Title: Association between lung capacity and abnormal glucose metabolism: Findings from China and Australia

Short title: lung capacity and abnormal glucose metabolism

Dahai Yu 1,2, Tao Chen 1,3, Rui Qin 4, Yamei Cai 1, Zhixing Jiang 5, Zhanzheng Zhao 1*, David Simmons 6*

1. Department of Nephrology, the First Affiliated Hospital, Zhengzhou University, Zhengzhou 450052, China.
2. Arthritis Research UK Primary Care Centre, Research Institute for Primary Care & Health Sciences, Keele University, Keele ST5 5BG, UK.
3. Division of Health and Social Care, King College London, London SE1 3QD, UK
4. Jiangsu Province Hospital on Integration of Chinese and Western Medicine, Nanjing 210028, China
5. Jiangsu Province People's Hospital, Nanjing 210029, China
6. Western Sydney University, Campbelltown, Sydney NSW 2751, Australia.

*Correspondence 1 (China):
Professor Zhanzheng Zhao, Department of Nephrology, The First Affiliated Hospital Zhengzhou University, Zhengzhou 450052, CHINA
Email: zhanzhengzhao@zzu.edu.cn
TEL:+86 139 3852 5666
FAX:+86 371 6698 8753

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Correspondence 2 (Australia):
Professor David Simmons, Macarthur Clinical School, School of Medicine, Western Sydney University, Locked Bag 1797, Campbelltown NSW 2751, AUSTRALIA
Email: dworkster@gmail.com
TEL: (61+2) 4620 3899
FAX: (61+2) 4620 3890

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Author contributions:
DY: Acquisition of data, analysis and interpretation of the data, drafted the manuscript, has provided final approval of the version to be published.
TC: Validated the analysis, edited the manuscript and has provided final approval of the version to be published.
RQ and ZJ: Contributed to collect data from communities in Nanjing, edited the manuscripts and has provided final approval of the version to be published.
YC: Contributed to questionnaire design, data manipulation edited the manuscript and has provided final approval of the version to be published.
ZZ: Conception and design of the Nanjing study, interpretation of the data, co-led this joint study, edited the manuscript, has provided final approval of the version to be published.
DS: Conception and design of the Crossroads study, co-led the joint study, acquisition of data, analysis and interpretation of the data, revised the manuscript, has provided final approval of the version to be published, has agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ABSTRACT

Objective: Restricted pulmonary function is found among people with diabetes. This study aimed to investigate the dose-response relationship between pulmonary function measurements (forced expiratory volume in one second (FEV1) and forced vital capacity (FVC)) and risk of metabolic syndrome (MS) /type 2 diabetes.

Methods: 1,454 adults in rural Victoria, Australia and 5,824 adults in Nanjing, China from randomly selected households provided clinical history, oral glucose tolerance test, lipids, anthropometric, blood pressure and spirometric measurements. MS was defined by International Diabetes Federation criteria. Adjusted odds ratios for MS and type 2 diabetes with lung capacity measurements were estimated using logistic regression. Dose-response relationships were explored using restricted cubic spline models.

Results: There was a non-linear relationship between FEV1 and the risk of type 2 diabetes and MS (both P<0.0001) both in Australian and Chinese populations. The FEV1 associated with the lowest risk of type 2 diabetes and MS was above 2.70L (95%CI: 2.68 to 2.72L and 2.65 to 2.76L in Chinese and Australian populations respectively). The discrimination of the model could be significantly improved using the FEV1 threshold both in the Australian and Chinese populations.

Conclusions: In both Australian and Chinese populations, the risk of type 2 diabetes and MS is lowest with a FEV1 of 2.65-2.76 L. This might be used in clinical practice in different countries as a prompt to screen for type 2 diabetes and MS in patients with obstructive lung disease and to ensure there was no abnormal glucose metabolism before the commencement of steroids if indicated.

INTRODUCTION

Type 2 diabetes imposes significant health and economic burdens on both developed and developing countries 2 and its prevalence is increasing1. Although this increase may be due to increased obesity, other potential risk factors have been proposed such as impaired pulmonary function 3. Epidemiological and clinical studies suggest that adults with diabetes have lower forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) compared with their non-diabetic counterparts 4,5. Furthermore, the lung function of patients with diabetes is inversely related to blood glucose level, duration of diabetes and the severity of diabetes, independent of smoking or obesity 6,7.

