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Ideal cardiovascular health, glycaemic status and incident type 2 diabetes mellitus: the REasons for Geographic and Racial Differences in Stroke (REGARDS) study

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Abstract

Aims/hypothesis—Ideal cardiovascular health (CVH) is associated with lower diabetes risk. However, it is unclear whether this association is similar across glycaemic levels (normal [<5.6 mmol/l] vs impaired fasting glucose [IFG] [5.6–6.9 mmol/l]).

Methods—A secondary data analysis was performed in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. Incident diabetes was assessed among 7758 participants without diabetes at baseline (2003–2007) followed over 9.5 years. Baseline cholesterol, blood pressure, diet, smoking, physical activity and BMI were used to categorise participants based on the number (0–1, 2–3 and ≥4) of ideal CVH components. Risk ratios (RRs) were calculated using modified Poisson regression, adjusting for cardiovascular risk factors.

Results—Among participants (mean age 63.0 [SD 8.4] years, 56% female, 73% white, 27% African-American), there were 891 incident diabetes cases. Participants with ≥4 vs 0–1 ideal CVH components with normal fasting glucose (n = 6, 004) had 80% lower risk (RR 0.20; 95% CI 0.10, 0.37), while participants with baseline IFG (n = 1754) had 13% lower risk (RR 0.87; 95% CI 0.58, 1.30) (*p* for interaction by baseline glucose status <0.0001). Additionally, the magnitude of the association of ideal CVH components with lower diabetes risk was stronger among white than African-American participants (*p* for interaction = 0.0338).

Conclusions/interpretation—A higher number of ideal CVH components was associated with a dose-dependent lower risk of diabetes for participants with normal fasting glucose but not IFG. Tailored efforts that take into account observed differences by race and glycaemic level are needed for the primordial prevention of diabetes.

Introduction

The American Heart Association (AHA) published 2020 Impact Goals for cardiovascular health (CVH) promotion aiming to improve CVH and reduce deaths from cardiovascular disease (CVD) and stroke by 20% from 2010 to 2020 [1]. Through this effort, the AHA identified ideal levels of seven health factors or behaviours that have been associated with healthy ageing without cardiovascular and other chronic diseases (also known as 'Life's Simple 7') [1]. The health factors include total cholesterol <5.18 mmol/l, blood pressure <120/<80 mmHg and fasting plasma glucose <5.6 mmol/l, all without the use of medication. The health behaviours include a healthy dietary pattern, no prior tobacco use or having stopped smoking more than 12 months previously, ≥150 min/week of moderate intensity or ≥75 min/week of vigorous intensity physical activity and BMI <25 kg/m^2. Adherence to these factors and behaviours has been associated with a lower incidence of CVD and all-cause mortality [2, 3].

There are many shared cardiovascular and diabetes risk factors, and we have previously shown that attainment of a higher number of ideal CVH factors is associated with lower risk of diabetes in multi-ethnic populations, with a greater magnitude of risk reduction among non-Hispanic white participants [4, 5]. Recent analyses have challenged whether attainment

of more optimal levels of classic risk factors is associated with similar risk reductions among individuals with lower or higher diabetes risk [5, 6]. Thus, we examined whether the association of ideal CVH with diabetes risk differed for participants with higher levels of diabetes risk (i.e. impaired fasting glucose [IFG], African-Americans) compared with participants at lower baseline risk (i.e. normal fasting glucose, whites).

Methods

This paper reports the results of a secondary analysis of data from the REGARDS cohort. The REGARDS study is a prospective national cohort of 30,239 community-dwelling African-American and white adults 45 years of age from the 48 contiguous US states that was designed to examine regional and racial influences on stroke mortality [7, 8]. Full details are described elsewhere [7]. Briefly, participants—English-speaking adults aged 45 years or older—were enrolled between January 2003 and October 2007, with commercially available lists combining mail and telephone contacts used for recruitment. Race and sex were balanced by design, with oversampling from the south-eastern USA; the final cohort composition was 58% women and 42% African-American. Overall, 56% of participants resided in the stroke belt (NC, SC, GA, AL, MS, TN, AR and LA) with the rest from the other 40 contiguous states. An initial telephone interview was used to survey participants and establish eligibility. Following verbal consent, demographic information and medical history, including data on stroke risk factors and sociodemographic, lifestyle and psychosocial characteristics were collected via computer-assisted telephone interviews using validated questionnaires. Participants were asked to fast for 10–12 h and physical and physiological measures including BP, anthropometric measures, blood samples, urine samples, electrocardiogram and medication use by pill bottle review were collected during an in-home examination by trained staff following standardised, quality-controlled protocols. Blood and urine samples were shipped overnight on ice to the REGARDS central laboratory in Burlington, VT, USA. Participants were contacted via telephone at 6 month intervals to ascertain hospitalisations and vital status. A second in-person assessment was conducted 10 years (2013–2016) following baseline and included a telephone interview and an in-home examination to collect physical and physiological measures. Study methods were reviewed and approved by the institutional review board at the participating institutions and all participants gave written informed consent.

Exposure

The primary exposure was ideal CVH, assessed using six baseline metrics: cigarette smoking status; diet; physical activity; BMI; serum cholesterol; and blood pressure [4]. The blood glucose metric was excluded in the analyses, as diabetes was the outcome of interest. Each baseline metric was evaluated separately using poor, intermediate and ideal categories (electronic supplementary material [ESM] Table 1) [1]. Additionally, the number of ideal CVH metrics was summed across the six individual metrics and categorised as poor (0–1 ideal metrics), intermediate (2–3 ideal metrics) and ideal (4+ ideal metrics) CVH [4].

