ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1

CHINA CDC WEEKLY

Vol. 5 No. 45 Nov. 10, 2023

中国疾病预防控制中心周报

World Diabetes Day

Novemeber 14, 2023

Access to diabetes care

WORLD DIABETES DAY ISSUE

ISSN 2096-7071

China CDC Weekly

Cover Image: adapted from the International Diabetes Federation, https://worlddiabetesday.org/resources/wdd2021-23/toolkit/.

This week's issue was organized by Guest Editor An Pan.

Foreword

Modifiable Risk Factors in the Prevention and Management of Type 2 Diabetes: Implications and Future Directions for China

Tingting Geng[1]; Gang Liu[2]; An Pan[2,#]

Diabetes, marked by an elevated concentration of blood glucose, presents a substantial global public health challenge. It is estimated that around 537 million adults(20-79 years) globally suffer from diabetes, primarily type 2 diabetes in 2021. This figure is projected to increase to 783 million by 2045. As of 2021, the countries with the greatest number of adults living with diabetes are China, India, and Pakistan (*1*). According to data obtained from the China Chronic Disease and Risk Factors Surveillance, the estimated prevalence of diabetes was 12.4% in 2018 (*2*). Diabetes is acknowledged as a multifaceted cardiorenal-metabolic ailment associated with diverse metabolic and homeostatic disturbances that evolve over time (*3*). Although genetics contribute to the susceptibility to diabetes, increasing evidence suggests that modifiable risk factors, such as lifestyle (including nutrition and physical activity) and socioeconomic status (SES), play a pivotal role in both preventing and managing the disease.

This special issue contains a collection of articles that explore the relationship between lifestyle choices, SES, and diabetes, along with its related complications. Physical activity proves to be a key aspect of diabetes prevention and control. Drawing from the China Kadoorie Biobank (CKB) data, Li et al. (*4*) underline that patients with diabetes were more prone to engage in low-level physical activities compared to non-diabetic counterparts. Corroborating this notion, Yu et al. (*5*), based on objectively measured physical activity, infers that an increase in daily step counts was correlated with lower odds of cardiovascular events among patients with type 2 diabetes in China.

The third paper in this issue of *China CDC Weekly* underlines the important role of dietary factors, particularly the consumption of red and processed meat, can have on diabetes prevention, specifically in East Asian populations. The research confirmed the positive relationship between the consumption of processed meat and the risk of diabetes (*6*). While moderate intake of unprocessed red meat was not related to higher diabetes risk, surpassing a certain consumption threshold could pose a risk for type 2 diabetes.

The concluding paper in this series delves into various risk factors for diabetes such as age, sex, SES, lifestyle choices, and metabolic factors. The study emphasizes the need for forming prevention strategies tailored to distinct age-specific risk profiles. In addition, it discourses on diabetes being a key risk contributor to cardiovascular complications and elaborates on its impacts across age categories (*7*).

This special issue emphasizes the modifiable risk factors such as diet, physical activity, and SES, for the prevention and management of diabetes within China. However, there remains an urgent need for additional research on the Chinese population. First, there should be an expansion in the scope of dietary factors considered in the studies, including but not limited to cooking styles (*8*), dietary chronotype (*9*), and microplastics from take-out foods (*10*). These additions could enhance the understanding of the relationship between dietary habits and the susceptibility to diabetes and related complications among Chinese population. Furthermore, the emerging implications of wearable technology, such as accelerometers, relating to health outcomes have been gaining prominence (*11–12*). The implementation of this wearable technology could potentially facilitate the prevention and management strategies for diabetes; hence, more empirical evidence derived from Chinese cohorts is crucial. Lastly, the realm of precision medicine, which entails multi-omics and pharmacogenomics, is showing great potential for increasing our understanding of physiology and can contribute to proactive prevention strategies and targeted therapies.

Conflicts of interest: No conflicts of interest.

Funding: Supported by grants 81930124 from the National Natural Science Foundation of China and grant 2022YFC3600600 from the National Key Research and Development Program of China.

doi: 10.46234/ccdcw2023.187

[#] Corresponding author: An Pan, panan@hust.edu.cn.

[1] School of Public Health & Institute of Nutrition, Fudan University, Shanghai, China; [2] School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China.

