07	1.09
		肥満（BMI）>=25.0未変化群	618	6.65	16.91	3.07	11.20	6.45	24.84	0.61	1.51	2.48	12.75	1.93	17.75	4.50	30.74	-0.65	8.67	10.99	24.01	16.29	89.52	0.09	0.46	0.09	1.40
	55→59	やせ（BMI）<18.5未変化群	277	5.17	15.92	1.71	9.31	0.95	21.53	0.03	0.97	0.29	5.46	-0.36	7.55	0.82	11.01	-0.01	10.52	5.31	19.10	4.47	41.31	-0.01	0.21	-0.18	0.73
		基準内（BMI）<25.0未変化群	2440	5.19	15.72	1.66	9.60	1.52	20.22	0.12	0.78	0.78	22.61	0.42	23.73	1.49	42.45	-0.80	9.44	6.52	20.43	4.77	57.36	0.01	0.23	-0.02	1.05
		肥満（BMI）>=25.0未変化群	432	6.42	16.59	2.53	10.84	2.55	22.65	0.18	0.93	0.84	10.97	0.21	16.35	0.79	27.72	-0.86	8.17	3.79	23.49	5.56	71.71	0.07	0.45	0.16	1.39
	60→64	やせ（BMI）<18.5未変化群	85	3.69	14.03	1.06	7.47	3.64	17.38	0.15	0.60	-0.49	5.03	-1.02	6.44	1.47	9.48	0.58	9.12	4.82	18.82	1.40	37.73	0.00	0.24	-0.31	0.71
		基準内（BMI）<25.0未変化群	828	4.67	16.37	0.54	9.25	1.86	20.51	0.08	0.68	0.19	8.71	-0.36	10.55	-0.23	15.24	-0.56	9.29	5.41	20.29	6.54	55.68	0.01	0.29	-0.14	1.07
		肥満（BMI）>=25.0未変化群	158	7.49	14.90	2.01	9.90	1.49	20.59	0.05	0.65	-0.08	9.18	-1.20	11.27	-2.04	14.08	-0.77	8.16	0.94	23.07	3.76	54.77	0.06	0.67	0.24	1.32
	65→69	やせ（BMI）<18.5未変化群	34	3.79	14.42	2.79	9.87	-3.85	13.88	-0.15	0.58	-0.88	4.16	-0.56	4.61	0.76	13.59	1.09	9.61	4.15	17.95	2.41	33.03	-0.01	0.21	-0.43	0.78
		基準内（BMI）<25.0未変化群	251	5.90	17.55	0.77	9.88	3.83	20.53	0.08	0.77	0.17	5.51	-0.43	7.32	-1.58	23.32	0.49	8.91	7.16	22.82	1.14	61.78	-0.06	0.25	-0.19	1.03
		肥満（BMI）>=25.0未変化群	63	7.89	18.00	2.37	9.94	2.55	16.39	0.13	0.49	-0.03	6.53	-1.03	7.15	-0.29	7.58	-0.86	7.37	1.65	22.00	19.35	69.93	-0.01	0.42	-0.14	1.35
	70→74	やせ（BMI）<18.5未変化群	3	4.67	16.07	2.00	7.21	-15.33	44.29	-0.37	1.19	0.67	4.73	6.33	7.57	4.33	3.21	-2.33	17.04	-3.00	39.66	14.67	30.66	-0.16	0.27	-0.83	0.48
		基準内（BMI）<25.0未変化群	48	3.88	18.70	-0.71	10.47	1.15	19.30	0.05	0.71	-0.35	4.71	-0.58	5.76	-1.38	10.91	0.29	11.09	9.13	17.79	-1.23	45.33	-0.05	0.26	-0.03	0.86
		肥満（BMI）>=25.0未変化群	10	4.10	21.50	-0.70	10.97	-4.10	19.45	0.06	0.65	-6.40	11.82	-6.10	10.79	-5.30	17.65	-4.60	11.86	-0.30	20.44	24.50	51.60	0.04	0.19	0.76	1.33
	75→79	やせ（BMI）<18.5未変化群	1	-1.00	0.00	1.00	0.00	0.00	0.00	-0.60	0.00	-2.00	0.00	-1.00	0.00	3.00	0.00	19.00	0.00	-13.00	0.00	-39.00	0.00	0.35	0.00	0.20	0.00
		基準内（BMI）<25.0未変化群	12	0.42	24.92	0.33	10.07	-6.36	27.50	-0.34	1.22	3.92	8.90	3.17	9.40	1.00	6.16	-0.08	10.22	-2.00	22.91	13.00	69.35	0.07	0.24	0.26	1.17
		肥満（BMI）>=25.0未変化群	3	-16.67	15.95	-7.67	5.69	-2.50	21.92	-0.23	0.15	3.00	3.61	-1.67	3.21	-9.67	10.97	-0.67	7.51	14.33	27.15	-38.33	28.01	-0.09	0.33	-0.24	0.34

図 6-1　やせ内未変化群における性別年齢階級別個人検査値の経年推移（5 年間）の平均値

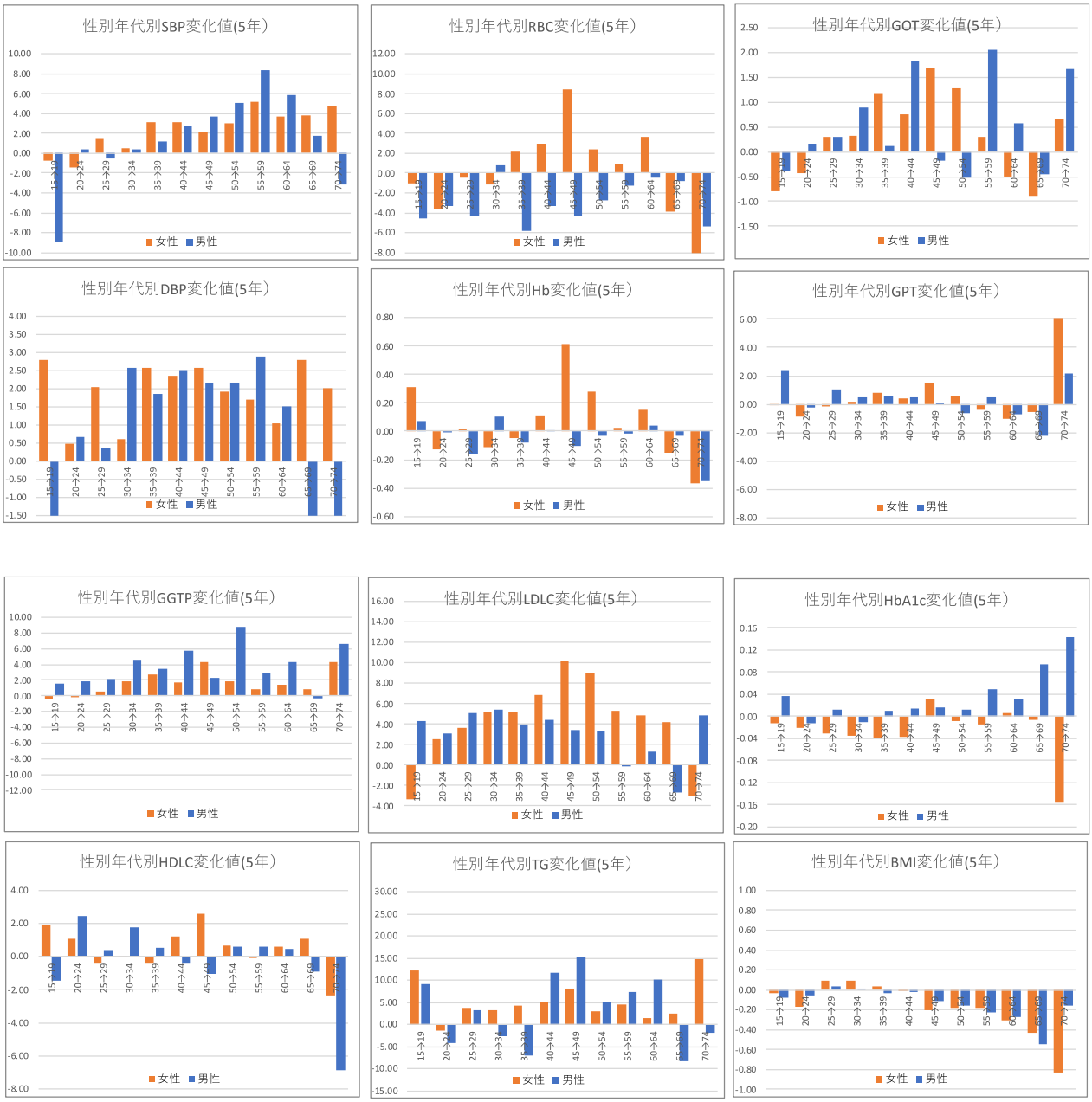


図 6-2　基準値内未変化群における性別年齢階級別個人検査値の経年推移（5 年間）の平均値

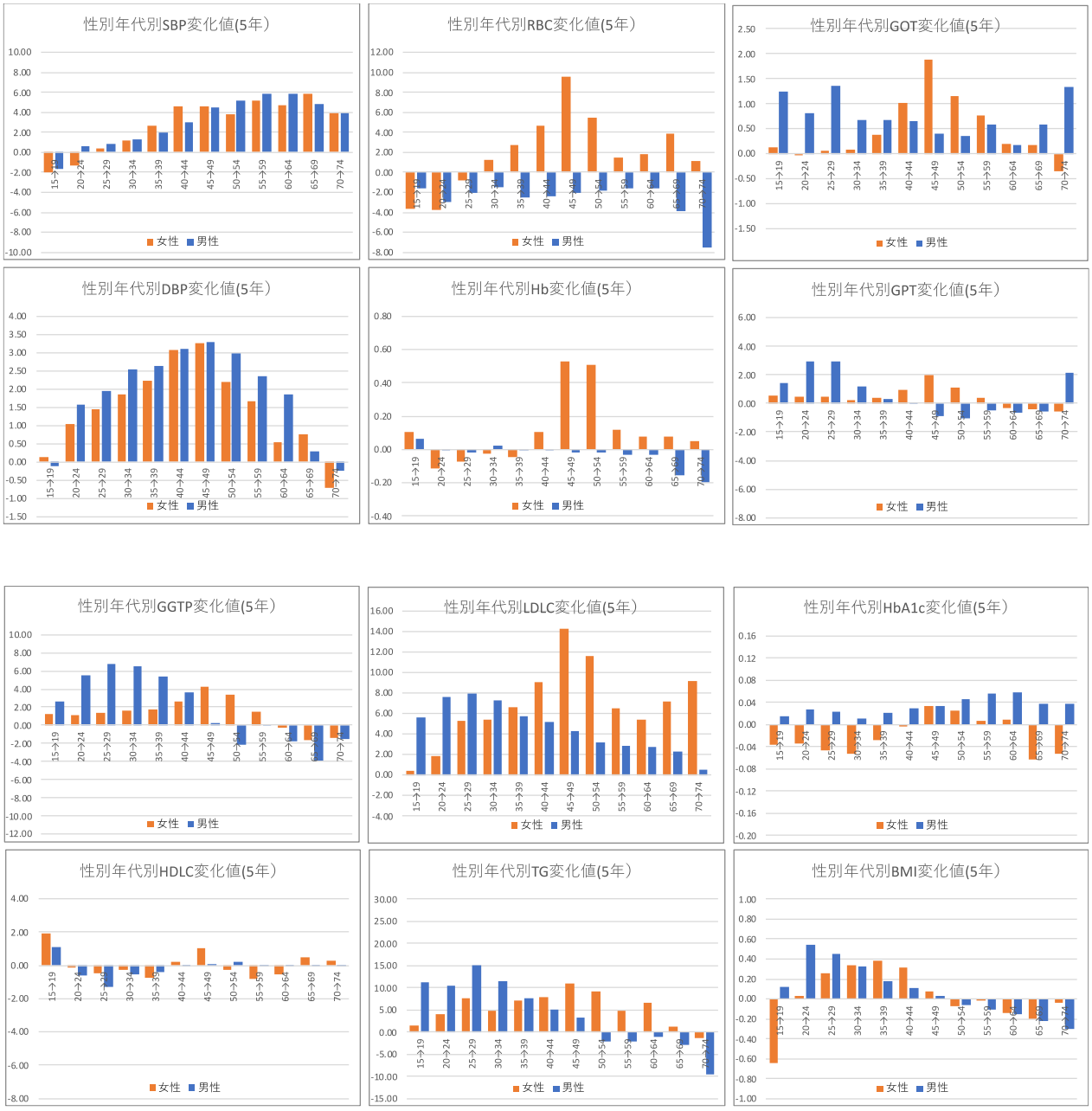


図 6-3　肥満未変化群における性別年齢階級別個人検査値の経年推移（5 年間）の平均値

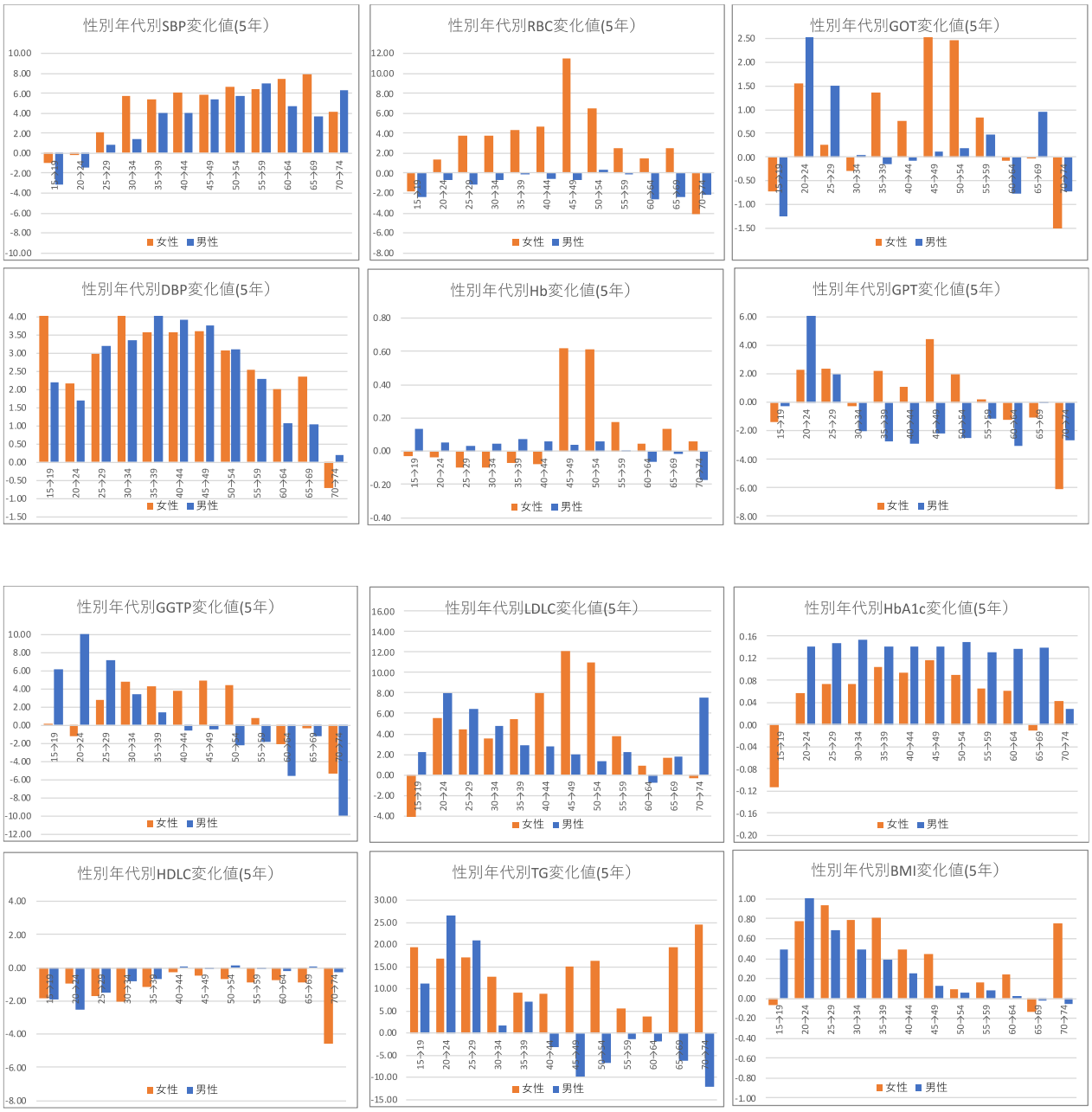


表８　基準値内未変化群におけるカットオフ値の算出

性別	年代	n	SBP		DBP		RBC		Hb		GOT		GPT		GGT		HDLC		LDLC		TG		HbA1c	
男性	30→34	5733	1.31	12.60	2.54	9.41	-1.46	22.32	0.02	0.76	0.68	11.28	1.18	19.29	6.52	38.88	-0.52	9.39	7.25	20.26	11.51	94.08	0.01	0.25
	35→39	8155	1.99	12.84	2.65	9.37	-2.51	22.54	0.00	0.74	0.67	11.83	0.29	20.25	5.38	44.24	-0.37	9.68	5.68	20.99	7.57	103.17	0.02	0.27
女性	30→34	1426	1.23	12.19	1.87	9.41	1.25	25.34	-0.02	1.04	0.08	5.08	0.23	8.41	1.61	9.81	-0.29	10.43	5.37	19.78	4.77	41.94	-0.05	0.26
	35→39	2711	2.66	12.67	2.24	9.36	2.73	24.95	-0.04	1.24	0.39	6.77	0.41	8.63	1.79	20.43	-0.74	9.94	6.57	18.43	7.22	45.74	-0.03	0.28

男性	受診勧奨値	140.0		90.0		360.0		12.0		51.0		51.0		101.0		34.0		140.0		300.0		6.5	
	指導勧奨値	130.0		85.0		400.0		13.0		31.0		31.0		51.0		39.0		120.0		150.0		5.6	
女性	受診勧奨値	140.0		90.0		300.0		11.0		51.0		51.0		101.0		34.0		140.0		300.0		6.5	
	指導勧奨値	130.0		85.0		360.0		12.0		31.0		31.0		51.0		39.0		120.0		150.0		5.6	

受診勧奨

30歳判定基準算出	男性	136.7	84.8	364.0	12.0	49.6	49.5	89.1	34.9	127.1	280.9	6.5
	女性	136.1	85.9	296.0	11.1	50.5	50.4	97.6	35.0	128.1	288.0	6.6
35歳判定基準算出	男性	138.0	87.3	362.5	12.0	50.3	50.7	95.6	34.4	134.3	292.4	6.5
	女性	137.3	87.8	297.3	11.0	50.6	50.6	99.2	34.7	133.4	292.8	6.5

指導勧奨

30歳判定基準算出	男性	126.7	79.8	404.0	13.0	29.6	29.5	39.1	39.9	107.1	130.9	5.6
	女性	126.1	80.9	356.0	12.1	30.5	30.4	47.6	40.0	108.1	138.0	5.7
35歳判定基準算出	男性	128.0	82.3	402.5	13.0	30.3	30.7	45.6	39.4	114.3	142.4	5.6
	女性	127.3	82.8	357.3	12.0	30.6	30.6	49.2	39.7	113.4	142.8	5.6

受診勧奨

30歳判定基準カットオフ	男性	136.0	84.0	363.0	11.0	49.0	49.0	89.0	34.0	127.0	280.0	6.4
	女性	136.0	85.0	296.0	11.0	50.0	50.0	97.0	35.0	128.0	288.0	6.5
35歳判定基準カットオフ	男性	138.0	87.0	362.0	12.0	50.0	50.0	95.0	34.0	134.0	292.0	6.4
	女性	137.0	87.0	297.0	11.0	50.0	50.0	99.0	34.0	133.0	292.0	6.5

指導勧奨

30歳判定基準カットオフ	男性	126.0	79.0	403.0	12.0	29.0	29.0	39.0	39.0	107.0	130.0	5.5
	女性	126.0	80.0	356.0	12.0	30.0	30.0	47.0	40.0	108.0	138.0	5.6
35歳判定基準カットオフ	男性	128.0	82.0	402.0	13.0	30.0	30.0	45.0	39.0	114.0	142.0	5.5
	女性	127.0	82.0	357.0	12.0	30.0	30.0	49.0	39.0	113.0	142.0	5.6

表９-1 表８を基に設定した性別年代別　検査基準許容値

項目		受診勧奨値				指導勧奨値			
	性別	男性		女性		男性		女性	
	年齢	30	35	30	35	30	35	30	35
SBP		136	138	136	137	126	128	126	127
DBP		84	87	85	87	79	82	80	82
GOT		49	50	50	50	29	30	30	30
GPT		49	50	50	50	29	30	30	30
GGT		89	95	97	99	39	45	47	49
HDLC		34	34	35	34	39	39	40	39
LDLC		127	134	128	133	107	114	108	113
TG		280	292	288	292	130	142	138	142
HbA1c		6.4	6.4	6.5	6.5	5.5	5.5	5.6	5.6

表 9 -2 表 9-1 を基に設定した性別年代別検査基準許容値に基づく有所見率(%)

項目		受診勧奨				指導勧奨			
	性別	男性		女性		男性		女性	
	年齢	30	35	30	35	30	35	30	35
SBP	勧奨値	9.1	10.9	2.1	3.8	22.2	24.7	5.9	8.8
	許容値	12.9	12.7	3.0	4.8	30.9	28.6	9.0	11.8
DBP	勧奨値	4.6	7.6	1.9	3.3	9.1	14.3	3.9	6.3
	許容値	10.3	11.3	3.9	5.0	20.9	19.8	7.7	9.1
GOT	勧奨値	2.0	2.3	0.5	0.5	10.6	12.1	2.2	2.5
	許容値	2.3	2.4	0.5	0.5	13.4	13.5	2.5	2.8
GPT	勧奨値	9.9	10.7	1.3	1.3	25.6	28.5	3.6	4.2
	許容値	10.7	11.2	1.3	1.4	28.7	30.2	3.9	4.5
GGT	勧奨値	4.3	6.2	0.5	0.7	16.1	11.4	2.3	3.2
	許容値	5.5	7.1	0.6	0.7	25.0	26.0	2.7	3.6
HDLC	勧奨値	2.1	2.4	0.2	0.3	7.4	7.9	1.0	1.2
	許容値	2.1	2.4	0.3	0.3	7.4	7.9	1.3	1.2
LDLC	勧奨値	19.3	25.7	8.7	9.2	39.7	48.9	22.9	27.8
	許容値	31.6	31.8	16.0	15.7	56.9	56.9	37.8	36.3
TG	勧奨値	4.3	5.3	0.5	0.6	22.9	25.9	5.5	6.3
	許容値	5.2	5.7	0.6	0.7	30.0	28.7	7.1	7.3
HbA1c	勧奨値	0.9	1.8	0.5	0.7	7.5	13.2	5.3	8.4
	許容値	1.0	1.9	0.5	0.7	13.1	19.4	5.3	8.4

