

Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa: a systematic review and meta-analysis

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Objective To assess differences between men and women in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa.

Methods In September 2011, the PubMed and Web of Science databases were searched for community-based, cross-sectional studies providing sex-specific prevalences of any of the three study conditions among adults living in parts of sub-Saharan Africa (i.e. in Eastern, Middle and Southern Africa according to the United Nations subregional classification for African countries). A random-effects model was then used to calculate and compare the odds of men and women having each condition.

Findings In a meta-analysis of the 36 relevant, cross-sectional data sets that were identified, impaired fasting glycaemia was found to be more common in men than in women (OR: 1.56; 95% confidence interval, CI: 1.20–2.03), whereas impaired glucose tolerance was found to be less common in men than in women (OR: 0.84; 95% CI: 0.72–0.98). The prevalence of diabetes mellitus – which was generally similar in both sexes (OR: 1.01; 95% CI: 0.91–1.11) – was higher among the women in Southern Africa than among the men from the same subregion and lower among the women from Eastern and Middle Africa and from low-income countries of sub-Saharan Africa than among the corresponding men.

Conclusion Compared with women in the same subregions, men in Eastern, Middle and Southern Africa were found to have a similar overall prevalence of diabetes mellitus but were more likely to have impaired fasting glycaemia and less likely to have impaired glucose tolerance.

Abstracts in **عربي, 中文, Français, Русский and Español** at the end of each article.

Introduction

Increasing urbanization and the accompanying changes in lifestyle are leading to a burgeoning epidemic of chronic non-communicable diseases in sub-Saharan Africa.^{1,2} At the same time, the prevalence of many acute communicable diseases is decreasing.^{1,2} In consequence, the inhabitants of sub-Saharan Africa are generally living longer and this increasing longevity will result in a rise in the future incidence of noncommunicable diseases in the region.^{1–3}

Diabetes mellitus is one of the most prominent noncommunicable diseases that are undermining the health of the people in sub-Saharan Africa and placing additional burdens on health systems that are often already strained.^{4,5} In 2011, 14.7 million adults in the African Region of the World Health Organization (WHO) were estimated to be living with diabetes mellitus.⁶ Of all of WHO's regions, the African Region is expected to have the largest proportional increase (90.5%) in the number of adult diabetics by 2030.⁶

Sex-related differences in lifestyle may lead to differences in the risk of developing diabetes mellitus and, in consequence, to differences in the prevalence of this condition in women and men.³ However, the relationship between a known risk factor for diabetes mellitus – such as obesity – and the development of symptomatic diabetes mellitus may not be simple. For example, in many countries of sub-Saharan Africa, women are more likely to be obese or overweight than men and might therefore be expected to have higher prevalences of diabetes mellitus.^{3,7} Compared with the corresponding men, women in Cameroon⁸, South Africa⁹ and Uganda¹⁰ were indeed found

to have higher prevalences of diabetes mellitus. However, women in Ghana,¹¹ Nigeria,¹² Sierra Leone¹³ and rural areas of the United Republic of Tanzania¹⁴ were found to have lower prevalences of diabetes mellitus than the men in the same study areas. No significant differences between men and women in the prevalence of diabetes mellitus were detected in studies in Guinea,¹⁵ Mali,¹⁶ Sudan¹⁷ and urban areas of the United Republic of Tanzania,¹⁸ or in a meta-analysis of data collected in several studies in West Africa.¹⁹ Although wide variations in the distribution of diabetes mellitus by sex have been documented in several review articles,^{3–5,7,20} the possible causes of this heterogeneity have never been examined in detail.

Like obesity, impaired fasting glycaemia and impaired glucose tolerance appear to be risk factors in the development of diabetes mellitus.^{21,22} According to the International Diabetes Federation, the estimated age-adjusted prevalence of impaired fasting glycaemia in WHO's African Region was substantially higher in 2011 than the corresponding global mean value – 9.7% versus 6.5%, respectively – and is expected to have risen further by 2030.²³

Impaired fasting glycaemia and impaired glucose tolerance are reported to be metabolically distinct entities that affect different subpopulations, albeit with some degree of overlap.^{22,24} In Mauritius, the prevalence of impaired fasting glycaemia was found to be significantly higher in men than in women, whereas the prevalence of impaired glucose tolerance was found to be higher in women than in men.^{24,25}

Differences between men and women in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in much of sub-Saharan Africa have yet

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Table 1. Countries comprising sub-Saharan Africa, by African subregion^a

Subregion			
Eastern	Middle	Southern	Western
Burundi	Angola	Botswana	Benin
Comoros	Cameroon	Lesotho	Burkina Faso
Djibouti	Central African Republic	Namibia	Cape Verde
Eritrea	Chad	South Africa	Côte d'Ivoire
Ethiopia	Congo	Swaziland	Gambia
Kenya	Democratic Republic of the Congo		Ghana
Madagascar	Equatorial Guinea		Guinea-Bissau
Malawi	Gabon		Liberia
Mauritius	Sao Tome and Principe		Mali
Mozambique			Mauritania
Rwanda			Niger
Seychelles			Nigeria
Somalia			Senegal
Sudan			Sierra Leone
Uganda			Togo
United Republic of Tanzania			
Zambia			
Zimbabwe			

^a As designated by the United Nations.⁶

Box 1. Strategy followed in searching PubMed and the Web of Science

Various medical subject headings (MeSH) and search terms, including "prevalence", "incidence", "epidemiology", "proportion", "rate", "diabetes mellitus", "hyperglycaemia", "abnormal* blood glucose", "glucose intolerance", "dysglycaemia", "insulin resistance", "metabolic* syndrome", "insulin resistance syndrome X", "cardiovascular syndrome", "hypertension", "increase* blood pressure", "obesity", "overweight", "hypercholesterolaemia", "hyperlipidaemia", "dyslipidaemia", "physical inactivity", "smoking", "cardiovascular diseases risk factors" and "Africa South of the Sahara" – and alternative spellings such as "hyperglycemia" were used. Searches were combined with the names of each country in Eastern, Middle and Southern Africa (Table 1) – except Cameroon, which was included in a previous study on West Africa³⁴ – by using the Boolean operators "OR" or "AND".

to be reviewed. Given the variation in health care, culture, environment, human behaviour and other determinants of health across sub-Saharan Africa,²⁶ the conclusions drawn from a recent meta-analysis of data from West Africa¹⁹ should not be assumed to apply to the whole of sub-Saharan Africa. The sex-specific prevalence of at least one risk factor for diabetes mellitus – obesity – is known to differ across different parts of sub-Saharan Africa.^{7,27}

The main aims of the present systematic review were to examine differences between men and women in the prevalence of three conditions – diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance – in Eastern, Middle and Southern Africa (i.e. all in sub-Saharan Africa according to the United Nations subregional classification for African countries),²⁸ and to explore the possible

causes of any variation observed. We followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group's guidelines for the reporting of systematic reviews of observational studies.²⁹

Methods

Data sources

In September 2011, we searched PubMed and Web of Science for studies that presented the sex-specific prevalences of diabetes mellitus, impaired fasting glycaemia and/or impaired glucose tolerance in Eastern, Middle and/or Southern Africa (Table 1). The medical subject headings (MeSH) and search terms we used are described in Box 1. We limited our search to human studies but placed no restrictions on the language of publication. We also used Google, Google Scholar and WHO's InfoBase to search

the "grey" literature for relevant studies and reports. The citations in articles that appeared to be relevant were examined for other articles that might hold useful data. When it seemed possible that relevant data had been recorded but not published, the authors of published study reports were contacted via e-mail to see if they could provide such data.

Inclusion and exclusion criteria

Data were included in the meta-analysis if they came from studies that fulfilled all of the following criteria:

- community-based;
- cross-sectional;
- reported prevalence of diabetes mellitus, impaired fasting glycaemia and/or impaired glucose tolerance;
- reported either odds ratios (ORs) for differences between men and women in the prevalence of diabetes mellitus, impaired fasting glycaemia and/or impaired glucose tolerance or data that allowed the computation of such ORs;
- conducted in apparently healthy, non-pregnant subjects;
- most subjects are adults (i.e. aged ≥ 15 years) and residing in the UN-designated Eastern, Middle or Southern subregions of Africa;
- both men and women investigated;
- employed any of WHO's diagnostic criteria – or the equivalent criteria of the American Diabetic Association – for diabetes mellitus, impaired fasting glycaemia and/or impaired glucose tolerance;^{34–38}
- reported results either in English or in another language with an abstract in English.

When multiple reports of the same study were retrieved, only the most informative report was selected. Clinic-, hospital- and laboratory-based studies, anonymous reports, letters, commentaries, case studies and reviews were excluded.

Data abstraction

After reading each article that appeared relevant and met the inclusion criteria, one of the authors (EHH) made notes of the year of study and publication, sampling method, sample size, response rate, study design, diagnostic criteria, study area, mean age and/or age range of the subjects, mean blood glucose level, the recorded prevalences of diabetes mellitus, impaired fasting glycaemia and/or

or impaired glucose tolerance, and, if available, the OR and corresponding 95% confidence intervals (CIs) that indicated the type and significance of any differences in these prevalences by sex. When articles presented data separately for urban and rural subjects, information for these two groups of subjects was extracted separately. When articles presented data stratified by subject age, only the data for subjects aged 15 years or older were included in the analysis. All of the extracted data were independently reviewed by a second author (HY).

Quality appraisal

A checklist – adopted from one created by the University of Wisconsin³⁹ – was used to assess the quality of the included studies. The checklist had eight questions relating to the research question, selection of study subjects, comparability of study groups, handling of withdrawals, measurement of outcomes, statistical analyses, results and conclusions, and funding or sponsorship. If the answers to five or more of these questions were positive, the study involved was categorized as “positive” and considered to be of good quality. If the answers to five or more of these questions were negative, the study involved was categorized as “negative” and considered to be of poor quality. All other studies were categorized as “neutral”.