Submitted: November 04, 2023; Accepted: November 05, 2023

REFERENCES

1. Ogurtsova K, Guariguata L, Barengo NC, Ruiz PLD, Sacre JW, Karuranga S, et al. IDF diabetes Atlas: global estimates of undiagnosed diabetes in adults for 2021. Diabetes Res Clin Pract 2022;183:109118. http://dx.doi.org/10.1016/j.diabres.2021.109118.
2. Wang LM, Peng W, Zhao ZP, Zhang M, Shi ZM, Song ZW, et al. Prevalence and treatment of diabetes in China, 2013–2018. JAMA 2021;326(24):2498 – 506. http://dx.doi.org/10.1001/jama.2021.22208.
3. Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. A synopsis of the evidence for the science and clinical management of Cardiovascular-Kidney-Metabolic (CKM) syndrome: a scientific statement from the American heart association. Circulation 2023. http://dx.doi.org/10.1161/cir.0000000000001186.
4. Li AL, Lyu J, Chen YY, Shao ZL, Sun DJY, Yu CQ, et al. Comparative study on physical activity in diabetic and non-diabetic individuals and influential factors — China, 2020–2021. China CDC Wkly 2023;5(45):1001 – 5. http://dx.doi.org/10.46234/ccdcw2023.188.
5. Yu P, Ni XJ, Xu L, Zhang L, Cao L, Chen QY, et al. Impact of daily step count on diabetes management and complications among elderly individuals — Jiangsu Province, China, 2020–2022. China CDC Wkly 2023;5(45):1006 – 11. http://dx.doi.org/10.46234/ccdcw2023.189.
6. Yu HC, Zhang JJ, Xie JC, Li XL, Wang YJ, Yang YJ, et al. Dose-response meta-analysis on risk of diabetes in relation to red and processed meat consumption — Asian populations, 2006–2021. China CDC Wkly 2023;5(45):1012 – 6. http://dx.doi.org/10.46234/ccdcw2023.190.
7. Dou C, Liu D, Wang TG. Risk factors for diabetes and cardiovascular complications in the Chinese population. China CDC Wkly 2023;5(45):1017 – 21. http://dx.doi.org/10.46234/ccdcw2023.191.
8. Liu G, Zong G, Wu KN, Hu Y, Li YP, Willett WC, et al. Meat cooking methods and risk of type 2 diabetes: results from three prospective cohort studies. Diabetes Care 2018;41(5):1049 – 60. http://dx.doi.org/10.2337/dc17-1992.
9. Hou WY, Han TS, Sun XY, Chen YY, Xu JX, Wang Y, et al. Relationship between carbohydrate intake (quantity, quality, and time eaten) and mortality (total, cardiovascular, and diabetes): assessment of 2003-2014 national health and nutrition examination survey participants. Diabetes Care 2022;45(12):3024 – 31. http://dx.doi.org/10.2337/dc22-0462.
10. Du FN, Cai HW, Zhang Q, Chen QQ, Shi HH. Microplastics in take-out food containers. J Hazard Mater 2020;399:122969. http://dx.doi.org/10.1016/j.jhazmat.2020.122969.
11. Ho FK, Zhou ZY, Petermann-Rocha F, Para-Soto S, Boonpor J, Welsh P, et al. Association between device-measured physical activity and incident heart failure: a prospective cohort study of 94 739 UK biobank participants. Circulation 2022;146(12):883 – 91. http://dx.doi.org/10.1161/circulationaha.122.059663.
12. Stamatakis E, Ahmadi MN, Gill JMR, Thøgersen-Ntoumani C, Gibala MJ, Doherty A, et al. Association of wearable device-measured vigorous intermittent lifestyle physical activity with mortality. Nat Med 2022;28(12):2521 – 9. http://dx.doi.org/10.1038/s41591-022-02100-x.

An Pan
Dean and Professor of School of Public Health,
Tongji Medical College, Huazhong University of Science and Technology

Preplanned Studies

Comparative Study on Physical Activity in Diabetic and Non-Diabetic Individuals and Influential Factors — China, 2020–2021

Aolin Li[1]; Jun Lyu[1,2,3]; Yuanyuan Chen[1]; Zilun Shao[1]; Dianjianyi Sun[1,3,#]; Canqing Yu[2,3,#]; Liming Li[1,2,3]

Summary

What is already known about this topic?

The majority of Chinese patients with diabetes failed to achieve the level of physical activity recommended by clinical guidelines.

What is added by this report?

The prevalence of low-level physical activity was found to be greater in individuals diagnosed with diabetes. It was observed that patients with a protracted duration of diabetes demonstrated a propensity to participate in lower levels of physical activity compared to those with a shorter disease trajectory. The likelihood of engaging in low-level physical activity associated with diabetes was higher in rural inhabitants, those with medium-tier education, employed individuals, and individuals who had longer sleep durations.

What are the implications for public health practice?

Developing strategies and interventions to encourage greater involvement of Chinese diabetic patients in physical activity is essential. However, these strategies must take population characteristics into account.

