SUPPLEMENTARY DATA

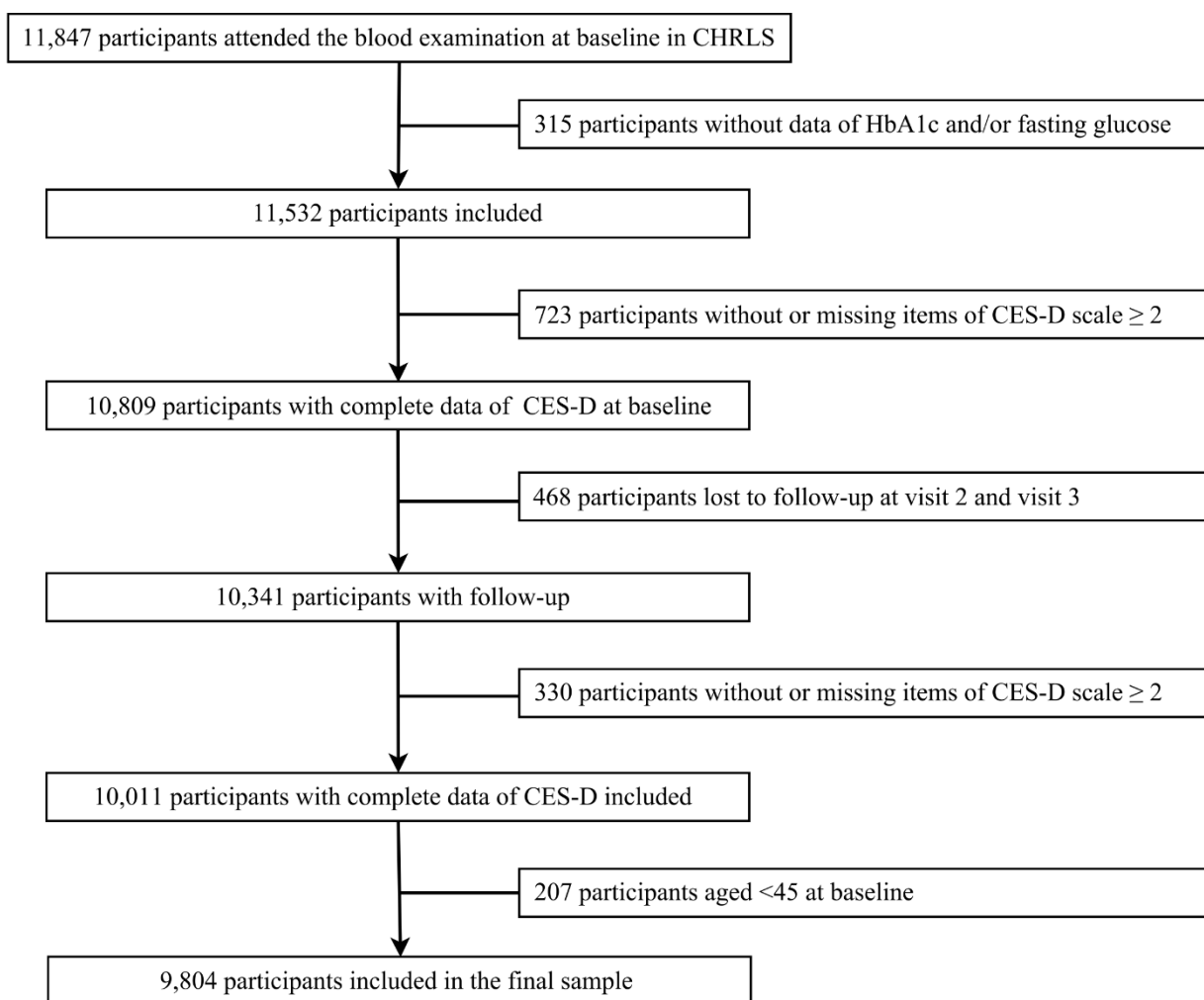# Prospective Study of Glycated Hemoglobin and Trajectories of Depressive Symptoms: The China Health and Retirement Longitudinal Study