Cigarette smoking

Self-reported cigarette smoking was categorised as: current = poor; former 12 months (smoking at least 100 cigarettes in a lifetime) = intermediate; or never or quit 12 months = ideal.

Dietary intake

Dietary intake was assessed with the Block 98 food frequency questionnaire (FFQ), a validated semi-quantitative FFQ that assessed usual dietary intake of 110 food items (NutritionQuest, Berkeley, CA, USA) [9]. The FFQ was self-administered by participants after the baseline in-home visit and mailed to the REGARDS operations centre, where it was checked for completeness, scanned and forwarded to NutritionQuest for processing and analysis. The amounts of each food on the FFQ consumed by a participant were calculated by multiplying the frequency of consumption of that food by the usual amount consumed; the food groups were constructed as has been described previously [10]. The REGARDS questionnaire had some slight differences from the 2020 guidelines regarding units of servings, which required modification of the metrics. Components of the modified ideal diet score were: fruits and vegetables 4.5 cups/day; fish 2 × 98 g servings per week (non-fried); fibre-rich whole grains 3 × 28 g-equivalent servings/day; sodium <1500 mg/day; and sugar-sweetened beverages 1884 kJ/week. Participants were given one point per dietary component at goal for a total score ranging from 0 to 5. Participants were classified as ideal (4–5 of 5 components), intermediate (2–3 of 5 components) or poor (0–1 of 5 components).

Physical activity

Participants in REGARDS were asked 'How many times per week do you engage in intense physical activity, enough to work up a sweat?' We defined ideal physical activity as a frequency of four or more times per week, intermediate as 1–3 times per week, and poor as none, as previously [11].

Serum cholesterol, BMI, BP, plasma glucose

Serum concentrations of total cholesterol were measured using colorimetric reflectance spectrophotometry. Poor, intermediate and ideal levels of total cholesterol were categorised as 6.21 mmol/l, 5.18–<6.21 mmol/l or treated to goal, < 5.18 mmol/l, respectively. Calibrated devices were used to measure participants' weight and height to calculate BMI as weight (kg)/height^2 (m^2). BMI was categorised as poor, intermediate and ideal as follows: 30 kg/m^2, 25–29.9 kg/m^2 and <25 kg/m^2, respectively. Resting seated BP was measured following a standard protocol in the left arm. The average of two seated BP measurements was used for analysis. BPs were categorised as poor, intermediate and ideal as follows: systolic (S)BP 140 or diastolic (D)BP 90 mmHg, SBP 120–139 or DBP 80–89 mmHg or treated to goal, <120/<80 mmHg, respectively. Fasting plasma glucose was categorised as intermediate or ideal as 5.6–6.9 mmol/l and <5.6 mmol/l, respectively. Because participants with diabetes at baseline were excluded from this analysis, no participants were in the poor category for glucose (7.0 mmol/l).

Outcome

The primary outcome was incident diabetes, defined as fasting glucose 7.0 mmol/l, non-fasting glucose 11.1 mmol/l or diabetes medication use at the follow-up examination in those without prevalent diabetes at baseline. Glucose was measured using colorimetric reflectance spectrophotometry on the Ortho Vitros 950 IRC Clinical Analyzer (Johnson & Johnson Clinical Diagnostics, Rochester, NY, USA) with a coefficient of variation of 1% [12].

Covariates

Age, race, sex, annual household income and education were self-reported. Self-reported alcohol use was categorised as none, moderate (1–7 drinks/week for women or 1–14 drinks/week for men) or heavy (>7 drinks/week for women or >14 drinks/week for men) [7]. Estimated GFR (eGFR) was calculated according to the 2012 Chronic Kidney Diseases Epidemiology Collaboration (CKD-EPI) equation, which includes both creatinine and cystatin C, and urinary albumin concentrations [13]. Serum creatinine was measured and calibrated to isotope dilution mass spectrometry-traceable methods [13]. Cystatin C was measured by means of a particle-enhanced immunonephelometry assay (N Latex Cystatin C on a BNII nephelometer [Siemens, Munich, Germany]) [9]. Urine albumin was measured by nephelometry using a BNII ProSpec nephelometer (Siemens) and urine creatinine was measured by the rate Jaffe method using the Modular-P chemistry analyser (Roche/Hitachi, Basel, Switzerland) [13] to calculate the urinary albumin-to-creatinine ratio (ACR). High-sensitivity C-reactive protein (hsCRP) was measured by particle-enhanced immunonephelometry using the BNII nephelometer (N High Sensitivity CRP; Siemens) with interassay coefficients of variation of 2.1–5.7%.

Statistical analysis

In this secondary analysis using data collected from the REGARDS cohort, we included participants who completed the follow-up visit or computer-assisted telephone interview (n=16, 150), then excluded participants with diabetes at baseline (n=2,729) and those who were missing diabetes status at baseline (n=521), diabetes status at follow-up (n=1,580), one of the CVH metrics (n=3,202) or data on baseline covariates (n=360) (ESM Fig.1). The 5,663 participants excluded because of missing diabetes and covariate status had a higher percentage of African-Americans, higher BMI, higher smoking, higher blood pressure, lower education and were less physically active (all p<0.01; ESM Table 2). Descriptive statistics were used to compare the baseline characteristics overall and by baseline glycaemic status and race (Table 1; ESM Table 3). Risk ratios (RR) for incident diabetes were calculated using modified Poisson regression adjusting for age, sex, race, education, income, alcohol use, eGFR, ACR and hsCRP.