Diabetes mellitus (DM) is a chronic metabolic disorder marked by high blood glucose levels, often resulting in multi-organ and systemic insufficiency or failure. Over the last three decades, there's been a noted increase in DM prevalence in China (*1*). Previous research has suggested that sufficient, appropriate physical activity (PA) can assist DM patients in regulating their blood glucose levels (*2*), and numerous national guidelines for comprehensive DM management advocate for regular PA (*1*,*3*). Prior studies exploring the PA level of DM patients in China typically suffered from small sample sizes and lacked comparative analysis with the general population (*4*–*5*). Thus, this study aims to examine the variations in PA between Chinese individuals with and without DM and to identify influential factors utilizing data from the third resurvey of the China Kadoorie Biobank (CKB).

The CKB constitutes one of the largest prospective cohort studies globally, surveying across 10 sites within China. The CKB obtains crucial sociodemographic data, lifestyle factors, and histories of common chronic diseases through direct, face-to-face interviews. Additionally, trained technicians perform on-site physical examinations, including height and weight measurements, adhering to a standard operating procedure.

The initial baseline data (2004–2008) of the CKB incorporated more than 512,000 participants, with the third resurvey data (2020–2021) focusing on a randomly selected subset constituting approximately 5% of the initial participant pool. This resurvey examined a total of 25,087 participants, aged between 40 and 95 years old, across the 10 original study sites and collected relevant data in a method consistent with the baseline study. Participants were selectively excluded based on certain criteria. These included missing value data related to PA, DM status, and other important covariates. Individuals with self-reported histories of tumors or asthma were also omitted from the study.

The PA level was assessed by calculating the sum of the product of the metabolic equivalent of task (MET) multiplied by the duration of each PA, measured in unit time. Within the CKB, PA levels were stratified by gender and age (either ≥65 or <65 years). Low-level PA was characterized as those falling below the lowest tertile of their corresponding gender and age group. Participants reporting a history of DM were classified as DM patients.

Continuous variables were described using mean±standard deviation, while frequencies and proportions were used for categorical variables. The chi-squared test or *t*-test was utilized to identify differences between groups. DM and PA level relationships were separately assessed through multiple logistic regression, adjusted for social demographic factors such as age, gender, region, educational level, and occupational status. This model also took into account body mass index (BMI), lifestyle factors

(smoking, drinking, and sleep time), and history of other chronic diseases.

The effects of blood glucose control (characterized by fasting glucose: <7.0 mmol/L and ≥7.0 mmol/L; random glucose: <11.1 mmol/L and ≥11.1 mmol/L) and length of DM course (≤5, 5–10, and >10 years) on PA level were further explored. Stratified analysis ensued, in which the relationship between DM and PA level was examined at each covariate level with other covariates serving as controls. The interaction was assessed through the construction of a logistic regression model, with PA level as the dependent variable, and the product of one discrete covariate and DM as the independent variable(s). The statistical significance of the interaction between the covariate and DM was determined by the *P*-value from the likelihood ratio test for the product term, also adjusted for additional covariates. Linear trends of DM course impact on PA level were tested. To mitigate the risk of reverse causation, analyses were rerun while excluding DM patients diagnosed within the previous year. Data analysis for this study was executed using SPSS software (version 27.0: IBM Corp., Armonk, NY, USA), coupled with a bilateral test and a test level of $P<0.05$.

This study incorporated a total of 24,494 participants drawn from the CKB, the mean age being 65.5±9.1 years (Table 1), with 3,107 individuals, or 12.7%, having DM. Statistically significant differences were observed in PA levels among DM patients, with a higher prevalence of low-level PA compared to non-DM individuals ($P<0.001$). Additionally, variations were evident between the two groups regarding age, gender, geographic region, education level, profession, lifestyle, BMI, and history of chronic diseases.

Upon adjusting for potential confounders, we found no heightened likelihood of diminished PA in patients with DM compared to their non-DM counterparts [odds ratio (*OR*): 1.04, 95% confidence interval (*CI*): 0.95–1.13] (Table 2). Notably, individuals with a DM history surpassing a decade exhibited the highest propensity towards low-level PA, corresponding to an *OR* (95% *CI*) at 1.12 (1.00, 1.26). We also observed a significant linear trend linking the course of DM with reduced PA levels ($P_{trend}<0.001$, Table 2). However, the contrast in the likelihood of diminished PA between DM patients exhibiting poor versus good glucose control did not reach statistical significance.

The interaction between all population characteristics and DM was found to be statistically significant ($P<0.05$), with the exception of smoking ($P=0.052$). When conducting stratified analyses, instances of DM-associated low-level PA were found to be more prevalent among rural, medium-educated, employed individuals and those with sleep durations of ≥9 h (Table 3).

The sensitivity analysis, excluding DM patients diagnosed within 1 year, yielded results that were

TABLE 1. Basic characteristics of CKB research subjects.