**Haibin Li[1,2], Anxin Wang[1,2], Wei Feng[1,2], Deqiang Zheng[1,2], Qi Gao[1,2], Lixin Tao[1,2], Jin Guo[3], Xiaonan Wang[1,2], Xia Li[4], Wei Wang[5], Xiuhua Guo[1, 2*]**
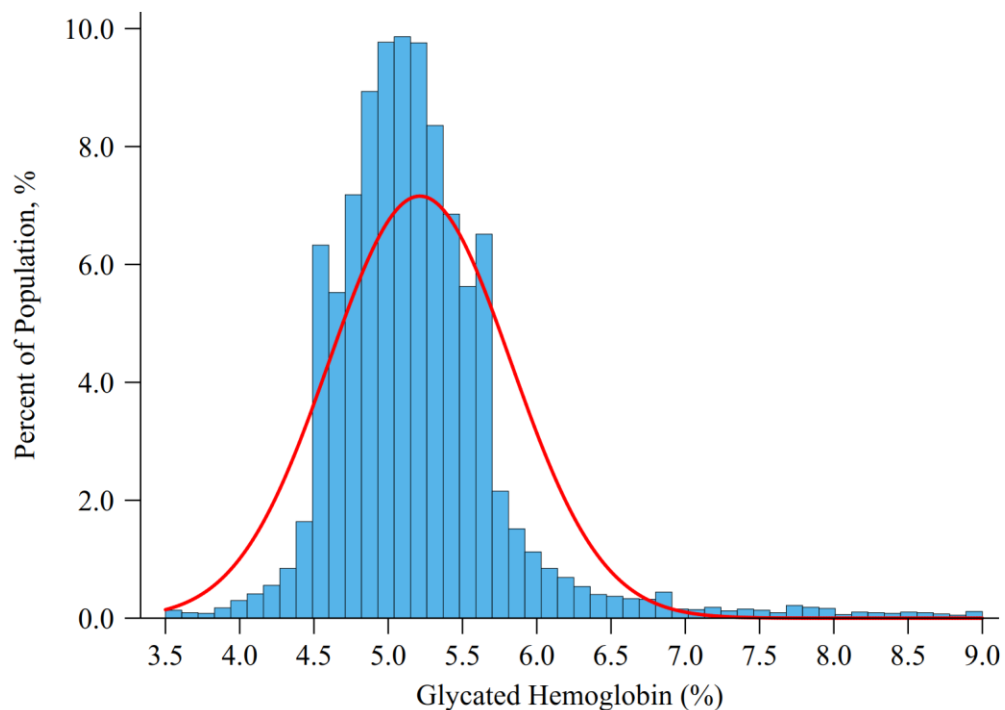
[1]Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, Beijing, China. [2]Beijing Municipal Key Laboratory of Clinical Epidemiology, Capital Medical University, Beijing, China. [3]Greenwood Medical Company, 300 Highway Burwood, Melbourne, Melbourne, Victoria, Australia. [4]Department of Mathematics and Statistics, La Trobe University, Victoria, Australia. [5]Global Health and Genomics, School of Medical Sciences and Health, Edith Cowan University, Perth, Western Australia, Australia.
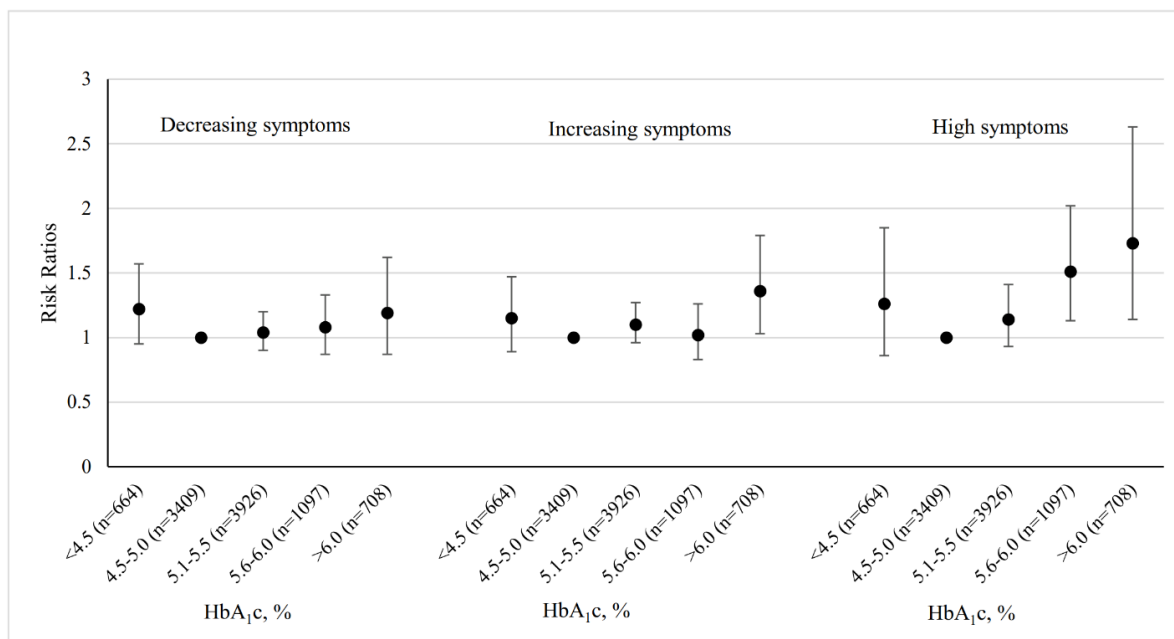
# SUPPLEMENTARY DATA