However the association between lung capacity and type 2 diabetes is not consistent. This might be due to different research design, ethnic variation or different analytical methods. The association between lung capacity and metabolic syndrome (MS) has also not been investigated. We therefore

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undertook a joint analysis between Chinese and Australian populations to assess the dose response relationship between lung capacity measures (FEV1 and FVC) for MS and type 2 diabetes.

METHODS
The Crossroads study was carried out between June 2001 and March 2003 among residents of the seven main towns in the Goulburn Valley, Victoria, Australia (populations 2094–35,828), as previously described⁸,⁹,¹⁰.

The Nanjing Community Cardiovascular Risk Survey was carried out, using random cluster sampling¹¹, between 2011 and 2013 among the residents of 6 communities in Nanjing, Jiangsu Province, China (population 0.7 million-1.3 million). In each community, one street district or township was randomly selected. All households (n=6,445) in the selected street or town were included with only one participant aged ≥ 20 years selected from each household, without replacement. Overall, 5,824 residents completed the survey and examination (response rate of 90%).

In both studies, questionnaires were completed, wherever possible, through face-to-face interviews by trained research staff. Questions included age, sex, education, cigarette smoking, a self-reported history of asthma, chronic obstructive pulmonary disease (COPD), and known diabetes.

In both studies, blood pressure and body measurements were taken three times using a standardized methodology and the mean of the two closest recordings was used. Overweight/obesity were defined as 25.0–29.9/≥30.0 kg/m² respectively⁹.

Measurements of FEV1 and FVC were obtained using spirometry (Vitalograph, Buckingham, UK). Each participant completed two spirometry attempts while seated. Where the two readings differed significantly, a third measurement was taken¹⁰.

Fasting blood specimens were processed at the examination center¹². Plasma glucose and lipid levels were measured by automated analyser (Australian: Hitachi 917R autoanalyser (Hitachi, Tokyo, Japan); Nanjing: Olympus AU600 autoanalyser (Olympus Optical, Tokyo, Japan)). Type 2 diabetes was defined using WHO criteria³ or by self-report if previously diagnosed, and MS using International Diabetes Federation (IDF) criteria¹³. Hypertension was considered present if reported as having been diagnosed by a doctor or nurse¹⁴,¹⁵. Patients with Type 2 diabetes overlapping within the MS definition were only defined as having ‘Type 2 diabetes’ in the analysis.
Statistics

Continuous variables were compared using the Kruskal–Wallis test and categorical variables using the chi-squared test. Multiple linear regression was used to investigate the association between lung capacity measures (FEV1 and FVC) and linear variables including glucose, lipid profiles. The relationship between lung capacity measurements and the odds ratios of MS and diabetes were estimated using a linear model (unconditional Logistic Model), a natural cubic spline model with four equally spaced knots determined from the levels of lung capacity measurements, and a quadratic spline model\textsuperscript{16,17}. The natural cubic spline model was chosen as the best fit model for the relationship curve by its minimum Akaike information criterion (AIC) compared with the linear model or quadratic spline model\textsuperscript{18}.

The break-point test was carried out to target the potential thresholds (the 5\textsuperscript{th} percentile (P\textsubscript{5}) to the 95\textsuperscript{th} percentile (P\textsubscript{95}) of lung capacity measures) by incorporating the piecewise term into the cubic spline model\textsuperscript{19}. The threshold with a significant break in the regression coefficients and achieving the minimum AIC was chosen as the final threshold\textsuperscript{20}. The 95\% CI of the threshold was obtained from 1000 bootstrap samples\textsuperscript{21}.

For sensitivity analysis, the natural cubic spline models for the overall dataset were repeated using other potential knots, chosen to lie within the range for minimum to maximum measure of lung capacity\textsuperscript{20}. Modelling in the data rich range (in the 5\textsuperscript{th} percentile to the 95\textsuperscript{th} percentile of measure of lung capacity) was processed as another sensitivity analysis\textsuperscript{20}. The linear test was used in the natural cubic spline model to test the linearity of the relationship\textsuperscript{22,23}.

All analyses were two-tailed, performed using STATA (STATA/SE 13.0 Stata Corp., College Station, TX, USA) with P value < 0.05 were considered statistically significant.