The number of ideal CVH components and each CVH metric separately were evaluated to estimate the proportion of cases in the population that might be attributable to suboptimal levels of CVH (population-attributable risk [PAR]%). The PAR% was calculated using the formula p(RR−1)/(1 + p[RR−1]), where p is the prevalence of individuals not in the low-risk

group and RR is the associated multivariable-adjusted relative risk of those individuals. Upper and lower 95% CIs of the PAR% were derived using this formula and the upper and lower 95% CI estimates of the multivariable-adjusted RR [14]. Given that the association of ideal CVH with diabetes risk may differ by age, sex, race, glycaemic status (normal <5.6 mmol/l vs IFG 5.6–6.9 mmol/l) and history of coronary heart disease, we tested for interaction by these factors with CVH measures by inserting an interaction term in the model and using the likelihood ratio test.

We performed sensitivity analyses (ESM Tables 4–8) to confirm the robustness of our findings. These analyses included: (1) adjusting for baseline fasting glucose in the main analysis (ESM Table 4); (2) using the World Health Organization classification of IFG (< 6.1 mmol/l vs 6.1–6.9 mmol/l in stratified models (ESM Table 5); (3) examining RRs for incident dysglycaemia (IFG and diabetes combined [ESM Table 6]; IFG only [ESM Table 7]) among participants with normal fasting glucose at baseline; and (4) performing the main analysis with full adjustment except for eGFR, ACR and hsCRP, as these may be in the pathway from risk to diabetes (ESM Table 8). Statistical significance was defined as two-sided $\alpha<0.05$ for all analyses except for interactions ($p<0.10$). Analyses were performed using SAS 9.4 (SAS, Cary, NC, USA).

Results

Characteristics of the cohort

Among the 7,758 included participants, the 1754 with IFG had significantly higher smoking prevalence, BMI, waist circumference, BP, fasting glucose and hsCRP than the 6004 participants with normal fasting glucose. Additionally, participants with IFG had fewer ideal CVH components compared with those with normal fasting glucose (all p<0.05; Table 1). Similar to the IFG group vs normal fasting glucose, African-American participants had a more adverse cardiometabolic profile compared with white participants (ESM Table 3).

Incidence of diabetes

During a median follow-up of 9.5 years (interquartile range [IQR] 8.6–9.9 years), there were 891 participants who developed diabetes (incidence rate 11.5 per 1000 person-years). The incidence rates were higher among participants with IFG vs normal fasting glucose (30.4 vs 6.0 per 1000 person-years) (Table 1) and among African-American vs white participants (17.3 vs 9.4 per 1000 person-years) (ESM Table 3).

Ideal CVH and incident diabetes

The unadjusted and adjusted RRs for incident diabetes associated with baseline ideal CVH are presented in Table 2. The RRs for 2–3 ideal CVH components or 4 ideal CVH components compared with 0–1 ideal CVH components were 0.70 (95% CI 0.62, 0.79) and 0.29 (95% CI 0.20, 0.41), respectively. Among the individual CVH components, ideal vs poor status was associated with a decreased risk of incident diabetes for blood pressure (RR 0.39, 95% CI 0.31, 0.49), BMI (RR 0.23, 95% CI 0.18, 0.29), current smoking (RR 0.75, 95% CI 0.63, 0.89) and dietary intake (RR 0.81, 95% CI 0.68, 0.97) in adjusted analyses (Table 3).

Cardiovascular health and incident diabetes by glycaemic status

There were significant differences by glycaemic status (p for interaction <0.0001) in the association of baseline CVH components with risk of diabetes. Having 4 ideal CVH components vs 0–1 ideal CVH components was associated with a greater magnitude of diabetes risk-lowering in participants with normoglycaemia than in those with IFG (RR 0.20, 95% CI 0.10, 0.37 vs RR 0.87, 95% CI 0.58, 1.30; Table 2). Among the individual CVH components, there were significant differences for BMI, blood pressure, smoking and dietary intake by glycaemic status (all p<0.05; Table 3).

Cardiovascular health and incident diabetes by race

There were significant differences by race (p for interaction=0.0338) in the association of baseline CVH components with risk of diabetes. Participants having 2–3 and 4 ideal CVH components vs 0–1 ideal CVH components was associated with a greater magnitude of diabetes risk-lowering in white (39% and 73%) than in African-American (14% and 66%) participants. In Table 3, among the individual CVH components, there were significant differences for BMI and BP by race (both p<0.05).

Age (p for interaction = 0.2385), sex (p for interaction = 0.4420) and history of coronary heart disease (p for interaction = 0.5464) did not modify the association of ideal CVH with incident diabetes. Findings were similar in sensitivity analyses: (1) adjusted for glucose in the main analysis (ESM Table 4); (2) using the World Health Organization classification of IFG <6.1 mmol/l vs 6.1–6.9 mmol/l in stratified models (ESM Table 5); (3) evaluating incident IFG and diabetes combined (ESM Table 6) and incident IFG alone at follow-up (ESM Table 7) among those with normal fasting glucose at baseline; and (4) excluding adjustment for eGFR, ACR and hsCRP from the main analysis (ESM Table 8). The exception was that there were no significant racial/ethnic differences in the association of CVH with incident IFG alone.

Population-attributable diabetes risk

We present the results of the evaluation of diabetes risk by baseline number of CVH components and categories at baseline, compared with all others not in that group in Table 4. Overall, participants with 4 ideal CVH components at baseline (10% of participants) had a 70% lower risk of diabetes, and 6.8 out of ten new cases of diabetes appeared attributable to not being in the ideal CVH group at baseline. Participants with normal fasting glucose in the 4 ideal CVH components category at baseline (12% of participants) had a 79% lower risk of diabetes and 7.6 out of ten new cases of diabetes appeared attributable to not being in the ideal CVH group at baseline; among individuals with IFG, this was only 1.9 out of ten new cases.