表 10　肥満未変化群と肥満改善群の性別年齢階級別個人検査値の経年推移（5 年間）の比較

被験者内効果の検定		SBP								DBP								RBC								Hb							
		肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率
		n	M	SD	n	M	SD					M	SD		M	SD						M	SD		M	SD						M	SD		M	SD					
男性	20代	1808	0.21	13.94	273	-4.33	12.15	4.72	343.84	2.20	0.06	2.75	10.29		-1.58	9.25		4.60	229.59	2.45	***0.04***	-0.99	22.15		-12.41	25.01		4.44	638.94	1.72	0.14	0.04	0.71		-0.28	0.76		3.85	0.50	1.03	0.39
	30代	5530	2.99	14.35	1008	-2.36	12.89	4.31	182.24	0.96	0.44	3.88	10.53		-0.33	10.29		4.40	152.78	1.53	0.18	-0.33	21.50		-9.29	24.03		4.31	1697.83	4.64	***0.00***	0.06	0.72		-0.15	0.77		4.34	1.29	3.44	***0.01***
	40代	5531	4.65	15.00	1154	-0.72	15.24	4.46	599.81	3.34	***0.01***	3.85	10.43		-0.55	10.42		4.43	587.32	6.83	***0.00***	-0.62	22.03		-11.55	26.51		4.37	3728.12	10.63	***0.00***	0.05	0.76		-0.25	0.88		4.27	2.95	7.57	***0.00***
	50代	3047	6.27	15.81	851	0.79	16.36	4.43	685.74	3.71	***0.00***	2.77	10.56		-1.03	10.84		4.53	524.18	6.93	***0.00***	0.18	22.11		-8.62	25.74		4.43	9404.63	29.18	***0.00***	0.04	0.76		-0.19	0.88		4.34	7.26	19.55	***0.00***
	60代	700	4.40	16.80	202	1.89	18.08	4.66	503.61	2.80	***0.02***	1.06	10.43		-0.60	11.61		4.65	196.87	2.93	***0.01***	-2.58	22.15		-12.06	27.88		4.39	1796.51	5.16	***0.00***	-0.05	0.84		-0.35	0.96		4.19	3.53	8.33	***0.00***
	70代	56	5.61	15.75	12	-2.50	18.28	4.91	234.94	1.23	0.29	0.88	9.19		-1.92	8.12		4.97	99.12	1.60	0.16	-0.89	20.26		-10.67	29.84		4.47	261.41	0.84	0.51	-0.15	0.82		-0.37	0.68		4.22	0.94	2.34	0.05
女性	20代	311	1.25	13.59	69	-3.26	12.57	4.03	98.48	0.60	0.66	2.70	10.21		0.22	9.78		3.79	136.54	1.30	0.28	2.92	23.86		-7.14	26.77		5.00	161.05	0.47	0.80	-0.08	0.93		-0.34	0.94		4.67	0.53	1.23	0.30
	30代	855	5.55	15.08	117	-0.21	13.14	4.00	304.93	1.22	0.30	3.80	11.35		-0.19	10.14		4.23	207.85	1.91	0.10	4.13	23.31		2.27	28.92		4.57	1609.43	4.64	***0.00***	-0.08	1.23		0.06	1.12		4.18	4.69	5.64	***0.00***
	40代	1567	5.97	16.04	286	0.91	15.56	4.18	246.86	1.12	0.35	3.59	10.46		0.17	10.10		4.37	148.80	1.73	0.14	7.90	26.44		1.11	28.84		4.52	1727.62	4.21	***0.00***	0.25	1.62		0.13	1.67		3.70	1.07	0.82	0.50
	50代	1050	6.56	16.77	239	3.44	16.29	4.45	426.90	2.21	0.06	2.85	11.05		0.33	10.73		4.51	135.43	1.96	0.09	4.85	24.03		0.08	28.78		4.54	407.08	1.71	0.14	0.43	1.32		0.28	1.32		3.29	0.32	0.57	0.65
	60代	221	7.61	15.80	53	2.91	14.52	4.72	155.89	0.88	0.49	2.11	9.89		-0.64	10.75		4.78	36.89	0.60	0.69	1.79	19.46		-3.81	26.12		4.35	943.47	3.89	***0.00***	0.07	0.61		-0.24	1.37		4.13	0.92	3.45	***0.01***
	70代	13	-0.69	21.73	9	12.00	34.86	4.16	310.74	1.25	0.29	-2.31	10.24		-5.11	13.60		4.74	87.82	1.27	0.28	-3.83	18.80		-14.11	37.36		3.87	159.62	0.33	0.85	-0.01	0.58		-0.31	1.05		3.92	0.18	0.48	0.75

		AST								ALT								GGTP								HDL							
		肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率
		n	M	SD	n	M	SD					M	SD		M	SD						M	SD		M	SD						M	SD		M	SD					
男性	20代	1808	2.10	15.73	273	-4.33	11.55	4.21	221.30	0.87	0.49	4.07	35.19		-15.57	25.67		3.88	1042.60	0.81	0.51	9.14	40.19		-9.89	27.04		3.64	718.51	0.95	0.43	-1.81	7.57		4.36	9.25		4.50	169.22	6.51	***0.00***
	30代	5530	-0.08	13.15	1008	-3.50	10.53	2.18	2120.57	2.80	0.06	-2.43	28.48		-13.56	21.43		3.74	7321.21	8.81	***0.00***	2.20	39.21		-12.22	32.09		2.12	11233.81	1.99	0.13	-0.74	7.29		5.28	9.10		4.63	401.65	13.50	***0.00***
	40代	5531	0.01	12.51	1154	-2.98	13.31	4.48	638.19	5.02	***0.00***	-2.60	22.77		-11.11	21.28		4.50	4863.07	15.00	***0.00***	-0.56	45.84		-14.52	53.44		4.07	17526.35	15.58	***0.00***	0.00	7.59		5.23	9.65		4.58	1420.93	45.08	***0.00***
	50代	3047	0.30	11.13	851	-2.36	12.18	4.49	1269.43	10.18	***0.00***	-1.92	17.59		-7.96	18.11		4.31	5386.28	19.78	***0.00***	-2.07	42.19		-15.85	49.82		4.31	15234.37	12.90	***0.00***	0.05	7.42		4.01	8.96		4.60	1539.95	47.93	***0.00***
	60代	700	-0.30	15.13	202	-0.97	11.45	4.48	169.37	2.70	***0.02***	-2.20	20.20		-4.32	15.36		4.31	571.48	3.96	***0.00***	-4.36	37.21		-12.69	61.29		3.91	2414.63	1.84	0.12	-0.12	7.81		2.02	7.92		4.61	347.18	11.21	***0.00***
	70代	56	-0.64	4.80	12	0.25	4.67	4.30	71.37	1.42	0.22	-2.48	8.17		-1.58	6.73		4.05	234.68	2.12	0.08	-8.93	35.21		-1.75	12.42		2.73	2148.52	1.87	0.14	-0.48	5.26		3.33	6.83		4.44	15.19	0.55	0.72
女性	20代	311	0.72	16.16	69	-1.06	8.62	3.72	119.21	0.71	0.58	2.33	29.12		-3.58	14.90		3.63	173.62	0.27	0.88	1.40	29.67		-4.13	12.85		3.51	66.74	0.15	0.95	-1.43	8.56		3.72	10.68		4.20	18.52	0.33	0.86
	30代	855	0.76	11.20	117	-1.48	7.98	3.66	53.20	0.60	0.65	1.29	19.26		-4.72	18.58		4.02	185.86	0.92	0.45	4.50	22.55		-3.79	26.40		3.80	315.72	1.51	0.20	-1.45	9.04		2.85	10.14		4.47	21.79	0.59	0.69
	40代	1567	1.69	12.60	286	0.63	24.78	4.35	97.15	1.07	0.37	2.68	17.36		-1.53	30.51		4.25	530.99	2.18	0.06	4.39	23.79		-1.33	41.91		3.81	478.57	1.01	0.40	-0.38	8.53		4.76	9.82		4.57	158.81	4.24	***0.00***
	50代	1050	1.80	12.07	239	-0.81	8.33	4.38	327.39	5.77	***0.00***	1.22	17.20		-2.53	12.48		4.22	1092.19	8.09	***0.00***	2.97	29.58		-3.12	21.46		4.28	1188.38	3.26	***0.01***	-0.74	8.46		3.13	8.94		4.59	314.31	9.07	***0.00***
	60代	221	-0.06	8.50	53	-0.64	8.79	4.19	52.66	1.30	0.27	-1.15	10.25		-1.40	14.18		4.23	271.38	3.19	***0.01***	-1.54	12.58		-5.43	13.25		4.11	407.29	1.87	0.11	-0.80	7.93		0.36	8.54		4.53	122.30	3.53	***0.01***
	70代	13	-4.23	11.13	9	-0.78	2.73	2.59	68.92	0.72	0.52	-5.08	9.63		-3.67	4.47		2.65	82.43	0.86	0.45	-6.31	16.04		-0.67	6.95		1.52	668.63	1.48	0.23	-3.69	10.86		-1.89	7.29		5.00	14.04	0.52	0.77

		LDLC								TG								BS								HbA1c							
		肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率	肥満未変化群			肥満改善群			自由度	平均平方	F 値	有意確率
		n	M	SD	n	M	SD					M	SD		M	SD						M	SD		M	SD						M	SD		M	SD					
男性	20代	1808	6.92	22.44	273	-5.82	21.61	4.22	233.73	0.44	0.79	22.68	136.29		-39.25	117.64		3.18	9498.43	0.32	0.83	1.79	15.17		0.77	8.30		3.29	131.70	0.08	0.98	0.15	0.61		-0.04	0.22		4.00	0.56	0.63	0.64
	30代	5530	3.61	22.72	1008	-4.81	23.81	4.18	692.62	1.19	0.31	4.98	131.53		-49.89	118.46		3.87	62178.35	1.89	0.11	2.84	18.46		-2.23	13.20		4.40	1479.73	1.91	0.10	0.15	0.60		-0.01	0.71		3.98	3.13	4.42	***0.00***
	40代	5531	2.48	22.68	1154	-5.38	24.85	4.16	1369.35	2.63	***0.03***	-5.90	137.30		-43.68	150.95		4.75	112626.37	7.99	***0.00***	3.17	17.30		0.46	20.76		4.56	1306.12	1.82	0.11	0.14	0.59		0.01	0.72		3.83	4.22	7.31	***0.00***
	50代	3047	1.71	21.52	851	-2.54	23.03	4.19	2339.02	5.58	***0.00***	-4.61	122.31		-41.40	111.99		4.58	102512.29	9.30	***0.00***	2.45	19.07		-0.02	16.33		4.63	1189.49	2.09	0.07	0.14	0.54		0.01	0.70		3.99	3.19	9.07	***0.00***
	60代	700	-0.05	21.45	202	-1.46	22.46	4.07	1180.89	3.30	***0.01***	-3.18	79.58		-21.22	87.18		4.68	36651.01	6.39	***0.00***	3.23	16.07		-0.63	9.13		4.32	304.34	0.56	0.71	0.14	0.50		0.02	0.77		3.55	1.44	5.88	***0.00***
	70代	56	8.00	21.06	12	-3.92	41.26	4.57	163.68	0.60	0.69	-9.18	45.07		-66.50	123.78		4.78	1734.62	0.68	0.63	3.75	14.48		-2.67	10.26		2.84	915.89	2.22	0.09	0.01	0.32		-0.24	0.39		3.68	0.13	0.99	0.41
女性	20代	311	4.84	20.78	69	-5.13	17.37	4.10	375.84	0.83	0.51	16.96	54.12		-12.94	47.37		4.94	906.87	0.40	0.85	-0.64	10.00		-3.50	7.63		2.00	3354.85	2.30	0.12	0.07	0.28		-0.09	0.25		2.95	1.79	1.73	0.17
	30代	855	4.78	21.78	117	-4.54	24.35	4.10	431.67	0.87	0.49	10.41	66.82		-32.89	71.42		3.89	16530.10	3.53	***0.01***	2.96	21.76		-3.50	8.40		2.05	601.12	0.68	0.51	0.09	0.50		-0.12	0.41		2.48	0.32	0.60	0.59
	40代	1567	9.92	22.60	286	1.48	25.50	4.11	1593.00	2.75	***0.03***	11.74	63.33		-17.26	73.95		3.77	19854.26	3.62	***0.01***	1.27	12.56		-2.38	10.93		3.89	270.73	0.43	0.78	0.10	0.48		-0.04	0.61		3.86	1.79	4.69	***0.00***
	50代	1050	8.03	24.05	239	2.98	23.98	4.02	389.51	0.66	0.62	11.88	82.79		-15.10	62.40		4.22	13293.45	2.63	***0.03***	1.11	20.01		0.49	30.76		4.17	1188.20	2.40	***0.05***	0.08	0.46		-0.03	0.62		3.91	2.40	9.81	***0.00***
	60代	221	1.14	22.72	53	-1.47	19.73	4.14	357.99	0.68	0.61	8.20	59.74		-12.32	54.62		4.36	3176.78	1.18	0.32	0.84	13.19		0.92	4.96		4.41	130.28	0.40	0.82	0.04	0.61		-0.12	0.58		3.62	0.39	2.03	0.10
	70代	13	3.08	21.85	9	-3.00	28.39	3.85	655.89	1.34	0.26	10.00	53.73		10.78	27.38		4.15	3680.30	1.87	0.12	0.60	5.64		-20.00	8.49		3.53	132.67	0.69	0.58	0.01	0.22		-0.18	0.39		2.86	0.09	0.55	0.64

労災疾病臨床研究事業費補助金
分担研究報告書

2-2．就労者集団の検査値に影響する要因に関する検討

研究分担者　山本　健也　　東京大学環境安全本部　准教授

研究要旨

糖尿病予防に喫煙や運動、適正体重の維持といった健康的な生活習慣が関わることはよく知られており、これらを実践するほどより健康効果が得られると期待されている。しかしながら、日常環境下において健康的な生活習慣の経時的な推移と糖尿病発症について検証した報告はない。職域多施設研究（J-ECOH スタディ）のサブコホート（1 社）の縦断データを用いて、3 年間の生活習慣パターンを同定したうえで、糖尿病発症との関連を検証した。全体的に健康的な習慣であるほど、糖尿病発症リスクは低く、さらに健康的な生活習慣に変わるとリスクが低下することも示唆された。

協力研究者：　桑原恵介（帝京大学大学院公衆衛生学研究科　講師）

A.研究背景および目的

背景：

定期健康診断は職域において毎年ルーチンに実施されるが、この健診項目を見直し、改善していくには定期健診項目と有所見との関連を定量的に評価することが求められる。この職域健康診断の縦断的検討を実現するには、同一コホートを大規模に長期間追跡しているデータベースの構築が不可欠である。

健康診断の有所見に寄与すると考えられる要因として生活習慣要因はよく知られているが、複数の生活習慣要因を組み合わせてかつ経時的に活用しようとする試みはない。

本研究では、職域多施設研究（J-ECOH スタディ）でこれまで収集した各種データを整理・統合し、本研究の目的を達成するための専用データベースの構築を図るとともに、生活習慣について詳細なデータの得られたサブコホートのデータを用いて生活習慣の推移パターンと 2 型糖尿病発症との関連について検討した。

B.　研究方法

1）研究設定

J-ECOH スタディに参加する関東・東海地方に本社を置く 12 企業、13 施設のうち、通勤に関する情報を健診時に収集している企業 1 社

2）研究デザイン

経時的疫学データベースを用いた観察研究。

3）研究対象者

生活習慣に関する詳細なデータを収集している研究に参加する事業場において、2009 年度に当該事業場に在籍しており、かつ産業医の健康管理下にある社員約 5 万名。

4）研究で収集するデータ

健康診断などの健康管理情報を収集する。

5)　上記１）の各企業において匿名化された従業員の健康診断等の記録を、事業場内での研究利用目的の承認を経たうえで収集されたデータを統合したデータベースが、J-ECOH スタディとして国立国際医療センター内に倫理審査委員会の承認を経て構築・運用されている。本調査研究については J-ECOH スタディの一環として実施された。

6)データ分析

3 年間の生活習慣の推移パターンと糖尿病発症との関連の評価

2009 年度（ベースライン）に健診を受診した労働者を対象とした。生活習慣は 5 つの低リスク習慣：非喫煙、多量飲酒なし、睡眠不足なし、運動あり、適切な体重コントロールによって定義し、低リスクな生活習慣には 1 点、そうでない習慣には 0 点をそれぞれ与え、その合計得点（0 点は最も不健康、5 点は最も健康的）を 2006 年度から 2009 年度まで年度ごとに求めた。さらに、この生活習慣の推移パターンを Group-based trajectory modeling を用いて同定した。糖尿病は定期健康診断時の空腹時または随時血糖、HbA1c、自己申告に基づき評価し、ベースライン時点以降 2017 年度までの発症を評価した。コックス比例ハザードモデルを用いて、生活習慣の推移パターンと糖尿病発症との関連を評価した。多変量モデルでは 2009 年度時点の仕事関連要因や糖尿病家族歴などを調整した。

C. 研究結果

対象者 26,647 名から、3 年間の生活習慣の推移について 5 パターンが抽出された（継続して不健康な生活習慣、継続してやや健康的な生活習慣、継続して概ね健康的な生活習慣、概ね健康的な生活習慣から十分に健康的な生活習慣に改善、継続して十分に健康的な生活習慣）。

平均 6.6 年間の追跡期間（約 17 万人年）中に 2,223 名が 2 型糖尿病を発症した。糖尿病発症リスクは生活習慣が健康的なパターンになるほど低下した。調整済みハザード比（95%信頼区間）は、継続して不健康な生活習慣と比べて、継続してやや健康的な生活習慣では 0.71 (0.63, 0.79)、継続して概ね健康的な生活習慣では 0.48 (0.43, 0.55)、概ね健康的な生活習慣から十分に健康的な生活習慣に改善したパターンでは 0.37 (0.28, 0.49)、継続して十分に健康的な生活習慣では 0.29 (0.23, 0.37) であった。2009 年度時点の HbA1c 値や body mass index を調整すると関連は弱まったが、健康的な生活習慣ほどリスクが低下する関連は変わらなかった。

D. 考察

日本の大企業の従業員において、生活習慣は 3 年間を通じてあまり変わっておらず、一部の集団でのみ改善していた。全体的に健康的な生活習慣パターンであるほど 2 型糖尿病発症リスクは低下した。継続して概ね健康的な生活習慣であったパターンと比べ、概ね健康的な生活習慣から十分に健康的な生活習慣に改善したパターンでは糖尿病リスクは低かったことから、介入研究以外の日常生活環境下においても、生活習慣を改善することで糖尿病リスクは低下する可能性が示された。

ベースライン時点の健康的な生活習慣パターンと糖尿病発症に関するコホート研究のメタ分析においても、全体的に健康的な生活習慣であるほど、糖尿病リスクは低下

することが報告されている。生活習慣を経時的に評価した観察研究はないが、今回の日本の労働者で得られた結果の方向性は先行研究と同様であったと考えられる。

E. 結論

J-ECOH スタディに参加する一部の企業の縦断データを用いて、3 年間の生活習慣の推移パターンとその後の 2 型糖尿病発症との関連について検証したところ、生活習慣が健康的であるほど、糖尿病リスクは低下することが示された。定期健康診断で得られる情報を縦断的に用いることで、介入すべき集団を同定しやすくなるだけでなく、有所見率の変化をより強力に予測できる可能性がある。

F. 健康危険情報

特記事項なし

G. 研究発表

1．論文発表

特記事項なし

2．学会発表等

1）桑原恵介, 中川徹, 山本修一郎, 本多融, 林剛司, 溝上哲也. 日本の労働者における 3 年間の生活習慣パターンと 2 型糖尿病発症との関連. 第 4 回日本糖尿病・生活習慣病ヒューマンデータ学会年次学術集会, 新潟, 12 月, 2019

2）桑原恵介, 中川徹, 山本修一郎, 本多融, 林剛司, 溝上哲也. 労働者における 3 年間の生活習慣の推移パターンと 2 型糖尿病発症：糖代謝レベル別のサブグループ解析結果. 第 30 回日本疫学会学術総会, 京都, 2 月, 2020

H. 知的財産権の出願・登録状況

特記事項なし

労災疾病臨床研究事業費補助金
分担研究報告書

3．糖尿病及び心血管疾患のリスク予測に関する研究

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研究要旨
職域の定期健康診断データを心血管疾患発症のリスク層別化に役立てるため、職域多施設研究（J-ECOH スタディ）で収集された 2011 年度の定期健康診断データおよび 2019 年 3 月までの心血管疾患の発症登録データを用いて、5 年間の発症リスクを予測するスコアを作成した。統計的検討の結果、年齢、喫煙、収縮期血圧、HDL コレステロール、LDL コレステロール、糖尿病が予測変数として選ばれた。これらの β 値を 10 倍し、四捨五入して、各変数カテゴリーのスコアとした。各スコアを合計することでリスクスコアが得られる。時間依存型ＲＯＣ分析により予測精度を評価したところ、0.8 と同程度の予測精度が得られた。本研究によって、勤労者向けの精度のよい心血管疾患リスクスコアが開発された。

研究協力者：　胡歓歓（国立国際医療研究センター疫学・予防研究部・上級研究員）

A. 研究目的

心血管疾患は代表的な生活習慣病のひとつであり、就業人口においては死亡や長期疾病休業に至る重大な原因疾病である。その予防対策として、職域では定期健康診断において血圧、血糖値、脂質といった循環器疾患の危険因子に関する検査が行われ、有所見者には医療機関への受診や生活習慣の改善の勧告がなされているほか、メタボリックシンドローム該当者には保健指導が行われている。

職域集団において疾病の高危険群を同定することは、産業保健リソースの効率的かつ効果的な投入の基礎である。また労働者が自らの発症リスクを把握することは、予防や治療の動機づけにもなる。心血管疾患のハイリスク群同定のため、これまで国内外で多くのリスク評価ツールが開発されてきた。しかしながら、心血管疾患の発症率には人種差が大きいこと、また日本で開発されたリスクスコアは主に非都市部の地域住民データにもとづいていることより、勤労者集団のデータに基づくリスク予測モデルの開発が望まれる。

職域多施設研究（J-ECOH スタディ）における 2019 年 3 月までの疾病登録データを用いて、心血管疾患発症を予測するリスクスコアを開発した。

B.　研究方法

1）職域多施設研究（J-ECOH スタディ）

J-ECOH スタディは関東・東海地方に本社を置く 12 企業（社員約 10 万名）が参加した多施設共同研究である。研究では定期健康診断（2008 年度以降）のほか、長期病休、心血管疾患発症、全死亡のイベントデータ（2012 年度以降）を定期的に収集している。本年度は 2018 年度の定期健康診断データと 2018 年度末までのイベントデータを収集・整理し、それ以前のデータと突合する作業を進めた。

2）5 年間の心血管疾患リスクスコアの開発

2011 年度（欠損の場合は 2010 年度）の健康診断を受けた労働者約 10 万人のうち、心血管疾患の既往者、リスクスコア作成に必要な変数が欠損している人、ベースライン以降 1 回も定期健康診断を受診しなかった人（発症者以外）を除いた 30 歳以上の 63,454 名を解析対象とした。2012 年 4 月以降に各施設で発症した心血管疾患（心筋梗塞、脳卒中）を産業医からの報告にもとづいて登録した。2019 年 3 月まで追跡した（最大 7 年間の観察)。最後の健康診断受診日までを在籍と見做した。

心血管疾患発症のリスク予測因子の候補として、性、年齢、肥満度（BMI)、喫煙、血圧、高血圧、高血圧治療、ヘモグロビン A1c、空腹時血糖、糖尿病、糖尿病治療、HDL コレステロール、LDL コレステロール、脂質異常症治療をまず選んだ。未調整のコックス比例ハザードモデルにより、これらの要因と心血管疾患発症との関連を調べた。ついで、多重解析の変数減少法（p<0.1）により予測変数を選択した。各予測変数の β 値にもとづき各カテゴリーにスコアを与えた。これらを合計することで各人のリスクスコアが計算される。リスクモデルの予測能評価を時間依存型 ROC 曲線下面積により定量化した。

（倫理面での配慮）

国立国際医療研究センター倫理委員会にて承認を得た。健康診断成績や疾病罹患など通常の産業医業務の中で取得されるデータについては個別に調査説明や同意は行わず、事業場に研究実施の情報公開文書を事業所内に掲示し、データ提供を拒否する場合には調査担当者に申し出る。データは企業側で匿名化を行った上で研究事務局に提供する方式とした。

C. 研究結果

追跡期間中、236 名が新規に心血管疾患を発症した。内訳は、脳卒中 163 名、心筋梗塞 73 名である。未調整での関連分析では、いずれの変数も心血管疾患との有意な関連を認めた。意味上の重複や過去に開発されたモデルを参考に変数を選択して多変量モデルに投入した。その結果、統計的に有意であった変数は、年齢、喫煙、収縮期血圧、HDL コレステロール、LDL コレステロール、糖尿病であった。これらの予測変数の β 値を 10 倍し、四捨五入して、各変数カテゴリーのスコアとした。各人についてすべてのスコアを合計することで心血管疾患リスクスコアを算出した。時間依存型ＲＯＣ分析により予測精度を評価したところ、0.8 であった。

D. 考察

本研究では、職域多施設模研究である J-ECOH スタディのデータを用いて、定期健康診断成績から心血管疾患発症のリスク予測モデルを開発した。予測に用いる変数は、年齢、喫煙、収縮期血圧、HDL コレステロール、LDL コレステロール、糖尿病である。

書者らが知る限り、日本ではこれまで 6 件のリスクスコアが作成されており、冠動脈心疾患と脳卒中を併せたものをアウトカムとした研究が 1 件、冠動脈心疾患が 2 件、心筋梗塞が 1 件、脳卒中が 2 件であった。すべて地域住民を対象にした研究で、ベースライン調査は 1988 年から 1995 年までに行われていた。予測変数として、年齢、性、喫煙、糖尿病、血圧（高血圧）はすべてのモデルに含まれていた。HDL コレステロールは 5 件に含まれていたが、LDL コレステロールを含むモデルは 2 件しかなかった。c-統計量は 0.78 から 0.83 の範囲であった。

今回作成したリスクスコアは本研究のベースラインは 2008 年から 2010 年までであり、最近の危険因子の動向を反映した、働く人に

おける心血管疾患の発症を予測するモデルとして特徴づけられよう。予測精度は既存のモデルと同程度であった。本研究のアウトカムは産業医が把握しえた症例であるため、長期病休や死亡に至った比較的、重症な心血管疾患が主である。逆に、治療日数が短く、有給休暇として済ませるなど休業届を出さなかった場合には把握されない。本対象集団は大企業の勤務者であり、健康労働者効果（healthy worker effect）のため、一般人口より発生率は低い。こうした点は絶対リスクを解釈する上で留意したい。