Statistical analysis

ORs were used as “effect estimates” to quantify the relationship between sex and the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance. If no OR had been reported, it was calculated from the raw data. Since the studies included in the meta-analysis used different standard populations, crude prevalences were preferred to the age-adjusted values when both were available. The DerSimonian and Laird random-effects model was used to estimate the mean OR for all of the studies included in the meta-analysis.⁴⁰

Statistical heterogeneity across the studies was evaluated using both the *Q* and *I*² statistics.⁴⁰ In the *Q*-tests, a *P*-value of < 0.1 was considered indicative of statistically significant heterogeneity. We performed subgroup analyses to assess the potential influence of the following study-level covariates on the OR for any sex-specific differences: area of residence (urban or rural), subgroup

of residence in sub-Saharan Africa (i.e. Eastern, Middle or Southern Africa), study year, ethnicity of the study subjects, and the World-Bank-determined income level of the study country.⁴¹ Random-effects univariate meta-regression analysis⁴⁰ was also performed as an extension of the subgroup analyses.

The potential influence of each individual study on the overall summary estimates was assessed by rerunning the meta-analysis while omitting one study at a time. Sensitivity analysis was performed to assess the impact of the quality of the studies on the overall effect estimates. For those studies that reported both crude and age-adjusted prevalences, we also assessed if the effect estimates would have been substantially altered if the age-adjusted values had been used instead of the crude ones.

Publication bias⁴⁰ was assessed using a funnel plot to examine the relationship between the effect size and study precision. Begg and Mazumdar's rank-correlation test⁴⁰ was then used to test this relationship statistically. Finally, Duval and Tweedie's “trim and fill” analysis was used to assess the possible impact of publication bias on the effect size.⁴⁰

Version 2 of the Comprehensive Meta-Analysis software package (Biostat, Englewood, United States of America) was used for all of the statistical analyses. All statistical tests were two-sided. A *P*-value of < 0.05 was generally considered indicative of statistical significance.

Results

Literature search

Although the PubMed and Web of Science searches revealed 5129 potentially useful reports, only 25 of these reports were found to satisfy all of the inclusion criteria (Fig. 1). Four additional reports that met all of the inclusion criteria were identified via a Google search (*n* = 2), a search of the WHO InfoBase (*n* = 1) or contact with authors (*n* = 1). The meta-analysis therefore included data from 29 reports that, together, covered 36 studies in which cross-sectional data were collected.^{14,17,42–68}

Study characteristics

Table 2 (available at: <http://www.who.int/bulletin/volumes/91/9/12-113415>) provides detailed descriptive information for the 36 studies included in the

meta-analysis. These studies involved 75 928 subjects and were conducted between 1983 and 2009 in Angola, the Democratic Republic of the Congo, Kenya, Malawi, Mauritius, Mozambique, Seychelles, South Africa, Sudan, Uganda, the United Republic of Tanzania, Zambia or Zimbabwe. Most (92%) of the studies included in the meta-analysis employed probability- or census-sampling techniques and had response rates of 62–99%. Sex-specific prevalences of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance were included in the reports of 35, 21 and 11 of the studies, respectively. Almost half (45%) of the studies were conducted in both urban and rural areas. The other studies were conducted exclusively in urban (26%), rural (23%) or periurban (6%) areas. In terms of quality, the studies were categorized as either “positive” (*n* = 31) or “neutral” (*n* = 5)^{42,49,58,61,63} (Appendix A, available at: <http://www.med.nagoya-u.ac.jp/intnl-h/swfu/d/auto-UZzMJC.pdf>).

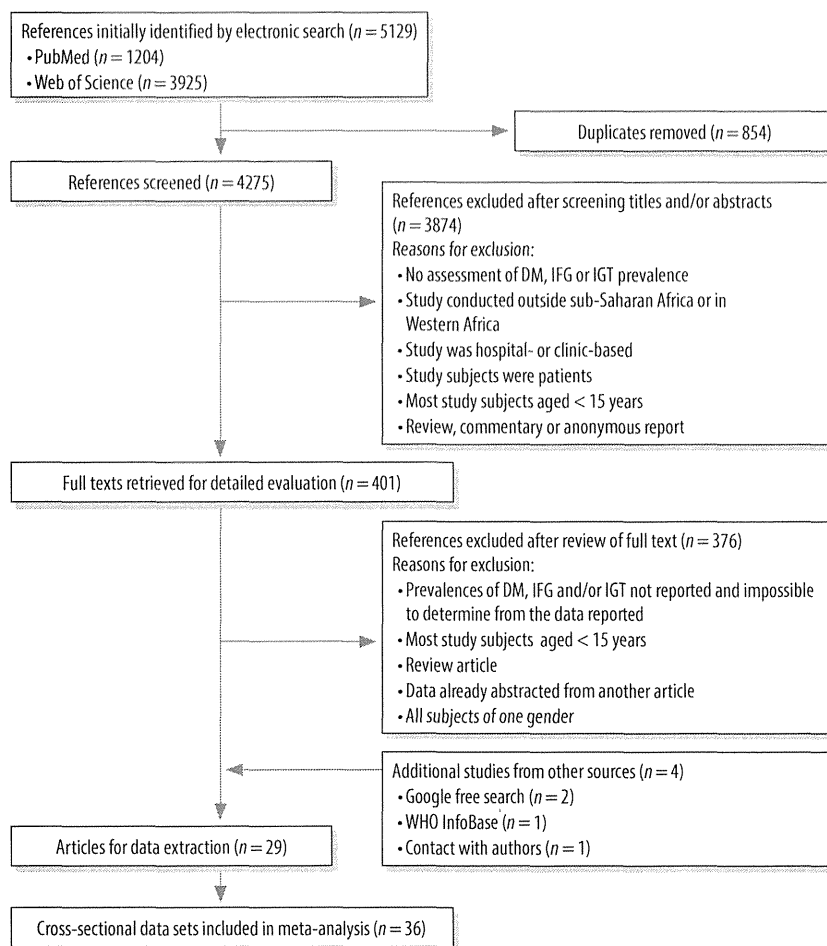
Sex-specific prevalences

The prevalence of diabetes mellitus was 5.7% (95% CI: 4.8–6.8) overall, with a slight difference between the men (5.5%; 95% CI: 4.1–7.2) and women (5.9%; 95% CI: 4.6–7.6) included in the meta-analysis. The prevalence of impaired fasting glycaemia was 4.5% (95% CI: 3.3–6.1) overall – 5.7% (95% CI: 3.7–8.6) among the men and 3.5% (95% CI: 2.1–5.8) among the women – whereas the prevalence of impaired glucose tolerance was 7.9% (95% CI: 6.7–9.2) overall – 7.3% (95% CI: 6.0–8.8) among the men and 8.5% (95% CI: 6.7–10.7) among the women.

Odds ratios

The prevalence of diabetes mellitus among men was not significantly different from that among women (OR: 1.01; 95% CI: 0.91–1.11). However, impaired fasting glycaemia appeared to be significantly more common among men than among women (OR: 1.56; 95% CI: 1.20–2.03), whereas impaired glucose tolerance appeared to be significantly less common among men than among women (OR: 0.84; 95% CI: 0.72–0.98) (Fig. 2). These significant differences between the sexes were still observed when the analysis was restricted to those studies in which the prevalences of both impaired fasting glycaemia and impaired glucose tolerance were

Fig. 1. Flow diagram of the study selection procedure



DM, diabetes mellitus; IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance.

determined in the same study cohorts (data not shown). A moderate to substantial level of heterogeneity between studies was detected in the data for diabetes mellitus ($I^2 = 54.62\%$; $P < 0.001$ in Q-test), impaired fasting glycaemia ($I^2 = 85.38\%$; $P < 0.001$ in Q-test) and impaired glucose tolerance ($I^2 = 74.13\%$; $P < 0.001$ in Q-test).

Subgroup analyses

Table 3 summarizes the results of the subgroup analyses. Significant heterogeneity in the OR for diabetes mellitus was observed by area of residence (i.e. urban or rural), subregion of residence in Africa, ethnicity of the study subjects, and country income level – each of which gave a P -value of < 0.05 in a Q-test. The prevalence of diabetes mellitus was found to be significantly higher in men than in women in studies conducted in a mix of urban and rural areas, in Middle or Eastern Africa or in low-income countries. However, in

studies conducted in Southern Africa or among subjects of Indian ethnicity, the prevalence of diabetes mellitus was significantly higher among women than among the corresponding men.

Significant heterogeneity in the OR for impaired fasting glycaemia was observed by subregion of residence in Africa ($P = 0.02$) and country income level ($P = 0.006$). In studies conducted in Eastern Africa or upper-middle-income countries, impaired fasting glycaemia appeared to be significantly more common among men than among women.

With impaired glucose tolerance, significant heterogeneity in the OR was observed by area of residence ($P < 0.001$), subregion of residence in Africa ($P = 0.001$), ethnicity ($P = 0.002$), and country income level ($P = 0.03$). The odds of impaired glucose tolerance were found to be higher in men than in women in studies conducted on urban residents or subjects of Indian ethnicity.