Ethics, consent and permissions

The Goulburn Valley Health Ethics Committee approved the Crossroads study (approval number GVH – 3/99). The Institutional Review Board of Jiangsu Province Hospital on Integration of Chinese and Western Medicine approved the Nanjing study (approval number 11-006). Signed, informed consent was obtained from all participants.

RESULTS AND DISCUSSION

Results

MS/type 2 diabetes were present in 28.9%/9.4% in Crossroads and 24.1%/8.1% in Nanjing. In both populations, mean ages and gender proportions were similar overall (Table 1) and participants with MS/type 2 diabetes were more likely to be older and male.
Both Chinese and Australian participants with MS or type 2 diabetes were more likely to have lower lung capacity measurements. Figure 1 shows that the median (interquartile range) of FEV1 was 2.42 (2.07, 2.89)L, 2.12 (1.81, 2.43)L, and 2.15 (1.81, 2.52)L among Chinese participants and 2.95 (2.44, 3.49)L, 2.73 (2.12, 3.38)L, and 2.35 (1.92, 2.94)L among Australian participants without MS/ type 2 diabetes, with MS and with type 2 diabetes, respectively.

Figure 1 also shows that the median (interquartile range) of FEV1 was 2.99 (2.50, 3.56)L, 2.55 (2.16, 3.00)L, and 2.60 (2.18, 3.15)L among Chinese participants and 3.67 (3.06, 4.42)L, 3.45 (2.69, 4.17)L, and 2.99 (2.42, 3.63)L among Australian participants without MS/ type 2 diabetes, with MS and with type 2 diabetes, respectively.

The relationships between clinical measurements and lung capacity measurements (both FEV1 and FVC) are shown in Figures 1 and 2. Significant reverse associations were identified between lung capacity measurements (both FEV1 and FVC) and both fasting glucose and lipids in the Chinese and Australian general populations. (Tables 2 and 3).

**Dose-response relationship between lung capacity measurements and type 2 diabetes/Metabolic syndrome**

There was a non-linear relationship (Linear test: both P<0.0001) between FEV1 and adjusted odds ratios for both type 2 diabetes and MS, with clear evidence of a threshold estimated at 1.76L (95%CI: 1.74 to 1.78L and 1.73 to 1.79L in both the Chinese and Australian populations respectively) (Figures 2 and 3) and 2.70 (95%CI: 2.68 to 2.72)L only in the Chinese population by threshold models. Similar non-linear relationships (Linear test: both P<0.0001) were observed between FVC and adjusted odds ratios for type 2 diabetes and a threshold was identified at 2.00L (95%CI: 1.82 to 2.21L and 1.61 to 2.42L in Chinese and Australian populations respectively) (Figure 2). A non-linear association (Linear test: both P<0.0001) between FEV1 and adjusted odds ratio of both type 2 diabetes and MS with a threshold 2.70L (95%CI: 2.68 to 2.72L and 2.65 to 2.76L in Chinese and Australian populations respectively) were also found in sensitivity analysis modelling the association within the data rich range (1.5 to 3.5L for FEV1; e-Figures 3 and 4). Below the threshold, the adjusted odds ratio decreased with the increase of FEV1. Above the threshold, the adjusted odds ratio remained unchanged. A similar analysis for FVC was not significant, as the adjusted odds ratio decreased linearly with the increase in FVC in both populations.

The adjusted odds ratios of MS decreased between an FEV1 of 1.76 and 2.70L in both populations although neither increased nor decreased risk was observed below 1.76L. The adjusted odds ratio did not decrease above 2.70L of FEV1 in the Chinese but not Australian population. A linear association between FVC and adjusted odds ratio of MS was found in both populations.

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Discussion

This joint study was undertaken to relate pulmonary function measurements to the risk of MS/type 2 diabetes in both Chinese and Australian populations in the light of the growing evidence of the existence of their mutual association. We focused our investigation on the shape of the relationship, assessing the evidence for non-linearity and, in particular, on the existence of a threshold. In our analyses, we found consistent evidence that the associations are non-linear between FEV1 and metabolic disorders (both type 2 diabetes and MS). Threshold analysis demonstrated two FEV1 thresholds for type 2 diabetes and MS in both the Chinese and Australian populations: 1.76 L and 2.70L of FEV1. The risk of type 2 diabetes and MS decreased in the 1.76 to 2.70 range of FEV1 but neither increased nor decreased risk was observed below 1.76L or above 2.70L.