性別は過去の日本のすべてのモデルにおいて予測変数に用いられているが、本モデルでは選択されなかった。本対象集団の 8 割が男性であり、かつ女性の発症数が少ないため、統計的な検出力が低かったことが一因かもしれない。あるいは喫煙や高血圧などによって性差のほとんどは、説明されるのかもしない。

E. 結論

職域健康診断の成績から心血管疾患の発症を予測する簡便で精度のよいリスクスコアを開発した。

F. 研究発表

1. 論文発表

1） Hu H, Mizoue T, et al. Low serum creatinine and risk of diabetes: The Japan Epidemiology Collaboration on Occupational Health Study. J Diabetes Investig. 2019;10(5):1209-1214.
2） Xiang M, Mizoue T, et al. Association between anthropometric indices of obesity and risk of cardiovascular disease in Japanese men. J Occup Health. 2020;62(1):E12098.
3） Hu H, Mizoue T, et al. Trajectories of body mass index and waist circumference before the onset of diabetes among people with prediabetes. Clin Nutr (印刷中)

2. 学会発表

なし

G. 知的財産権の出願・登録状況

なし

図１．心血管疾患リスクスコア：J-ECOHスタディ

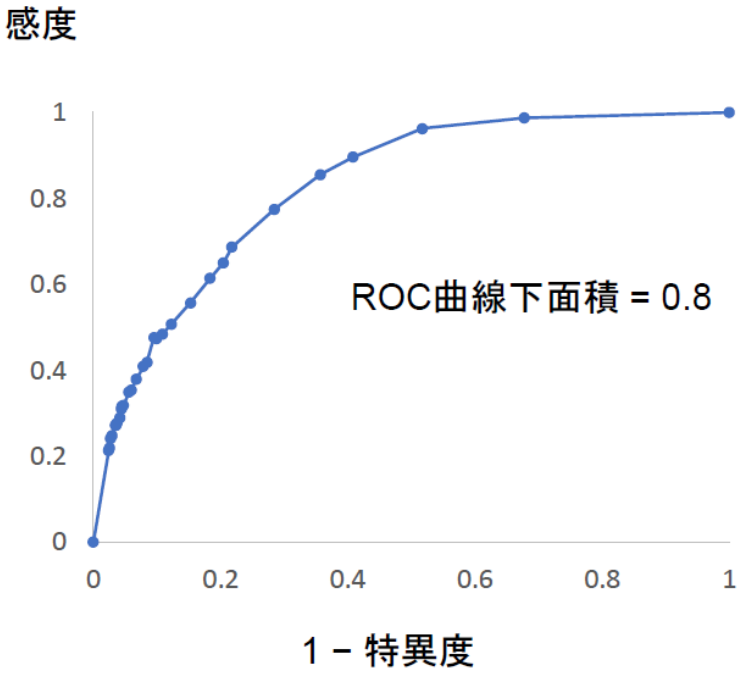
	スコア
年齢	
30-39	0
40-49	14
≥50	20
喫煙	
非喫煙/過去喫煙	0
現在喫煙　1-20 本 /日	8
現在喫煙　21 本以上 /日	11
収縮期血圧 (mmHg)	
<120	0
120-139	10
140-159	16
≥160	18
HDLコレステロール (mg/dL)	
≥60	0
40-59	5
<40	10
LDLコレステロール (mg/dL)	
<140	0
≥140	5
糖尿病*	
なし	0
あり	9

＊ヘモグロビンA1c 6.5%以上、空腹時血糖 126mg/dL以上、随時血糖 200mg/dL以上、糖尿病治療のいずれかに該当

合計スコア	5年間の推定発症リスク
≤14	<0.07%
15-24	0.07%-0.14%
25-30	0.15%-0.30%
31-38	0.31%-0.50%
≥39	0.51%-3.00%

図２．リスクモデルの予測精度

ROC 曲線



労災疾病臨床研究事業費補助金
分担研究報告書

４．一般健康診断の事後措置の有効性に関する調査

(Effective coverage(EC)による評価)

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研究要旨
労働安全衛生法に基づく健康診断は、企業に実施義務が課されており、単に健診を行うのみでなく、健康診断の事後措置を適切に行うことが法令で規定されている。2017 年度の質的調査では、就業制限が必要か否かの判断が必要な人への対応に次いで、要受診レベルの人への対応が、優先順位が高かった。本研究では、某企業（製造業）において、産業保健専門職（産業医、保健師等）が健診事後措置に関与することにより、対象者が医療機関に受診し、かつ、治療による疾患のコントロールが良好となるか否かについて、Effectiveness coverage(EC)の指標を用いて検討した。53,720 名で検討した結果、専属の産業保健スタッフがいる事業所で EC が高血圧と糖尿病は有意に高く(高血圧 aOR 1.41: 95%CI 1.20-1.66、糖尿病　aOR 1.53: 95%CI 1.17-2.00)、一方で脂質異常症は有意な差を認めなかった。(脂質異常症　aOR 1.11: 95%CI 0.92-1.34)。特に生活習慣に関連する疾患に対して、産業保健スタッフが本人の疾患に対する理解を高めながら介入を行うことが有効であり、また、その効果を Crude coverage (CC)や Effectiveness coverage(EC)等のベンチマークを活用しながら評価することが重要である。

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Ａ．はじめに

労働安全衛生法に基づく健康診断は、企業に実施義務が課されており、単に健診を行うのみでなく、健康診断の事後措置を適切に行うことが法令で規定されている（労働安全衛生法第 66 条の 4～7)。具体的な内容は「健康診断結果に基づき事業者が講ずべき措置に関する指針」に記述されている。具体的には、就業上の配慮の要否の判断や受診勧奨、栄養・運動指導等であり、この順に優先順位が高いことが専門家によるフォーカス・グループ・ディスカッションで明らかになっている。

本研究では、受診勧奨に注目し、2018 年度は、某企業（製造業）において、産業保健専門職（産業医、保健師等）が健診事後措置に関与することにより、受診勧奨が促されか否かについて検討した。その結果、高血圧は有意に高く受診している一方で、糖尿病と脂質異常症は有

意な差を認めなかった。ただし、糖尿病は両群とも受診率が高いという背景があった。

受診勧奨の目的は、受診することのみでなく、受診したうえで適切に治療が行われ、当該疾患のコントロールが良好となることである。

本研究では、某企業（製造業）（2018 年度報告書の調査対象企業と同一）において、産業保健専門職（産業医、保健師等）が健診事後措置に関与することにより、対象者が医療機関に受診し、かつ、治療による疾患のコントロールが良好となるか否か、について明らかにすることを目的とした。

B．研究の方法

本研究は、某企業での断面調査である。一般健康診断、人事データ、診療報酬明細書（レセプト）を用い、2011 年 4 月から 2012 年 3 月まで所属する男性社員 91351 人を対象とした。対象者を 40〜59 歳に絞り、心筋梗塞、脳卒中、悪性腫瘍、腎不全または透析の者、また、データ欠損がある者を除外し、最終的に残った 53720 人を本研究の対象とした。

産業保健専門職の有無

2011 年度において、対象者は 1914 事業所で勤務していた。研究対象企業では、1914 事業所のうち、265 事業場(8,559 名)が産業医および保健師が不在、146 事業場(3,872 名)が嘱託の産業医および保健師が執務、393 事業場(14,690 名）が嘱託の産業医と専属の保健師が執務、そして、555 事業場(26,599 名)が専属の産業医および保健師が執務していた。

研究対象企業においては、健康診断実施後に各個人に健診結果が返却される。健診結果には、「要受診（医療機関での治療が必要）」「要保健指導（治療は必要ないが生活習慣を改善する必要がある）」「異常なし」の判定が行われ、個人に通知される。専属の産業保健スタッフがいる事業所では、産業保健スタッフが、「要受診」の判定を受けた人が適切に受診したかどうかの確認を行い、また、「要保健指導」の判定を受けた人に対して保健指導を実施することが通常行われるが、専属の産業保健スタッフがいない事業所では、そのようなきめ細かいフォローアップが実施できていない。そこで、専属の産業保健スタッフ（産業医または産業看護職）がいる事業所（948 事業場、41,289 名）を OH 群、専属の産業保健スタッフがいない事業所(411 事業場、12,431 名)を non-OH 群と定義した。

健康情報

2011 年度に実施された定期健康診断のデータのうち、属性（性・年齢、職種)、自記式の質問票（喫煙歴、現在の内服状況（血糖、血圧、脂質の内服)、および既往歴（心筋梗塞、脳卒中、悪性腫瘍および腎不全・透析））と客観的な検査結果（body mass index (BMI)、空腹時血糖、脂質（low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides)、収縮期血圧/拡張期血圧を用いた。

社会経済的情報

2011 年度の標準報酬月額を用いた。研究参加企業における母集団の標準報酬月額がおよそ 3 分位となるように分類し、low (≥41 万円); middle (41-56 万円)、high (>56 万円)とした。

医療機関への受診記録

各個人が医療機関に受診したかどうかを把握する目的で診療報酬明細書（レセプト）を用いた。レセプトには、受診日、傷病名、医療費等の情報が記載されている。2011 年 4 月 1 日から 2012 年 3 月 31 日までのレセプトを用いて、高血圧、糖尿病、脂質異常症の病名で受診

したか否かを把握した。ここで把握した受診は、各疾患の治療薬が内服されているか否かに関わらず、受診したか否かのみで判断した。

Need の定義

医療サービスを必要とする人を、本研究では高血圧、糖尿病、脂質異常症毎に、以下の通りに定義した。

Need（高血圧）: 収縮期血圧 160mmHg 以上、または、拡張期血圧 100mmHg 以上、または、降圧薬の内服あり

Need（糖尿病）: FBS160mg/dL 以上、または、血糖降下薬・インスリンの使用あり

Need（脂質異常症）: LDL コレステロール 160mg/dL 以上、または、HDL コレステロール 35mg/dL 未満、または、中性脂肪(TG)300mg/dL 以上、または、コレステロールを改善する薬の内服あり

この基準は、健診で「要受診」の判定となり、かつ、研究参加企業において専属の産業保健スタッフが個別の介入を行う基準である。

Crude coverage (CC)の定義

各疾患での受療ありのものを、Use（高血圧）、Use（糖尿病）、Use（脂質異常症）とし、Crude coverage (CC)を次の通り定義した。
Crude coverage (CC)は、特定の医療サービスを必要とする人のうち、医療サービスの利用している者の割合であり、
Crude coverage (CC) = Use / Need

Effectiveness の定義
各疾患での受療ありのもので、かつ、各疾患のコントロールが良好なものを、Effectiveness（高血圧）、Effectiveness（糖尿病）、Effectiveness（脂質異常症）と定義した。

Effectiveness（高血圧）:降圧薬の内服ありであり、かつ、「収縮期血圧 140mmHg 未満、かつ、拡張期血圧 90mmHg 未満」のもの

Effectiveness（糖尿病）:血糖降下薬・インスリンの使用ありであり、かつ、FBS126mg/dL 未満のもの

Effectiveness（脂質異常症）:コレステロールを改善する薬の内服ありであり、かつ、「LDL コレステロール 140mg/dL 未満、かつ、HDL コレステロール 40mg/dL 以上、かつ、中性脂肪(TG)150mg/dL 未満」のもの

Effectiveness coverage (EC)の定義

Effectiveness coverage (EC)は、特定の医療サービスを必要とする人のうち、医療サービスの利用しており、かつ、疾患のコントロールが良好である者の割合であり、
EC = Effectiveness / Need
とする。

統計

Non-OH 群と OH 群の年齢、BMI、喫煙歴、職種、標準報酬月額の各カテゴリーの割合を計算した。また、non-OH 群と OH 群の Crude coverage (CC) および Effectiveness coverage(EC)を計算した。

次に、医療サービスを必要とする人（Need）を対象とし、「実際に医療機関に受療し、かつ、コントロール良好であること（Effectiveness）」をアウトカムとし、nonOH 群と比較して OH

群のオッズ比および95%信頼区間を、高血圧、糖尿病、脂質異常症の疾患毎に、ロジスティック回帰で分析した。年齢、標準報酬月額、職種を調整した。本解析は、個人を一次レベル、事業所を二次レベルとしたマルチレベル分析を行った。

C．結果

対象者の詳細を Table 1.に示す。53,720 名のうち、12,431 名が non-OH 群、41,289 名が OH 群であった。

Crude coverage（CC）および Effectiveness coverage(EC)を Figure 1.に示す。OH-群の方が、高血圧、糖尿病、脂質異常症のいずれの所見においても CC、EC ともに高かった。

高血圧、糖尿病、脂質異常症ごとに、治療が必要な人が、実際に医療機関に受診し、かつ、コントロール良好であるオッズ比を Table 2.に示す。nonOH 群と比較して、OH 群の受診は、高血圧と糖尿病で有意に高く（高血圧 aOR 1.41: 95%CI 1.20-1.66、糖尿病　aOR 1.53: 95%CI 1.17-2.00)、一方で脂質異常症は有意な差を認めなかった（脂質異常症　aOR 1.11: 95%CI 0.92-1.34)。

D．考察

本研究では、健康診断の事後措置において、産業保健専門職（産業医、保健師等）が健診事後措置に関与することにより、受診勧奨が促され、また、治療による疾患のコントロールが良好となるか否かについて検討した。

所属する事業場に産業医や産業看護職といった産業保健スタッフが常勤し、日常的に産業保健サービスを提供していることが、高血圧の Crude coverage（CC)が有意に良好な効果を及ぼしていた。また、高血圧および糖尿病の Effectiveness coverage（EC)に有意に良好な効果を及ぼしていた。高血圧と糖尿病においては、産業保健スタッフが受診勧奨の取り組みを行っていること、また、保健指導等の機会を含め受療後もフォローアップを行うことにより、疾患のコントロールも良好となっていることが考えられる。中小企業において保健師による保健指導がある場合には精密検査の受診が有意に増加していたとの報告[1)]や、保健所の成人健診後の医療機関受診の指示の際に紹介状の発行によって医療機関受診が向上したことなどが報告されている[2)]。脂質については、CC、EC ともに有意に良好な効果を認めなかった。Tateishi et al. は、プロフェッショナルレベルの産業医は血圧や血糖の異常高値については単独でも就業制限を検討するが、脂質項目の異常高値では就業制限を検討する割合が低いことを報告しており、産業保健スタッフの指導が積極的でない可能性が想定される[3)]。また脂質異常については、直接的な指導があっても、治療開始をさせることが容易ではないことが示唆されている。Tatemichi et al.は、産業保健体制が整っている大規模事業場において、健康診断の結果で高コレステロール血症に対する治療が必要と判断された労働者のうち、3 か月間の食事療法によって改善しなかった対象に対して保健専門職が服薬治療を指導したが、そのうち治療に応じた対象者は約半数であり、応じなかった対象者のうち 3 分の 1 は食事療法にも応じなかったことを報告している[4)]。その背景として、脂質のコントロール不良であっても他の疾病に比べて自覚症状が乏しく、プレゼンティーイズムが生じにくいこと[5)]が影響している可能性がある。

以上から、特に生活習慣に関連する疾患に対して、産業保健スタッフが本人の疾患に対する

理解を高めながら介入を行うことが有効であり、また、その効果を Crude coverage (CC)や Effectiveness coverage (EC)のベンチマークを活用しながら評価することが重要である。

1) Aono Y, Aisaka A, Gohno M, Hida T, Shimizu T (2000): Visiting a doctor by individuals who need medical diagnosis after screening and kinds of screening. Sangyo Igaku Journal 23, 43-49 (in Japanese)
2) Goto E, Ishikawa H, Okuhara T, Kato M, Okada M, Kiuchi T (2018): Factors associated with adherence to recommendations to visit a physician after annual health checkups among Japanese employees: a cross-sectional observational study. Ind Health 56: 155-159.
3) Tateishi S, Watase M, Fujino Y, Mori K (2016): The opinions of occupational physicians about maintaining healthy workers by means of medical examinations in Japan using the Delphi method. J Occup Health 58: 72-80.
4) Tatemichi M, Hamaguchi T, Hashira et al (2002): Acceptability and long-term compliance with drug treatment for hypercholesterolemia in Japanese male worker: I. Acceptability of drug treatment. J Occup Health 44: 166-175.
5) Burton WN, Chen CY, Conti DJ, Schultz AB, Pransky G, Edington DW (2005): The association of health risks with on-the-job productivity. J Occup Environ Med 47: 769-77.

Ｅ．倫理的配慮

本調査に関して、研究１、研究２ともに、産業医大学倫理委員会の承認を得て実施した。

Ｆ．健康危険情報

該当せず。

Ｇ．研究発表

１．論文発表

Hashiguchi K, Nagata T, Mori K, Nagata M, Fujino Y, Ito M. Occupational health services improve effective coverage for hypertension and diabetes mellitus at Japanese companies. JUOEH. 2019: 41(3):271-282.

２．学会発表

永田智久，橋口克頼，森晃爾，永田昌子，藤野善久，伊藤正人．産業保健サービスは企業における高血圧および糖尿病の Effective Coverage を向上させる．2019 年度日本産業衛生学会九州地方会学会．福岡．2019 年 7 月．

Table 1. Baseline characteristics of employees

	non-OH	OH
Number of subjects	12,431	41,289
Age categories (%)		
40-44	16.4	9.8
45-49	33.6	34.0
50-54	27.2	34.1
55-59	22.8	22.2
BMI (%)		
≤18.4	2.6	2.8
18.5-24.9	64.0	67.8
25.0-29.9	28.2	25.5
30.0-34.9	4.5	3.4
≥35.0	0.7	0.6
missing	0.1	0.0
Smoking status (%)		
Non-smoker	47.1	44.3
Ex-smoker	10.6	18.9
Smoker	42.1	36.6
Missing	0.2	0.1
Job classification (%)		
Sales	37.3	10.5
Research and development, and product	29.0	64.0
Office work and others	33.7	25.5
Standard remuneration monthly fee（JPY）(%)		
Low ≤ 410,000	35.4	23.2
Middle 410,000-560,000	41.6	34.8
High >560,000	23.0	42.0

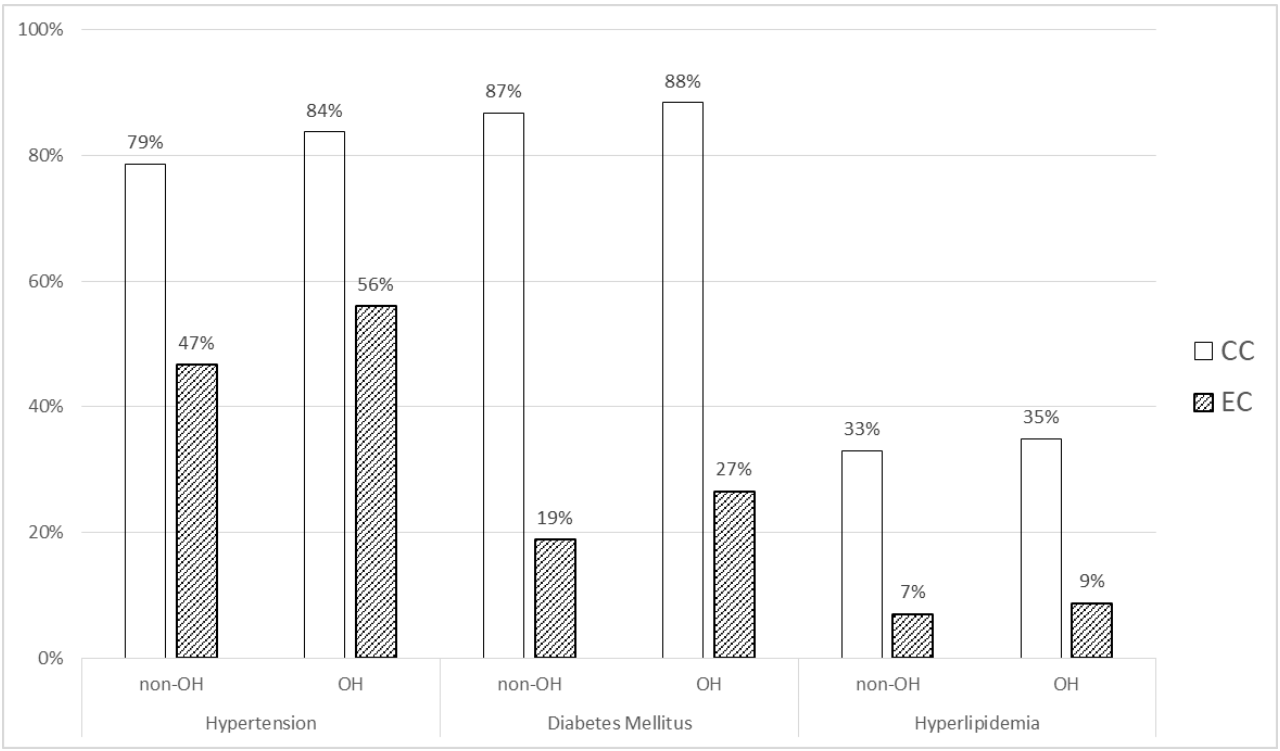

Figure 1. Crude coverage and effective coverage for hypertension, diabetes mellitus and hyperlipidemia in workplaces without or with full-time occupational health practitioners respectively (non-OH / OH).

Table 2. Odd ratios for whether or not diseases were well controlled among employees found to require medical treatment for hypertension, diabetes mellitus, and hyperlipidemia

	Number needing treatment	Number with effective control	Odds ratio for effective control			
			adjusted OR*	95%CI**		p
Hypertension						
Workplaces without full-time occupational health practitioners	1461	1148	reference			
Workplaces with full-time occupational health practitioners	4661	3901	1.41	1.20	1.66	<0.001
Diabetes mellitus						
Workplaces without full-time occupational health practitioners	474	411	reference			
Workplaces with full-time occupational health practitioners	1300	1149	1.53	1.17	2.00	<0.001
Hyperlipidemia						
Workplaces without full-time occupational health practitioners	2905	959	reference			
Workplaces with full-time occupational health practitioners	9363	3267	1.11	0.92	1.34	0.283

* Univariate logistic regression analysis adjusted for age, job type and standard remuneration monthly fee

** CI: Confidence interval

Ⅲ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
該当なし							

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Hu H, Mizoue T, et al.	Low serum creatinine and risk of diabetes: The Japan Epidemiology Collaboration on Occupational Health Study	J Diabetes Investig	10(5)	1209-1214	2019
Xiang M, Mizoue T, et al.	Association between anthropometric indices of obesity and risk of cardiovascular disease in Japanese men	J Occup Health	62(1)	E12098	2020
Hu H, Mizoue T, et al.	Trajectories of body mass index and waist circumference before the onset of diabetes among people with prediabetes	Clin Nutr			印刷中
Hashiguchi K, Nagata T, Mori K, Nagata M, Fujino Y, Ito M.	Occupational health services improve effective coverage for hypertension and diabetes mellitus at Japanese companies	JUOEH	41(3)	271-282	2019

Ⅳ．研究成果の刊行物・別刷

JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
ORIGINAL ARTICLE

Low serum creatinine and risk of diabetes: The Japan Epidemiology Collaboration on Occupational Health Study

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Keywords
Diabetes, Serum creatinine, Skeletal muscle

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ABSTRACT

Aims/Introduction: We examined a prospective association between serum creatinine levels and diabetes.

Materials and Methods: The present study included 31,343 male workers without diabetes, and aged between 20 and 64 years at baseline. We calculated the cumulative average of their serum creatinine over the study period. We defined diabetes as either glycated hemoglobin levels ≥6.5%, random glucose levels ≥200 mg/dL, fasting glucose levels ≥126 mg/dL or receiving antidiabetic treatment. Cox proportional hazards regression analysis was carried out to estimate the hazard ratio (HR) and 95% confidence interval (CI).

Results: With a median observation of 7.7 years, 2,509 participants developed diabetes. After adjusting for age, smoking, body mass index, hypertension and dyslipidemia, lower cumulative average serum creatinine levels were related to a greater diabetes risk: HRs were 1.56 (95% CI 1.35–1.82), 1.22 (1.09–1.35) and 1.06 (0.96–1.17) for the participants with serum creatinine <0.70, 0.70–0.79 and 0.80–0.89 mg/dL, respectively, compared with those with 0.90–1.20 mg/dL (*P* for trend <0.001). The serum creatinine-diabetes association was more pronounced among older adults (serum creatinine <0.70 vs 0.90–1.20 mg/dL, HR 1.66, 95% CI 1.37–2.00) than younger adults (HR 1.32, 95% CI 1.02–1.71; *P* for interaction by age group = 0.001).

Conclusions: Low serum creatinine is associated with an increased risk of diabetes. Screening serum creatinine levels can be used to identify those who are at high risk of diabetes.