Meta-regression

In general, the univariate random-effects meta-regression revealed similar associations – between the OR and study-level covariates – as seen in the subgroup analyses (Appendix A). For example, the OR for the sex-specific prevalences of diabetes mellitus appeared to be significantly affected by area of residence (rural versus urban; $P = 0.018$), subregion of residence in Africa (Southern and Middle Africa versus Eastern Africa; $P < 0.001$), ethnicity of the study subjects (multi-ethnic versus Indian; $P = 0.013$), study year (1990s versus 2000s; $P = 0.039$), and country income level (low versus upper middle; $P < 0.001$). Subregion of residence (Eastern versus Southern Africa; $P = 0.047$) and country income level (low versus upper-middle; $P = 0.006$) also had a significant effect on the OR for impaired fasting glycaemia, whereas subregion of residence (Eastern versus Southern Africa; $P < 0.001$), ethnicity of study subjects (multi-ethnic versus Indian; $P < 0.001$), country income level (low versus upper-middle; $P < 0.001$), and area of residence – both rural versus urban ($P < 0.001$) and rural versus urban and rural combined ($P = 0.003$) – had significant effects on the OR for impaired glucose tolerance.

Sensitivity and influence analyses

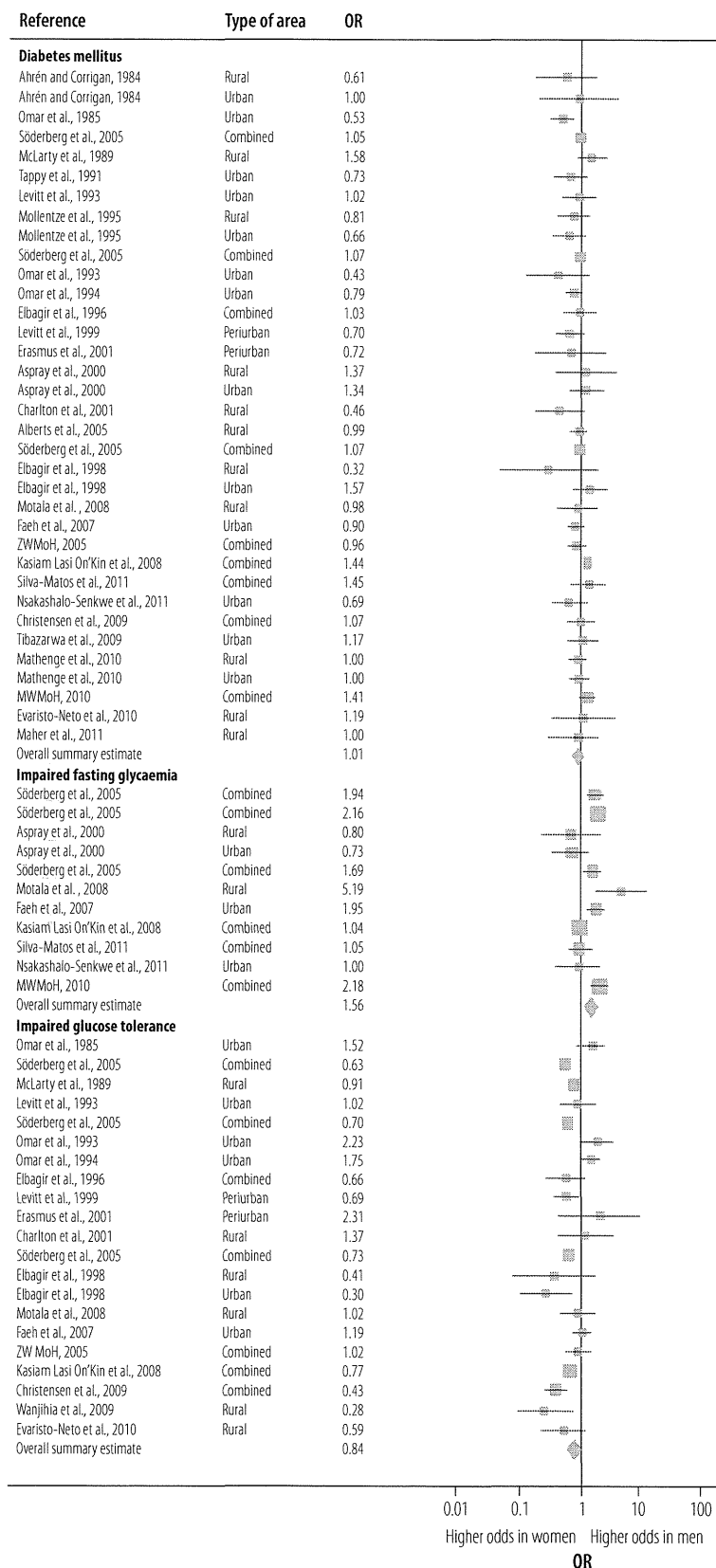
No meaningful change in the OR was evident when the meta-analysis was rerun either with the data from the five studies of “neutral” quality omitted or using age-adjusted prevalences instead of the crude values (data not shown).

The results of the influence analysis indicated that the omission of the data from any of seven studies – described in five reports^{43,44,47,48,57} – could eliminate the statistical significance of the overall differences between men and women in the prevalence of impaired glucose tolerance. However, even when the data from one of these studies were omitted, women still showed a higher prevalence of impaired glucose tolerance than the corresponding men, with a P -value of > 0.05 but < 0.1 . The pooled results for diabetes or impaired fasting glycaemia were not substantially affected by the omission of the data from any one study.

Publication bias

The funnel plots for diabetes mellitus and impaired fasting glycaemia were asymmetric, indicating possible publi-

Fig. 2. Forest plot of main meta-analysis results, showing sex-specific odds ratios for diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa



DM, diabetes mellitus; IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance; MW MoH, Malawi Ministry of Health; OR, odds ratio; ZW MoH, Zimbabwe Ministry of Health and Child Welfare. Note: The ORs shown are for differences in prevalence between the sexes (i.e. odds in men versus odds in women). For each study, the plot indicates the mean OR (midpoint of the square), the corresponding 95% confidence interval (horizontal lines) and the weight given to the study (area of the square).

tion bias. However, the corresponding results from Begg and Mazumdar's rank-correlation tests – *P*-values of 0.93 and 0.64, respectively – were not statistically significant. Duval and Tweedie's “trim and fill” analysis indicated that the meta-analysis would have benefitted from the inclusion of data from more studies – nine for diabetes mellitus and one for impaired fasting glycaemia – and that, if the asymmetry seen in the funnel plots was the result of publication bias, the summary estimates of the sex-specific (i.e. men versus women) OR for diabetes mellitus and impaired fasting glycaemia should be 1.09 (95% CI: 0.98–1.20) and 1.65 (95% CI: 1.27–2.14), respectively (Appendix A).

There were no indications of publication bias in the data on impaired glucose tolerance.

Discussion

To our knowledge, this study is the first systematic review of possible associations between sex and the prevalences of impairments in glucose tolerance and fasting glycaemia in Eastern, Middle and Southern Africa. Previous narrative reviews have reported on the prevalence of diabetes mellitus and, briefly, on the variation in the sex distribution of this illness in sub-Saharan Africa.^{3–5,7,20} However, there appears to have been only one previous meta-analysis of data on the prevalence of diabetes mellitus in sub-Saharan Africa and that was limited to data collected in West Africa.¹⁹

The present results reveal considerable between-country variation in the prevalence of diabetes mellitus among adults. However, the relatively high value recorded for all of the studies combined (5.7%) is a reflection of the rapid transition – from a predominance of communicable disease to one of non-communicable disease – that much of sub-Saharan Africa is facing. In this vast area of Africa, important risk factors for diabetes mellitus, such as impaired glucose tolerance, appear to be increasing in prevalence while humans are tending to live longer. The prevalence of diabetes mellitus in sub-Saharan Africa will therefore probably rise further unless prevention efforts are intensified.²³

In the present meta-analysis – as in most^{22,24,69} – but not all⁷⁰ – previous studies on this risk factor for diabetes mellitus – impaired fasting glucose was found to be significantly more common among

Table 3. Pooled odds ratios (ORs)^a for diabetes mellitus and two associated risk factors

Variable	Diabetes mellitus			Impaired fasting glycaemia			Impaired glucose tolerance		
	n ^b	OR (95% CI)	P ^c	n ^b	OR (95% CI)	P ^c	n ^b	OR (95% CI)	P ^c
All data sets	35	1.01 (0.91–1.11)		11	1.56 (1.20–2.03)		21	0.84 (0.72–0.98)	
Area of residence			0.009			0.56			<0.001
Combined	9	1.17 (1.04–1.31)		6	1.61 (1.14–2.26)		7	0.69 (0.59–0.81)	
Periurban	2	0.70 (0.42–1.18)					2	0.79 (0.46–1.37)	
Rural	11	0.98 (0.80–1.20)		2	2.21 (0.87–5.64)		6	0.82 (0.61–1.09)	
Urban	13	0.86 (0.73–1.01)		3	1.24 (0.71–2.19)		6	1.33 (1.03–1.72)	
Subregion of residence			<0.001			0.019			0.001
Middle Africa	2	1.44 (1.31–1.59)		1	1.04 (0.65–1.65)		2	0.73 (0.49–1.09)	
Eastern Africa	21	1.08 (1.01–1.15)		9	1.65 (1.35–2.02)		11	0.71 (0.59–0.84)	
Southern Africa	12	0.80 (0.69–0.92)		1	5.19 (1.75–15.38)		8	1.30 (0.99–1.70)	
Ethnicity of subjects			0.012			0.066			0.002
African	24	1.12 (1.00–1.25)		7	1.30 (0.96–1.74)		11	0.81 (0.66–0.99)	
Indian	2	0.69 (0.52–0.94)					2	1.66 (1.10–2.50)	
Multi-ethnic	9	1.00 (0.87–1.14)		4	1.93 (1.42–2.62)		8	0.73 (0.60–0.89)	
Study year			0.125			0.81			0.61
Before 1991	9	0.90 (0.73–1.11)		1	1.94 (0.84–4.48)		4	0.90 (0.62–1.31)	
1991–1999	13	0.96 (0.83–1.12)		4	1.41 (0.88–2.27)		10	0.90 (0.68–1.19)	
After 1999	13	1.13 (0.99–1.30)		6	1.58 (1.09–2.30)		7	0.74 (0.55–1.01)	
Country income level			0.008			0.006			0.028
Low	14	1.21 (1.06–1.37)		6	1.18 (0.89–1.57)		5	0.70 (0.52–0.95)	
Lower middle	4	1.16 (0.75–1.80)					4	0.50 (0.29–0.87)	
Upper middle	17	0.93 (0.83–1.03)		5	2.05 (1.56–2.69)		12	0.99 (0.80–1.23)	

CI, confidence interval.