Both FEV1 and FVC as lung capacity measurements have been identified as possible predictors for the development of type 2 diabetes in cross-sectional studies and cohort studies24–26. It has been widely accepted that low lung function is associated with the subsequent occurrence of diabetes and related conditions6,27. For example, in the Normative aging study25, it was found that a lower FEV1 and lower FVC at baseline predicted hyperinsulinemia and estimated insulin resistance over 20 years of follow-up, independent of age, adiposity, and smoking. It was also found in a Swedish study that 4,637 non diabetic middle-aged men, baseline mean vital capacity was 10% lower among 116 men who developed diabetes during 6-years follow-up than those who did not develop diabetes28.

However, in most scenarios, the underlying associations between lung capacity measurements and risk of type 2 diabetes were assumed to be linear, eg Ford et al (2004) assessed the risk of incident type 2 diabetes by each 10ml decrease and 10% decrease of FEV1 and FVC29; Engstrom et al (2003) evaluated the decile decrease of FVC in prediction of the incident type 2 diabetes28. Few studies have set out to investigate the possible dose-response relationship between lung capacity measurements and risk of type 2 diabetes or MS.

To our knowledge, this is the first study that has explored the dose-response relationship between lung capacity measurements and both type 2 diabetes and MS using two independent representative samples from two different countries. Our results extend previous findings, suggesting that a non-linear relationship exists between lung capacity measurements, FEV1 in particular, and glucose metabolism disorders, both type 2 diabetes and metabolism: The risk of type 2 diabetes and MS decreased over the 1.76 to 2.70L range of FEV1 but neither increased nor decreased below 1.76L or above 2.70L. This was remarkably consistent in these two independent samples from two different countries.

We wonder if this new information suggests that patients with obstructive lung disease below the...
FEV1 threshold should be screened for diabetes and MS. This might reduce the potential to aggravate, unknowingly, undiagnosed dysglycaemia when commencing insulin antagonists such as steroids. Under the linear assumption of a dose-response relationship, there are no thresholds of lung capacity measurements, and therefore, it was previously difficult to propose a point for heightened awareness of the risk of significant hyperglycaemia. In the ARIC study, it was found that risk of incident diabetes was similar between women with average 2.6L of FEV1 and women with 2.9L of FEV1. However in our refined explorations of the dose-response relationship and thresholds, a relatively precise threshold has now been generated.

In our study, the threshold of 2.70L of FEV1 independent of age, gender, smoking, previous lung diseases, and adiposity, was identified both for type 2 diabetes and MS in both Chinese and Australian populations. An increased risk of type 2 diabetes and MS was more likely to be found among those with FEV1 below the threshold. Further studies should investigate whether the use of this threshold is cost-effective in both Western and Eastern populations.

Our results are generally consistent with previous studies on graded lung capacity in MS and type 2 diabetes, but this is the first time that a similar risk threshold has been reported. A similar FEV1 threshold for type 2 diabetes and MS suggests that the pathological process (assumed to be inflammation, but potentially glycation) commences early. This is supported by the relationship between fasting glycaemia and lung function in the general populations in both populations.

Comparisons of independent survey data between countries allow opportunities to study the similarities and differences in the association between lung capacity and dysglycaemia. Both cross-sectional survey datasets will incorporate variation by ethnicity, methodology and medical systems, potentially leading to variation in the prevalence of disease and clinical measurements. For this reason, we have not merged these datasets for analysis.

There may also be underlying differences in the distribution of lung capacity and metabolic markers between countries and in the delivery and effectiveness of healthcare, contributing to observed difference in associations between lung capacity and metabolic disorders. However, it has been feasible to compare associations between nations by using a rigorous approach to data analysis.

The approach we have used included a comparison of participant characteristics, levels of metabolic markers and the association between lung capacity measurements and metabolic markers. This suggests that the two datasets in the two countries were comparable and this is supported by the consistency in the association between lung capacity measurements and metabolic disorders between the two populations.

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The differences we observed were expected and may be partially explained by the smaller Australian sample size and ethnic differences. The latter could reflect different genetic backgrounds and anthropometry.