INTRODUCTION

Skeletal muscle is a primary target for insulin action[1]. Thus, decreased skeletal muscle mass could potentially trigger insulin resistance[2,3], which is an underlying mechanism of diabetes. Two cohort studies from Korea have shown that low muscle mass, defined using relative muscle mass and muscle mass index (appendicular), respectively, is linked with a greater risk of incident diabetes in both young and old people[4,5].

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Creatinine is the only metabolite of creatine phosphate in the skeletal muscle. Under the steady state, it is created at a relatively constant rate by the body depending on the total skeletal muscle mass[6]. Because of the close association between muscle mass and creatinine (correlation coefficient ≥0.7)[7,8], serum creatinine is also used as an inexpensive, easily available surrogate of muscle mass when the kidney functions are stable and protein intake is normal. Thus, it would be interesting to examine a potential association between low serum creatine and the development of diabetes. Three cohort studies from Japan and one from China reported that low serum creatinine was

associated with an elevated risk (hazard ratios [HRs] ranging from 1.4 to 2.0) of diabetes[9–12]. However, these cohort studies had some limitations, including short mean follow-up periods (≤4 years)[9,12], lack of adjustment for potentially important diabetes risk factors (for example, smoking and dyslipidemia)[10,11] or the use of fasting glucose only for diagnosing diabetes[9,11]. Furthermore, all of these studies assessed serum creatinine at baseline only. In addition, no study has examined the creatinine–diabetes association among those with prediabetes, which represents a high risk for diabetes.

Thus, we investigated a prospective association between serum creatinine levels and diabetes risk using repeated measures of creatinine in a male working population in Japan.

METHODS

Study design

We analyzed data from the Japan Epidemiology Collaboration on Occupational Health Study, which is an ongoing cohort study among workers of 12 companies in Japan (study description in the Appendix S1)[13,14]. Briefly, the workers in the participating companies underwent a health checkup every year. They also completed a questionnaire about their medical history and lifestyle. The study protocol, including the consent procedure, was approved by the ethics committee of the National Center for Global Health and Medicine, Japan. In the present study, the 2008 health checkup was considered as the baseline. Two companies had large amounts of missing data in 2008, thus the dataset of 2009 and 2010, respectively, for each company was used as the baseline. We determined the outcome of the present prospective analysis using data of a maximum 8-year follow up from the baseline through March 2017.

Study participants

The present study included only male workers, because the number of women was small (only approximately 100 women had serum creatinine <0.50 mg/dL). Workers were considered initially eligible for the study if they were aged between 20 and 64 years, and had data on serum creatinine at baseline. Of the 38,028 male workers who met the inclusion criteria for participation, we excluded those with diabetes at baseline (n = 2,754), or with missing data on blood glucose (n = 397), glycated hemoglobin (HbA1c; n = 190) or diabetes treatment (n = 154). We further excluded those with a self-reported history of kidney disease (n = 193), hepatitis (n = 186), cardiovascular disease (n = 417) or cancer (n = 239) at baseline to eliminate the influence, if any, of these diseases on serum creatinine. Workers with serum creatinine >1.2 mg/dL, suggestive of renal dysfunction, were also excluded (n = 193)[15]. After further excluding those with missing data on smoking, body mass index (BMI), dyslipidemia and hypertension (n = 388), 32,917 participants remained. We further excluded those who did not attend any subsequent health checkups (n = 1,245) or who attended, but did not receive, glucose measurement (n = 329). Finally, 31,343 participants remained in the analysis.

Exposure

We assessed the levels of serum creatinine using the enzymatic method. To minimize misclassification of exposure, we calculated the cumulative average of serum creatinine from baseline examination up to the start of each follow-up interval. For example, the incidence of diabetes between 2009 and 2010 was related to the average serum creatinine measured at the 2008 and 2009 health checkups, and the incidence of diabetes between 2010 and 2011 was related to the average serum creatinine measured at the 2008, 2009 and 2010 health checkups. The cumulative average of serum creatinine was divided into four categories (<0.7, 0.7–0.79, 0.8–0.89 and 0.9–1.2 mg/dL) according to serum creatinine distribution among participants and with reference to the cut-off points used in previous studies[9–11].

Outcome

Based on the American Diabetes Association criteria, we defined diabetes as either HbA1c levels ≥6.5%, random glucose levels ≥200 mg/dL, fasting glucose levels ≥126 mg/dL or receiving antidiabetic treatment[16]. The participants who met any of the aforementioned conditions during follow up were treated as incident cases of type 2 diabetes.

Covariates

Covariates included baseline age, worksite, smoking, BMI, hypertension and dyslipidemia. We refer to Appendix S1 for the data collection methods, which have been described in previous studies[13,14].

Statistical analysis

Basic characteristics of the present study participants were determined as means (standard deviations) and percentages for continuous and categorical variables, respectively. We tested trend association by carrying out a linear regression analysis for continuous variables and the Cochran–Armitage trend test for categorical variables.

Person-time for each participant was counted by subtracting the date of the baseline survey from the date when incident diabetes was first identified or the date of last health checkup, whichever happened first. We used Cox proportional hazards regression analysis to calculate the HR and 95% confidence interval (CI) for risks of incident diabetes related to cumulative average serum creatinine, which was treated as a time-varying variable. In model 1, we adjusted for worksite and age. Furthermore, we adjusted for BMI, dyslipidemia, smoking and hypertension in model 2. Additionally, we examined the creatinine–diabetes association among the participants with prediabetes at baseline, defined as HbA1c 5.7–6.4% and/or fasting glucose 100–125 mg/dL[16].

Stratified analysis was carried out by the baseline age (<45 or ≥45 years), BMI (<21, 21–24.9 and ≥25 kg/m^2), smoking (yes/no), dyslipidemia status (yes/no) and hypertension status (yes/no), which are associated with both diabetes risk and serum

creatinine levels[17–19]. All of the statistical analyses were carried out using SAS version 9.3 (SAS Institute, Cary, NC, USA. Statistical significance was established as two-sided $P < 0.05$.

RESULTS

Table 1 presents participants' characteristics according to the baseline serum creatinine categories. Those with lower serum creatinine were older, tended to be current smokers, and had higher mean high-density lipoprotein cholesterol, blood pressure and fasting glucose.

With a median observation of 7.7 years (range 0.2–9.1 years), 2,509 of the participants developed diabetes. The crude incident rate was 12.3 per 1,000 person-years. As presented in Table 2, worksite- and age-adjusted HR for diabetes among the participants with serum creatinine <0.70 mg/dL was 1.36 (95% CI 1.18–1.58) compared with people with serum creatinine 0.9–1.2 mg/dL (P for trend <0.001). After further adjusting for dyslipidemia, BMI, smoking and hypertension, the association was strengthened (HR 1.56, 95% CI 1.35–1.82). Among the participants with prediabetes at baseline, the multivariable-adjusted HR was 1.45 (95% CI 1.23–1.70) for those with creatinine <0.70 mg/dL compared with serum creatinine 0.90–1.20 mg/dL (P for trend <0.001).

Table 3 presents the association of the cumulative average serum creatinine with diabetes in the stratified analysis. The creatinine–diabetes association was more pronounced among older adults compared with younger adults (P for interaction by age group = 0.001). The serum creatinine–diabetes association did not differ by BMI levels, smoking status, hypertension status or dyslipidemia status (all P for interactions >0.05).

DISCUSSION

Using repeated measurements of serum creatinine, we found that lower levels of cumulative average serum creatinine were associated with an increased risk of diabetes. Similar findings were observed among the participants with prediabetes at baseline. The serum creatinine–diabetes association was more pronounced among the older adults than the younger adults.

The present findings are consistent with those studies using baseline creatinine only[9–12]. In a 4-year follow-up study of Japanese male workers (n = 8,570), the adjusted odds ratio of diabetes was 1.91 for the participants with creatinine 0.40–0.60 mg/dL compared with 0.71–0.80 mg/dL[9]. In another Japanese study of male workers (n = 3,313, with a median observation of 6.7 years), the adjusted HR was 1.9 for the participants with creatinine 0.38–0.69 mg/dL compared with 0.90–1.10 mg/dL[11]. In a study of a general population in Japan (n = 9,667, with a mean observation of 5 years), the adjusted HR was 1.40 for men with creatinine ≤0.7 mg/dL compared with 0.9–1.2 mg/dL, and 1.7 for women with serum creatinine ≤0.5 mg/dL compared with 0.7–1.1 mg/dL[10]. A Chinese study of the general population (n = 57,587, with a mean observation of 3.6 years) also showed that serum creatinine values at baseline were inversely associated with diabetes risk[12]. The present study had a bigger sample (n = 31,343) and longer observation period (median follow-up period of 7.7 years) than previous studies. In addition, we used cumulative average serum creatinine over the study period to minimize the misclassification of exposure. Furthermore, we found low concentrations of serum creatinine were associated with the progression from prediabetes to diabetes, extending the serum creatinine–diabetes association to those with prediabetes. With these methodological advantages and extended findings, the present study provides strong evidence that people with lower serum creatinine are at a greater risk of diabetes.

In the stratified analyses, we observed that the serum creatinine–diabetes association did not differ by BMI or smoking status, which is consistent with previous studies[9,10,12].

Table 1 | Characteristics of participants according to baseline serum creatinine categories

	Serum creatinine (mg/dL)				*P* for trend
	<0.7	0.7 0.79	0.8 0.89	0.9 1.2	
n	1,492	6,405	10,848	12,598	
Age (years)	44.9 ± 10.4	42.6 ± 10.4	42.1 ± 10.2	43.6 ± 9.7	<0.001
BMI (kg/m^2)	22.9 ± 3.5	23.0 ± 3.3	23.3 ± 3.1	23.7 ± 3.0	<0.001
Current smoker (%)	62.1	52.7	44.5	34.6	<0.001
SBP (mmHg)	123.1 ± 14.5	121.5 ± 14.2	120.6 ± 13.7	120.9 ± 14.0	<0.001
DBP (mmHg)	77.0 ± 10.0	75.8 ± 10.1	75.6 ± 9.9	76.5 ± 10.2	0.07
Hypertension (%)	19.2	15.9	14.6	18.1	0.003
FPG (mg/dL)	97.2 ± 10.2	96.4 ± 9.8	96.2 ± 9.8	96.6 ± 9.6	0.03
HbA1c (%)	5.5 ± 0.4	5.5 ± 0.4	5.5 ± 0.4	5.5 ± 0.4	0.02
TG (mg/dL)	128.4 ± 127.1	124.3 ± 100.1	125.8 ± 95.1	130.0 ± 95.7	0.57
HDL-C (mg/dL)	58.0 ± 15.5	57.6 ± 14.7	56.5 ± 14.0	56.3 ± 14.1	<0.001
LDL-C (mg/dL)	114.6 ± 31.7	117.4 ± 30.8	120.0 ± 30.5	123.4 ± 30.3	<0.001
Dyslipidemia (%)	41.3	42.5	44.9	49.0	<0.001

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting blood glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglycerides.

Table 2 | Associations between cumulative average serum creatinine and incidence of diabetes

	Cumulative average serum creatinine (mg/dL)				*P* for trend
	<0.7	0.7 <0.8	0.8 <0.9	0.9 1.2	
Overall					
Cases	228	636	832	813	
Person-years	11,599	47,950	73,878	69,866	
Model 1	1.36 (1.18, 1.58)	1.09 (0.98, 1.21)	0.98 (0.89, 1.08)	Reference	<0.001
Model 2	1.56 (1.35, 1.82)	1.22 (1.09, 1.35)	1.06 (0.96, 1.17)	Reference	<0.001
People with prediabetes at baseline					
Cases	198	582	742	745	
Person-years	5,698	21,038	30,377	29,540	
Model 1	1.29 (1.11, 1.52)	1.09 (0.98, 1.22)	0.99 (0.89, 1.10)	Reference	<0.001
Model 2	1.45 (1.23, 1.70)	1.19 (1.06, 1.33)	1.05 (0.95, 1.16)	Reference	<0.001
People with normoglycemia at baseline					
Cases	30	54	90	68	
Person-years	5,900	26,911	43,501	40,325	
Model 1	2.54 (1.64, 3.95)	1.11 (0.77, 1.60)	1.18 (0.86, 1.62)	Reference	0.005
Model 2	2.48 (1.59, 3.89)	1.18 (0.82, 1.68)	1.22 (0.89, 1.68)	Reference	0.003

Model 1: adjusted for age and worksite. Model 2: adjusted for age, worksite, smoking, body mass index, hypertension and dyslipidemia.

Table 3 | Associations between cumulative average serum creatinine and diabetes in subgroups

Subgroup	Cases	Person-years	Cumulative average serum creatinine (mg/dL)				*P* for trend
			<0.7	0.7 <0.8	0.8 <0.9	0.9 1.2	
Age (years)†							
<45	902	122,370	1.32 (1.02, 1.71)	0.95 (0.79 1.14)	0.91 (0.77, 1.06)	Reference	<0.001
≥45	1,607	80,920	1.66 (1.37, 2.00)	1.37 (1.20, 1.57)	1.15 (1.01, 1.30)	Reference	<0.001
	P-interaction = 0.001						
BMI (kg/m^2)†							
<21.0	233	45,210	1.51 (0.94, 2.41)	1.33 (0.91, 1.93)	1.09 (0.75, 1.57)	Reference	0.044
21.0 24.9	1,054	106,383	1.42 (1.12, 1.80)	1.21 (1.03, 1.43)	1.06 (0.91, 1.23)	Reference	<0.001
≥25.0	1,222	51,697	1.64 (1.32, 2.05)	1.19 (1.02, 1.37)	1.05 (0.91, 1.20)	Reference	<0.001
	P-interaction = 0.69						
Smoking‡							
Current	1,212	87,770	1.57 (1.29, 1.91)	1.24 (1.06, 1.45)	0.98 (0.85, 1.15)	Reference	<0.001
Never/former	1,297	115,521	1.47 (1.15, 1.87)	1.17 (1.01, 1.36)	1.11 (0.98, 1.27)	Reference	<0.001
	P-interaction = 0.16						
Hypertension§							
Yes	750	29,299	1.24 (0.93, 1.66)	1.35 (1.12, 1.64)	1.02 (0.85, 1.22)	Reference	0.01
No	1,759	173,992	1.70 (1.42, 2.03)	1.18 (1.03, 1.34)	1.07 (0.96, 1.21)	Reference	<0.001
	P-interaction = 0.48						
Dyslipidemia§							
Yes	1,634	91,162	1.43 (1.18, 1.74)	1.21 (1.06, 1.38)	1.04 (0.92, 1.17)	Reference	<0.001
No	875	112,189	1.72 (1.36, 2.18)	1.22 (1.02, 1.47)	1.09 (0.91, 1.29)	Reference	<0.001
	P-interaction = 0.24						

†Adjusted for age, worksite, smoking, body mass index, hypertension, and dyslipidemia. ‡Adjusted for age, worksite, body mass index, hypertension and dyslipidemia. §Adjusted for age, worksite, smoking, body mass index and dyslipidemia (or hypertension).

Furthermore, we found no effect modification by chronic diseases (for example, hypertension or dyslipidemia). With regard to age, we found that the creatinine–diabetes association was significantly stronger in the older participants (aged 45–64 years) than in the younger adults (aged 20–44 years). In contrast, a small cohort study of Japanese male workers (207 cases of incident diabetes) reported no material differences in the association between serum creatinine and diabetes by age[11]. The present findings based on a much larger number of cases of incident diabetes (n = 2,509) would not only be statistically

reliable, but also reasonable from a mechanistic viewpoint. As creatinine is created proportionally to total skeletal muscle mass[6], low creatinine levels could be an indication of age-associated loss of muscle mass. This aging-related muscle loss has been proposed to increase diabetes risk through several pathways: (i) skeletal muscle tissue is a major target of insulin action, therefore, muscle loss with age results in a diminished target of insulin, and worsens insulin sensitivity and glucose regulation; (ii) aging-related declines in muscle quality can lead to oxidation and inflammation, which cause insulin resistance by inhibiting insulin signal transduction;[20,21] and (iii) fatty infiltration in skeletal muscle that occurs with aging can lead to insulin resistance[22]. Given that aging is also associated with the impairment of β-cell function[23], it is assumed that older adults are more likely to develop diabetes than younger adults in the presence of insulin resistance. If this is the case, older people might benefit more than younger people from strength training, which increases muscle and consequently improves insulin sensitivity. In fact, a study in Japan reported a greater reduction in diabetes risk related to strength training in people aged ≥50 years than their younger counterparts[24]. More studies are required to confirm these findings.

The present study had several strengths, including the large cohort, long-term observation, use of blood glucose and HbA1c for diagnosing diabetes, sufficient cases of diabetes, and annual assessment of serum creatinine. Some limitations also warrant attention. First, serum creatinine was measured in different laboratories in the Japan Epidemiology Collaboration on Occupational Health study. Given that all the laboratories in the present study received high-quality control scores from external agencies, we believe that the measurement is reliable and comparable across participating companies. To further confirm this, we repeated the analysis with data from a big company and found that the adjusted HR was 1.52 (95% CI 1.27–1.81) for men with creatinine <0.70 mg/dL compared with 0.90–1.20 mg/dL, which is similar to the overall analysis. Second, two worksites (approximately 5% of the total study population) did not have disease history data (e.g., kidney disease, hepatitis, cardiovascular disease and cancer) that might have influenced the level of serum creatinine. We confirmed, however, that the results were materially unchanged after excluding people at the two worksites (serum creatinine <0.70 vs 0.90–1.20 mg/dL, adjusted HR 1.56, 95% CI 1.34–1.81). Third, because of the lack of data on potential confounders, such as meat intake, we were unable to control for the potential effects of these factors. Last, the small number of women, especially few (approximately 100) women with serum creatinine <0.50 mg/dL, precluded the assessment of the association between low serum creatinine and diabetes in women.

In conclusion, the present cohort study based on repeated measurements of serum creatinine shows that low serum creatinine is associated with an increased risk of diabetes. Screening serum creatinine levels can be used to identify those at a high risk of diabetes.

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DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Zierath JR, Krook A, Wallberg-Henriksson H. Insulin action and insulin resistance in human skeletal muscle. *Diabetologia* 2000; 43: 821–835.
2. Moon SS. Low skeletal muscle mass is associated with insulin resistance, diabetes, and metabolic syndrome in the Korean population: the Korea National Health and Nutrition Examination Survey (KNHANES) 2009-2010. *Endocr J* 2014; 61: 61–70.
3. Srikanthan P, Hevener AL, Karlamangla AS. Sarcopenia exacerbates obesity-associated insulin resistance and dysglycemia: findings from the National Health and Nutrition Examination Survey III. *PLoS One* 2010; 5: e10805.
4. Son JW, Lee SS, Kim SR, *et al.* Low muscle mass and risk of type 2 diabetes in middle-aged and older adults: findings from the KoGES. *Diabetologia* 2017; 60: 865–872.
5. Hong S, Chang Y, Jung HS, *et al.* Relative muscle mass and the risk of incident type 2 diabetes: a cohort study. *PLoS One* 2017; 12: e0188650.
6. Heymsfield SB, Arteaga C, McManus C, *et al.* Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. *Am J Clin Nutr* 1983; 37: 478–494.
7. Baxmann AC, Ahmed MS, Marques NC, *et al.* Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C. *Clin J Am Soc Nephrol* 2008; 3: 348–354.
8. Woo KS, Choi JL, Kim BR, *et al.* Clinical usefulness of serum cystatin C as a marker of renal function. *Diabetes Metab J* 2014; 38: 278–284.
9. Harita N, Hayashi T, Sato KK, *et al.* Lower serum creatinine is a new risk factor of type 2 diabetes: the Kansai healthcare study. *Diabetes Care* 2009; 32: 424–426.
10. Kashima S, Inoue K, Matsumoto M, *et al.* Low serum creatinine is a type 2 diabetes risk factor in men and women: the Yuport Health Checkup Center cohort study. *Diabetes Metab* 2017; 43: 460–464.
11. Takeuchi M, Imano H, Muraki I, *et al.* Serum creatinine levels and risk of incident type 2 diabetes mellitus or dysglycemia in middle-aged Japanese men: a retrospective cohort study. *BMJ Open Diabetes Res Care* 2018; 6: e000492.

12. Bao X, Gu Y, Zhang Q, *et al.* Low serum creatinine predicts risk for type 2 diabetes. *Diabetes Metab Res Rev* 2018; 24: e3011.
13. Hu H, Nagahama S, Nanri A, *et al.* Duration and degree of weight change and risk of incident diabetes: Japan Epidemiology Collaboration on Occupational Health Study. *Prev Med* 2017; 96: 118–123.
14. Hu H, Kurotani K, Sasaki N, *et al.* Optimal waist circumference cut-off points and ability of different metabolic syndrome criteria for predicting diabetes in Japanese men and women: Japan Epidemiology Collaboration on Occupational Health Study. *BMC Public Health* 2016; 16: 220.
15. Evaluation of elevated creatinine. Available from https://bestpractice.bmj.com/topics/en-us/935 Accessed July 28, 2018.
16. American Diabetes Association Standards of medical care in diabetes–2015. *Diabetes Care* 2015; 38(Suppl 1): 1–94.
17. Bellou V, Belbasis L, Tzoulaki I, *et al.* Risk factors for type 2 diabetes mellitus: an exposure-wide umbrella review of meta-analyses. *PLoS One* 2018; 13: e0194127.
18. Stevens LA, Coresh J, Greene T, *et al.* Assessing kidney function–measured and estimated glomerular filtration rate. *N Engl J Med* 2006; 354: 2473–2483.
19. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem* 1992; 38: 1933–1953.
20. de Luca C, Olefsky JM. Inflammation and insulin resistance. *FEBS Lett* 2008; 582: 97–105.
21. Hurrle S, Hsu WH. The etiology of oxidative stress in insulin resistance. *Biomed J* 2017; 40: 257–262.
22. Scott D, de Courten B, Ebeling PR. Sarcopenia: a potential cause and consequence of type 2 diabetes in Australia's ageing population? *Med J Aust* 2016; 205: 329–333.
23. Chang AM, Halter JB. Aging and insulin secretion. *Am J Physiol Endocrinol Metab* 2003; 284: E7–E12.
24. Kuwahara K, Honda T, Nakagawa T, *et al.* Strength training and risk of type 2 diabetes in a Japanese working population: a cohort study. *J Diabetes Investig* 2015; 6: 655–661.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1 | Japan Epidemiology Collaboration on Occupational Health Study design and data collection methods.

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ORIGINAL ARTICLE

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Association between anthropometric indices of obesity and risk of cardiovascular disease in Japanese men

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Abstract

Objectives: We aimed to compare the association of body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR) with risk of cardiovascular disease (CVD) among middle-aged working Japanese men.

*Japan Epidemiology Collaboration on Occupational Health Study Group are included in the Appendix.

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Methods: A nested case-control study was performed among middle-aged male employees who underwent periodic health checkup. A total of 241 CVD cases were identified and matched individually on age, gender, and worksite with 1205 controls. Data on BMI, WC, WHtR, smoking, hypertension, diabetes, and dyslipidemia collected at 4 years before the event/index date were retrieved. Associations between BMI, WC, WHtR, and CVD risk were assessed by using conditional logistic regression models.
Results: The strength of the association of BMI, WC, and WHtR with CVD risk was similar. The smoking-adjusted odds ratio (95% confidence interval) for CVD was 1.60 (1.38-1.85), 1.53 (1.33-1.78), and 1.56 (1.35-1.81) for a 1 SD unit increase in BMI, WC, and WHtR respectively. After further adjustment for hypertension, diabetes, and dyslipidemia, these associations were attenuated but remained statistically significant.
Conclusions: Measures of general (BMI) and abdominal (WC and WHtR) obesity were similarly associated with CVD in middle-aged Japanese men.

KEYWORDS
body mass index, cardiovascular disease, waist circumference, waist-to-height ratio

1 | INTRODUCTION

Cardiovascular disease (CVD) is a major cause of death worldwide.[1] Obesity is a strong predictor of CVD risk.[2] To assess risk for CVD, a variety of anthropometric indices have been used as a proxy for general obesity (ie, body mass index [BMI]) or abdominal obesity (ie, waist circumference [WC] and waist-to-height ratio [WHtR]).[2] There is controversy, however, as to whether these measures of obesity are similarly related to CVD risk. A systematic review of 22 prospective studies showed that WHtR and WC were significant predictors of cardio-metabolic outcomes more often than BMI.[3] In contrast, a meta-analysis using individual records from 58 prospective studies indicated that there was no significant difference in the strength of the association with CVD risk between BMI and abdominal obesity measures (WC and waist-to-hip ratio).[4] These reviews included few studies in the Japanese population, which is characterized by a low prevalence of obesity.