^a ORs represent the odds in men versus the odds in women.^b Number of data sets included in the analysis.^c P-value for the category, estimated in a Q-test.

men than among women, irrespective of the subgroup that was investigated. One possible explanation for this difference is that men tend to have lower hepatic sensitivity to insulin and may, in consequence, have generally higher fasting levels of plasma glucose.⁶⁹ Another possible explanation or contributing factor is that, within sub-Saharan Africa, men are more likely to smoke than women⁷¹ and smoking appears to increase the risk of impaired fasting glucose, by decreasing insulin sensitivity.^{72–74}

In earlier research, impaired glucose tolerance has generally been found to be more common among women than among men.^{22,24,69} The same difference between the sexes was detected in most of the subgroups that were investigated in the present meta-analysis. In general, women have a smaller mass of muscle than men and therefore less muscle available for the uptake of the fixed glucose load (75 g) used in the oral glucose-tolerance test.^{69,75} Women also have relatively high levels of estrogen

and progesterone, both of which can reduce whole-body insulin sensitivity.⁷⁶ Physical inactivity⁷⁷ and unhealthy diet⁷⁸ have also both been associated with impaired glucose tolerance. In many countries in sub-Saharan Africa, women are more likely to be physically inactive than the corresponding men.^{79,80}

The differences in the sex distribution of both impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa need to be considered in evaluating the probability that individuals will develop diabetes mellitus and in efforts to prevent the disease. Impairments in glucose tolerance and in fasting glycaemia are not metabolically equivalent, and the people classified as having each condition are different as well.^{22,81} If screening programmes were based only on the measurement of “fasting plasma glucose”, most individuals with impaired glucose tolerance would go undetected and the population identified as being at risk would probably be biased towards males. The glycated

haemoglobin (HbA1c) assay⁶⁹ may offer a way of evaluating the risk of diabetes mellitus that is relatively sex-neutral, although this assay is currently too expensive for routine use in Africa and it can also be affected by disorders such as malaria.⁸² Screening for both impaired fasting glycaemia and impaired glucose tolerance might eliminate most of the sex bias in the identification of those who are at risk of developing diabetes mellitus. Even then, the dose of glucose used in the oral glucose-tolerance test may have to be made lower for women than for men – or tailored to the height of the individual to be tested – to allow for the lower mean muscle mass in women and so prevent the over-diagnosis of impaired glucose tolerance in women.⁷²

In the present meta-analysis, despite the differences seen by sex in impaired fasting glycaemia and impaired glucose tolerance, the overall prevalence of diabetes mellitus in men was found to be very similar to that in women. However, subgroup analyses revealed

that diabetes mellitus was more common in the men who lived in Middle and Eastern Africa than in the women who lived in the same African subregions, whereas the women who lived in Southern Africa were more likely to have diabetes mellitus than the corresponding men. Such differences between the sexes were not seen in the earlier study on diabetes mellitus in West Africa.¹⁹ Some of these differences may be related to differences between the sexes in the prevalence of central obesity, which, as a risk factor for diabetes mellitus, is more predictive than peripheral obesity.⁸³ Central obesity has been found to be more common in men than in women in Eastern Africa^{84,85} and more common in women than men in Southern Africa.⁸⁶ However, such obesity cannot be used to explain why the men of Middle Africa are more likely to have diabetes mellitus than the women, as central obesity is more common among the women in this area than among the men.⁸⁷ Behavioural risk factors, such as smoking and alcohol use, which are more common among the men of sub-Saharan Africa than among the women,^{3,71} might contribute to the prevalence of diabetes mellitus among the men of Middle Africa.

In the present meta-analysis, the income level of the country of residence – a proxy indicator of the economic status of the people in the country – appeared to contribute to the heterogeneity seen in the association between sex and the prevalence of diabetes mellitus. Women of low socioeconomic status in Australia,⁸⁸ Canada,⁸⁹ Germany⁹⁰ and the United States of America⁹¹ appear to be at markedly higher risk of diabetes mellitus than the corresponding men. In a recent meta-analysis, the incidence of Type 2 diabetes mellitus among adults with low socioeconomic status was found to be generally higher in women than in men; it was suggested that the women who lived in impoverished areas were more likely to be obese, physically inactive and under high levels of psychosocial stress than the men in the same areas.⁹² In contrast, the results of the present meta-analysis indicated that men who lived in the low-income countries of sub-Saharan Africa were more likely to be diagnosed with diabetes mellitus than the corresponding

women. This difference between the sexes may be a consequence of differences between men and women in the distribution of risk factors for diabetes mellitus (e.g. obesity, physical inactivity, poor diet and smoking, etc.) in low-income countries. Another possibility is that women in low-income countries have particularly poor access to health-care services and therefore little chance of being diagnosed with diabetes.^{88,89,91,92} In addition, as Africa is one of the most inequitable parts of the world in terms of income,⁹³ the income level recorded for an African country might not correlate with the socioeconomic status of a study cohort in that country. There appear to be no published data sets that would allow sex-based differences in the relationship between individual socioeconomic status and diabetes mellitus in sub-Saharan Africa to be investigated.

The present meta-analysis had several limitations. First, the studies that provided the data for the meta-analysis were conducted under different circumstances in different countries and the prevalences of diabetes mellitus, impaired fasting glycaemia and/or impaired glucose tolerance were not the primary outcomes of some of the studies. A random-effects model was therefore employed to embrace this considerable heterogeneity.⁴⁰ Second, the studies had to be cross-sectional in design to be included in the meta-analysis and may therefore have been affected by confounding and biases. However, we attempted to minimize selection bias by employing predefined study selection criteria and a quality appraisal checklist. Potential sources of heterogeneity were also assessed in subgroup and meta-regression analyses. Third, since our subgroup and meta-regression analyses were entirely observational in nature, the relationships recorded – across all of the studies – between some study-level characteristics and the effect estimate could be subject to confounding by other study-level characteristics. Unfortunately, the studies included in the meta-analysis were too few to allow for a reasonable assessment of interactions between the study-level covariates. Fourth, we used the income levels of the countries of residence to stratify the studies because of a general lack of infor-

mation on the socioeconomic status of study participants. The relationships that we observed between a country's income level and the sex-specific prevalences of interest may therefore not reflect the relationships between the socioeconomic status of the subjects and their risks of impaired fasting glycaemia, impaired glucose tolerance or diabetes mellitus. Finally, our conclusions may have been affected by publication bias. The asymmetric funnel plots were indicative of possible publication bias in the data for diabetes mellitus and impaired fasting glucose. Furthermore, our study selection criteria excluded reports that did not have an abstract in English and may have excluded some reports that were not recorded in the PubMed or Web of Science databases, although we did try to search the "grey" literature for relevant data. The results of the "trim and fill" analyses indicated that the impact of any publication bias on our conclusions was probably trivial.

In summary, our meta-analysis demonstrated that, compared with the corresponding women, the men in Eastern, Middle and Southern Africa had a significantly higher prevalence of impaired fasting glycaemia and a lower prevalence of impaired glucose tolerance. Although the overall prevalence of diabetes mellitus did not significantly differ by sex, the prevalence of diabetes mellitus was found to be lower or higher in women than in men when analysed by African subregion. Sex-based differences in the relationship between individual socioeconomic status and impaired fasting glycaemia, impaired glucose tolerance and diabetes mellitus still need to be investigated in sub-Saharan Africa. Our observations may help in the targeting of appropriate – and perhaps sex-specific – interventions to prevent diabetes mellitus in sub-Saharan Africa. ■

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ملخص

دور الاختلافات حسب الجنس في معدل انتشار داء السكري، واختلال سكر الدم مع الصيام واختلال تحمل الجلوكوز في أفريقيا جنوب الصحراء الكبرى: استعراض منهجي وتحليل وصفي

2.03)، في حين تم التوصل إلى أن اختلال تحمل الجلوكوز أقل شيوعاً لدى الرجال عنه لدى النساء (نسبة الاحتمال: 0.84؛ فاصل الثقة 95٪: من 0.98 إلى 0.72) وكان معدل انتشار داء السكري - الذي تشابه عموماً في كلا الجنسين (نسبة الاحتمال: 1.01؛ فاصل الثقة 95٪: من 0.91 إلى 1.11) - أعلى بين النساء في أفريقيا الجنوبية عنه بين الرجال من نفس المنطقة دون الإقليمية وأقل بين النساء من أفريقيا الشرقية والوسطى ومن بلدان أفريقيا جنوب الصحراء الكبرى المنخفضة الدخل عنه بين الرجال المقابلين لهم.

الاستنتاج مقارنة بالنساء من نفس المناطق دون الإقليمية، تم التوصل إلى أن الرجال في أفريقيا الشرقية والوسطى والجنوبية لديهم معدل انتشار عام مشابه لداء السكري غير أنه ازدادت لديهم احتمالية الإصابة باختلال سكر الدم مع الصيام في حين قلت لديهم احتمالية الإصابة باختلال تحمل الجلوكوز.

الغرض تقييم الاختلافات بين الرجال والنساء في معدل انتشار داء السكري، واختلال سكر الدم مع الصيام واختلال تحمل الجلوكوز في أفريقيا جنوب الصحراء الكبرى.