Discussion

In this large contemporary cohort study, a higher number of ideal CVH components at baseline showed a graded, inverse association with incident diabetes, consistent with previous studies [4, 5, 14, 15]. However, the magnitude of the association of ideal CVH with lower diabetes risk varied by glycaemic status, with a strong inverse association observed

among those with normal glucose and no association observed among those with IFG. These findings suggest population-level public health promotion of the AHA 2020 ideal CVH metrics may be beneficial for primordial prevention of diabetes, but may not be as beneficial for preventing progression to diabetes from IFG over 10 years in black and white middle-aged and older adults.

Ideal CVH, baseline glycaemic status and incident diabetes

Our study is consistent with previous analyses examining the association of ideal CVH with incident diabetes, revealing a dose-dependent inverse association with incident diabetes [4, 5, 16], both continuously and categorically. These findings confirm the importance of focusing on increased attainment of ideal CVH in the USA as only 27.9% of the REGARDS participants in this analysis had 4 out of seven ideal CVH metrics. Among participants with IFG, the prevalence of 4 out of six ideal CVH metrics was low at 4.4% compared with 11.9% among those with normal fasting glucose. These differences in baseline ideal CVH for individuals with IFG are even more concerning given the lower (nonsignificant) magnitude of risk reduction with higher levels of ideal CVH among individuals with IFG. Previously, we evaluated modifiable lifestyle factors, including exercise, diet, cigarette smoking, television watching and sleep-disordered breathing, among African-Americans in the Jackson Heart Study and showed lower risk of incident diabetes with more ideal levels of these risk factors. However, similar to this analysis, the results were driven by individuals at the lower end of the diabetes-risk spectrum (BMI < 30 kg/m^2 and normoglycaemia) [6], suggesting broader public health interventions may work well for primordial prevention but not as well for those with IFG. As noted by Tuomilehto et al [17], lower-intensity population-level interventions involving multiple stakeholders are well suited for primordial prevention of diabetes, but individuals later in the natural history of glucose dysregulation with significant pathophysiological derangements (i.e. IFG [hepatic insulin resistance and decreased first-phase insulin response], impaired glucose tolerance [skeletal muscle insulin resistance and reduced early- and late-phase insulin response]) may require participation in higher intensity interventions. Interestingly, while high-intensity interventions among participants with impaired glucose tolerance, such as the diabetes prevention programme [18], have been successful in reducing the development of diabetes, high-intensity interventions in isolated IFG have not produced the same response [17, 19]. Thus, our findings support the need for further investigation of novel approaches including newer pharmacotherapies such as glucagon-like peptide-1 receptor agonists in individuals with IFG [20].

Racial differences

Consistent with prior studies [4, 21, 22], African-American participants in the REGARDS cohort had a lower prevalence of ideal CVH at baseline compared with white participants (17.2% vs 31.8%). The racial differences are concerning given that ideal CVH in African-Americans was associated with lower magnitude of diabetes risk-lowering, especially for individuals with attainment of 2–3 ideal metrics, which represented 55% of African-Americans. Notably, there were no racial differences in incident IFG (ESM Table 7). In addition to overall ideal CVH differences, ideal vs poor levels of blood pressure and BMI were associated with much lower risk among white vs African-American participants (81%

vs 66%, p=0.0309 and 69% vs 37%, p=0.0194), respectively. Physical activity and dietary intake were associated with significantly lower risk of incident diabetes among white participants but not among African-Americans. In the Multi-Ethnic Study of Atherosclerosis [4], more ideal levels of BP were associated with lowest risk among white participants, consistent with REGARDS, but there were no racial differences for BMI. The findings for discrepancy of the association of BP with insulin resistance and incident diabetes have also been reported in prior race-stratified analyses [23, 24]. These differences may result from co-existing cardiometabolic risk factors including adiposity, fasting hyperinsulinaemia, inflammation, endothelial dysfunction and socioeconomic status. In this analysis, we adjusted for inflammation (hsCRP) and socioeconomic status and the findings persisted. Consistent with prior studies, African-Americans had higher waist circumference and fasting glucose, which may partly explain the findings for BP [25]. Investigations have also shown that hormonal actions underlying hypertension and diabetes, including aldosterone, may be different in African-American vs white participants. Aldosterone is associated with a dose-dependent higher risk of incident diabetes among African-Americans [26]. African-Americans are sensitive to the effects of aldosterone and mineralocorticoid receptor agonists, as evidenced by studies showing that aldosterone and 9-α fludrocortisone (mineralocorticoid receptor agonist) increase BP in African-American but not white participants [27]. Given the high rates of hypertension and diabetes among African-Americans, further research exploring mechanistic links explaining pathophysiological racial differences is of paramount importance. The lower magnitude of diabetes risk-lowering with ideal CVH in AfricanAmericans provides one potential explanation for the continued rise in incident diabetes among African-Americans, which contrasts with the plateauing of risk among the white population over the last 20 years [28].