In Japan, risk of CVD has been linked to either general obesity (BMI)[5-7] or abdominal obesity (WC and WHtR).[8] Only one cohort study among the general population compared the association of BMI and WC with CVD risk, suggesting that abdominal obesity is a better predictor for CVD than general obesity in women.[8] However, no obesity measure was appreciably associated with CVD risk in men.[8] Given that CVD remains the leading cause of deaths in Japan,[9] clarifying the impact of obesity on CVD in Japanese is important.

Previous studies on the strength of associations between general obesity, abdominal obesity, and CVD are mainly based on cohort studies with a median follow-up of ≥10 years.[3,4,8] The long length of follow-up can avoid reverse causality bias and link obesity to the initiation and development of CVD. On the other hand, it can introduce bias due to loss to follow-up and cannot account for the change of obesity status over the long follow-up period. More importantly, it cannot answer the association between obesity and the development of a clinical CVD from a latent precursor (a few years prior to the onset of CVD). To the best of our knowledge, no previous study has compared the risk of CVD associated with general obesity and abdominal obesity assessed a few years before the onset of CVD.

Thus, using a nested case-control study design which can be used to investigate the risk of diseases associated with exposures assessed at a particular time point, we compared the association of CVD with BMI, WC, and WHtR collected at 4 years (data collected between 1 year and 3 years were not used for minimizing reverse causality bias) before the CVD event among middle-aged working Japanese men.

2 | METHODS

2.1 | Study design

This is a case-control study nested in the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) Study, an ongoing multi-company study of workers in Japan. Details on the J-ECOH Study and the CVD registration has been described elsewhere.[10,11] As the present study aimed to examine whether BMI, WC, and WHtR collected at 4 years before the CVD event were similarly associated with the development of CVD, we retrieved obesity data and other annual health checkup data collected from more than 100 000 workers between January 2008 and December 2013 or between

April 2008 and March 2014 in 11 participating companies (12 worksites) and their CVD data collected between April 2012 and March 2018. The study protocol, including the consent procedure, was approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan (NCGM-G-001140-15).

2.2 | Ascertainment of CVD cases and control selection

Incident CVD cases, including fatal and non-fatal myocardial infarction (MI) and stroke, were identified through a CVD registry. Within the J-ECOH Study, the CVD registry was set up in participating companies in April 2012 to collect data on CVD events. For most nonfatal cases, the occupational physician confirmed the diagnosis of each CVD event on the basis of medical certificates written by a treating physician and submitted to the company by the worker. Because the submission of a medical certificate is required when taking a long-term sick leave, this registry primarily covers relatively severe cases. For fatal cases, occupational physicians judged the cause of death based on available information, including death certificates and information obtained from the bereaved family or colleagues. Each case was coded according to the 10th revision of the International Classification of Diseases (ICD). Event date was defined as the date of CVD diagnosis recorded in the registry.

From April 2012 to March 2018, 249 males and 20 females with incident CVD were registered. Emerging evidence suggests that sex hormones and sex-specific patterns of adiposity and fat distribution can lead to sex differences in the association between obesity and CVD.[12] In the present study, the number of female CVD cases was too small (n = 20) to analyses the association between obesity and CVD among women. Thus, we excluded women from the current analyses. Among these 249 male cases, we excluded eight patients without matched controls. Finally, 241 CVD cases (51 fatal cases), including 81 with MI (ICD-10: I21), and 160 with stroke (ICD-10: I60, I61, and I63), remained in the present study.

Controls were selected from study participants who did not self-report stroke or MI at J-ECOH Study entry and did not develop CVD during the follow-up period. Those who self-reported a history of CVD at annual health checkups during the study period were also excluded. For each case, we created a pool of controls who were matched by worksite, gender, and date of birth (±2 years). We then allocated an index date, which was the same as the event date of its matched case. We excluded people who did not attend health checkup at 4 years before the index date. Finally, for a given case, we randomly selected up to five controls from the pool of eligible controls. Once a control was sampled, we did not allow the control to be again chosen as the control of other cases. A total of 1,205 matched controls were included in the present study.

2.3 | Exposure

Measurements of body height, body weight, and waist circumference obtained 4 years prior to the event/index date were used for both cases and controls. The body height and weight were measured using a scale while the participant wore light clothes and no shoes. BMI was calculated as the weight in kilograms divided by the squared height in meters. WC was measured at the umbilical level in the standing position. WHtR was calculated as WC (cm) divided by height (cm).

2.4 | Covariates

The covariates included smoking, hypertension, diabetes, and dyslipidemia. We retrieved data collected at 4 years before the event/index date. Data collection methods have been described in detail in previous papers.[10,11,13] Smoking status was divided in to the following five groups: never smokers, past smokers, current low-intensity smokers (1-10 cigarettes/day), medium-intensity smokers (11-20 cigarettes/day), or high-intensity smokers (≥21 cigarettes/day). Hypertension was defined as systolic blood pressure of at least 140 mmHg, diastolic blood pressure of at least 90 mmHg, or use of treatment for hypertension.[14] Diabetes was defined as a fasting plasma glucose level of at least 126 mg/dL, or a random plasma glucose level of at least 200 mg/dL, an HbA1c level of at least 6.5%, or medical treatment of diabetes.[15] Dyslipidemia was defined as an low-density lipoprotein-cholesterol level of at least 140 mg/dL, high-density lipoprotein-cholesterol level of less than 40 mg/dL, triglyceride level of at least 150 mg/dL, or use of medications for dyslipidemia.[16]

2.5 | Statistical analysis

In the present study, about 20% of study participants had one or more missing values. To improve efficiency and reduce bias, we handled missing data with multiple imputation using matching variables and full-conditional specification.[17] Fifty imputed data sets were produced, and analyses were combined using Rubin's rules.

The characteristics of the study participants were expressed as means (standard deviation) for continuous variables and as percentages for categorical variables. To examine differences in characteristics between cases and controls, we performed conditional logistic regression for categorical variables. For continuous variables, paired t-test was performed. There were five controls for each case. We first calculated the mean of matched controls, and then compared it with their case using paired *t* test.

Conditional logistic regression was used to estimate odds ratio (OR) and 95% confidence interval (CI) for the development of CVD associated with a one standard deviation (SD) unit change in BMI, WC, and WHtR respectively. We adjusted for smoking status in model 1. In model 2, we further adjusted for hypertension (yes or no), diabetes (yes or no), and dyslipidemia (yes or no). In addition, ORs were estimated at tertiles of BMI, WC, and WHtR respectively. BMI, WC, and WHtR were categorized into tertiles among controls, separately. The lowest tertile was used as the reference group. Trend association was assessed with ordinal scores 0-2 assigned to the three groups of BMI, WC and WHtR.

We also performed a sensitivity analysis using individuals with complete data. A two-sided $P < .05$ was considered statistically significant. Multiple imputation was performed in StataMP 15 (StataCorp). All other statistical analyses were performed using SAS version 9.4 (SAS Institute).

3 | RESULTS

The characteristics of cases and controls at 4 years prior to the CVD event/index date are summarized in Table 1. The mean (standard deviation) age of cases was 50.5 (6.2) years, and 80% of the individuals were ages less than 60 years. The mean values of BMI, WC, and WHtR were higher among cases than those among controls. Cases had higher prevalence of hypertension, diabetes, and dyslipidemia as well as smoking than controls.

As shown in Table 2, BMI, WC, and WHtR demonstrated generally similar strength of association with CVD risk. In model 1, the ORs (95% CIs) for CVD were 1.60 (1.38-1.85), 1.53 (1.33-1.78), 1.56 (1.35-1.81) for 1 SD increase in BMI, WC, and WHtR respectively. After additionally adjusting for hypertension, diabetes, and dyslipidemia (model 2), these associations were attenuated but remained statistically significant. The ORs (95% CIs) for CVD in the highest versus lowest tertile of BMI, WC, and WHtR were 2.94 (1.99-4.33), 2.61 (1.75-3.89), and 2.61 (1.76-3.87) respectively (model 1). Similar findings were observed in the sensitivity analysis using complete data (Table S1).

In Table 3, the three obesity measures (BMI, WC, and WHtR) were similarly and positively associated with all CVD subtypes. The ORs (95% CIs) for MI were 1.70 (1.34-2.17), 1.73 (1.35-2.23), 1.75 (1.35-2.27) for 1 SD increase in BMI, WC, and WHtR respectively. For stroke, the corresponding ORs (95% CIs) were 1.54 (1.28-1.85) for BMI, 1.44 (1.20-1.73) for WC, 1.47 (1.23-1.77) for WHtR. These associations were attenuated after additional adjustment for hypertension, diabetes, and dyslipidemia (model 2).

TABLE 1 Characteristics of cases and controls at 4 years before the date of CVD event, J-ECOH Study, Japan[a]

	Cases	Controls	*P*-value*
N	241	1,205	
Age (y)	50.5 (7.2)	50.4 (7.3)	<.001
Smoking status, %			
Never smokers	26.3	35.3	<.001
Past smokers	15.6	27.9	
Current low-intensity smokers[b]	8.4	6.9	
Medium-intensity smokers[b]	33.0	21.5	
High-intensity smokers[b]	16.8	8.5	
BMI (kg/m^2)	25.3 (3.8)	23.7 (3.1)	<.001
WC (cm)	87.9 (9.5)	84.0 (8.4)	<.001
WHtR	0.52 (0.05)	0.49 (0.05)	<.001
Hypertension, %	48.8	26.6	<.001
Hypertension treatment[c], %	52.5	59.6	<.001
Diabetes, %	27.1	10.9	<.001
Diabetes treatment[d], %	51.9	57.7	<.001
Dyslipidemia, %	68.5	60.2	<.001
Lipid-lowering treatment[e], %	11.2	14.6	.84

Note: Data were expressed as mean (standard deviation) or as percentages.
Abbreviations: BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; FPG, fasting plasma glucose; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein-cholesterol levels; J-ECOH Study, the Japan Epidemiology Collaboration on Occupational Health Study; LDL-C, low-density lipoprotein-cholesterol; TG, Triglyceride; WC, waist circumference; WHtR, waist-to-height ratio.
[a]Dataset without multiple imputation was used for Table 1.
[b]Current low-intensity smokers, 1-10 cigarettes/d; medium-intensity smokers, 11-20 cigarettes/d; high-intensity smokers, ≥21 cigarettes/d.
[c]The denominator is the total number of people with hypertension (systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or current medical care for hypertension).
[d]The denominator is the total number of people with diabetes (FPG ≥ 126 mg/dL, random plasma glucose ≥ 200 mg/dL, HbA1c ≥ 6.5%, or current medical care for diabetes).
[e]The denominator is the total number of people with dyslipidemia (LDL-C ≥ 140 mg/dL, HDL-C < 40 mg/dL, TG ≥ 150 mg/dL, or use of medications for dyslipidemia).
*Paired *t* test for continuous variables and conditional logistic regression for categorical variables.

4 | DISCUSSION

In this nested case-control study among middle-aged Japanese working men, we found that both general (BMI) and abdominal (WC and WHtR) obesity showed a significant and positive association with CVD, and that they demonstrated generally similar strength of association with CVD.

TABLE 2 Associations among BMI, WC, and WHtR and the risk of CVD, J-ECOH Study, Japan

	OR (95% CI)					
	1st tertile	2nd tertile	3rd tertile	*P* for trend	OR (95% CI) per SD increment	*P*
BMI (kg/m^2)	<22.2	22.2 to <24.5	≥24.5			
Model 1	1.00	1.43 (0.93–2.18)	2.94 (1.99–4.33)	<.001	1.60 (1.38–1.85)	<.001
Model 2	1.00	1.06 (0.67–1.65)	1.75 (1.14–2.68)	.01	1.29 (1.10–1.52)	.002
WC (cm)	<80	80 to <86.5	≥86.5			
Model 1	1.00	1.03 (0.66–1.62)	2.61 (1.75–3.89)	<.001	1.53 (1.33–1.78)	<.001
Model 2	1.00	0.70 (0.44–1.13)	1.46 (0.94–2.26)	.09	1.24 (1.05–1.46)	.01
WHtR	<0.47	0.47 to <0.51	≥0.51			
Model 1	1.00	1.12 (0.73–1.73)	2.61 (1.76–3.87)	<.001	1.56 (1.35–1.81)	<.001
Model 2	1.00	0.77 (0.48–1.22)	1.41 (0.91–2.18)	.10	1.25 (1.05–1.48)	.01

Notes: Model 1 adjusted for smoking status (never smokers, past smokers, current low-intensity smokers (1-10 cigarettes/d), medium-intensity smokers (11-20 cigarettes/d), or high-intensity smokers (≥21 cigarettes/d))

Model 2 additionally adjusted for hypertension (systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or current medical care for hypertension), diabetes (FPG ≥ 126 mg/dL, random plasma glucose ≥ 200 mg/dL, HbA1c ≥ 6.5%, or current medical care for diabetes), dyslipidemia (LDL-C ≥ 140 mg/dL, HDL-C < 40 mg/dL, TG ≥ 150 mg/dL, or use of medications for dyslipidemia).

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; FPG, fasting plasma glucose; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein-cholesterol levels; J-ECOH Study, the Japan Epidemiology Collaboration on Occupational Health Study; LDL-C, low-density lipoprotein-cholesterol; MI, myocardial infarction; OR, odds ratio; SD, standard deviation; TG, Triglyceride; WC, waist circumference; WHtR, waist-to-height ratio.

Our finding is in line with that of a meta-analysis mainly based on cohort studies,[4] suggesting that general obesity and abdominal obesity show similar associations with CVD. The current finding is also compatible with that of our previous report showing that BMI, WC, and WHtR showed similar associations with the clustering of cardio-metabolic risk factors in the cross-sectional analysis of the J-ECOH Study data.[10] In contrast, Browning et al[3] reviewed 22 prospective studies on cardiometabolic outcomes and concluded that WHtR and WC are more strongly associated with CVD than BMI. That systematic review, however, included only seven publications with CVD as an outcome and did not perform a meta-analysis. Our study and previous meta-analysis[4] provided evidence that the strength of association for each measure (WC, WHtR, and BMI) was similar, suggesting that general and abdominal obesity can be equally used in the assessment of the risk of CVD.

In the analysis by CVD subtypes, we found that the three obesity measures (BMI, WC and WHtR) were equally strongly associated with stroke and MI. The strength of the association with stroke observed in the present study is similar to that in the above-mentioned meta-analysis.[4] Specifically, in age group of 40-59 years in the meta-analysis, the age-, gender-, and smoking-adjusted ORs (95% CIs) of stroke for 1 SD increase in BMI and WC were 1.34 (1.21-1.48) and 1.45 (1.30-1.60) respectively. In the present study (mean age, 54 years), the corresponding ORs (95% CIs) were 1.54 (1.28-1.85) and 1.44 (1.20-1.73) (Table 3, Model 1). With regard to MI, we observed a somewhat stronger association (BMI, OR = 1.70, 95% CI, 1.34-2.17; WC, OR = 1.73, 95% CI, 1.35-2.23), compared to that for coronary heart disease (BMI, OR = 1.41, 95% CI, 1.30-1.53; WC, OR = 1.50, 95% CI, 1.37-1.63) in the above-mentioned meta-analysis. This may be due to the difference in study design, outcome (MI vs coronary heart disease), or to chance, given the fewer MI events in our study. The findings based on stratified analyses in our study and previous meta-analysis[4] provide further evidence that general obesity and abdominal obesity are similarly associated with CVD regardless of its subtypes.

The mechanisms underlying the association between obesity and CVD remain incompletely understood. Hypertension, diabetes, and dyslipidemia are established conditions linking obesity to CVD.[18,19] Yet, we found that after adjustment for these risk factors, the associations of BMI, WC and WHtR with CVD risk still remained statistically significant, a finding consistent with previous reports.[20,21] These results may suggest a pathway other than those through traditional CVD risk factors, such as obesity-induced prothrombotic state and inflammation, which may additionally contribute to the development of CVD.[18,19]

Strengths of the current study include its prospective design as a nested case-control study within a well-defined cohort; objective measures of obesity based on measured height, weight, and WC; and assessment of confounding (smoking) and mediating (hypertension, diabetes, and dyslipidemia) variables at 4 years prior to the CVD event for cases and the index date for controls. There are several limitations that warrant mention. First, due to the lack of data on socioeconomic status, family history of CVD, and lifestyles other than smoking (eg, alcohol drinking, diet, physical activity), we were unable to control for potential effects of these factors. Further, residual confounding may

TABLE 3 Associations among BMI, WC, and WHtR and the risk of MI and Stroke, J-ECOH Study, Japan

	OR (95% CI)					
	1st tertile	2nd tertile	3rd tertile	*P* for trend	OR (95% CI) per SD increment	*P*
MI						
BMI (kg/m^2)	<22.2	22.2 to <24.5	≥24.5			
Model 1	1.00	2.16 (1.00–4.66)	3.58 (1.75–7.33)	<.001	1.70 (1.34–2.17)	<.001
Model 2	1.00	1.36 (0.59–3.15)	1.92 (0.87–4.28)	.09	1.33 (1.01–1.76)	.04
WC (cm)	<80	80 to <86.5	≥86.5			
Model 1	1.00	2.27 (0.93–5.54)	5.43 (2.29–12.9)	<.001	1.73 (1.35–2.23)	<.001
Model 2	1.00	1.53 (0.60–3.90)	2.69 (1.05–6.89)	.02	1.37 (1.02–1.82)	.04
WHtR	<0.47	0.47 to <0.51	≥0.51			
Model 1	1.00	1.71 (0.78–3.77)	3.64 (1.68–7.87)	<.001	1.75 (1.35–2.27)	<.001
Model 2	1.00	1.03 (0.43–2.43)	1.52 (0.63–3.66)	.24	1.36 (0.99–1.84)	.05
Stroke						
BMI (kg/m^2)	<22.2	22.2 to <24.5	≥24.5			
Model 1	1.00	1.43 (0.93–2.18)	2.71 (1.70–4.33)	<.001	1.54 (1.28–1.85)	<.001
Model 2	1.00	0.92 (0.54–1.58)	1.75 (1.05–2.92)	.01	1.29 (1.05–1.58)	.02
WC (cm)	<80	80 to <86.5	≥86.5			
Model 1	1.00	0.77 (0.45–1.31)	2.05 (1.30–3.22)	<.001	1.44 (1.20–1.73)	<.001
Model 2	1.00	0.52 (0.29–0.91)	1.23 (1.75–2.04)	.15	1.20 (0.97–1.47)	.09
WHtR	<0.47	0.47 to <0.51	≥0.51			
Model 1	1.00	0.93 (0.55–1.57)	2.30 (1.46–3.45)	<.001	1.47 (1.23–1.77)	<0.001
Model 2	1.00	0.77 (0.48–1.22)	1.41 (0.91–2.18)	.07	1.22 (0.99–1.50)	0.05

Notes: Model 1 adjusted for smoking status (never smokers, past smokers, current low-intensity smokers (1-10 cigarettes/d), medium-intensity smokers (11-20 cigarettes/d), or high-intensity smokers (≥21 cigarettes/d)).

Model 2 additionally adjusted for hypertension (systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or current medical care for hypertension), diabetes (FPG ≥ 126 mg/dL, random plasma glucose ≥ 200 mg/dL, HbA1c ≥ 6.5%, or current medical care for diabetes), dyslipidemia (LDL-C ≥ 140 mg/dL, HDL-C < 40 mg/dL, TG ≥ 150 mg/dL, or use of medications for dyslipidemia).

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; FPG, fasting plasma glucose; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein-cholesterol levels; J-ECOH Study, the Japan Epidemiology Collaboration on Occupational Health Study; LDL-C, low-density lipoprotein-cholesterol; MI, myocardial infarction; OR, odds ratio; SD, standard deviation; TG, Triglyceride; WC, waist circumference; WHtR, waist-to-height ratio.

also exist due to the incomplete assessment of covariates such as smoking (the lack of data on smoking duration). Second, the number of CVD cases for each subtype was not sufficiently large to detect a modest association with statistical significance. Third, the small number of female CVD cases (n = 20) precludes us to compare the strength of association for general obesity and abdominal obesity in women. In addition, our study is a Japanese occupational cohort. Thus, our findings may not be generalizable to female workers, the general population, or other racial/ethnic groups.

5 | CONCLUSIONS

General (BMI) and abdominal (WC and WHtR) obesity demonstrated generally similar strength of association with CVD and its subtypes among middle-aged Japanese men.

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DISCLOSURE

Approval of the research protocol: The study protocol, including the consent procedure, was approved by the Ethics Committee of the National Center for Global Health and

Medicine, Japan. Prior to the collection of the data, the format of the J-ECOH Study was announced in each company by using posters that explained the purpose and procedure of the study. *Informed consent:* Participants did not provide their verbal or written informed consent to join the study but were allowed to refuse their participation. This procedure conforms to the Japanese Ethical Guidelines for Epidemiological Research, where the procedure for obtaining consent may be simplified for observational studies that use existing data. *Registry and the registration no. of the study/trial:* N/A. *Animal studies:* N/A. *Conflict of interest:* Authors declare no conflict of interests for this article.

AUTHOR CONTRIBUTIONS

SD and T Mizoue were involved in the design of the study as the principal investigators; TI, A Nishihara, NS, TO, AH, TN, SY, TH,HO, AU, MY, T Miyamoto, TK, ME, T Murakami, MS, KT, SN, I Kabe, and SD collected health check-up data; MK and A Nanri cleaned CVD data; T Mizoue, MK, and KK created database; MX, HH, T Mizoue, SA, I Kashino, MY, KK and NK drafted the plan for the data analysis; HH and MX conducted data analysis; MX drafted manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Mendis S, Puska P, Norrving B. *Global atlas on cardiovascular disease prevention and control*. World Health Organization; 2011.
2. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol*. 2009;53(21):1925-1932.
3. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev*. 2010;23(2):247-269.
4. Collaboration ERF, Wormser D, Kaptoge S. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *The Lancet*. 2011;377(9771):1085-1095.
5. Yatsuya H, Yamagishi K, Iso H. Adiposity and risk of cardiovascular diseases in Japan: secular trend, individual level associations and causal pathway–implications for the prevention of cardiovascular diseases in societies with rapid economic development. *EPMA Journal*. 2011;2(1):65-73.
6. Saito I, Iso H, Kokubo Y, Inoue M, Tsugane S. Body mass index, weight change and risk of stroke and stroke subtypes: the Japan Public Health Center-based prospective (JPHC) study. *Int J Obes (Lond)*. 2011;35(2):283-291.
7. Kawate N, Kayaba K, Hara M, Kotani K, Ishikawa S; Jichi Medical School Cohort Study Group. Body mass index and stroke incidence in Japanese community residents: The Jichi Medical School (JMS) Cohort Study. *J Epidemiol*. 2017;27(7):325-330.
8. Furukawa Y, Kokubo Y, Okamura T, et al. The relationship between waist circumference and the risk of stroke and myocardial infarction in a Japanese urban cohort: the Suita study. *Stroke*. 2010;41(3):550-553.
9. Ministry of Health, Labour and Welfare. Summary of demographic statistics 2015. https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei15/ (in Japanese). Accessed July 18, 2019.
10. Hori A, Nanri A, Sakamoto N, et al. Comparison of body mass index, waist circumference, and waist-to-height ratio for predicting the clustering of cardiometabolic risk factors by age in Japanese workers. *Circ J*. 2014;78(5):1160-1168.
11. Hu H, Mizoue T, Sasaki N, et al. Prediabetes and cardiovascular disease risk: A nested case-control study. *Atherosclerosis*. 2018;278:1-6.
12. Coromilas EJ, Bello NA. Gender differences in obesity-associated cardiac remodeling. *Gender and the Genome*. 2017;1(2):76-79.
13. Hu H, Sasaki N, Ogasawara T, et al. Smoking, smoking cessation, and the risk of hearing loss: Japan epidemiology collaboration on occupational health study. *Nicotine Tob Res*. 2019;21(4):481-488.
14. Shimamoto K, Ando K, Fujita T, et al. The Japanese society of hypertension guidelines for the management of hypertension (JSH 2014). *Hypertens Res*. 2014;37(4):253-390.
15. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37(Suppl. 1):S81-S90.
16. Teramoto T, Sasaki J, Ishibashi S, et al. Executive summary of the Japan atherosclerosis society guidelines for the diagnosis and prevention of atherosclerotic cardiovascular diseases in Japan – 2012 version. *J Atherosclerosis Thromb*. 2013;20(6):517-523.
17. Seaman SR, Keogh RH. Handling missing data in matched case-control studies using multiple imputation. *Biometrics*. 2015;71(4):1150-1159.
18. Csige I, Ujvárosy D, Szabó Z, et al. The impact of obesity on the cardiovascular system. *J Diabetes Res*. 2018;2018:3407306.
19. Marinou K, Tousoulis D, Antonopoulos AS, Stefanadi E, Stefanadis C. Obesity and cardiovascular disease: from pathophysiology to risk stratification. *Int J Cardiol*. 2010;138(1):3-8.
20. Choi S, Kim K, Kim SM, et al. Association of obesity or weight change with coronary heart disease among young adults in South Korea. *JAMA Intern Med*. 2018;178(8):1060-1068.
21. Flint AJ, Rexrode KM, Hu FB, et al. Body mass index, waist circumference, and risk of coronary heart disease: a prospective study among men and women. *Obes Res Clin Pract*. 2010;4(3):e171-e181.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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APPENDIX

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Original article

Trajectories of body mass index and waist circumference before the onset of diabetes among people with prediabetes

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SUMMARY

Background & aims: To investigate trajectories of body mass index (BMI) and waist circumference (WC) among prediabetic people who progressed to diabetes, people who remained with prediabetes, and those who returned to normoglycemia.