الطريقة في أيلول/سبتمبر 2011، تم البحث في قواعد بيانات PubMed و Web of Science عن الدراسات المجتمعية متعددة القطاعات التي تقدم معدلات انتشار لأي من حالات الدراسة الثلاث بين البالغين الذين يسكنون مناطق من أفريقيا جنوب الصحراء الكبرى (أي في أفريقيا الشرقية والوسطى والجنوبية وفقاً لتصنيف المنطقة دون الإقليمية للبلدان الأفريقية حسب الأمم المتحدة). وتم استخدام نموذج التأثيرات العشوائية لحساب الاحتمالات بين الرجال والنساء في كل حالة.

النتائج في تحليل وصفي لثلاث البيانات متعددة القطاعات ذات الصلة التي تم تحديدها البالغ عددها 36 فئة، تم التوصل إلى أن اختلال سكر الدم مع الصيام أكثر شيوعاً لدى الرجال عنه لدى النساء (نسبة الاحتمال: 1.56؛ فاصل الثقة 95٪: من 1.20 إلى

الخلاصة

الخلاصة: الاختلافات بين الجنسين في معدل انتشار داء السكري، واختلال سكر الدم مع الصيام واختلال تحمل الجلوكوز في أفريقيا جنوب الصحراء الكبرى: استعراض منهجي وتحليل وصفي

الغرض تقييم الاختلافات بين الرجال والنساء في معدل انتشار داء السكري، واختلال سكر الدم مع الصيام واختلال تحمل الجلوكوز في أفريقيا جنوب الصحراء الكبرى.

الطريقة في أيلول/سبتمبر 2011، تم البحث في قواعد بيانات PubMed و Web of Science عن الدراسات المجتمعية متعددة القطاعات التي تقدم معدلات انتشار لأي من حالات الدراسة الثلاث بين البالغين الذين يسكنون مناطق من أفريقيا جنوب الصحراء الكبرى (أي في أفريقيا الشرقية والوسطى والجنوبية وفقاً لتصنيف المنطقة دون الإقليمية للبلدان الأفريقية حسب الأمم المتحدة). وتم استخدام نموذج التأثيرات العشوائية لحساب الاحتمالات بين الرجال والنساء في كل حالة.

النتائج في تحليل وصفي لثلاث البيانات متعددة القطاعات ذات الصلة التي تم تحديدها البالغ عددها 36 فئة، تم التوصل إلى أن اختلال سكر الدم مع الصيام أكثر شيوعاً لدى الرجال عنه لدى النساء (نسبة الاحتمال: 1.56؛ فاصل الثقة 95٪: من 1.20 إلى

التأثيرات العشوائية لحساب الاحتمالات بين الرجال والنساء في كل حالة. النتائج في تحليل وصفي لثلاث البيانات متعددة القطاعات ذات الصلة التي تم تحديدها البالغ عددها 36 فئة، تم التوصل إلى أن اختلال سكر الدم مع الصيام أكثر شيوعاً لدى الرجال عنه لدى النساء (نسبة الاحتمال: 1.56؛ فاصل الثقة 95٪: من 1.20 إلى

النتائج في تحليل وصفي لثلاث البيانات متعددة القطاعات ذات الصلة التي تم تحديدها البالغ عددها 36 فئة، تم التوصل إلى أن اختلال سكر الدم مع الصيام أكثر شيوعاً لدى الرجال عنه لدى النساء (نسبة الاحتمال: 1.56؛ فاصل الثقة 95٪: من 1.20 إلى

Résumé

Les différences entre les sexes dans la prévalence du diabète sucré, de la glycémie à jeun anormale et de l'intolérance au glucose en Afrique subsaharienne: examen systématique et méta-analyse

Objectif Évaluer les différences entre hommes et femmes en termes de prévalence du diabète sucré, de la glycémie à jeun anormale et de l'intolérance au glucose en Afrique subsaharienne.

Méthodes En septembre 2011, on a recherché dans les bases de données PubMed et Web of Science des études communautaires transversales fournissant les prévalences spécifiques au sexe des trois maladies faisant l'objet de l'étude, chez des adultes vivant dans certaines régions d'Afrique subsaharienne (par exemple en Afrique orientale, centrale et australe, selon la classification sous-régionale des Nations Unies pour les pays africains). Un modèle à effets aléatoires a ensuite été utilisé pour calculer et comparer les cotes des hommes et des femmes affectés par chacune de ces maladies.

Résultats Dans une méta-analyse des 36 séries de données transversales pertinentes identifiées, on a découvert que la glycémie à jeun anormale

était plus fréquente chez les hommes que chez les femmes (RC: 1,56, intervalle de confiance de 95%, IC: 1,20 à 2,03), tandis que la tolérance au glucose s'est révélée moins fréquente chez les hommes que chez les femmes (RC: 0,84, IC de 95%: 0,72 à 0,98). La prévalence du diabète sucré - généralement semblable chez les deux sexes (RC: 1,01, IC de 95%: 0,91 à 1,11) - était plus élevée chez les femmes d'Afrique australe que chez les hommes de la même sous-région, et plus faible chez les femmes d'Afrique orientale et centrale et des pays à faible revenu d'Afrique subsaharienne que chez les hommes des mêmes pays.

Conclusion Par rapport aux femmes des mêmes sous-régions, on a découvert que la prévalence globale du diabète sucré était similaire chez les hommes d'Afrique orientale, mais que ceux-ci étaient plus susceptibles de souffrir de glycémie à jeun anormale et moins susceptibles d'être affectés par une intolérance au glucose.

Резюме

Половые различия в распространенности сахарного диабета, нарушенной гликемии натощак и нарушенной переносимости глюкозы в Африке южнее Сахары: систематический обзор и мета-анализ

Цель Оценить различия между мужчинами и женщинами в распространенности сахарного диабета, нарушенной гликемии натощак и нарушенной переносимости глюкозы в Африке южнее Сахары.

Методы В сентябре 2011 года был осуществлен поиск в базах данных PubMed и Web of Science территориальных поперечных исследований, предоставляющих данные в половом разрезе о распространенности любого из трех исследуемых заболеваний среди взрослых, живущих в Африке южнее Сахары (то есть в Восточной, Средней и Южной Африке, согласно субрегиональной классификации африканских стран Организацией Объединенных Наций). Затем для расчета и сопоставления риска мужчин и женщин подвергнуться каждому из заболеваний была использована модель случайных эффектов.

Результаты Мета-анализ идентифицированных 36 релевантных поперечных наборов данных показал, что нарушение гликемии

натощак чаще встречается у мужчин, чем у женщин (соотношение риска, СР: 1,56; 95% доверительный интервал, ДИ: 1,20–2,03), в то время как нарушенная переносимость глюкозы у мужчин встречается реже, чем у женщин (СР: 0,84; 95% ДИ: 0,72–0,98). Распространенность сахарного диабета, которая в целом была аналогична у обоих полов (СР: 1,01; 95% ДИ: 0,91–1,11), в Южной Африке была выше среди женщин, чем среди мужчин из того же субрегиона, и ниже среди женщин из стран Восточной и Центральной Африки, а также из малообеспеченных стран Африки южнее Сахары, чем среди мужчин из той же выборки.

Вывод У мужчин в Восточной, Средней и Южной Африке была обнаружена аналогичная с женщинами в тех же субрегионах общая распространенность сахарного диабета, но чаще встречались нарушения гликемии натощак и реже – нарушенная толерантность к глюкозе.

Resumen

Las diferencias entre sexos en la prevalencia de la diabetes mellitus, las alteraciones de la glucemia en ayunas y la intolerancia a la glucosa en África subsahariana: revisión sistemática y metaanálisis

Objetivo Evaluar las diferencias entre hombres y mujeres respecto a la prevalencia de la diabetes mellitus, las alteraciones de la glucemia en ayunas y la intolerancia a la glucosa en África subsahariana.

Métodos En septiembre de 2011, se realizaron búsquedas en las bases de datos de PubMed y Web of Science a fin de hallar estudios comunitarios transversales que proporcionaran datos sobre las prevalencias específicas de cada sexo de cualquiera de las tres enfermedades de estudio entre los adultos residentes en zonas de África subsahariana (es decir, en el Este, Centro y Sur de África, según la clasificación subregional de las Naciones Unidas para los países africanos). Se empleó un modelo de efectos aleatorios para calcular y comparar las probabilidades por parte de hombres y mujeres de padecer cada una de las enfermedades.

Resultados En un metaanálisis de los 36 conjuntos de datos de carácter transversal pertinentes que se identificaron, se halló que las alteraciones

de la glucemia en ayunas eran más comunes en hombres que en mujeres (OR: 1,56; intervalo de confianza del 95%, IC: 1,20 a 2,03), por el contrario, se descubrió que la intolerancia a la glucosa era menos común en los hombres que en las mujeres (OR: 0,84; IC del 95%: 0,72 a 0,98). La prevalencia de la diabetes mellitus (la cual fue, por lo general, similar en ambos sexos (OR: 1,01; IC 95%: 0,91 a 1,11) fue mayor entre las mujeres del Sur de África que entre los hombres de la misma subregión, y menor entre las mujeres del Este y Centro de África, así como en los países de ingresos bajos de África subsahariana, que entre los hombres correspondientes.

Conclusión En comparación con las mujeres de las mismas subregiones, se halló que los hombres del Este, Centro y Sur de África tienen una prevalencia general similar de la diabetes mellitus, pero son más propensos a padecer alteraciones de la glucemia en ayunas y menos propensos a padecer intolerancia a la glucosa.