Strengths/limitations

The strengths of our analysis include a large, biracial population-based cohort with a decade of follow-up and rigorously ascertained physiological measures. We used validated questionnaires and an objective assessment of diabetes using fasting glucose and medication use. This study also has several potential limitations. Dietary data were obtained using an FFQ of usual diet over the previous year and was modified from the original definition. Additionally, we did not scale the dietary components based on total energy intake because of the difficulty in ascertaining an accurate estimate and this may have resulted in misclassification. In our study, the majority of participants (78.5%) were in the poor category for diet, which is consistent with findings reported in other studies [21]. Our study assessed the frequency of intense physical activity. Although geographic region and season may influence the intensity of physical activity required to work up a sweat, this widely used measure of physical activity is well validated [29]. We did not collect data on physical activity duration, thus our measure may over- or underestimate the actual adherence to the original definition of the AHA physical activity goal, which is based on minutes of physical activity per week. Our findings of a non-significant relationship between ideal CVH and incident diabetes in those with IFG could be due to several factors that could not be evaluated, such as genetic susceptibility and lifestyle changes after being identified as high risk for diabetes. We were unable to distinguish between type 1 diabetes and type 2 diabetes,

but in this age range, incident type 1 diabetes is extremely uncommon, so we assumed a predominance of type 2 diabetes in our population.

Conclusions

Our study demonstrated that increasing levels of ideal CVH were associated with a lower risk of diabetes, especially among participants with normal fasting glucose at baseline. However, only one in four participants overall and fewer than one in 20 participants with IFG had ≥4 ideal CVH components at baseline. The lower magnitude of risk reduction with ideal CVH among those with IFG warrants further investigation and suggests this group requires higher intensity interventions to lower long-term diabetes risk. Primordial prevention through attainment of ideal CVH has the potential to dramatically reduce the burden of diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Abbreviations:

ACR	Albumin-to-creatinine ratio
AHA	American Heart Association
CVD	Cardiovascular disease
CVH	Cardiovascular health
CKD-EPI	Chronic Kidney Diseases Epidemiology Collaboration
eGFR	Estimated GFR
FFQ	Food frequency questionnaire
hsCRP	high-sensitivity C-reactive protein
IFG	Impaired fasting glucose

IQR	Interquartile range
PAR	Population-attributable risk
REGARDS	REasons for Geographic and Racial Differences in Stroke
RR	Risk ratio

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Research in Context

What is already known about this subject?

- In 2010, the American Heart Association identified seven health factors/ behaviours associated with healthy ageing without cardiovascular disease, based on total cholesterol, blood pressure, fasting plasma glucose, dietary pattern, smoking, exercise and BMI

- Attainment of 2−3 and 4 ideal cardiovascular health (CVH) components vs 0−1 components has been associated with significantly lower diabetes risk

What is the key question?

- Does the associated of ideal CVH with lower diabetes risk vary by glycaemic status (normal fasting glucose vs impaired fasting glucose)?

What is the new findings?

- Participants with 2−3 and 4 vs 0−1 ideal CVH components with normal fasting glucose at baseline had 36% and 80% lower risk of diabetes, respectively

- Participants with 2−3 and 4 vs 0−1 ideal CVH components with impaired fasting glucose at baseline did not have a significantly lower risk

How might this impact on clinical practice in the foreseeable future?

- Focusing clinical practice on attainment of ideal CVH among individuals with normal blood glucose levels will dramatically reduce the burden of diabetes

- Futher research is necessary to develop best practices to prevent diabetes among individuals with impaired fasting glucose

Table 1

Characteristics of participants, by fasting glucose status in REGARDS

Characteristic	Overall n= 7,758	Normal fasting glucose (<5.6 mmol/l) n=6004	IFG (5.6–6.9 mmol/l) n=1754	p value
Age	63.0 (8.4)	62.9 (8.5)	63.4 (8.2)	0.0237
Female (%)	56.5	58.6	49.1	<0.0001
African-American (%)	26.5	24.9	32.0	<0.0001
Current smoking (%)	10.7	10.1	12.7	<0.0001
Ideal cardiovascular diet score (0–5)[a]	0.9 (0.8)	0.9 (0.8)	0.8 (0.8)	<0.0001
Current alcohol use (%)	62.1	62.4	61.1	0.0937
Education: college graduate and above (%)	46.2	47.1	42.9	0.0096
Income				0.1446
<$20k	9.9	9.5	11.1	
$20k-$34k	21.1	21.1	21.0	
$35k-$74k	34.7	34.4	35.9	
$75 and above	23.7	24.2	22.4	
Refused to give details	10.5	10.7	9.7	
History of CHD	11.5	10.8	13.7	0.0010
BMI (kg/m^2)	28.4 (5.6)	27.9 (5.4)	30.4 (5.7)	<0.0001
Waist circumference (cm)	93.0 (14.5)	91.3 (14.0)	98.9 (14.6)	<0.0001
Systolic BP (mmHg)	124.4 (15.1)	123.4 (14.9)	127.6 (15.3)	<0.0001
Diastolic BP (mmHg)	76.2 (9.1)	75.7 (9.0)	77.7 (9.2)	<0.0001
eGFR CKD-EPI (ml min^{-1} 1.73 m^{-2})	87.5 (15.9)	87.3 (15.8)	88.0 (16.5)	0.1294
Urine ACR (mg/mmol)[b]	0.69 (0.72)	0.67 (0.68)	0.73 (0.87)	<0.0001
Total cholesterol (mmol/l)	5.1 (1.0)	5.1 (1.0)	5.0 (1.0)	0.0039
Fasting glucose (mmol/l)	5.1 (0.6)	4.9 (0.4)	5.9 (0.3)	<0.0001
Statin medication usage	28.3	26.5	34.6	<0.0001
hsCRP[b]	1.8 (3.2)	1.6 (3.0)	2.4 (4.1)	<0.0001
Incident diabetes per 1000 person- years	11.5	6.0	30.4	<0.0001
Glucose[c]				<0.0001
Poor(%)	NA	NA	NA	
Intermediate (%)	22.6	0.0	100.0	
Ideal (%)	77.4	100.0	0.0	
BP[c]				<0.0001
Poor (%)	16.5	15.1	21.4	
Intermediate (%)	59.0	57.8	63.2	
Ideal (%)	24.5	27.2	15.3	
BMI[c]				<0.0001
Poor (%)	32.2	27.9	46.9	
Intermediate (%)	40.1	40.4	38.9	