The principal limitation of the present study is the use of cross-sectional data in both China and Australia, whereby spirometry variables and disease status were assessed at the same time. If disease progression changed lung function, it is difficult to deduce causation from the association between pulmonary function and metabolic disease. Analysis of longitudinal study data would be the next step in examining these relationships further. Another limitation of this joint study is the data were not collected within the same survey: the data do appear comparable though. The temporary difference in data collection from the two nations might also have some impact on the research population.

CONCLUSION

In summary, our results suggest a non-linear relationship between FEV1 and risk of MS and type 2 diabetes exists in both Chinese and Australian populations. The threshold of FEV1 for the lowest risk of type 2 diabetes and MS was above 2.70L (95%CI: 2.68 to 2.72L and 2.65 to 2.76L in Chinese and Australian population respectively). FEV1 below 2.70L was associated with a high risk of MS and type 2 diabetes.

References

7. Walter RE, Beiser A, Givelber RJ, O'Connor GT, Gottlieb DJ. Association between

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Legends

**Figure 1. Forced expiratory volume in 1s and of forced vital capacity distribution by disease status.**

The figure shows the 25th, 50th (Median) and 75th percentile of the distribution of forced expiratory volume in 1s and of forced vital capacity (vertical lines on each box).
‘Whiskers’ on each box indicate values at 1.5 times the median (interquartile range) from the median and dots indicate the more extreme values, including the maximum and minimum of the distribution.

MS, metabolic syndrome; DM, diabetes mellitus.

(a) Distribution of FEV1 by disease status in Nanjing survey;
(b) Distribution of FVC by disease status in Nanjing survey;
(c) Distribution of FEV1 by disease status in Crossroads study;
(d) Distribution of FVC by disease status in Crossroads study;

Figure 2. Dose-response relationship between lung capacity measures (FEV1 and FVC) and odds ratios for type 2 diabetes both in Nanjing survey and Crossroads study

All odds ratios were adjusted for age, gender, body mass index, smoking status, history of COPD or asthma, systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high density lipoprotein cholesterol. The solid line indicates the odds ratio and the dashed lines represent the 95% CI.

(a) Dose-response relationship between FEV1 and odds ratios for type 2 diabetes in Nanjing survey;
(b) Dose-response relationship between FEV1 and odds ratios for type 2 diabetes in Crossroads study;
(c) Dose-response relationship between FVC and odds ratios for type 2 diabetes in Nanjing survey;
(d) Dose-response relationship between FVC and odds ratios for type 2 diabetes in Crossroads study.

Figure 3. Dose-response relationship between lung capacity measures (FEV1 and FVC) and odds ratios for metabolic syndrome both in Nanjing survey and Crossroads study

All odds ratios were adjusted for age, gender, body mass index, smoking status, history of COPD or asthma, systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high density lipoprotein cholesterol. The solid line indicates the odds ratio and the dashed lines represent the 95% CI.

a) Dose-response relationship between FEV1 and odds ratios for metabolic syndrome in Nanjing survey;

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b) Dose-response relationship between FEV1 and odds ratios for metabolic syndrome in Crossroads study;

c) Dose-response relationship between FVC and odds ratios for metabolic syndrome in Nanjing survey;

d) Dose-response relationship between FVC and odds ratios for metabolic syndrome in Crossroads study.
Table 1. Characteristics of participants in all and by metabolic diseases status