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Table 2. Descriptions of the cross-sectional data sets included in the meta-analysis

Authors	Year		Study area		Sampling method	Response rate (%)	Target population	Age (years)	No. of adults		Mean age ^a (years)	Diagnosis Criteria	Diagnosis Method Specimen		Outcomes assessed	Prevalence (%) ^b	
	Publication	Study	Location	Type					Men	Women			Method	Specimen		Men	Women
Ahrén and Corrigan ⁵¹	1984	1983	Mwanza, URT	Urban	Cluster	95	All inhabitants	≥ 20	161 ^c	215 ^c	35.4 ^c	WHO 1980	FBG and/or OGTT	cWB	DM	1.87 ^c	1.86 ^c
Ahrén and Corrigan ⁵¹	1984	1983	Kahangala and Ndolage, URT	Rural	Cluster	90	All inhabitants	≥ 20	360 ^c	489 ^c	43.3 ^c	WHO 1980	FBG and/or OGTT	cWB	DM	1.1 ^c	1.84 ^c
Omar et al. ⁴⁶	1985	NR	Durban, South Africa	Urban	Cluster	77	Adults	≥ 15	368	498	42.5	WHO 1985	FBG and OGTT	VP	DM IGT	7.6 7.1	13.5 4.8
Söderberg et al. ⁴³	2005	1987	Mauritius	Combined	Multistage cluster	86	Adults	25–74	2339	2652	43.3	WHO 1999	FBG and OGTT	VP	DM IFG IGT	14.3 5.1 13.2	13.7 2.7 (2.6) 19.4 (19.1)
McLarty et al. ¹⁴	1989	1988 ^d	Morogoro and Kilimanjaro, URT	Rural	Random	92.6	Adults	≥ 15	2623	3460	37	WHO 1985	FBG and/or OGTT	vWB	DM IGT	1.1 7.3	0.7 8.0
Tappy et al. ⁶⁶	1991	1989	Mahe, Seychelles	Urban	Stratified random	86.4	Adults	25–64	511	567	NR	ADA 1988	FBG	vWB	DM	NR (3.4)	NR (4.6)
Levitt et al. ⁵³	1993	1990	Cape Town, South Africa	Urban	Cluster	79	Adults	> 30	210	504	45.1	WHO 1985	FBG and OGTT	VP	DM IGT	6.5 6.0	6.4 (7.4) 5.9
Mollentze et al. ⁶⁸	1995	1990	QwaQwa, South Africa	Rural	Random	68	Adults	≥ 25	279	574	52.3	WHO 1985	FBG and OGTT	VP	DM	5.4	6.6
Mollentze et al. ⁶⁸	1995	1990	Mangaung, South Africa	Urban	Random	62	Adults	≥ 25	290	468	48.6	WHO 1985	FBG and OGTT	VP	DM	5.8	8.5
Söderberg et al. ⁴³	2005	1992	Mauritius	Combined	Multistage cluster	90	Adults	≥ 25	2986	3477	46	WHO 1999	FBG and OGTT	VP	DM IFG IGT	19.3 8.5 13.0	18.3 4.1 (3.9) 17.7 (16.3)
Omar et al. ⁶⁴	1993	NR	Umlazi, South Africa	Urban	Cluster	78	Adults	≥ 15	141	338	32.9	WHO 1985	FBG and OGTT	VP	DM IGT	2.3 11.5	5.2 5.5

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Authors	Year		Study area		Sampling method	Response rate (%)	Target population	Age (years)	No. of adults		Mean age ^a (years)	Diagnosis			Outcomes assessed	Prevalence (%) ^b	
	Publication	Study	Location	Type					Men	Women		Criteria	Method	Specimen		Men	Women
Omar et al. ⁵⁹	1994	NR	Durban, South Africa	Urban	Cluster	92	Adults	≥ 15	1038	1441	NR	WHO 1985	FBG and OGTT	VP	DM	8.6 (10.4)	10.6 (15.0)
															IGT	7.6 (8.9)	4.5 (5.8)
Elbagir et al. ¹⁷	1996	NR	Sudan	Combined	Multistage	NR	Adults	≥ 25	461	823	46.1	WHO 1985	OGTT	cWB	DM	3.5	3.4
															IGT	2.2	3.3
Levitt et al. ⁵²	1999	1996	Mamre, South Africa	Periurban	Cluster	64.5	Adults	≥ 15	428	545	37.6	WHO 1985	OGTT	VP	DM	5.8	8.1
															IGT	6.5	9.2
Erasmus et al. ⁶⁷	2001	1997 ^d	Umtata, South Africa	Periurban	NR	73	Adults	20–69	237	137	37.9	WHO 1985	FBG and OGTT	VP	DM	2.1	2.9
															IGT	3.4	1.5
Aspray et al. ⁴⁵	2000	1997	Ilala Ilala and Dar es Salaam, URT	Urban	Random	73.25	Adults	≥ 15	332	438	30.6	WHO 1998	FBG	cWB	DM	5.3 (5.9)	4.0 (5.7)
															IFG	4.0 (3.6)	5.4 (4.7)
Aspray et al. ⁴⁵	2000	1997	Shari, URT	Rural	Random	82.5	Adults	≥ 15	401	527	42.1	WHO 1998	FBG	cWB	DM	1.5 (1.7)	1.1 (1.1)
															IFG	1.2 (0.8)	1.5 (1.6)
Charlton et al. ⁶¹	2001	1997	St Helena Bay and Velddrif, South Africa	Rural	Convenience	NR	Adults	> 55	46	106	65.4	WHO 1985; ADA 1997	FBG and OGTT	VP	DM	15.8	28.9
															IGT	13.2	10.0
Alberts et al. ⁵⁶	2005	1997 ^d	Limpopo, South Africa	Rural	Census	66	Adults	> 30	498	1608	57.5	ADA 1997	FBG	VP	DM	9.9 (8.5)	10.0 (8.8)
Söderberg et al. ⁴³	2005	1998	Mauritius	Combined	Multistage cluster	87	Adults	≥ 20	2392	3000	48.8	WHO 1999	FBG and OGTT	VP	DM	25.2 (18.3)	23.8 (17.6)
															IFG	5.7 (6.2)	3.5 (2.9)
															IGT	13.2 (11.2)	17.2 (16.2)
Elbagir et al. ⁴⁸	1998	NR	Northern State, Sudan	Urban	Multistage	NR	Adults	≥ 25	118	197	38	WHO 1985	OGTT	cWB	DM	NR (15.8)	NR (10.7)
															IGT	NR (4.5)	NR (13.5)

(continues...)

(...continued)

Authors	Year		Study area		Sampling method	Response rate (%)	Target population	Age (years)	No. of adults		Mean age ^a (years)	Diagnosis			Outcomes assessed	Prevalence (%) ^b	
	Publication	Study	Location	Type					Men	Women		Criteria	Method	Specimen		Men	Women
Elbagir et al. ⁴⁸	1998	NR	Northern State, Sudan	Rural	Multistage	NR	Adults	≥ 25	43	126	39	WHO 1985	OGTT	cWB	DM	NR (2.8)	NR (8.3)
															IGT	NR (4.4)	NR (10.2)
Motala et al. ⁵⁰	2008	2000 ^d	Ubombo district, South Africa	Rural	Cluster	78.9	Adults	≥ 15	200	799	46.9	WHO 1998	FBG and OGTT	VP	DM	4.5 (3.5)	4.6 (3.9)
															IFG	4.5 (4.0)	0.9 (0.8)
															IGT	6.5 (4.0)	6.4 (4.7)
Faeh et al. ⁵⁵	2007	2004	Seychelles	Urban	Stratified random	80.2	Adults	25–64	568	687	45.2	ADA 2004	FBG and/or OGTT	VP	DM	NR (11.0)	NR (12.1)
															IFG	NR (30.4)	NR (18.0)
															IGT	NR (11.2)	NR (9.6)
ZWMOH ⁶³	2005	2005	Zimbabwe	Combined	Multistage cluster	72.1	Adults	≥ 25	402	1264	48	WHO 1999	FBG and OGTT	VP	DM	2.2	1.3
															IGT	5.3	5.2
Kasiam Lasi On'Kin et al. ⁵⁷	2008	2005	Kinshasa, DRC	Combined	Multistage cluster	90.3	All inhabitants	> 12	4580	5190	46	WHO/ADA 2003	FBG and OGTT	cWB	DM	NR (23.7)	NR (17.7)
															IFG	NR (9.5)	NR (9.2)
															IGT	NR (6.4)	NR (8.2)
Silva-Matos et al. ⁶⁰	2011	2005	Mozambique	Urban ^e	Cluster	70.5	Adults	25–64	NR	NR	39	WHO 1998	FBG	cWB	DM	5.5	4.9
															IFG	3.2	2.0
Silva-Matos et al. ⁶⁰	2011	2005	Mozambique	Rural ^e	Cluster	70.5	Adults	25–64	NR	NR	39	WHO 1998	FBG	cWB	DM	2.4	1.2
															IFG	2.3	2.6
Nsakashalo-Senkwe et al. ⁴⁹	2011	2005	Lusaka, Zambia	Urban	Multistage cluster	NR	Adults	25–64	620	1260	42.1	WHO ^f	FBG	cWB	DM	2.1	3.0
															IFG	1.3	1.3
Christensen et al. ⁴⁷	2009	2006	Luo, Kamba, Maasai and Nairobi, Kenya	Combined	Random	98.2	All inhabitants	≥ 17	640	819	37.5	WHO 1999	FBG and OGTT	vWB	DM	NR (4.5)	NR (4.2)
															IGT	NR (6.1)	NR (13.1)
Tibazarwa et al. ⁴²	2009	2007	Soweto, South Africa	Urban	Convenience	94	Adults	NR	594	1097	46	WHO 1985	RBG	cWB	DM	3.5	3.0

(continues...)