Characteristic	Overall n= 7,758	Normal fasting glucose (<5.6 mmol/l) n=6004	IFG (5.6–6.9 mmol/l) n=1754	p value
Ideal (%)	27.8	31.8	14.1	
Total cholesterol[c]				0.0129
Poor(%)	11.9	12.2	10.9	
Intermediate (%)	52.5	51.6	55.6	
Ideal (%)	35.6	36.2	33.5	
Smoking[c]				0.0008
Poor (%)	10.6	10.0	12.7	
Intermediate (%)	1.4	1.3	1.9	
Ideal (%)	87.9	88.7	85.4	
Dietary intake[c]				<0.0001
Poor (%)	78.5	77.2	82.8	
Intermediate (%)	21.6	22.8	17.2	
Ideal (%)	0.0	0.0	0.0	
Physical activity[c]				0.0002
Poor(%)	27.6	26.5	31.5	
Intermediate (%)	40.1	40.7	37.9	
Ideal (%)	32.3	32.9	30.6	
Using 6 components[d]				
Total no. ideal components	2.1 (1.1)	2.2 (1.1)	1.8 (1.0)	<0.0001
0–1 ideal CVH components (%)	32.1	29.3	41.5	<0.0001
2–3 ideal CVH components (%)	57.8	58.8	54.1	
4 ideal CVH components (%)	10.2	11.9	4.4	

Data are mean (SD) or percentages

[a]Adapted for REGARDS, with one point given for: fruits and vegetables 4.5 cups/day; fish × 98 g servings per week (non-fried); fibre-rich whole grains 3 × 28 g-equivalent servings/day; sodium <1500 mg/day; and sugar-sweetened beverages 1884 kJ/week

[b]Median and interquartile range (IQR) are listed, kruskal-Wallis test used for comparsion

[c]See ESM Table 1 for description of poor, intermediate and ideal classifications for each individual CVH component

[d]Using six components, excluding glucose as a component p values were calculated using X^2 (categorical variables), ANOVA (continuous variables) and logrank test (incident diabetes)

NA, not applicable; no., number

Table 2

Diabetes RRs for baseline levels of ideal CVH

Diabetes RR	n/cases	Unadjusted	Multivariable adjusted[a]	NFG[a,b]	IFG[a,c]	White[a,d]	African-American[a,e]
By no. of ideal CVH components[f]							
0	262/64	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
1	2226/335	0.62 (0.49, 0.78)	0.71 (0.56, 0.91)	0.55 (0.38, 0.80)	0.97 (0.73, 1.29)	0.68 (0.49, 0.94)	0.71 (0.51, 1.01)
2	2816/336	0.49 (0.39, 0.62)	0.59 (0.46, 0.75)	0.45 (0.31, 0.65)	0.94 (0.70, 1.25)	0.51 (0.36, 0.71)	0.69 (0.49, 0.98)
3	1664/127	0.31 (0.24, 0.41)	0.40 (0.30, 0.52)	0.29 (0.19, 0.44)	0.82 (0.59, 1.14)	0.32 (0.22, 0.46)	0.55 (0.36, 0.83)
4	652/24	0.15 (0.10, 0.24)	0.21 (0.13, 0.32)	0.11 (0.05, 0.23)	0.81 (0.49, 1.34)	0.19 (0.11, 0.32)	0.22 (0.09, 0.54)
5	138/5	0.15 (0.06, 0.36)	0.24 (0.10, 0.58)	0.15 (0.04, 0.61)	1.01 (0.38, 2.65)	0.19 (0.07, 0.52)	0.75 (0.16, 3.62)
p for trend[g]		<0.0001	<0.0001	<0.0001	0.1009	<0.0001	0.0002
p for interaction[h]				<0.0001		0.1846	
For 0–1, 2–3 and 4 ideal CVH components							
0–1	2488/399	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
2–3	4480/463	0.64 (0.57, 0.73)	0.70 (0.62, 0.79)	0.65 (0.53, 0.80)	0.93 (0.80, 1.08)	0.61 (0.52, 0.72)	0.86 (0.71, 1.05)
4	790/29	0.23 (0.16, 0.33)	0.29 (0.20, 0.41)	0.20 (0.10, 0.37)	0.87 (0.58, 1.30)	0.27 (0.17, 0.40)	0.34 (0.16, 0.72)
p for trend[g]		<0.0001	<0.0001	<0.0001	0.1898	<0.0001	0.0037
p for interaction[h]				<0.0001		0.0338	

Data are RR with 95% CI; cases are incident cases of diabetes during the study

[a] Adjusted for age, education, sex, race, income, alcohol use, eGFR, urine ACR, hsCRP; race-stratified analyses were not adjusted for race

[b] NFG group (n total/cases) by no. ideal CVH components and for 0–1, 2–3 and 4: 0, 166/29; 1, 1594/131; 2, 2156/134; 3, 1375/53; 4, 587/8; 5, 126/2; 0–1, 1760/160; 2–3, 3531/187; and 4, 713/10