Methods: We used data from 22,945 prediabetic people who received an annual health checkup for up to eight years. The development of diabetes was defined using the American Diabetes Association criteria. People who did not progress to diabetes during the observation period were classified as 'remained with prediabetes' or 'returned to normoglycemia', based on their last health checkup data. Trajectories of BMI and WC were evaluated using linear mixed models for repeated measures, with adjustment for a wide range of covariates.

Results: During the study period, 2972 people progressed to diabetes, 4706 returned to normoglycemia, and 15,267 remained with prediabetes. People who progressed to diabetes had a larger increase in mean BMI from 7 years to 1 year prior to diagnosis, which was about three times that of people who remained with prediabetes (annual change rate, 0.20 [95% confidence interval; 0.15 to 0.24] vs 0.06 [0.04 to 0.08] kg/m^2 per year, $P < 0.001$), regardless of their BMI levels at the initial health checkup. Among people who returned to normoglycemia, mean BMI remained almost the same over time (−0.04 [-0.09 to 0.002] kg/m^2 per year), except for those with obesity (−0.16 [-0.28 to −0.05] kg/m^2 per year). As for WC, the annual change rate among people who developed diabetes was about 7 times that of people who remained with prediabetes (0.38 [0.32 to 0.45] vs 0.05 [0.03 to 0.08] cm per year, $P < 0.001$). We also observed a constant

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mean WC over time among people who had no central obesity and later returned to normoglycemia (0.02 [0.06 to 0.03] cm per year), and an annual decrease in mean WC among those who had central obesity and later returned to normoglycemia (0.40 [0.47 to 0.32] cm per year).

Conclusions: Our study provides strong evidence that avoiding weight gain could help prediabetic people minimize the risk of developing diabetes, regardless of whether they are obese. Losing weight could help obese people restore normoglycemia from a prediabetic state, whereas maintaining current weight may help nonobese people return to normoglycemia.

1. Introduction

Prediabetes is a growing public health problem and affects 20–50% of adults worldwide [1]. People with prediabetes represent a heterogeneous group with different glycemic outcomes; some could progress to diabetes within a few years, while others may remain with prediabetes or return to normoglycemia [2]. Although major clinical trials have consistently shown the effect of weight loss with lifestyle intervention on reducing the risk of diabetes among prediabetic people [3–7], it is unclear how weight varies during the natural history of progression from prediabetes to diabetes or during the reversion from prediabetes to normoglycemia. Exploring longitudinal changes in body mass index (BMI) could provide insight into the heterogeneity of prediabetes, inform monitoring practices for physicians and prediabetic people, and improve risk stratification for targeted diabetes prevention programs.

Several cohort studies have examined weight change in relation to glycemic outcomes of prediabetes [8–11]. A study among 405 prediabetic people in Germany showed that people who had a relatively constant BMI level (BMI difference between baseline and end of study, > -1 and ≤ 1 kg/m^2) or weight loss ($\leq$-1 kg/m^2) were more likely to return to normoglycemia [8]. Two studies from Singapore and Japan also showed that weight loss was associated with regression from prediabetes to normoglycemia [9,10]. In addition, a study among 979 prediabetic people in France showed that people who developed diabetes had more weight gain over the follow-up period than those who did not develop diabetes [11]. In all these studies, however, BMI was measured only at 2 time points (baseline and final examinations) [8–11]. Due to the lack of information on BMI preceding outcome assessments, it remains unclear whether weight decreases or remains stable during the transition from prediabetes to normoglycemia. Such data are important for knowing whether weight loss is necessary for normalization of prediabetes. Moreover, although prediabetic people seem to gain weight in the years before a diabetes diagnosis [11], current data leave unanswered the shape of BMI trajectories in the years prior to diagnosis and how these trajectories differ in people who remain with prediabetes. Knowing this allows us to identify those persons at a high risk of diabetes by monitoring BMI among prediabetic people over time.

To address these issues, we conducted a study among over 20,000 prediabetic people who received an annual health checkup for up to 8 years. The large sample size and repeated measurements provide a unique opportunity to investigate trajectories of BMI separately among prediabetic people who progressed to diabetes, people who remained with prediabetes, and those who returned to normoglycemia. Given that waist circumference (WC) is a better indicator of visceral fat than BMI and data on WC change has been rarely reported in previous studies [11], we also plotted the trajectories of WC in the present study.

2. Materials and methods

2.1. Study design

We used data from the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) Study, which is an ongoing cohort study among workers from several companies in Japan. Under the Industrial Safety and Health Act, nearly all workers in the participating companies attend their annual health checkup. They also completed a questionnaire that covered medical history and health-related lifestyle at the health checkup each year. Detailed information about the J-ECOH Study can be found in previous papers [12,13]. To date, annual health checkup data between January 2008 and December 2016 or between April 2008 and March 2017 have been collected. The study protocol, including the consent procedure, was approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan.

2.2. Participants

We extracted 2008–2016 health checkup data. The initial health checkup was mainly conducted in 2008. Because two companies had a great deal of missing data in 2008, we used 2009 or 2010 health checkup data (one company each) as the initial health checkup. Eligible participants were 20–64 years of age at the initial health checkup and had prediabetes defined by American Diabetes Association criteria [14]. Of the 28,961 people with prediabetes, we excluded those with missing information on BMI, WC, smoking, hypertension, or dyslipidemia at the initial health checkup (n = 1450). In addition, we excluded people with a self-reported history of cancer or cardiovascular disease at the initial health checkup (n = 776). We also excluded people who did not have any health checkup data between 2009 (2010 or 2011 for two companies) and 2016 or who had health checkup data but did not receive any glucose measurement (n = 1575), as we could not ascertain their glycemic outcomes (progressed to diabetes, remained with prediabetes, or returned to normoglycemia). Because at least two measurements of BMI and WC were required for studying trends longitudinally, we further excluded people who had only one measurement before the diagnosis of diabetes or before the last health checkup for those who did not develop diabetes (n = 2215). Finally, 22,945 participants remained in the analysis.

2.3. Health checkup

The participants in the J-ECOH Study underwent routine physical and laboratory examinations each year. In brief, the physical examinations included items such as body height, weight, WC, and blood pressure. Blood pressure was measured with the participants in a sitting position using an automatic blood pressure monitor. The data on smoking status, history of cardiovascular disease (stroke and ischemic heart disease) and cancer, and use of anti-

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hypertensive, anti-diabetic, and lipid-lowering medications were obtained by a self-administered questionnaire. The laboratory examinations included items such as blood glycemia and lipids. Plasma glucose was measured with either the enzymatic or glucose oxidase peroxidative electrode method. HbA1c was measured using a latex agglutination immunoassay, high-performance liquid chromatography, or the enzymatic method. Triglyceride, low-density lipoprotein-cholesterol, and high-density lipoprotein-cholesterol levels were measured with the enzymatic method. All of the laboratories involved in the health check-ups of the participating companies received satisfactory scores (rank A or a score >95 out of 100) from external quality control agencies.

2.4. Glycemic outcomes of prediabetes

Using data collected after the initial health checkup, glycemic outcomes of prediabetes were classified as progressed to diabetes, remained with prediabetes, or returned to normoglycemia. Diabetes was defined as either fasting plasma glucose ≥126 mg/dL, a random plasma glucose level ≥200 mg/dL, HbA1c ≥ 6.5%, or receiving medical treatment for diabetes according to the American Diabetes Association criteria [14]. People who did not progress to diabetes during the observation period were classified as 'remained with prediabetes' or 'returned to normoglycemia', based on their last health checkup data. 'Remained with prediabetes' was defined as fasting plasma glucose 100–125 mg/dL and/or HbA1c 5.7–6.4%, and 'returned to normoglycemia' was defined as fasting plasma glucose <100 mg/dL and HbA1c <5.7% [14].

2.5. Assessment of BMI and WC

The body height and weight were measured using a scale while the participant wore light clothes and no shoes. BMI was calculated as the weight in kilograms divided by the square of the height in meters. In stratified analyses, BMI at initial health checkup was divided into three groups (<23, 23-<27.5, and ≥27.5 kg/m^2) according to the Asian BMI criteria [15]. WC was measured at the umbilical level using a measuring tape, with the subjects in the standing position [16]. In stratified analyses, WC at initial health checkup was divided into two groups (<90 cm or ≥90 cm for men, <80 cm or ≥80 cm for women) [17].

2.6. Covariates

The fixed covariates included sex and worksite. The time-dependent covariates included age, smoking, hypertension, and dyslipidemia. Hypertension was defined as a systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or receiving medical treatment for hypertension [18]. Dyslipidemia was defined as a triglyceride level ≥150 mg/dL, low-density lipoprotein-cholesterol level ≥140 mg/dL, high-density lipoprotein-cholesterol level <40 mg/dL, or as receiving medical treatment for dyslipidemia [19].

2.7. Statistical analysis

The characteristics of the study participants at the initial health checkup and the last health checkup were described as means for continuous variables and percentages for categorical variables. Trajectories of BMI and WC were modeled using a backward timescale. For participants who progressed to diabetes, year 0 was the year of the health checkup when diabetes was first identified. For those who did not develop diabetes during the observation period, year 0 was the year of the last health checkup. Participants were then tracked backward to the initial health checkup. For example, a participant who was identified as having diabetes in the 2012 health checkup (year 0) had a maximum of four BMI measurements: BMI in 2011 (year −1), 2010 (year −2), 2009 (year −3), and 2008 (year −4).

First, we plotted the least-square means and 95% confidence intervals (CIs) of BMI and WC during the study period according to glycemic outcomes of prediabetes (progressed to diabetes, remained with prediabetes, and returned to normoglycemia), using linear mixed models for repeated measures. The linear mixed model accommodates within-subject correlations and unequal numbers of observations per subject [20]. Interaction terms for time by glycemic outcomes of prediabetes were included.

Second, we evaluated slopes (annual change rate) of BMI and WC change over time using a piecewise linear mixed model that allows the slope to differ among time segments [20]. The entire observation period was divided into two time segments (one knot at year −7) because we observed that the change in the least-square means of BMI and WC between year −8 and year −7 was somewhat different from the change between year −7 and year −1. We did not investigate weight change in the last year (from year −1 to 0) before diabetes diagnosis because patients may experience weight loss during this period [21]. Given that the observation period between year −8 and year −7 was short, and almost half of the people did not have data at year −8 (for people who progressed to diabetes, only approximately 10% had data at year −8), the estimated slopes for year −8 and year −7 may have limited clinical meaning. Thus, we mainly reported annual change rates and 95% CIs from year −7 and year −1 in the present study. To examine whether the annual change rate in BMI and WC over time differed by sex, initial BMI, and WC, we tested the interactions of sex*time (P for interaction = 0.57), initial BMI*time (P for interaction = 0.007), and initial WC*time (P for interaction <0.001). Based on the statistical significance of the interaction terms, we included the initial BMI*time and initial WC*time in the model. To show the effect of initial BMI and WC, stratified analyses were conducted. We adjusted all analyses for worksite, sex, and time-varying variables, including age, smoking, hypertension, and dyslipidemia.

Because the linear mixed model can handle missing data and <5% of BMI, WC, and covariate values were missing in our study, we chose not to impute values. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). A two-sided $P < 0.05$ was considered statistically significant.

3. Results

Of the 22,945 people with prediabetes at the initial health checkup, 2972 progressed to diabetes, 15,267 remained with prediabetes, and 4706 returned to normoglycemia during the observation period. Among the people who progressed to diabetes, the proportions of people who had 2, 3, 4, 5, 6, 7, or 8 BMI (WC) measurements before diagnosis were 24 (25), 20 (20), 14 (14), 13 (12), 12 (12), 10 (10), and 7 (7)%, respectively; for people who remained with prediabetes, the corresponding proportions were 6 (6), 8 (8), 7 (7), 7 (8), 11 (11), 15 (16), and 46 (44)%, respectively; And for people who returned to normoglycemia, the corresponding proportions were 3 (3), 5 (6), 7 (7), 8 (8), 13 (13), 17 (17), and 47 (46)%, respectively.

Table 1 shows the characteristics of study participants at the initial health checkup and the last health checkup. Compared with people who remained with prediabetes or returned to normoglycemia, people who progressed to diabetes had a higher prevalence of smoking and higher means of WC, BMI, blood pressure, triglyceride, and blood glucose at both the initial health checkup and the last health checkup. The longitudinal changes in blood pressure, lipids, and blood glucose were provided in Supplemental Figures S1–S7. People who progressed to diabetes had a gradual increase

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Table 1
Characteristics of study participants at the initial health checkup and the last health checkup.

	Progressed to diabetes		Remained with prediabetes		Returned to normoglycemia	
	Initial health checkup	Last health checkup	Initial health checkup	Last health checkup	Initial health checkup	Last health checkup
N	2972		15,267		4706	
Men, %	92.9		89.8		85.2	
Age, mean (SD), years	48.2 (7.2)	52.5 (7.1)	47.8 (7.8)	54.4 (7.2)	45.2 (8.0)	52.0 (7.6)
Current smoker, %	44.0	34.4	38.8	30.7	36.3	30.6
FPG, mean (SD), mg/dL	108.2 (8.7)	125.2 (14.6)	102.0 (7.4)	105.2 (7.6)	98.0 (7.3)	93.5 (4.9)
HbA1c, mean (SD), %	5.9 (0.3)	6.3 (0.6)	5.7 (0.3)	5.7 (0.3)	5.6 (0.3)	5.5 (0.2)
BMI, mean (SD), kg/m^2	25.2 (3.7)	26.0 (4.2)	23.8 (3.1)	24.2 (3.3)	23.3 (3.2)	23.2 (3.1)
WC, mean (SD), cm	87.7 (9.3)	89.9 (10.3)	84.0 (8.5)	84.7 (8.8)	82.3 (8.9)	81.7 (8.4)
SBP, mean (SD), mmHg	127.5 (15.8)	129.2 (15.4)	123.1 (14.9)	125.2 (14.9)	120.5 (15.1)	122.1 (15.3)
DBP, mean (SD), mmHg	81.3 (10.5)	82.0 (10.1)	78.4 (10.2)	79.3 (10.1)	76.4 (10.4)	76.9 (10.8)
Hypertension, %	34.0	53.3	22.9	44.6	16.9	36.9
Antihypertensive treatment, %	17.9	30.0	11.3	21.2	7.3	13.4
TG, mean (SD), mg/dL	159.3 (123.8)	171.2 (143.7)	132.1 (91.9)	131.6 (92.4)	121.4 (81.5)	115.6 (83.6)
HDL, mean (SD), mg/dL	53.8 (14.2)	53.8 (14.6)	56.9 (14.7)	58.0 (15.3)	58.4 (15.4)	60.4 (15.9)
LDL, mean (SD), mg/dL	128.2 (30.7)	129.7 (31.0)	125.6 (29.6)	126.6 (29.6)	120.8 (29.2)	122.7 (29.4)
Dyslipidemia, %	64.1	71.3	52.5	58.2	44.4	47.8
Lipid-lowering treatment, %	10.1	19.2	6.3	13.6	3.9	8.6

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride; WC, waist circumference.

in blood glucose from 7 years to 1 year prior to diagnosis, and people who returned to normoglycemia had a slight decrease in blood glucose (Supplemental Figures S1 and S2). No distinct difference in trajectories of blood pressure or lipids was observed among prediabetic people who progressed to diabetes, people who remained with prediabetes, and those who returned to normoglycemia (Supplemental Figures S3-S7).

Figure 1 shows BMI trajectories prior to the diabetes diagnosis or the last health checkup for those who did not develop diabetes. The annual change rate of BMI was different among the three groups ($P < 0.001$ for glycemic outcome*time interaction). People who progressed to diabetes had a significantly larger increase in mean BMI from 7 years to 1 year prior to diagnosis than people who remained with prediabetes (0.20 [95% CI: 0.15 to 0.24] vs 0.06 [0.04 to 0.08] kg/m^2 per year, $P < 0.001$), whereas the annual change rate was not statistically significant among people who returned to normoglycemia (−0.04 [-0.09 to 0.002] kg/m^2 per year, $P < 0.001$ vs people who remained with prediabetes).

Figure 2 displays BMI trajectories stratified by BMI at the initial health checkup. Table 2 shows that people who later developed diabetes had a larger annual increase in mean BMI than those who remained with prediabetes in each BMI group (0.20 [0.11 to 0.29] vs 0.09 [0.06 to 0.12] kg/m^2 per year for BMI <23 kg/m^2 group, $P = 0.018$; 0.13 [0.07 to 0.20] vs 0.05 [0.02 to 0.07] kg/m^2 per year for BMI 23-< 27.5 kg/m^2 group, $P = 0.016$; 0.25 [0.16 to 0.35] vs 0.05 [-0.01 to 0.10] kg/m^2 per year for BMI ≥27.5 kg/m^2 group, $P < 0.001$]. People who returned to normoglycemia had a similar annual increase in mean BMI (0.06 [0.01 to 0.11] kg/m^2 per year, $P = 0.37$) to people who remained with prediabetes in the BMI <23 kg/m^2 group. On the other hand, people who returned to normoglycemia had a constant mean BMI over time (−0.03 [-0.09 to 0.02] kg/m^2 per year, $P = 0.013$ vs people who remained with prediabetes) in the BMI 23-<27.5 kg/m^2 group, and a decrease in mean BMI (−0.16 [-0.28 to −0.05] kg/m^2 per year, $P = 0.002$ vs people who remained with prediabetes) in the BMI ≥27.5 kg/m^2 group.

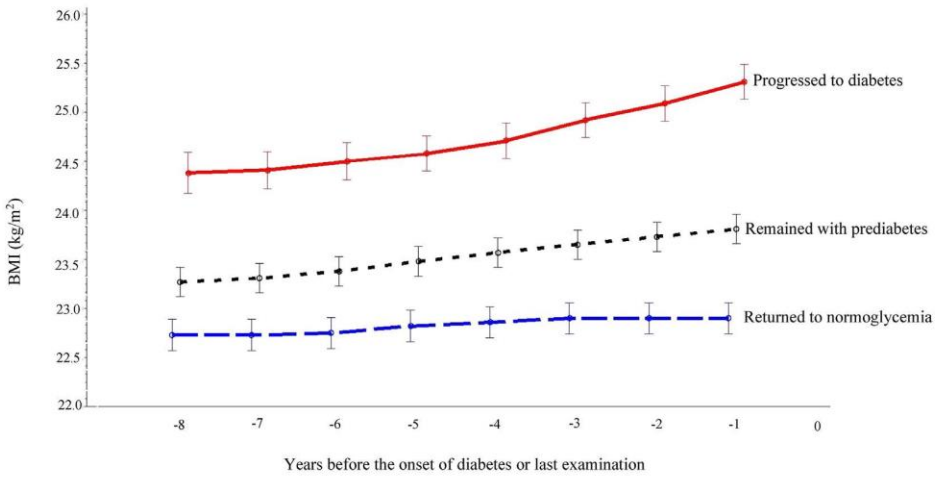

Fig. 1. Trajectories of body mass index (BMI) before the onset of diabetes or the last health checkup. Solid line (red), people who progressed to diabetes; dotted line (black), people who remained with prediabetes; dashed line (blue), people who returned to normoglycemia. Adjusted for worksite, sex, and time-varying age, smoking, hypertension, dyslipidemia, time, and time*glycemic outcomes of prediabetes. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

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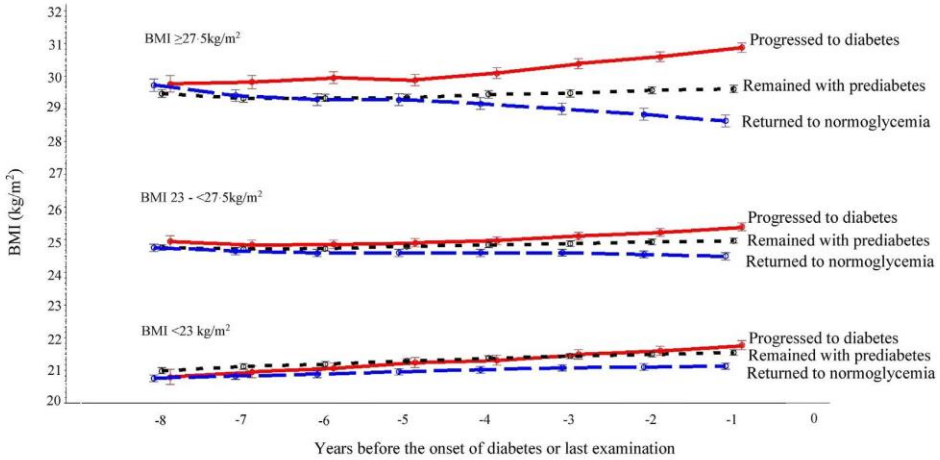

Fig. 2. Trajectories of body mass index (BMI) before the onset of diabetes or the last health checkup stratified by BMI at the initial health checkup. Solid line (red), people who progressed to diabetes; dotted line (black), people who remained with prediabetes; dashed line (blue), people who returned to normoglycemia. Adjusted for worksite, sex, and time-varying age, smoking, hypertension, dyslipidemia, time, and time*glycemic outcomes of prediabetes. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Annual mean change in BMI and WC (95% confidence interval) before the onset of diabetes or last health checkup.

	Progressed to diabetes		Remained with prediabetes		Returned to normoglycemia	
	Year −8 to −7	Year −7 to −1	Year −8 to −7	Year −7 to −1	Year −8 to −7	Year −7 to −1
BMI (kg/m^2)	−0.02 (−0.21 to 0.18)	0.20 (0.15–0.24)	−0.09 (−0.13 to −0.04)	0.06 (0.04–0.08)	−0.20 (−0.28 to −0.12)	−0.04 (−0.09 to 0.002)
Stratified by BMI at the initial health checkup						
<23 kg/m^2	0.11 (−0.23 to 0.45)	0.20 (0.11–0.29)	0.15 (0.09–0.20)	0.09 (0.06–0.12)	0.09 (0.004–0.18)	0.06 (0.01–0.11)
23-<27.5 kg/m^2	−0.10 (−0.37 to 0.16)	0.13 (0.07–0.20)	−0.11 (−0.16 to 0.05)	0.05 (0.02–0.07)	−0.18 (−0.28 to −0.08)	−0.03 (−0.09 to 0.02)
≥27.5 kg/m^2	−0.06 (−0.44 to 0.32)	0.25 (0.16–0.35)	−0.30 (−0.41 to −0.19)	0.05 (−0.01 to 0.10)	−0.51 (−0.73 to −0.30)	−0.16 (−0.28 to - 0.05)
WC (cm)	−0.33 (−0.90 to 0.25)	0.38 (0.32–0.45)	−0.24 (−0.37 to −0.12)	0.05 (0.03–0.08)	−0.44 (−0.67 to −0.21)	−0.21 (−0.25 to −0.16)
Stratified by WC at the initial health checkup						
<90 cm (80 cm for women)	0.22 (0.53–0.97)	0.38 (0.30–0.46)	0.33 (0.21–0.46)	0.12 (0.10–0.15)	0.29 (0.08–0.50)	−0.02 (−0.06 to 0.03)
≥90 cm (80 cm for women)	−0.87 (−1.74 to 0.01)	0.38 (0.28–0.48)	−0.82 (−1.03 to −0.61)	−0.02 (−0.06 to 0.02)	−1.16 (−1.57 to −0.75)	−0.40 (−0.47 to −0.32)

Adjusted for worksite, sex, initial BMI (WC), initial BMI (WC)*glycemic outcomes of prediabetes, and time-varying age, smoking, hypertension, dyslipidemia, time, time*initial BMI (WC), time*glycemic outcomes of prediabetes, and time*initial BMI (WC)*glycemic outcomes of prediabetes.