(. . .continued)

Authors	Year		Study area		Sampling method	Response rate (%)	Target population	Age (years)	No. of adults		Mean age ^a (years)	Diagnosis			Outcomes assessed	Prevalence (%) ^b	
	Publication	Study	Location	Type					Men	Women		Criteria	Method	Specimen		Men	Women
Wanjihia et al. ⁴⁴	2009	2008 ^d	Bondo and Kericho, Kenya	Rural	Random	99.6	All inhabitants	≥ 18	134	165	43	WHO 1999	FBG and OGTT	cWB	IGT	3.7	11.9
Mathenge et al. ⁴⁵	2010	2008	Nakuru district, Kenya	Urban	Cluster	88	Adults	≥ 50	707 ^d	730 ^d	60.8 ^d	WHO 1985	RBG	cWB	DM	9.9	9.9
Mathenge et al. ⁴⁵	2010	2008	Nakuru district, Kenya	Rural	Cluster	88	Adults	≥ 50	1399 ^d	1560 ^d	64.7 ^d	WHO 1985	RBG	cWB	DM	4.9	4.9
MWMOH ⁵⁴	2010	2009	Malawi	Combined	Multistage cluster	95.5	Adults	25–64	1690	3516	32.9	WHO 1999	FBG	cWB	DM IFG	6.5 5.7	4.7 2.7
Evaristo-Neto et al. ⁵⁸	2010	NR	Bengo, Angola	Rural	Multistage cluster	97	Adults	30–69	126	295	49.6	WHO 1985	FBG and OGTT	cWB	DM IGT	3.2 5.6	2.7 9.1
Maher et al. ⁶²	2011	2009	South-western Uganda	Rural	Census	65.6	All inhabitants	≥ 13	2719	3959	32.9	WHO 2006	RBG	VP	DM	NR (0.4)	NR (0.4)

ADA, American Diabetes Association; cWB, capillary whole blood; DM, diabetes mellitus; DRC, Democratic Republic of the Congo; FBG, fasting blood glucose; IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance; MWMOH, Malawi Ministry of Health; NR, not reported; OGTT, oral glucose-tolerance test; RBG, random blood glucose; URT, United Republic of Tanzania; VP, venous plasma; vWB, venous whole blood; WHO, World Health Organization; ZWMOH, Zimbabwe Ministry of Health and Child Welfare.

^a If never reported, estimated from the age distribution of subjects.

^b Values shown are crude prevalences followed, in parentheses, by the age-adjusted values (when reported).

^c Data for study subjects aged ≥ 20 years.

^d Previously unpublished information, supplied by an author of the cited report.

^e For the meta-analysis, pooled data for all of the study areas investigated by Silva-Matos et al.⁵⁹ (i.e. those for urban and rural areas combined) were used.

^f Year not reported.



Cohort Profile: The Fangshan Cohort Study of Cardiovascular Epidemiology in Beijing, China

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ABSTRACT

Background: Urbanizing rural areas in China face a rapidly growing cardiovascular disease burden. Epidemiologic studies and effective preventive strategies are urgently needed.

Methods: The Fangshan Cohort Study is a prospective study that began in 2008 and targets local residents aged 40 years or older living in 3 towns in the Fangshan district of Beijing. The baseline examination included a questionnaire on medical history, health knowledge, and behaviors related to cardiovascular disease, as well as physical and blood biochemical examinations. The questionnaire survey will be readministered every 2 years. A system for surveillance of mortality and morbidity of cardiovascular disease is under development.

Results: A total of 20 115 adults (6710 men and 13 405 women) were investigated at baseline (participation rate = 84.5%). The data indicate that overweight/obesity is a serious public health issue in Fangshan: average body mass index was 25.4 kg/m² among men and 26.5 kg/m² among women, and the prevalences of overweight and obesity were 43.6% and 10.3% among men and 47.0% and 17.7% among women.

Conclusions: The Fangshan Cohort Study will provide data on cardiovascular risk factors and disease profile, which will assist in developing appropriate prevention and control strategies for cardiovascular disease in rural Chinese communities.

Key words: risk factors; cardiovascular disease; rural population; cohort study; China

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the world and accounted for 23.6% of all deaths in 2008.¹ Mortality from CVD has declined in high-income countries but is increasing in many developing countries, such as China.² Indeed, China is facing a growing epidemic of CVD.

China is a large agricultural country. In 2006, 737 million people were living in rural communities—56% of the entire Chinese population.³ In China, an urban area is defined as a prefecture-level city or larger community and a rural area as a county or smaller community. There are 4 economic categories for rural areas. Annual per capita net income (in

renminbi) for rural residents is classified as 3000 RMB or higher, 2000 to 2999 RMB, 1500 to 1999 RMB, and less than 1500 RMB for first- to fourth-class rural areas, respectively.⁴ The income gap between urban and rural areas has widened with the increase in economic development that began in the 2000s. Therefore, many young workers migrate to large and medium-sized cities to seek jobs, leaving elderly people in the countryside. Along with the structural transformation of the economy, lifestyles (including diet and physical activity) have also changed. The traditional diet is made up mainly of cereals and is low in fat and calories and high in carbohydrate and dietary fiber. During the last 20 years, consumption of cereals has decreased rapidly and consumption of animal products has

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increased,⁵ which may have accelerated the epidemic of CVD.^{6,7} In some developed rural areas, cardiovascular disease morbidity and mortality exceed levels in urban areas.⁸⁻¹⁰ However, because of the lack of health awareness, uneven distribution of health resources, long distances to hospitals, and low incomes, rural areas in China may have more challenges in preventing and controlling CVD.

Large-scale cohort studies have examined the secular trend and epidemiologic characteristics of CVD in China.^{7,11-13} However, these cohort studies were conducted in the 1990s and ended in around 2000. Thus, data for recent years are lacking, especially for rural populations. In addition to academic research, the Chinese government is addressing the issue of chronic disease in rural areas. For example, the New Rural Cooperative Medical System was established in 2003.¹⁴ This health care system targets the rural population and is organized, led, and supported by the government, with the voluntary participation of rural residents. The system is jointly financed by individuals, collectives, and the government and attempts to reduce illness-induced poverty and reimburse the cost of major illnesses.¹⁵ Excepting Hong Kong and Macao, it covers all 22 provinces, 4 municipalities, and 5 autonomous regions in China. A total of 832 million rural residents (96% of the entire rural population of China) were covered by this system as of 2011.¹⁶ The Chronic Disease Record was started in 2009 and includes demographic information, family history, medical history, outpatient record, and other information for every resident (as recorded by community medical centers). In 2011, it included 30% of rural residents nationwide.¹⁷ All these policies and programs are important in preventing and controlling chronic diseases in rural areas.

Because the epidemiologic patterns of CVD change quickly in Chinese rural areas, we analyzed (1) CVD trends in rural populations, (2) awareness, treatment, and control of CVD, and their contributing factors, (3) the burden of chronic diseases, and local health needs, (4) medications commonly used for treating chronic diseases and their long-term beneficial effects, adverse effects, compliance, and pharmacoconomics, and (5) effective preventive and control strategies that were specially developed for rural populations. These data will be useful in devising health policies to address the epidemic of CVD.

METHODS

The main reason for developing the Fangshan cohort study was to analyze the changing epidemiologic characteristics of CVD among rural populations, including morbidity, mortality, prevalence, and risk factors. To investigate awareness, treatment, and control of CVD, we will conduct repeat surveys of medical history and medication adherence, as measured by the Morisky Scale.¹⁸ The burden of chronic disease will be measured by potential years of life lost (PYLL),¹⁹ disability-adjusted life years (DALYs),²⁰ and the

medical cost of the disease. Our ultimate goal is to collect data that assist in the development of suitable preventive strategies. This will require identification of the risk factor profile and sensitive biomarkers for CVD, and the establishing of intervention priorities, after which effective, economical treatment methods can be specially developed for rural populations.

Study design, setting, and participants

The prospective study started in 2008, and the targeted population was local rural residents aged 40 years or older living in the Fangshan district of Beijing, 12.5 miles southwest of downtown Beijing (Figure). People were excluded if they had a severe physical or mental disease that made them unable to answer the questionnaire or if they had a severe medical condition that made them unable to report to the survey location. Fangshan occupies an area of 2019 km² and comprises mountains, hills, and plateaus. It includes 8 subdistricts, 14 towns, and 6 townlets (the smallest administrative unit in China, based on the Constitution Law of 1982). The census population was 870 000, the rural population was greater than 400 000, and the population is relatively stable. Fangshan district has a high prevalence of CVD.²¹⁻²³ Local government and residents are cooperative, and the present authors have been involved in the area for other research projects since 1981.