[c] IFG group (n total/cases) by no. ideal CVH components and for 0–1, 2–3 and 4: 0, 96/35; 1, 632/204; 2, 660/202; 3, 289/74; 4, 65/16; 5, 12/3; 0–1, 728/239; 2–3, 949/276; and 4, 77/19

[d] White participants (n total/cases) by no. ideal CVH components and for 0–1, 2–3 and 4: 0, 159/33; 1, 1484/198; 2, 2028/200; 3, 1330/81; 4, 570/19; 5, 132/4; 0–1, 1643/231; 2–3, 3358/281; and 4, 702/23

[e] African-American participants (n total/cases) by no. ideal CVH components and for 0–1, 2–3 and 4: 0, 103/31; 1, 742/137; 2, 788/136; 3, 334/46; 4, 82/5; 5, 6/1; 0–1, 845/168; 2–3, 1122/182; and 4, 88/6

[f] Using six components, excluding glucose as a component; there were no participants with all six components in the ideal range

[g] p for trend calculated using the logrank test

[h]
p for interaction calculated using multiplicative interaction terms and application of the likelihood ratio test: interaction between NFG and IFG and between white and African-American NFG, normal fasting glucose; no., number

Table 3

Diabetes RRs by individual categories of baseline CVH components

Component	n/cases	Overall	Overall adjusted[a]	NFG[a,b]	IFG[a,c]	White[a,d]	African- American[a,e]
BP[f]							
Poor	1280/209	1 (Reference)[f]	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate	4579/580	0.78 (0.67, 0.90)	0.81 (0.70, 0.94)	0.74 (0.59, 0.94)	0.98 (0.82, 1.16)	0.78 (0.64, 0.95)	0.85 (0.69, 1.06)
Ideal	1899/102	0.33 (0.26, 0.41)	0.39 (0.31, 0.49)	0.27 (0.18, 0.40)	0.80 (0.62, 1.04)	0.31 (0.23, 0.42)	0.63 (0.44, 0.91)
p for interaction[g]				<0.0001		0.0194	
BMI[f]							
Poor	2496/505	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate	3107/304	0.48 (0.42, 0.55)	0.52 (0.46, 0.60)	0.51 (0.41, 0.64)	0.74 (0.63, 0.87)	0.47 (0.39, 0.56)	0.63 (0.51, 0.78)
Ideal	2155/82	0.19 (0.15, 0.24)	0.23 (0.18, 0.29)	0.21 (0.15, 0.30)	0.55 (0.42, 0.72)	0.19 (0.15, 0.26)	0.34 (0.23, 0.49)
p for interaction[g]				<0.0001		0.0309	
Total cholesterol[f]							
Poor	921/94	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate	4074/476	1.14 (0.93, 1.41)	1.18 (0.96, 1.45)	1.04 (0.76, 1.42)	1.23 (0.95, 1.60)	1.23 (0.93, 1.65)	1.11 (0.82, 1.50)
Ideal	2763/321	1.14 (0.92, 1.41)	1.11 (0.90, 1.38)	0.93 (0.67, 1.29)	1.34 (1.02, 1.75)	1.15 (0.85, 1.55)	1.06 (0.78, 1.45)
p for interaction[g]				0.2946		0.7897	
Smoking[f]							
Poor	825/142	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate	112/14	0.73 (0.44, 1.21)	0.78 (0.48, 1.28)	0.95 (0.47, 1.91)	0.62 (0.32, 1.20)	0.76 (0.37, 1.54)	0.79 (0.40, 1.58)
Ideal	6821/735	0.63 (0.53, 0.74)	0.75 (0.63, 0.89)	0.67 (0.51, 0.89)	0.92 (0.75, 1.12)	0.73 (0.57, 0.93)	0.76 (0.60, 0.98)
p for interaction[g]				0.0243		0.8873	
Dietary intake[f,h]							
Poor	6086/753	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate/ideal	1672/138	0.67 (0.56, 0.79)	0.81 (0.68, 0.97)	0.77 (0.58, 1.02)	1.00 (0.82, 1.23)	0.77 (0.62, 0.97)	0.91 (0.69, 1.20)
p for interaction[g]				0.0099		0.2247	

Component	n/cases	Overall	Overall adjusted[a]	NFG[a,b]	IFG[a,c]	White[a,d]	African- American[a,e]
Physical activity[f]							
Poor	2142/279	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Intermediate	3107/343	0.85 (0.73, 0.98)	0.90 (0.78, 1.05)	1.08 (0.85, 1.39)	0.93 (0.78, 1.10)	0.82 (0.68, 1.00)	1.03 (0.82, 1.29)
Ideal	2509/269	0.82 (0.70, 0.96)	0.88 (0.75, 1.03)	1.00 (0.76, 1.30)	0.95 (0.79, 1.13)	0.80 (0.65, 0.98)	1.02 (0.80, 1.31)
p for interaction[g]				0.7359		0.3161	

RRs (95% CI) calculated using modified Poisson regression with the poor category as the reference group

[a] Adjusted for age, education, sex, race, income, alcohol use, eGFR, urine ACR, hsCRP; race-stratified analyses were not adjusted for race

[b] NFG group (n total/cases): BP, poor 904/84, intermediate 3470/237, ideal 1630/36; BMI, poor 1673/192, intermediate 2424/129, ideal 1907/36; total cholesterol, poor 730/45, intermediate 3099/184, ideal 2175/128; smoking, poor 603/60, intermediate 78/7, ideal 5323/290; dietary intake, poor 4634/303, intermediate 1370/54, ideal (0/0); physical activity, poor 1589/97, intermediate 2442/150, ideal 1973/110