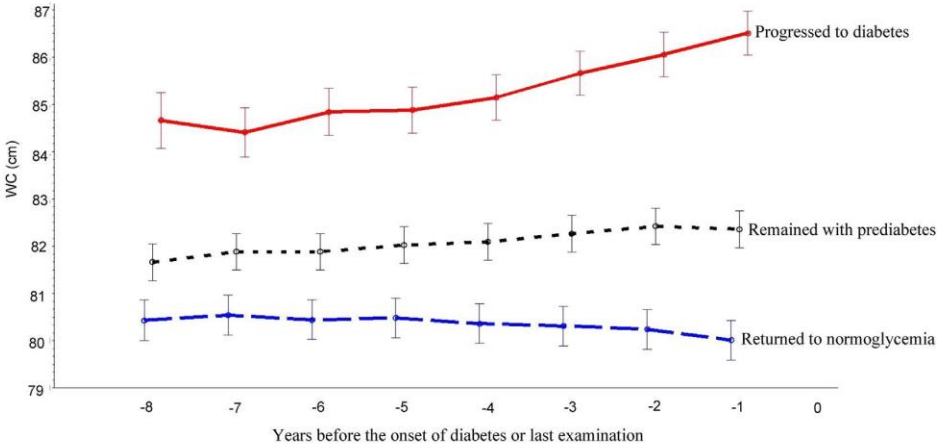

Fig. 3. Trajectories of waist circumference (WC) before the onset of diabetes or the last health checkup. Solid line (red), people who progressed to diabetes; dotted line (black), people who remained with prediabetes; dashed line (green), people who returned to normoglycemia. Adjusted for worksite, sex, and time-varying age, smoking, hypertension, dyslipidemia, time, and time*glycemic outcomes of prediabetes. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

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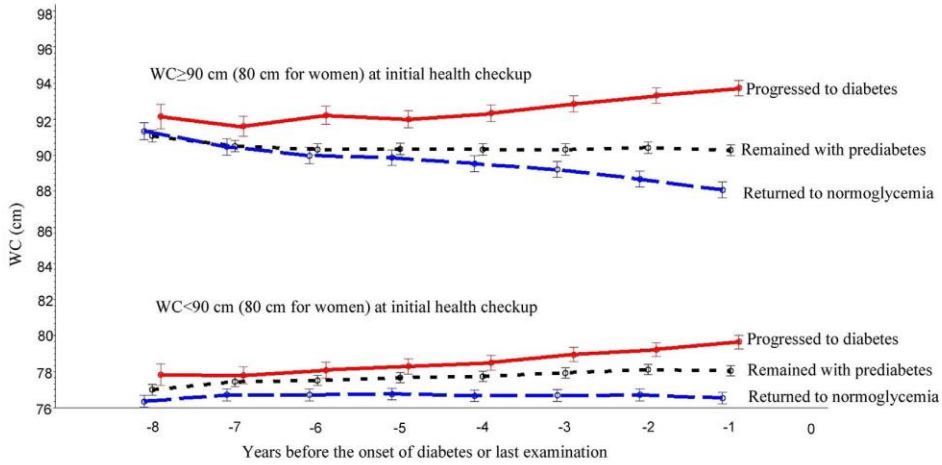

Fig. 4. Trajectories of waist circumference (WC) before the onset of diabetes or the last health checkup stratified by WC at the initial health checkup. Solid line (red), people who progressed to diabetes; dotted line (black), people who remained with prediabetes; dashed line (blue), people who returned to normoglycemia. Adjusted for worksite, sex, and time-varying age, smoking, hypertension, dyslipidemia, time, and time*glycemic outcomes of prediabetes. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Figures 3 and 4 show trajectories of WC. People who progressed to diabetes had a larger annual increase in WC compared with people who remained with prediabetes (0.38 [0.32 to 0.45] vs 0.05 [0.03 to 0.08] cm per year, $P < 0.001$), regardless of whether they had central obesity (WC $\geq$ 90 cm for men or 80 cm for women) at the initial health checkup (Table 2). A constant mean WC over time was observed among people who had no central obesity and later returned to normoglycemia (−0.02 [-0.06 to 0.03] vs 0.12 [0.10 to 0.15] cm per year for people who had no central obesity and remained with prediabetes, $P < 0.001$), whereas an annual decrease in WC was observed among those who had central obesity and later returned to normoglycemia (−0.40 [-0.47 to −0.32] vs −0.02 [-0.06 to 0.02] cm per year for people who had central obesity and remained with prediabetes, $P < 0.001$).

4. Discussion

Our results from over 20,000 prediabetic people with repeat BMI and WC measurements show that both mean BMI and WC increased faster and reached higher values in people who progressed to diabetes than that in people who remained with prediabetes. Among people who returned to normoglycemia, mean BMI and WC remained almost the same over time, except for those with obesity. To our knowledge, this is the first study to report trajectories of BMI and WC among prediabetic people with different glycemic outcomes.

We observed that prediabetic people who later developed diabetes experienced a greater annual increase in BMI and WC than those who did not. Two previous studies have examined weight change in relation to the progression from prediabetes to diabetes [10,11], although their findings are not directly comparable to those of the present study due to the difference in study design and data analysis. Using the BMI and WC assessed at the baseline visit and the visit when diabetes was screened, a French cohort study (n = 979) found that prediabetic people with greater increase in weight and WC had higher odds of developing diabetes [11]. In contrast, a small study in Singapore (n = 297) reported that people who developed diabetes appeared to have a smaller weight gain than those who remained with prediabetes (2 and 3 kg, respectively) [10]. However, both studies were based on weight and WC measured only at two time points [10,11]. People who developed diabetes between the two visits may have experienced weight loss due to the disease itself and/or dietary instructions [21]. It should be noted that neither of the two previous studies provided information on the longitudinal change in BMI or WC before the development of diabetes due to the lack of data in the years prior to diagnosis [10,11]. We used data repeatedly collected in the years before a diabetes diagnosis to depict the trajectories of BMI and WC. Several findings from our analysis bear mention. First, the annual change rate of BMI among people who developed diabetes was approximately three times that of people who remained with prediabetes (0.20 [0.15 to 0.24] vs 0.06 [0.04 to 0.08] kg/m^2 per year, $P < 0.001$). A more distinct difference in trajectories of WC was observed, with the annual change rate of WC among people who developed diabetes being about seven times that of people who remained with prediabetes (0.38 [0.32 to 0.45] vs 0.05 [0.03 to 0.08] cm per year, $P < 0.001$). Weight gain is an established risk factor for diabetes [12,22]. In addition, these distinct trajectories in our study suggest that monitoring BMI and/or WC over time can help identify those at a higher risk of diabetes. Second, the larger annual increase among prediabetic people who later developed diabetes (vs people who remained with prediabetes) was observed in all BMI and WC subgroups, indicating that preventing weight gain could help prediabetic people minimize the risk of developing diabetes, regardless of whether they are obese.

Our results showed that people who returned to normoglycemia had a slight increase in BMI over time in the BMI <23 kg/m^2 group (0.06 [0.01 to 0.11] kg/m^2 per year), a constant BMI in the BMI 23-<27.5 kg/m^2 group (−0.03 [-0.09 to 0.02] kg/m^2 per year), and an annual decrease in the BMI ≥27.5 kg/m^2 group (−0.16 [-0.28 to −0.05] kg/m^2 per year), while people who remained with prediabetes had a slight increase in BMI in all three BMI groups (0.05−0.09 kg/m^2 per year). WC also changed differently over time among people who had no central obesity and later returned to normoglycemia (−0.02 [-0.06 to 0.03] cm per year) and those who had central obesity and later returned to normoglycemia (−0.40 [-0.47 to −0.32] cm per year). Previous studies have reported differences in weight change between obese and nonobese prediabetic people who returned to normoglycemia, although different obesity definitions were used [8,9]. Using BMI assessed only at the

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baseline visit and the visit 7 years later, a German study (n = 405) showed that among obese people, BMI decline (≤ -1 kg/m^2), but not stable BMI (>-1, but ≤ 1 kg/m^2), increased the probability of returning from prediabetes to normoglycemia compared with people who had BMI increase (>1 kg/m^2) [8]. In contrast, among overweight people with prediabetes, both BMI decline and stable BMI were significantly associated with restoring normoglycemia compared with subjects who had BMI increase [8]. A Japanese study (n = 731) showed that weight change was significantly associated with reversion to normoglycemia in subjects who were obese or tended toward obesity but not in normal weight or slim individuals [9]. Both studies assessed BMI only at two time points with a long interval (7 years) or very short interval (only 1 year) [8,9]. With a large sample size and annual data on both BMI and WC for up to 8 years, our findings provided strong evidence that losing weight could help obese people restore normoglycemia from a prediabetes state, whereas maintaining current weight may help normal weight and overweight people return to normoglycemia.

Our study has many strengths, including the large sample size (n = 22,945); a maximum of 8 years of observation period; the fact that BMI, WC, and diabetes status were assessed ever year; and the use of a mixed linear model that accounts for the interrelationship between within-individual repeated measures. Our study also has limitations. First, we were not able to describe sex-specific trajectories because of the low proportion of women (approximately 10%) in the study. Although our study found no interaction between sex and time, suggesting that sex does not influence the change of BMI over time, caution may be still needed when applying our findings to women. Second, while we adjusted for a range of confounders, we cannot rule out residual confounding by unmeasured covariates such as diet and physical activity. Besides, the transition from prediabetes to diabetes can also be influenced by environmental factors and genetic and hereditary factors. The lack of these data did not allow us to control these factors in our study. Third, participants were informed about their annual health checkup results, and we cannot exclude the possibility that people with prediabetes might change lifestyle or may have started taking anti-diabetic drugs in response to the examination results. Fourth, misclassification may exist due to the lack of data on 2-h plasma glucose concentrations. Last, our study is a Japanese occupational cohort, so our findings may not be generalizable to the general population or other racial/ethnic groups.

In conclusion, we observed distinct trajectories of BMI and WC among prediabetic people who progressed to diabetes, people who remained with prediabetes, and those who returned to normoglycemia. This suggests that monitoring BMI and/or WC over time can help to identify people at high risk of developing diabetes. Our results indicate that avoiding weight gain could help prediabetic people minimize the risk of developing diabetes, regardless of whether they are obese. Losing weight could help obese people restore normoglycemia from a prediabetic state, whereas maintaining current weight may help nonobese people return to normoglycemia.

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Author contributions

SD and T Mizoue were involved in the design of the study as the principal investigators. TN, TH, SY, ME, TK, AN, TI, MY, HO, T Miyamoto, KT, AU, T Ogasawara, NS, AH, SN, MS, T Murakami, IK and SD collected health checkup data. T Mizoue and KK created database. HH conducted data analysis. YK provided support in statistical analysis methods. HH drafted the report. SC, TS and other authors contributed to the interpretation of study findings and had the opportunity to review and revise the manuscript. All authors were involved in the revision of the manuscript and approved the final manuscript.

Conflict of interest

The authors declare there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2019.12.023.

References

[1] Yip WCY, Sequeira IR, Plank LD, Poppitt SD. Prevalence of pre-diabetes across ethnicities: a review of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) for classification of dysglycaemia. Nutrients 2017;9:E1273.
[2] Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk state for diabetes development. Lancet 2012;379:2279–90.
[3] Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.
[4] Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.
[5] Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. Diabetes Res Clin Pract 2005;67:152–62.
[6] Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006;29:2102–7.
[7] Li G, Zhang P, Wang J, Gregg EW, Yang W, Gong Q, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008;371:1783–9.
[8] Kowall B, Rathmann W, Heier M, Holle R, Peters A, Thorand B, et al. Impact of weight and weight change on normalization of prediabetes and on persistence of normal glucose tolerance in an older population: the KORA S4/F4 study. Int J Obes (Lond) 2012;36:826–33.
[9] Shimizu S, Kawata Y, Kawakami N, Aoyama H. Effects of changes in obesity and exercise on the development of diabetes and return to normal fasting plasma glucose levels at one-year follow-up in middle-aged subjects with impaired fasting glucose. Environ Health Prev Med 2001;6:127–31.
[10] Wong MS, Gu K, Heng D, Chew SK, Chew LS, Tai ES. The Singapore impaired glucose tolerance follow-up study: does the ticking clock go backward as well as forward? Diabetes Care 2003;26:3024–30.
[11] Gautier A, Roussel R, Ducluzeau PH, Lange C, Vol S, Balkau B, et al. Increases in waist circumference and weight as predictors of type 2 diabetes in individuals with impaired fasting glucose: influence of baseline BMI: data from the DESIR study. Diabetes Care 2010;33:1850–2.
[12] Hu H, Nagahama S, Nanri A, Tomita K, Akter S, Okazaki H, et al. Duration and degree of weight change and risk of incident diabetes: Japan Epidemiology Collaboration on Occupational Health Study. Prev Med 2017;96:118–23.

Please cite this article as: Hu H et al., Trajectories of body mass index and waist circumference before the onset of diabetes among people with prediabetes, Clinical Nutrition, https://doi.org/10.1016/j.clnu.2019.12.023

[13] Hu H, Nakagawa T, Honda T, Yamamoto S, Nanri A, Konishi M, et al. Metabolic syndrome over four years before the onset of cardiovascular disease: nested case-control Study. Circ J 2018;82:430–6.
[14] American Diabetes Association. American Diabetes Association Standards of medical care in diabetes–2017. Diabetes Care 2017;40:S1–135.
[15] World Health Organization. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157–63.
[16] Matsushita Y, Tomita K, Yokoyama T, Mizoue T. Relations between waist circumference at four sites and metabolic risk factors. Obesity (Silver Spring) 2010;18:2374–8.
[17] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on Epidemiology and prevention; national heart, lung, and blood Institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation 2009;120:1640–5.
[18] Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M, et al. The Japanese society of hypertension guidelines for the management of hypertension (JSH 2014). Hypertens Res 2014;37:253–390.
[19] Teramoto T, Sasaki J, Ishibashi S, Birou S, Daida H, Dohi S, et al. Executive summary of the Japan atherosclerosis society guidelines for the diagnosis and prevention of atherosclerotic cardiovascular diseases in Japan -2012 version. J Atheroscler Thromb 2013;20:517–23.
[20] Fitzmaurice GM, Laird NM, Ware JH. Smoothing longitudinal data: semiparametric regression models. In: Fitzmaurice GM, Laird NM, Ware JH, editors. Applied longitudinal analysis. Hoboken: John Wiley & Sons; 2011. p. 553–79.
[21] Looker HC, Knowler WC, Hanson RL. Changes in BMI and weight before and after the development of type 2 diabetes. Diabetes Care 2001;24:1917–22.
[22] Wei GS, Coady SA, Reis JP, Carnethon MR, Coresh J, D'Agostino Sr RB, et al. Duration and degree of weight gain and incident diabetes in younger versus middle-aged black and white adults: ARIC, CARDIA, and the framingham heart study. Diabetes Care 2015;38:2042–9.

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[Original]

Occupational Health Services Improve Effective Coverage for Hypertension and Diabetes Mellitus at Japanese Companies

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Abstract : The World Health Organization (WHO) aims to enable all people to receive health services, and has proposed effective coverage (EC) as an index for this aim. EC refers to "the fraction of potential health gain that is actually delivered to the population through the health system, given its capacity," and is used to indicate the percentage of the population whose diseases are well controlled among those who require treatment or are receiving treatment. This study aimed to evaluate the effects of occupational health services on EC. We hypothesized that occupational health services provided to employees by full-time occupational health practitioners, such as occupational physicians and occupational health nurses, improve EC for hypertension, diabetes mellitus and hyperlipidemia compared to those services provided by part-time occupational health practitioners. We conducted a cross-sectional study to analyze the results of general medical examinations, personnel information, and medical expense claims in fiscal year 2011. A total of 91,351 male employees at a company group participated in the study. The EC for hypertension, diabetes mellitus and hyperlipidemia was measured and compared between the employees in workplaces with occupational health practitioners (OH group) and the employees in workplaces without occupational health practitioners (non-OH group). The EC for hypertension and diabetes mellitus was significantly greater in the OH group than in the non-OH group (aOR: 1.41, 95% CI: 1.20－1.66 for hypertension; aOR: 1.53, 95% CI: 1.17－2.00 for diabetes mellitus), while the EC for hyperlipidemia was comparable (aOR: 1.11, 95% CI: 0.92－1.34). Occupational health services provided by full-time occupational health practitioners greatly improve health management after a medical examination.

Keywords : UHC, EC, cross-sectional study, medical claim, occupational health practitioner.

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Introduction

The Industrial Safety and Health Act of Japan requires employers to provide their employees with annual general medical examinations and requires employees to undergo them. The objectives of the general medical examination are to assess fitness to work and the risk of cerebrocardiovascular disease. To attain these objectives, the Ministry of Health, Labour and Welfare (MHLW) established ordinances regarding mandatory tests required in medical examinations, including blood pressure, blood glucose, and lipid testing, which is a risk factor of cerebrocardiovascular disease [1]. These objectives can be attained if employees take appropriate action to prevent diseases based on the results of their general medical examination. To enable a high-risk approach for the prevention of cerebrocardiovascular disease based on the results of general medical examinations, employees who are found to require treatment must visit medical institutions and undergo diet therapy, exercise therapy and other appropriate treatment to maintain their condition at target levels.

Many employers commission third parties to conduct medical examinations due to a lack of facilities or personnel [2]. The third parties notify the employees of the results of the medical examination using their own formats, and advise them to visit medical institutions, improve their lifestyle, or take appropriate action, but many employees who are told they require treatment do not visit medical institutions [3]. To resolve this issue, the Industrial Safety and Health Act was established to urge employers to have physicians and nurses provide advice about health management to their employees [1]. The MHLW has issued "Guidelines on measures to be taken by employers based on results of health examination", which recommends employers to encourage their employees to undergo re-examinations or more detailed examinations or to visit medical institutions based on the results of their medical examination [4].

Aono *et al* reported that in small-to-medium-sized workplaces with more than 50 employees, the number of employees who underwent detailed examinations was significantly higher when nurses provided advice regarding health management [5]. Advice regarding health management is therefore expected to increase the number of employees who visit medical institutions. Such advice and increased numbers of visits would be useless, however, if continuous treatment and proper health management did not reduce the risk of cerebrocardiovascular disorders. The quality of medical services by physicians is thought to have a marked effect on whether or not high-risk employees continue treatment and make the required lifestyle changes. Additionally, various factors related to occupational health services, including improvement in health literacy through health education and work environments that encourage employees to visit medical institutions, may also be important factors [6, 7].

The World Health Organization (WHO) recommends that effective coverage (EC) be used over crude coverage (CC) as an index for the universal health coverage (UHC) of national/regional medical systems [8]. In health terms, those who require specific medical services are defined by the term "need", users of medical services by "use", and the percentage of those who show therapeutic effects by "quality". CC is defined as "use/need". This suggests that CC improves as health services improve. While a high CC is great, medical services do not always lead to preferable therapeutic outcomes due to a number of factors, including problems with the quality of medical services and user awareness. The WHO defines EC as CC*quality, which refers to "the fraction of potential health gain that is actually delivered to the population through the health system, given its capacity" [9]. EC was first used in Mexico to assess the medical services in each state [10], and it has been used mainly in developing countries since then [11, 12]. EC can also be used as an index for other contexts and subjects; it has been used to improve treatment for and prevention of non-infectious diseases in developed countries [13].

Few studies have assessed the usefulness of occupational health services. Large-scale research that compared the incidence of myocardial infarction between employees at large workplaces employing full-time occupational physicians and local residents showed that the incidence of myocardial infarction was lower among the male employees at large workplaces than among the local residents [14]. Similar results were also obtained in large-scale research comparing the mortality from myocardial infarction between em-

ployees at large workplaces employing full-time occupational physicians and local residents [15], although the results of these studies may have been affected by socioeconomic differences and job type, including differences in income and educational standards.

The present study was conducted to evaluate the effects of occupational health services based on objective information, including data from medical claims of the employees of a large company group. The Industrial Safety and Health Act of Japan requires the employment of full-time occupational physicians at workplaces with more than 1,000 employees and those with more than 500 employees engaged in special operations [1]. Many workplaces with fewer employees also employ full-time occupational health nurses. We hypothesized that occupational health services provided at workplaces employing full-time compared to part-time (one day a week or one day a month) occupational health practitioners (occupational physicians and occupational health nurses) would improve the EC for hypertension, diabetes mellitus and hyperlipidemia.

Methods

Study design and participants

We conducted a cross-sectional analysis of general medical exam data, human resources information, and medical claims data (inpatient and outpatient) from April 2011 to March 2012 of 90,658 male employees at a general electrical manufacturer in Japan. We excluded male employees over 60 years old (n=429) because they are beyond the basic retirement age in Japan and only continue to work if they desire and if they do not have significant health problems. We also excluded male employees under 39 years old (n=33,646) because their lifestyle-disease prevalence is relatively low. We also excluded 579 employees who had a lack of medical examination data and personal data. Additionally, because occupational health practitioners advised employees to visit medical institutions and continue to receive treatment for the prevention of stroke and myocardial infarction, those who were found to have any of the following diseases at the time of medical examination were also excluded from the analyses: myocardial infarction (n=557); stroke (n=357); malignant tumors (n=558); and kidney failure/dialysis (n=843). The remaining 53,720 employees were analyzed in the present study. A flow diagram of the participants in this study is shown in Fig. 1.

Our research protocol was approved by the Ethics Committee of Medical Research, University of Occupational and Environmental Health, Japan (H29−023).

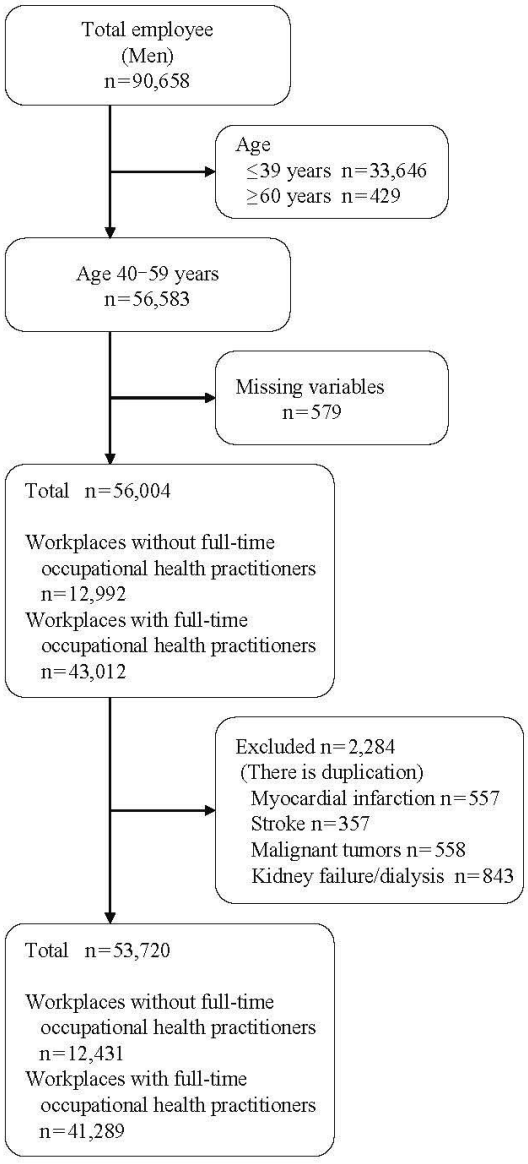

Fig. 1. Schematic diagram depicting study population.

Presence or absence of occupational health practitioners

The company had 1,359 business sites in fiscal year (FY) 2011. Workplaces in Japan with 50 or more employees are legally required to employ occupational physicians, and, as mentioned above, workplaces with more than 1,000 employees and those with more than 500 employees engaged in special hazardous operations are legally required to employ full-time occupational physicians [1]. Of the company's 1,359 sites, 265 sites employed neither occupational physicians nor nurses (8,559 employees), 146 sites employed part-time occupational physicians or nurses (3,872 employees), 393 sites employed part-time occupational physicians and full-time occupational health nurses (14,690 employees), and 555 sites employed both full-time occupational physicians and occupational health nurses (26,599 employees).

The company notifies each employee of the results of their medical examination, and the employees are classified under "hospital visit needed (treatment is needed at a medical institution)", "health management needed (although no treatment is needed, lifestyle must be improved)", or "no abnormalities". At workplaces with full-time occupational health practitioners, the occupational health practitioners ensure that those classified under "hospital visit needed" have visited medical institutions, and they provide advice regarding health management to those classified under "health management needed". In contrast, close follow up of employees at workplaces without full-time occupational health practitioners is difficult. In this study, workplaces with full-time occupational health practitioners (occupational physicians or occupational health nurses) were classified into the OH group (948 workplaces, 41,289 employees), and workplaces without full-time occupational health practitioners into the non-OH group (411 workplaces, 12,431 employees).

Health information

The following information was obtained from routine medical examinations conducted in FY 2011 and used for analyses: attributes (sex, age, and occupation categories); a self-administered questionnaire that included smoking status, current oral medications (blood pressure-lowering drugs, blood glucose-lowering drugs or insulin injections, and cholesterol- or neutral fat-lowering drugs) and disease history (myocardial infarction, stroke, malignant tumors, and kidney failure/dialysis); and objective test results (body mass index (BMI), smoking habits, occupation type, fasting blood glucose (FBG), lipids (low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides), systolic blood pressure, and diastolic blood pressure).