A stratified, multistage, cluster-sampling design was used in the present study. A random sample of 3 towns (Zhoukoudian, Dashiwo, and Qinglonghu) was selected to represent the 3 different topographical areas (mountain, hill, and plateau, respectively), because both health knowledge and the conditions of the residents differ among these areas. The 3 selected towns are located in the north, center, and south of Fangshan district (in ascending order of distance from downtown Beijing). As in previous preliminary studies, we used inference for a single proportion to calculate sample size²⁴ for the 3 towns, to detect regional differences in CVD prevalence.^{23,25} In Fangshan district the prevalence of stroke was lower than the prevalences of hypertension, coronary heart disease, and diabetes mellitus, according to our preliminary studies.^{23,25} Using inference for a single proportion to calculate sample size,²⁴ the absolute precision was set as 10 percentage points of the expected prevalence, and the confidence level was set as 95%. The expected prevalence of stroke was 4.9%, 4.8%, and 4.3% for people aged 40 years or older in Zhoukoudian, Dashiwo, and Qinglonghu, respectively, according to our pilot study. After calculating the sample size for each town, we used cluster sampling, with the village as the unit. We calculated the proportion of people that had to be sampled from the census population in each town. That proportion was almost equal to the proportion of the village that needed to be sampled from the town, because the census population of the village is nearly identical. After the calculation, 14, 10, and 18 villages

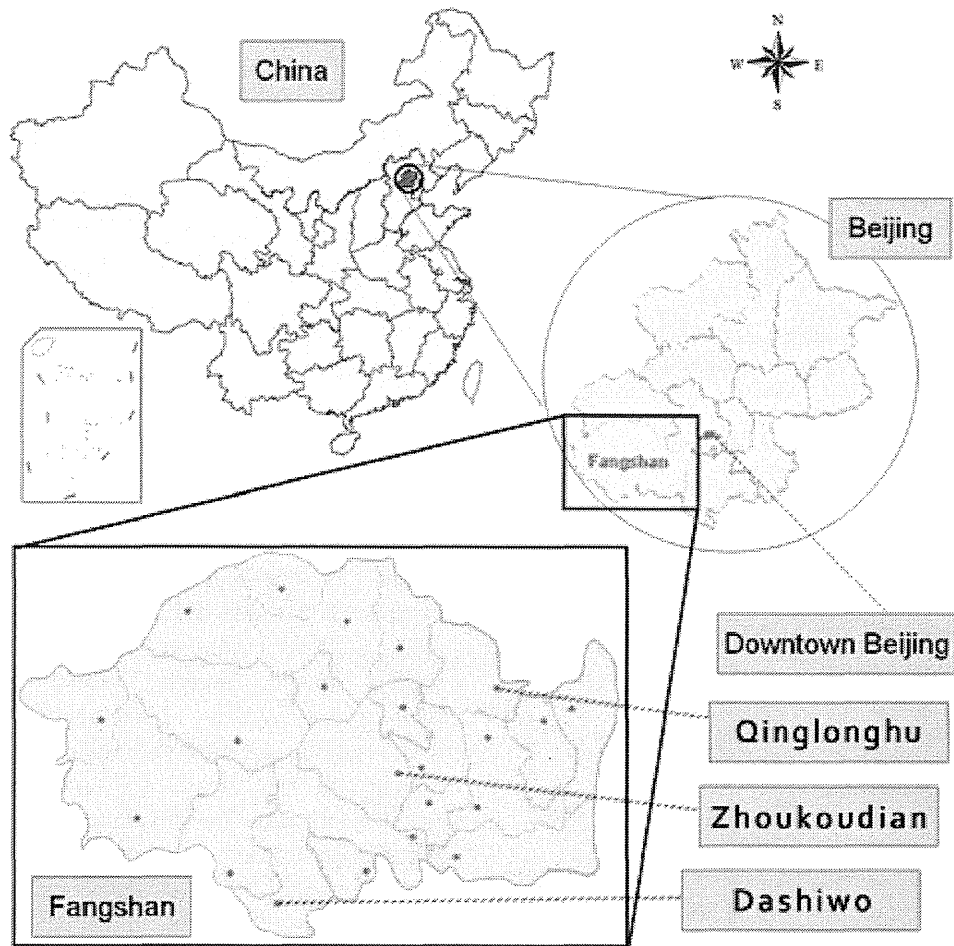


Figure. Map showing the locations of the 3 towns studied in the Fangshan Cohort Study.

needed to be sampled out of the 24, 24, and 20 villages in Zhoukoudian, Dashiwo, and Qinglonghu, respectively. Within towns we used simple random cluster sampling for villages, because there is no heterogeneity of characteristics among different villages in the same town. In 2008, the annual per capita net income for rural residents (US dollars) was \$1408 for Zhoukoudian, \$1218 for Dashiwo, and \$1254 for Qinglonghu. It ranged from \$651 to \$2446 for other areas and was \$1450 for the Fangshan district overall.²⁶ Therefore, the economic levels of the 3 towns did not substantially differ from that of the Fangshan district overall and were higher than the national average for rural areas (\$686 in 2008).

In 2008, the baseline survey was conducted for the sampling subjects ($n = 7514$) in Zhoukoudian town, which had a census population of 12 674 adults aged 40 years or older; 6047 chose to participate (participation rate = 80.5%). In 2009, the survey was conducted for the sampling subjects ($n = 7728$) in Dashiwo town, which had a census population of 17 872 adults aged 40 years or older; 6211 (80.4%) chose to participate. In 2010, the survey was conducted for the sampling subjects ($n = 8571$) in Qinglonghu town, which had a census population of 9753 adults aged 40 years or older; 7857 (91.7%) chose to participate. Thus, a total of 20 115

adults participated in the baseline survey of the 3 towns, and the overall participation rate was 84.5%.

The baseline survey included an interview and physical and blood biochemical examinations and was conducted at the community medical center of each sampled village. To recruit participants, the staffs of the local village governments publicized the survey through broadcasts and household telephone 1 day before and during the survey. The interview was done by trained investigators using a uniform questionnaire, the physical examination was conducted by research physicians and nurses, and the blood samples were processed by laboratory technicians.

Baseline measures

The main measures of the baseline examination are summarized in Table 1. Additional information for some items was investigated in the 2010 questionnaire survey.

The baseline questionnaire included the following individual-level information: demographic factors (age, sex, marriage status, education level, and occupation), medical history (year of diagnosis and medication used for hypertension, diabetes mellitus, coronary heart disease, and stroke diagnosed by a class 2 or higher hospital). To

Table 1. Summary of the baseline measures in Fangshan Cohort Study

Demographic information
Age
Sex
Ethnic group
Marital status
Education background
Occupation
Annual income
Medical history
Hypertension, diabetes mellitus, coronary heart disease, stroke
Family history of hypertension, diabetes mellitus, coronary heart disease, stroke
Health knowledge and behaviors
Willingness and methods to obtain health information
Smoking status
Alcohol consumption
Physical exercise (frequency of exercise, type of exercise)
Dietary pattern (preference for tea, meat, oil, sweet food, salty food)
Sleep duration
Quality of life
Assessed by self-rated health with 5 rating levels, or the EQ-5D scale ^a
Demand and utilization of health service ^a
Physical examination
(Resting blood pressure, height, weight, waist and hip circumferences, ^a 12-lead resting electrocardiogram)
Blood biochemical examination
Total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, blood glucose

Abbreviations: EQ-5D, European Quality of Life–5 Dimensions scale; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

^aAdditional information investigated in 2010 questionnaire survey.

investigate genetic epidemiology, we also obtained a detailed family history of CVD so that we could collect information on pedigrees, sib-pairs, and twins. Investigated lifestyle factors included smoking status and number of cigarettes smoked per day (current smokers were defined as people who had smoked more than 100 cigarettes in the past and had smoked during the previous 30 days; ex-smokers were defined as people who had smoked more than 100 cigarettes in the past but had not smoked during the previous 30 days), drinking status (current drinkers were defined as persons who reported current consumption of alcohol at least once a week; ex-drinkers were defined as people who reported consuming alcohol at least once a week in the past but not during the previous 30 days), regular physical exercise (defined as intentional exercise for at least 30 minutes at least once per week during the previous 6 months, not including housework or job-related work), dietary pattern (preference for tea, meat, oil, sweet food, or salty food), and hours of sleep per night. The definition of smoking was the same as that used in the Chinese National Health Services Survey in 2008,⁴ and the definitions for drinking and regular physical exercise were the same as those used in the Chinese National Health Services Survey in 2008 and National Nutrition and Health Survey in 2002.^{4,27} Regular physical exercise was determined by asking the question, “Do you intentionally exercise?”, and the responses “always”

(for at least 30 minutes ≥ 3 times per week) and “sometimes” (at least 30 minutes once or twice per week) were regarded as an affirmative response. Quality of life was assessed by the European Quality of Life–5 Dimensions (EQ-5D) scale²⁸ in 2010, and by self-rated health, with 5 rating levels, before that. Participant knowledge of CVD, and willingness and common approaches to obtain such knowledge, were also surveyed. We asked if they understood the relations between lifestyle and traditional risk factors and between risk factors and CVD. Further, we ascertained their willingness to obtain more information on healthy living, the media they most frequently consulted, and frequency of watching TV programs on the Fangshan Health Channel. We used some of the questions from the Chinese National Health Services Survey to measure resident health-service demands, utilization, and expenditure. Because the New Rural Cooperative Medical System was established in 2003, we also asked about participant satisfaction and comments regarding the system.

The physical examination comprised resting blood pressure, height, weight, waist circumference, hip circumference, and a 12-lead resting electrocardiogram (ECG). Systolic and fifth-phase diastolic blood pressures in the right arm were measured 3 times by trained physicians using standard mercury sphygmomanometers and a standard epidemiologic method. The participants were asked to sit and rest for 5 minutes before measurements.²⁹ Hypertension was defined as an average systolic blood pressure of 140 mm Hg or higher, an average diastolic blood pressure of 90 mm Hg or higher, and/or use of antihypertensive medications, according to the 1999 World Health Organization International Society of Hypertension Guidelines.³⁰ Diabetes mellitus was defined as a fasting glucose level of 7.0 mmol/l or higher, a random glucose level of 11.1 mmol/l or higher, and/or use of insulin or oral hypoglycemic agents, according to the 1999 World Health Organization Guidelines.³¹ Height was measured by using a fixed stadiometer. Participants were asked to remove their shoes and hats, stand with heels, hips, and shoulders to the wall, look straight ahead, and keep their shoulders horizontal. The measurements were accurate to 1 cm. Weight was measured by a calibrated weighing scale. Participants were asked to remove heavy clothes and shoes. Measurements were accurate to 1 kg. Waist and hip circumferences were measured while the participant was standing. Waist circumference was measured with the tape at the midpoint between the lower costal margin and the iliac crest; hip circumference was measured at the level of maximal extension of the buttocks. The 12-lead resting ECG was measured by a standard method.³²

Venous blood samples were sent to the laboratory of The First Hospital of Fangshan District for measurement of total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (measured directly), and blood glucose. Serum was used for the assay, and blood samples were stored at -20°C for DNA extraction. The lipids