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<th>No metabolic syndrome/Type 2 diabetes</th>
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<th>Type 2 diabetes</th>
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<td>Current smoking, %</td>
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<td>33.7%</td>
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<td>Asthma/COPD, %</td>
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<td>22.6 (20.7 to 24.5)</td>
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<td>Waist circumference in men, cm</td>
<td>82 (75 to 89)</td>
<td>80.0 (74.0 to 86.1)</td>
<td>97.6 (95.5 to 100.6)</td>
<td>88.0 (81.0 to 92.9)</td>
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<td>124.0 (114.0 to 137.0)</td>
<td>137.0 (124.0 to 151.0)</td>
<td>137.0 (125.9 to 157.0)</td>
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<td>Diastolic blood pressure, mmHg</td>
<td>80.5 (73.5 to 88.5)</td>
<td>78.5 (72.0 to 86.0)</td>
<td>85.5 (78.0 to 93.5)</td>
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<td>Fasting glucose, mmol/L</td>
<td>5.4 (4.9 to 5.9)</td>
<td>5.3 (4.9 to 5.7)</td>
<td>5.4 (5.0 to 5.9)</td>
<td>7.7 (7.1 to 9.8)</td>
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<td>Triglyceride, mmol/L</td>
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<td>1.0 (0.7 to 1.5)</td>
<td>1.5 (1.1 to 2.2)</td>
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<td>High density lipoprotein cholesterol, mmHg</td>
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<td>1.3 (1.1 to 1.5)</td>
<td>1.3 (1.1 to 1.5)</td>
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<td>Study 2</td>
<td>Study 3</td>
<td>p-value</td>
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<td>2.4 (2.0 to 2.9)</td>
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<td>Age, years</td>
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<td>18.9%</td>
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<td>13.5%</td>
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<td>Asthma/COPD, %</td>
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<td>BMI, kg/m2</td>
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<td>Waist circumference in men, cm</td>
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<td>95.0 (89.5 to 102.8)</td>
<td>105.6 (99.7 to 112.5)</td>
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<td>88.0 (79.0 to 99.0)</td>
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<td>130.0 (114.0 to 145.0)</td>
<td>122.0 (111.0 to 137.0)</td>
<td>139.0 (127.0 to 151.0)</td>
<td>143.0 (127.0 to 159.0)</td>
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</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>72.0 (65.0 to 79.0)</td>
<td>70.0 (64.0 to 77.0)</td>
<td>75.0 (69.0 to 82.0)</td>
<td>76.0 (68.0 to 83.0)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>5.1 (4.8 to 5.5)</td>
<td>4.9 (4.7 to 5.2)</td>
<td>5.4 (5.1 to 5.8)</td>
<td>7.3 (6.2 to 8.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.2 (0.9 to 1.7)</td>
<td>1.0 (0.8 to 1.3)</td>
<td>1.9 (1.4 to 2.4)</td>
<td>1.7 (1.2 to 2.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.2 (4.6 to 5.9)</td>
<td>5.2 (4.6 to 5.8)</td>
<td>5.4 (4.8 to 6.1)</td>
<td>4.7 (4.3 to 5.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol, mmol/L</td>
<td>1.4 (1.1 to 1.6)</td>
<td>1.5 (1.3 to 1.8)</td>
<td>1.2 (1.0 to 1.4)</td>
<td>1.3 (1.0 to 1.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Low density lipoprotein cholesterol, mmol/L</td>
<td>3.1 (2.6 to 3.7)</td>
<td>3.2 (2.6 to 3.7)</td>
<td>3.3 (2.7 to 3.9)</td>
<td>2.7 (2.3 to 3.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Metabolic markers</td>
<td>All Model 1‡</td>
<td>Model 2†</td>
<td>No metabolic syndrome/Type 2 diabetes Model 1‡</td>
<td>Model 2†</td>
<td>Metabolic syndrome Model 1‡</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>----------</td>
<td>---------------------------------</td>
<td>---------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td><strong>Nanjing Survey</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>-0.08 (-0.14 to -0.007)</td>
<td>-0.08 (-0.15 to -0.01)</td>
<td>0.02 (-0.02 to 0.06)</td>
<td>0.02 (-0.02 to 0.06)</td>
<td>-0.04 (-0.11 to 0.03)</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>0.02 (-0.05 to 0.08)</td>
<td>0.01 (-0.06 to 0.08)</td>
<td>0.02 (-0.04 to 0.09)</td>
<td>0.02 (-0.05 to 0.08)</td>
<td>-0.09 (-0.24 to 0.06)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>0.01 (-0.03 to 0.06)</td>
<td>0.02 (-0.02 to 0.07)</td>
<td>0.04 (-0.01 to 0.09)</td>
<td>0.06 (0.008 to 0.11)</td>
<td>-0.11 (-0.21 to -0.01)</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol, mmol/L</td>
<td>-0.001 (-0.17 to 0.15)</td>
<td>0.004 (-0.01 to 0.02)</td>
<td>0.006 (-0.013 to 0.02)</td>
<td>0.01 (-0.01 to 0.03)</td>
<td>-0.02 (-0.05 to 0.013)</td>
</tr>
<tr>
<td>Low density lipoprotein cholesterol, mmol/L</td>
<td>0.004 (-0.03 to 0.04)</td>
<td>0.02 (-0.02 to 0.005)</td>
<td>0.03 (-0.01 to 0.07)</td>
<td>0.04 (-0.002 to 0.08)</td>
<td>-0.11 (-0.19 to -0.018)</td>
</tr>
<tr>
<td><strong>Crossroad study</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>-0.12 (-0.19 to -0.05)</td>
<td>-0.12 (-0.23 to -0.002)</td>
<td>0.02 (-0.01 to 0.05)</td>
<td>0.02 (-0.04 to 0.07)</td>
<td>-0.03 (-0.09 to 0.03)</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>0.05 (-0.02 to 0.12)</td>
<td>0.04 (-0.04 to 0.12)</td>
<td>0.04 (0.0008 to 0.08)</td>
<td>0.04 (-0.01 to 0.09)</td>
<td>-0.14 (-0.31 to 0.032)</td>
</tr>
</tbody>
</table>
Table 3. Association between various markers of glycemic status and FVC both in Nanjing Survey and Crossroad study