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┌─────────────────────────────────────────────────────────────┐
│ 11,847 participants attended the blood examination at         │
│ baseline in CHRLS                                             │
└─────────────────────────────────────────────────────────────┘
                              │
                              ├──────────┐
                              │          ▼
                              │  ┌──────────────────────────────────────────┐
                              │  │ 315 participants without data of HbA1c     │
                              │  │ and/or fasting glucose                     │
                              │  └──────────────────────────────────────────┘
                              ▼
┌─────────────────────────────────────────────┐
│ 11,532 participants included                 │
└─────────────────────────────────────────────┘
                              │
                              ├──────────┐
                              │          ▼
                              │  ┌──────────────────────────────────────────┐
                              │  │ 723 participants without or missing items  │
                              │  │ of CES-D scale ≥ 2                         │
                              │  └──────────────────────────────────────────┘
                              ▼
┌─────────────────────────────────────────────┐
│ 10,809 participants with complete data of     │
│ CES-D at baseline                            │
└─────────────────────────────────────────────┘
                              │
                              ├──────────┐
                              │          ▼
                              │  ┌──────────────────────────────────────────┐
                              │  │ 468 participants lost to follow-up at       │
                              │  │ visit 2 and visit 3                        │
                              │  └──────────────────────────────────────────┘
                              ▼
┌─────────────────────────────────────────────┐
│ 10,341 participants with follow-up            │
└─────────────────────────────────────────────┘
                              │
                              ├──────────┐
                              │          ▼
                              │  ┌──────────────────────────────────────────┐
                              │  │ 330 participants without or missing items   │
                              │  │ of CES-D scale ≥ 2                         │
                              │  └──────────────────────────────────────────┘
                              ▼
┌─────────────────────────────────────────────┐
│ 10,011 participants with complete data of     │
│ CES-D included                               │
└─────────────────────────────────────────────┘
                              │
                              ├──────────┐
                              │          ▼
                              │  ┌──────────────────────────────────────────┐
                              │  │ 207 participants aged <45 at baseline       │
                              │  └──────────────────────────────────────────┘
                              ▼
┌─────────────────────────────────────────────┐
│ 9,804 participants included in the final      │
│ sample                                       │
└─────────────────────────────────────────────┘
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**Supplementary Figure 1. Flowchart of Study Profile.**

# SUPPLEMENTARY DATA



**Supplementary Figure 2. Histogram of Serum glycated hemoglobin Concentrations. Red Solid curve denotes the normality plot.**



**Supplementary Figure 3. The risk ratios of decreasing, increasing and high depressive symptoms by using an alternative HbA₁c category** (<4.5%, 4.5-5.0%, 5.1-5.5%, 5.6-6.0%, and >6.0%).