[c] IFG group (n total/cases): BP, poor 376/125, intermediate 1109/343; ideal 269/66; BMI, poor 823/313; intermediate 683/175; ideal 248/46; total cholesterol, poor 191/49, intermediate 975/292, ideal 588/193; smoking, poor 222/82, intermediate 34/7, ideal 1498/445; dietary intake, poor 1452/450, intermediate 302/84, ideal (0/0); physical activity, poor 553/182; intermediate 665/193; ideal 536/159

[d] White participants (n total/cases): BP, poor 819/117, intermediate 3255/350, ideal 1629/68; BMI, poor 1533/281, intermediate 2359/198, ideal 1811/56; total cholesterol, poor 644/50, intermediate 3079/300, ideal 1980/185; smoking, poor 527/72, intermediate 73/7, ideal 5103/456; dietary intake, poor 4408/450, intermediate 1295/85, ideal (0/0); physical activity, poor 1482/162, intermediate 2275/201, ideal 1946/172

[e] African-American participants (n total/cases): BP, poor 461/92, intermediate 1324/230, ideal 270/34; BMI, poor 963/224, intermediate 748/106, ideal 344/26; total cholesterol, poor 277/44, intermediate 995/176, ideal 783/136; smoking, poor 298/70, intermediate 39/7, ideal 1718/279; dietary intake, poor 1678/303, intermediate 377/53, ideal (0/0); physical activity, poor 660/117, intermediate 832/142, ideal 563/97

[f] See ESM Table 1 for description of poor, intermediate and ideal classifications for each individual CVH component

[g] p for interaction calculated using multiplicative interaction terms and application of the likelihood ratio test: interaction between NFG and IFG and between white and African-American

[h] Combined intermediate/ideal category for dietary intake as there were no participants in the ideal category NFG, normal fasting glucose

Table 4

Risk of incident diabetes mellitus and PAR according to number of baseline ideal CVH components and categorised by level of CVH

Variable	Number of ideal CVH components at baseline[a]						
	1	2	3	4	5	2–3	4
Overall							
Participants, % (n=7662)	28.7	36.3	21.5	8.4	1.8	57.8	10.2
RR (95% CI)	0.62 (0.49, 0.78)	0.74 (0.65, 0.85)	0.55 (0.46, 0.66)	0.30 (0.20, 0.44)	0.31 (0.13, 0.74)	0.64 (0.57, 0.73)	0.30 (0.21, 0.43)
PAR% (95% CI)[b]	31 (17, 43)	18 (10, 26)	39 (29, 48)	68 (54, 79)	68 (26, 87)	19 (14, 24)	68 (55, 78)
Normal fasting glucose							
Participants, % (n=6004)	26.6	35.9	22.9	9.8	2.1	58.8	11.9
RR (95% CI)	0.47 (0.33, 0.68)	0.68 (0.55, 0.85)	0.51 (0.39, 0.68)	0.21 (0.10, 0.42)	0.26 (0.07, 1.04)	0.58 (0.48, 0.71)	0.21 (0.11, 0.40)
PAR% (95% CI)[b]	45 (26, 60)	23 (10, 35)	42 (26, 55)	77 (55, 89)	73 (0, 93)	23 (14, 31)	76 (57, 87)
IFG							
Participants, % (n=1754)	36	37.6	16.5	3.7	0.7	54.1	4.4
RR (95% CI)	0.89 (0.66, 1.18)	0.93 (0.80, 1.09)	0.81 (0.65, 1.00)	0.80 (0.52, 1.23)	0.82 (0.31, 2.19)	0.89 (0.77, 1.02)	0.80 (0.54, 1.19)
PAR% (95% CI)[b]	8 (0, 24)	4 (0, 14)	17 (0, 31)	19 (0, 47)	18 (0, 69)	6 (0, 12)	19 (0, 45)
White							
Participants, % (n=5703)	26	35.6	23.3	10	2.3	58.9	12.3
RR (95% CI)	0.64 (0.46, 0.89)	0.70 (0.59, 0.84)	0.52 (0.41, 0.65)	0.33 (0.21, 0.51)	0.32 (0.12, 0.84)	0.60 (0.51, 0.70)	0.32 (0.21, 0.48)
PAR% (95% CI)[b]	29 (8, 46)	22 (11, 31)	42 (29, 52)	65 (46, 77)	68 (16, 88)	22 (15, 29)	65 (48, 76)
African-American							
Participants, % (n=2055)	36.1	38.4	16.3	4	0.3	54.6	4.3
RR (95% CI)	0.61 (0.44, 0.85)	0.87 (0.71, 1.06)	0.74 (0.56, 0.99)	0.34 (0.15, 0.81)	0.96 (0.16, 5.77)	0.82 (0.67, 0.99)	0.38 (0.18, 0.83)
PAR% (95% CI)[b]	29 (10, 45)	9 (0, 20)	23 (1, 40)	65 (19, 85)	4 (0, 84)	9 (1, 18)	61 (16, 82)

Analyses were adjusted for age, education, sex, race, income, alcohol use, eGFR, urine ACR and hsCRP; race-stratified analyses were not adjusted for race

[a]Using six components, excluding glucose as a component; there were no participants with all six components in the ideal range

[b]Compared with participants meeting a lower number of baseline ideal CVH components or lower categorical CVH status. The PAR is the percentage of new cases of diabetes in the population attributable to not adhering to a specified number of baseline ideal CVH components