<table>
<thead>
<tr>
<th>Metabolic markers</th>
<th>All</th>
<th>No metabolic syndrome/Type 2 diabetes</th>
<th>Metabolic syndrome</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1‡</td>
<td>Model 2†</td>
<td>Model 1‡</td>
<td>Model 2†</td>
</tr>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>-0.15 (-0.21 to -0.09)</td>
<td>-0.16 (-0.22 to -0.10)</td>
<td>-0.05 (-0.08 to -0.02)</td>
<td>-0.05 (-0.08 to -0.02)</td>
</tr>
</tbody>
</table>

‡ Results were adjusted for age, sex, and body mass index.
† Results were adjusted for age, sex, body mass index, smoking status, and history of COPD or asthma.
CI, confidence interval.
<table>
<thead>
<tr>
<th>Triglyceride, mmol/L</th>
<th>0.04 (-0.02 to 0.09)</th>
<th>0.03 (-0.03 to 0.09)</th>
<th>0.07 (0.01 to 0.12)</th>
<th>0.06 (0.01 to 0.12)</th>
<th>-0.003 (-0.13 to 0.12)</th>
<th>-0.005 (-0.13 to 0.12)</th>
<th>0.12 (-0.24 to 0.48)</th>
<th>0.11 (-0.27 to 0.48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>-0.05 (-0.08 to -0.01)</td>
<td>-0.04 (-0.08 to -0.003)</td>
<td>-0.02 (-0.06 to -0.02)</td>
<td>-0.01 (-0.05 to -0.03)</td>
<td>-0.10 (-0.19 to -0.02)</td>
<td>-0.11 (-0.19 to -0.02)</td>
<td>-0.05 (-0.23 to 0.12)</td>
<td>-0.05 (-0.23 to 0.13)</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol, mmol/L</td>
<td>-0.02 (-0.03 to -0.01)</td>
<td>-0.02 (-0.03 to -0.002)</td>
<td>-0.02 (-0.04 to -0.01)</td>
<td>-0.02 (-0.04 to 0.006)</td>
<td>-0.005 (-0.03 to 0.02)</td>
<td>0.0008 (-0.03 to 0.03)</td>
<td>0.009 (-0.04 to 0.06)</td>
<td>0.02 (-0.04 to 0.07)</td>
</tr>
<tr>
<td>Low density lipoprotein cholesterol, mmol/L</td>
<td>-0.06 (-0.09 to -0.03)</td>
<td>-0.05 (-0.08 to -0.02)</td>
<td>-0.04 (-0.07 to 0.002)</td>
<td>-0.03 (-0.06 to 0.02)</td>
<td>-0.14 (-0.21 to -0.02)</td>
<td>-0.15 (-0.23 to -0.07)</td>
<td>-0.09 (-0.22 to -0.05)</td>
<td>-0.08 (-0.22 to 0.06)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Crossroads study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose, mmol/L</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol, mmol/L</td>
</tr>
<tr>
<td>Low density lipoprotein cholesterol, mmol/L</td>
</tr>
</tbody>
</table>

† Results were adjusted for age, sex, and body mass index.

‡ Results were adjusted for age, sex, body mass index, smoking status, and history of COPD or asthma.

CI, confidence interval.

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