# SUPPLEMENTARY DATA

**Supplementary Table 1**. Sensitivity Analyses for the Association Between Quintile of Glycated Hemoglobin (HbA$_1$c) and Risk of Trajectories of Depressive Symptoms*

|  | Low symptoms | Decreasing symptoms | Increasing symptoms | High symptoms |
|---|---|---|---|---|
| Excluding participants who had antidepressant use (n=63) ¶ | | | | |
| Quintile 1 | | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| Quintile 2 | | 0.88 (0.73-1.07) | 1.05 (0.87-1.27) | 0.86 (0.64-1.15) |
| Quintile 3 | | 1.01 (0.84-1.22) | 1.00 (0.83-1.20) | 1.12 (0.85-1.47) |
| Quintile 4 | | 0.89 (0.73-1.07) | 1.20 (1.01-1.44) | 0.93 (0.71-1.22) |
| Quintile 5 | | 1.02 (0.83-1.26) | 1.12 (0.92-1.37) | 1.38 (1.03-1.85) |
| Excluding participants who had treatments for diabetes (n=394) † | | | | |
| Quintile 1 | | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| Quintile 2 | | 0.88 (0.73-1.08) | 1.07 (0.89-1.29) | 0.86 (0.64-1.16) |
| Quintile 3 | | 1.03 (0.86-1.24) | 0.99 (0.82-1.20) | 1.15 (0.87-1.51) |
| Quintile 4 | | 0.89 (0.74-1.08) | 1.23 (1.03-1.47) | 0.96 (0.73-1.27) |
| Quintile 5 | | 1.08 (0.88-1.34) | 1.11 (0.91-1.37) | 1.44 (1.07-1.94) |
| Excluding participants who had treatments for depression and/or diabetes (n=453) ‡ | | | | |
| Quintile 1 | | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| Quintile 2 | | 0.88 (0.72-1.07) | 1.07 (0.89-1.29) | 0.88 (0.65-1.18) |
| Quintile 3 | | 1.02 (0.85-1.23) | 1.00 (0.83-1.21) | 1.16 (0.88-1.53) |
| Quintile 4 | | 0.89 (0.74-1.08) | 1.23 (1.02-1.47) | 0.94 (0.71-1.25) |
| Quintile 5 | | 1.09 (0.88-1.35) | 1.12 (0.92-1.38) | 1.43 (1.06-1.93) |

*Data was reported as risk ratios (95%CI) from multinomial logistic regression.

¶ Model was adjusted for demographics [a], health behaviors [b], baseline health conditions [c], cardiac marker [d], and cognition scores.

† Model was adjusted for demographics [a], health behaviors [b], baseline health conditions (excluding treated diabetes) [c], cardiac marker [d], antidepressant use and cognition scores.

‡ Model was adjusted for demographics [a], health behaviors [b], baseline health conditions [c], cardiac (excluding treated diabetes) marker [d], and cognition scores.

**Supplementary Table 2**. Risk Ratios for the Association Between Quintile of Glycated Hemoglobin (HbA$_1$c) and Risk of Incident Depressive Symptoms During 4-year of follow-up Among Nondepressed Individuals at Baseline*

|  | No. cases | Crude IRRs | Adjusted IRRs ¶ |
|---|---|---|---|
| Quintile 1 (n=1325) | 259 | 1.00 (Reference) | 1.00 (Reference) |
| Quintile 2 (n=1080) | 246 | 1.17 (1.00-1.36) | 1.16 (1.00-1.35) |
| Quintile 3 (n=1116) | 247 | 1.13 (0.97-1.32) | 1.11 (0.96-1.30) |
| Quintile 4 (n=1174) | 309 | 1.35 (1.16-1.56) | 1.29 (1.12-1.49) |
| Quintile 5 (n=972) | 220 | 1.16 (0.99-1.36) | 1.12 (0.95-1.33) |

*Data was reported as incidence rate ratio (95%CI) from modified Poisson regression models with a robust error variance.

¶Model was adjusted for demographics [a], health behaviors [b], baseline health conditions [c], cardiac marker [d], antidepressant use and cognition scores (Model 5) plus baseline CES-D scores.