Workers were grouped by age according to five-year categories. Occupation was grouped as sales, research and development, and product, or office work and others. Smoking status was categorized as smoker, ex-smoker, or non-smoker. BMI was categorized as <18.4, $18.5-24.9$, $25.0-29.9$, $30.0-34.9$, or $\geq 35.0 kg/m^2$.

Socio-economic information

We extracted data on employees' standard monthly remuneration for FY2011, which is determined by health insurance unions as the total monthly income binned according to 50 appropriate categories for calculation of insurance premiums and benefits. The average standard monthly remuneration among employees of the participating company were divided into low ($\leq$410,000 yen), middle (410,000 – 560,000 yen), and high (> 560,000 yen).

Records of visits to medical institutions

To determine whether employees visited the required medical institutions, we referred to medical expense claims for the date of hospital visit, the name of the disease, medical fees, and other information. Medical expense claims of inpatients and outpatients between April 1, 2011 and March 31, 2012 were used to confirm that employees had visited a medical institution and had received the explanation that hypertension, diabetes mellitus or hyperlipidemia was suspected. We did not check whether or not employees had properly taken the oral drugs prescribed. Those who were treated for these diseases were referred to as "use (hypertension)", "use (diabetes mellitus)", and "use (hyperlipidemia)".

Crude coverage (CC) and effective coverage (EC)

Effective coverage is defined as the fraction of potential health gain that is actually delivered to the population through the health system, given its capacity [9]. It

is comprised of three factors: "Need", "Use", and "Quality". In this study "Need" refers to employees who need medical services; "Use" refers to received medical services among those who need them; and "Quality" refers to the rate at which level of health improves with medical service. Those who required medical services for hypertension, diabetes mellitus or hyperlipidemia were determined by the following criteria:

"Need (hypertension)": systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 100 mmHg, or treatment with oral antihypertensive drugs.

"Need (diabetes mellitus)": FBG ≥ 160 mg/dl or a history of treatment with hypoglycemic drugs or insulin.

"Need (hyperlipidemia)": LDL-cholesterol ≥ 160 mg/dl, HDL-cholesterol < 35 mg/dl, triglyceride ≥ 300 mg/dl, or treatment with oral cholesterol-regulating drugs.

Those who met any of these criteria were classified under "hospital visit needed" on the basis of the results of their medical examination and were noted as requiring consultations with full-time occupational health practitioners at the participating company.

Those who were well controlled for hypertension, diabetes mellitus or hyperlipidemia were determined by the following criteria:

"Effectiveness (hypertension)": systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg.

"Effectiveness (diabetes mellitus)": FBG < 126 mg/dl.

"Effectiveness (hyperlipidemia)": LDL-cholesterol < 140 mg/dl, HDL-cholesterol ≥ 40 mg/dl, and triglycerides < 150 mg/dl.

CC refers to the percentage receiving medical services among those who require specific medical services, and was calculated by the following formula:

Crude coverage (CC) = Use/Need.

The quality refers to the percentage showing therapeutic effects among those who use medical services, and was calculated by the following formula:

Quality = Effectiveness/Use.

EC refers to the quality and was calculated by the following formula:

Effectiveness (EC) = CC*Quality = Effectiveness/Need.

Statistical analyses

The percentage of employees in the OH group and non-OH group was determined according to age, BMI, smoking status, job classification and average standard monthly remuneration. CC and EC were calculated for the OH group and non-OH group. The odds ratio (OR) and its 95% confidence interval (CI) were determined by whether or not employees who were found to require medical services (need) actually did visit medical institutions, and were compared between the OH group and non-OH group using logistic regression for hypertension, diabetes mellitus and hyperlipidemia. Age, average standard monthly remuneration and job classification were adjusted, and multilevel analyses were performed using each employee as the primary level and each workplace as the secondary level of analysis. The OR and its 95% CI were also determined in regard to whether or not diseases were well controlled in employees who were found to require medical services (need), and were compared between the OH group and non-OH group using logistic regression for hypertension, diabetes mellitus and hyperlipidemia. Age, standard monthly remuneration and job classification were adjusted, and multilevel analyses were performed as described above.

Results

The employees' characteristics are shown in Table 1. Of the 53,720 employees, 12,431 comprised the non-OH group and 41,289 comprised the OH group. The proportion of obese individuals (BMI ≥ 25.0) in the non-OH group was slightly higher than in the OH group. The proportion of smokers was also higher in the non-OH group than in the OH group. The majority of employees in the non-OH group were engaged in sales, as opposed to research and product development and office/other work. The lowest standard monthly remuneration was higher in the non-OH group, while the highest standard monthly remuneration was lower in the non-OH group than in the OH group.

Both CC and EC in hypertension, diabetes mellitus and hyperlipidemia were higher in the OH group. The ORs for whether or not employees who were in need of medical treatment visited medical institutions for hypertension, diabetes mellitus and hyperlipidemia are shown in Table 2. The number of employees who visited medical institutions for treatment of hypertension was significantly higher in the OH group than in the non-OH group (aOR = 1.28, 95% CI = 1.07 − 1.54).

There were no significant intergroup differences in the number of employees who visited medical institutions for treatment of diabetes mellitus or hyperlipidemia (diabetes mellitus: aOR = 1.17, 95% CI = 0.85 – 1.62; hyperlipidemia: aOR = 1.00, 95% CI = 0.89 – 1.13).

The odds ratio for whether or not diseases were well controlled among employees who were found to require medical treatment for hypertension, diabetes mellitus and hyperlipidemia is shown in Table 3. Hypertension and diabetes mellitus were more effectively controlled in the OH group than the non-OH group (hypertension: aOR = 1.41, 95% CI = 1.20 – 1.66; diabetes mellitus: aOR = 1.53, 95% CI = 1.17 – 2.00). In contrast, there were no significant intergroup differences for the control of hyperlipidemia (aOR = 1.11, 95% CI = 0.92 – 1.34).

Table 1. Baseline characteristics of employees

	Workplace without full-time occupational health practitioners	Workplace with full-time occupational health practitioners
Number of subjects	12,431	41,289
Age categories (%)		
40–44	16.4	9.8
45–49	33.6	34.0
50–54	27.2	34.1
55–59	22.8	22.2
BMI (%)		
≤18.4	2.6	2.8
18.5–24.9	64.0	67.8
25.0–29.9	28.2	25.5
30.0–34.9	4.5	3.4
≥35.0	0.7	0.6
missing	0.1	0.0
Smoking status (%)		
Non-smoker	47.1	44.3
Ex-smoker	10.6	18.9
Smoker	42.1	36.6
Missing	0.2	0.1
Job classification (%)		
Sales	37.3	10.5
Research and development, and product	29.0	64.0
Office work and others	33.7	25.5
Standard remuneration monthly fee (JPY) (%)		
Low ≤410,000	35.4	23.2
Middle 410,000–560,000	41.6	34.8
High >560,000	23.0	42.0

Discussion

This study found that daily occupational health services provided at workplaces by full-time occupational health practitioners such as occupational physicians and occupational health nurses improved the CC and EC for hypertension and the EC for diabetes mellitus, but did not significantly affect the CC for diabetes mellitus. There were no significant inter-group differences in the CC or EC for hyperlipidemia.

Objective data on the difference in the occupational health service between the OH group and the non-OH group were available, but the company had a headquarters function that directed full-time occupational health practitioners and instructed them in the implementation of certain occupational health services, whereas part-time practitioners worked at their own discretion without any instructions from the headquarters, or many of them did not have sufficient time for such services that were available at the sites with full-time practitioners. It is possible that the CC and EC were affected more by the difference in the activities between the two groups rather than by the existence of full-time versus part-time practitioners.

The CC for hypertension, diabetes mellitus and hyperlipidemia in the non-OH group were 79%, 87% and 33%, respectively. These values were higher than those reported by Yamaguchi *et al* [16] and Fukuda [3], which may have been due to differences in criteria for hospital visit recommendations. The former study reported that less than 50% of employees visited medical institutions among those who were suspected of having diabetes mellitus based the results of occupational medical examinations, while the latter reported that 50%, 30% and 3% of employees visited medical institutions among those who were suspected of having diabetes mellitus, hypertension and hyperlipidemia, respectively, based the results of medical examinations conducted by health insurance unions

Table 2. Odds ratios for whether or not employees found to require medical treatment visited medical institutions for hypertension, diabetes mellitus, and hyperlipidemia

	Number needing treatment	Number visiting medical institusions for treatment	Crude coverage* (%)	Odds ratio for visiting medical institusions for treatment			
				adjusted OR**	95%CI		*p*
Hypertension							
Workplaces without full-time occupational health practitioners	1461	1148	78.6	reference			
Workplaces with full-time occupational health practitioners	4661	3901	83.7	1.28	1.07	1.54	0.008
Diabetes mellitus							
Workplaces without full-time occupational health practitioners	474	411	86.7	reference			
Workplaces with full-time occupational health practitioners	1300	1149	88.4	1.17	0.85	1.62	0.331
Hyperlipidemia							
Workplaces without full-time occupational health practitioners	2905	959	33.0	reference			
Workplaces with full-time occupational health practitioners	9363	3267	34.9	1.00	0.89	1.13	0.977

*: Crude coverage: Number visiting medical institusions for treatment / Number needing treatment × 100, **: Univariate logistic regression analysis adjusted for age, job type and standard remuneration monthly fee, OR: Odds ratio, CI: Confidence interval

Table 3. Odds ratios for whether or not diseases were well controlled among employees found to require medical treatment for hypertension, diabetes mellitus, and hyperlipidemia

	Number needing treatment	Number with effective control	Effective coverage* (%)	Odds ratio for effective control			
				adjusted OR**	95%CI		*p*
Hypertension							
Workplaces without full-time occupational health practitioners	1461	682	45.7	reference			
Workplaces with full-time occupational health practitioners	4661	2611	56.6	1.41	1.20	1.66	<0.001
Diabetes mellitus							
Workplaces without full-time occupational health practitioners	474	89	18.8	reference			
Workplaces with full-time occupational health practitioners	1300	345	26.5	1.53	1.17	2.00	<0.001
Hyperlipidemia							
Workplaces without full-time occupational health practitioners	2905	203	7.0	reference			
Workplaces with full-time occupational health practitioners	9363	817	8.7	1.11	0.92	1.34	0.283

*: Effective coverage: Number with effective control / Number needing treatment × 100, **: Univariate logistic regression analysis adjusted for age, job type and standard remuneration monthly fee, OR: Odds ratio, CI: Confidence interval

on employees over the age of 40 years at small-to-medium-sized workplaces. This suggests that medical interventions and advice regarding health management by part-time occupational physicians were effective even in the non-OH group.

We found that the CC for hypertension was greater in the OH group. This is likely attributable to thorough instructions provided by full-time occupational health practitioners after medical examinations. Studies have reported that a significantly greater number of employees at small-to-medium-sized workplaces visit medical institutions for detailed examinations after receiving such instructions from public health nurses [5], and that a higher number of employees visit medical institutions when the public health center issues a letter of introduction after an adult medical examination [17]. The present study found no differences in the CC for diabetes mellitus between the OH group and non-OH group, with the CC for diabetes mellitus being 87% in the non-OH group. This suggests that the majority of employees visit medical institutions based only on instructions written in medical examination reports.

In contrast, the CC for hyperlipidemia was 33% in the non-OH group and 35% in the OH group, indicating that occupational health services had no effect on subsequent health-promoting actions. Tateishi *et al* reported that while experienced occupational physicians advised employees to reduce their workload when either their blood pressure or blood glucose level was abnormally high, few occupational physicians advised employees to do so when their blood lipid levels were abnormally high. This suggests that some occupational health practitioners may not be keen to provide advice or instructions regarding blood lipid levels [18]. Furthermore, even when occupational health practitioners do provide advice to employees with hyperlipidemia, those employees are not inclined to receive such treatment. Tatemichi *et al* reported that when health experts advised employees at large workplaces who were found to require treatment for hypercholesterolemia to start drug therapy following a lack of response to three-month dietary therapy, approximately 50% agreed to receive drug therapy, while one-third of those who did not agree to receive drug therapy also rejected dietary therapy [19]. This was likely because employees with hypercholesterolemia have fewer subjective symptoms than those with other diseases and are unlikely to exhibit presenteeism despite poorly controlled cholesterol levels [20].

"Quality", a feature of EC that is affected by the quality of medical services, refers to the percentage who show therapeutic effects among those who use medical services, with those showing therapeutic effects defined by those whose medical condition is well controlled by treatment. The role of occupational health practitioners is to advise those who are found to require treatment based on the results of a medical examination to visit medical institutions and undergo appropriate treatment, rather than to provide treatment. The EC for hypertension and diabetes mellitus improved in the OH group, and the OR was greater for EC than for CC, which suggests that occupational health services contribute to the management of diseases even after medical treatment has started. The Industrial Safety and Health Act requires employees to take appropriate action regarding their work based on physicians' advice if the results of their medical examination suggest that their disease is poorly controlled. Therefore, employees must consider their health and reduce their workload even if they are receiving medical treatment [1, 4]. Occupational physicians and other occupational health practitioners often examine the progress of treatment and provide advice to employees in cooperation with physicians. Thorough health management is thought to contribute to the improvement of EC, especially in workplaces employing full-time occupational health practitioners. Tateishi *et al* reported that in cases of either abnormal blood pressure or blood glucose levels, occupational physicians should advise employers to reduce the affected employees' workload [18]. Employers are responsible for reducing employees' workload, and may be blamed for the occurrence of overwork-related hypertension, diabetes mellitus, other cerebrocardiovascular diseases or death if work conditions are poor.

At workplaces with well-established occupational health service systems, the human resources department and executive officers are likely to take appropriate action for health management based on advice from occupational physicians, while this is unlikely to occur at workplaces without occupational physicians,

leading to insufficient advice regarding health management and instructions for hospital visits. Occupational health services are provided by a team comprised of occupational physicians, occupational health nurses, and other staff members. In particular, occupational physicians have been required to perform a wide range of tasks in recent years [21]. Occupational health services include medical examinations, follow-ups based on the results of medical examinations, establishment of a health committee, health education, industrial hygiene education, and mental health services. The level of health literacy of employees is related to healthy lifestyle habits, including regular eating habits, regular exercise, and a smoke-free lifestyle [6]. Various occupational health services have improved the health literacy of employees in the OH group, enabling them to check the results of their medical examination, to voluntarily visit medical institutions, and to receive appropriate management of treatment, regardless of whether or not they were directly given such instructions from occupational health practitioners. There were no significant differences in the EC for hyperlipidemia between the OH group and non-OH group. The "quality" was 21% for the non-OH group and 25% for the OH group. Tatemichi *et al* reported that approximately 50% of patients with hypercholesterolemia who had started drug treatment after a medical examination discontinued hypercholesterolemia treatment within three years [22]. This suggests that those who are found to require treatment for hyperlipidemia based on the results of a medical examination are unlikely to visit medical institutions or to continue treatment.

Whether or not employees visit medical institutions after a medical examination is affected by various work and personal factors. Tsuda *et al* reported that when employees who were suspected of having diabetes mellitus were advised to visit medical institutions, those who could easily take a day off and those with well-managed jobs were more likely to do so. Those who worked 61 hours or more a week were less likely to visit medical institutions than those who worked less than 61 hours a week [23]. Goto *et al* reported that the factors for employees visiting medical institutions as advised after a medical examination despite not having visited a medical institution in the past three years included living alone, having a personal physician, low job demand, and lower-rated health [7]. It is important to continue treatment after the initial visit to a medical institution, even among those with low incidence of complications and low mortality rates. Goto *et al* also reported that there was no relationship between shift-work, overtime work, stress, or other work factors, and whether or not employees continued treatment [7]. Sato *et al* reported that full-time employees who had some symptoms were more likely to visit medical institutions if they did less overtime work, and that they were more likely to take supplements if they did more overtime work [24]. Azami *et al* reported that among employees with diabetes mellitus, those who did not visit medical institutions had higher HbA1c than those who did visit medical institutions, and that working long hours and having holidays other than Sunday increased the risk of not visiting medical institutions [25]. This suggests that better occupational health services and work environments that enable employees to engage in both treatment and work are essential for improving EC.

The present study has several limitations. The purpose of this study is to clarify the impact of differences in comprehensive occupational health services due to the presence or absence of full-time occupational health practitioners, but some objective data on the services, such as minutes spent with each employee, were not available. We adjusted for job type and standard monthly remuneration in our analyses as these may affect CC and EC and because they differed between the OH group and non-OH group, but because there was no information on other work or personal conditions, there is a possibility that other work and personal conditions may have affected the results of the study as confounding factors. We identified items for "need" by referring to the results of medical examinations and medical interview sheets from 2011, and identified items for "use" through medical expense claims from 2011. Therefore, depending on when the medical examination was performed, information on treatment in employees who were found to require treatment may not have been taken into consideration. Furthermore, because we examined employees from only one company group, our results may not be generalizable. However, an advantage of this study was that we identified treatment and outcomes by referring

to objective data such as medical expense claims and the results of medical examinations.

The Industrial Safety and Health Act requires that all employees undergo medical examinations, regardless of the size of their workplace. However, only a limited number of workplaces employ full-time occupational physicians, occupational health nurses and other occupational health practitioners. Workplaces with more than 50 employees are required to employ part-time occupational physicians, while those with fewer than 50 are unlikely to have occupational health practitioners to check the results of employees' medical examinations. The results of this study suggest that occupational health service systems greatly affect employees' health-related actions, such as visiting a medical institution and receiving appropriate health management after a medical examination. Appropriate action is therefore required to improve health management among employees of small-to-medium-sized workplaces.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Ministry of Health, Labour and Welfare (MHLW): Ordinance on Industrial Safety and Health. MHLW, Tokyo https://www.jaish.gr.jp/anzen/hor/hombun/hor1-2/hor1-2-1-m-0.htm (in Japanese) (Accessed 1 Feb 2019)
2. National Federation of Industrial Health Organization: Greeting. National Federation of Industrial Health Organization, Tokyo http://www.zeneiren.or.jp/about/index.html (in Japanese) (Accessed 1 Feb 2019)
3. Fukuda H (2016): Evaluation and future tasks of specified health examination and specific health guidance at health insurance associations based on employers and enterprises. Hoken No Kagaku 58: 162–171 (in Japanese)
4. Ministry of Health, Labour and Welfare (MHLW) (2008): Guidelines on measures to be taken by employers based on results of health examination. MHLW, Tokyo https://www.mhlw.go.jp/file/04-Houdouhappyou-11202000-Roudoukijunkyoku-Kantokuka/shishin.pdf. (in Japanese)
5. Aono Y, Aisaka A, Gohno M, Hida T & Shimizu T (2000): Visiting a doctor by individuals who need medical diagnosis after screening and kinds of screening. Sangyo Igaku Journal 23(5): 43–49 (in Japanese)
6. Ishikawa H, Nomura K, Sato M & Yano E (2008): Developing a measure of communicative and critical health literacy: A pilot study of Japanese office workers. Health Promot Int 23: 269–274
7. Goto E, Ishikawa H, Okuhara T, Kato M, Okada M & Kiuchi T (2018): Factors associated with adherence to recommendations to visit a physician after annual health checkups among Japanese employees: A cross-sectional observational study. Ind Health 56: 155–159
8. Shengelia B, Tandon A, Adams OB & Murray CJ (2005): Access, utilization, quality, and effective coverage: An integrated conceptual framework and measurement strategy. Soc Sci Med 61: 97–109
9. Ng M, Fullman N, Dieleman JL, Flaxman AD, Murray CJ & Lim SS (2014): Effective coverage: A metric for monitoring universal health coverage. PLoS Med 11: e1001730. doi: 10.1371/journal.pmed.1001730
10. Lozano R, Soliz P, Gakidou E, Abbott-Klafter J, Feehan DM, Vidal C, Ortiz JP & Murray CJ (2006): Benchmarking of performance of Mexican states with effective coverage. Lancet 368: 1729–1741
11. Rubinstein A, Zerbino MC, Cejas C & López A (2018): Making universal health care effective in Argentina: A blueprint for reform. Health Syst Reform 4: 203–213
12. Leslie HH, Malata A, Ndiaye Y & Kruk ME (2017): Effective coverage of primary care services in eight high-mortality countries. BMJ Glob Health 2: e000424. doi: 10.1136/bmjgh-2017-000424.
13. Sullivan R, Peppercorn J, Sikora K *et al* (2011): Delivering affordable cancer care in high-income countries.

Lancet Oncol 12: 933–980
14. Hirobe K, Terai T, Fujioka S, Goto K & Dohi S; 3M-Study Project Committee of the Japan Association of Occupational Physicians "San-yu-kai" (2005): Morbidity of Myocardial Infarction Multicenter Study in Japan (3M Study): Study design and event rates for myocardial infarction and coronary death by age category in Japanese workers. Circ J 69: 767–773
15. Horie S, Sone S, Nakano S, Taguchi M & Hirobe K (2005): Investigation of occupational mortality rate for 5 years in a workplace where a dedicated industrial physician is located. Sangyo Eiseigaku Zassi 47(suppl): 442 (in Japanese)
16. Yamaguchi N, Okubo T, Yamamura J, Takahashi K, Nakamura R & Funatani F (1990): A prospective study of access to medical services following a community-based screening program. Nihon Koshu Eisei Zasshi 37: 281–288 (in Japanese)
17. Adachi T, Matsumoto K, Irisawa Y, Ikuta J, Tashiro T, Konishi E, Okuma C, Yokota T & Tagami A (1989): Referral compliance improved by a letter of introduction to a specific physician following mass screening. Nihon Koshu Eisei Zasshi 36: 413–420 (in Japanese)
18. Tateishi S, Watase M, Fujino Y & Mori K (2016): The opinions of occupational physicians about maintaining healthy workers by means of medical examinations in Japan using the Delphi method. J Occup Health 58: 72–80
19. Tatemichi M, Hamaguchi T, Hashira M *et al* (2002): Acceptability and long-term compliance with drug treatment for hypercholesterolemia in Japanese male workers: I. Acceptability of drug treatment. J Occup Health 44: 166–175
20. Burton WN, Chen CY, Conti DJ, Schultz AB, Pransky G & Edington DW (2005): The association of health risks with on-the-job productivity. J Occup Environ Med 47: 769–777
21. Mori K (2018): Current status and issues for the role of occupational health physicians in Japan. JMA J 1: 15–21
22. Tatemichi M, Hamaguchi T, Hashira M *et al* (2002): Acceptability and long-term compliance with drug treatment for hypercholesterolemia in Japanese male workers: II. Long-term compliance with drug treatment. J Occup Health 44: 307–314
23. Tsuda K, Tsutsumi A & Kawakami N (2004): Work-related factors associated with visiting a doctor for a medical diagnosis after a worksite screening for diabetes mellitus in Japanese male employees. J Occup Health 46: 374–381
24. Sato K, Yamazaki S, Hayashino Y, Takegami M, Tokuda Y, Takahashi O, Shimbo T, Hinohara S, Fukui T & Fukuhara S (2011): Associations between hours worked, symptoms and health resource utilization among full-time male Japanese workers. J Occup Health 53: 197–204
25. Azami Y, Morita K, Nakada A & Suzuki M (2000): The factors associated with visiting a doctor for male diabetes workers. Practice 17: 177–182 (in Japanese)

産業保健サービスの存在は企業における高血圧および糖尿病のEffective Coverageを向上させる

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要　　旨：WHOは「各国・地域において，人々が経済的困難を伴わず保健医療サービスを享受すること」を目標としており，その指標としてEffective Coverage（EC）という概念を提唱している．ECとは“その国または地域における健康システムを通して，実際に人々に健康増進をもたらすことができる割合”と定義されており，産業保健の場面では治療が必要，もしくは治療を受けているうち，適切に疾病管理されている率に該当すると考えられる．本研究では産業保健サービスの効果を評価することを目的とし，「常勤の産業保健スタッフ（産業医または産業看護職）による労働者への産業保健サービスの提供は，高血圧，糖尿病，脂質異常症の各項目について，ECを向上させる」という仮説をたてて検証した．2011年度の一般健康診断，人事情報，及びレセプトからの個々のデータを分析した横断的研究である．特定の大規模企業グループの91,351人の男性労働者を対象とした．常勤の産業保健スタッフがいる事業場に所属する労働者（OH群）とそれ以外の事業場に所属する労働者（non-OH群）において高血圧，糖尿病，脂質異常症の各項目別にECを算出し，比較した．OH群はnon-OH群に比べて，高血圧・糖尿病において有意にECが高率であったが，脂質異常症については有意な差を認めなかった（高血圧aOR 1.41: 95%CI 1.20−1.66，糖尿病aOR 1.53: 95%CI 1.17−2.00，脂質異常症aOR 1.11: 95%CI 0.92−1.34）．常勤の産業保健スタッフによる産業保健サービスの提供は，健康診断後の適切な管理に大きく影響する．

キーワード：UHC，EC，横断的研究，診療報酬明細書，産業保健スタッフ．

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