Variables	Total	DM	Non-DM	*P*-value
n	24,494	3,107	21,387	
Age (years, $\bar{x}\pm s$)	65.5±9.1	65.5±9.1	65.5±9.1	<0.001
Male (%)	35.6	66.9	36.0	0.001
Region (%)				<0.001
Urban	49.7	39.7	41.0	
Rural	50.3	60.3	59.0	
Education level* (%)				0.032
Low	54.1	51.6	51.9	
Medium	41.9	43.8	43.6	
High	4.0	4.6	4.5	
Occupation (%)				<0.001
Employed	24.8	37.5	36.0	
Retired/unemployed	75.2	62.5	64.0	
Smoking (%)				<0.001
Never	74.6	71.1	71.5	
Previous	8.2	7.3	7.4	
Current	17.2	21.6	21.1	
Drinking (%)				<0.001
Never	70.6	65.8	66.4	
Previous	4.3	3.2	3.4	
Current	25.1	31.0	30.2	
Sleep duration (h, %)				<0.001
≤6	37.6	34.1	34.5	
7–8	42.6	47.0	46.4	
≥9	19.8	18.9	19.1	
BMI (kg/m^2, %)				<0.001
Low and normal	38.4	47.6	46.4	
Overweight	42.9	38.4	38.9	
Obesity	18.7	14.0	14.7	
Other chronic disease history† (%)	45.0	67.2	41.8	<0.001
Low-level PA (%)	33.3	39.8	32.3	<0.001

Abbreviation: DM=diabetes mellitus; BMI=body mass index; PA=physical activity; CKB=China Kadoorie Biobank.

* Low, medium, and high level of education in CKB refers to primary school and below, secondary school and college and above.

† Other chronic medical history includes cardiovascular disease, chronic obstructive pulmonary disease, and hypertension.

TABLE 2. Association of DM, DM course, and blood glucose control with low-level PA.

DM conditions	Low-Level PA*
DM diagnosis	
No	1.00
Yes	1.04 (0.95, 1.13)
The course of DM	
Non-DM	1.00
≤5 years	0.97 (0.84, 1.13)
5–10 years	0.94 (0.80, 1.12)
>10 years	1.12 (1.00, 1.26)
P_{trend}	<0.001
Blood glucose control	
Non-DM	1.00
Good	1.03 (0.93, 1.14)
Poor	1.04 (0.92, 1.19)

Abbreviation: DM=diabetes mellitus; PA=physical activity.
*Adjusted for age, gender, region, education level, occupation, smoking, drinking, sleep duration, BMI, and other chronic medical history.

consistent with the initial findings (Supplementary Tables S1–S2, available in https://weekly.chinacdc.cn/).

DISCUSSION

In the current investigation, we analyzed the third resurvey data from CKB and found that, while no significant disparity existed in the prevalence of low-level PA between Chinese individuals with and without DM, the occurrence of low-level PA was higher in those managing DM. Previous studies have primarily reported low adherence rates to the guideline-recommended level of PA in Chinese DM patients, absent any comparison with their non-DM cohorts (*4*–*5*). By contrasting the PA levels in subjects with and without DM, we were able to somewhat control the background PA levels.

Furthermore, our findings indicated that patients with a protracted duration of DM were more likely to participate in low-intensity PA. This trend suggests that as DM progresses, patients often face complications, including coronary heart disease, chronic kidney disease, and eye disease, significantly limiting their potential for PA (*6*). Our findings indicated a higher likelihood of decreased PA associated with DM amongst rural-dwelling, moderately educated individuals who routinely sleep for nine or more hours. Relative to urban patients, those residing in rural areas often receive inadequate health education and exhibit lower health management awareness. Consequently, their levels of PA are more susceptible to the influence of DM. Individuals with lower educational levels typically engage in occupations involving substantial PA, making their PA less vulnerable to the impacts of DM. Conversely, highly educated persons have a higher awareness of the critical role of PA and often engage in greater levels of leisure-time PA (*7*), thereby rendering moderately educated persons more susceptible to lower PA associated with DM compared to other education levels. Prior research has demonstrated an increased perception of exertion during physical activity in individuals with inadequate sleep, which influences upper and lower limb performance (*8*). Correspondingly, our study found that those sleeping for nine or more hours also exhibited lower PA levels. This suggests that both insufficient and excessive sleep could potentially be detrimental to PA.

Our research was based upon an extensive study conducted in China. The sizeable participant group, the wealth of information regarding exposure and disease specifics, and the impeccable data quality enhanced our findings. However, our study is not without limitations.

The study was subject to some limitations. The first limitation is inherent to a cross-sectional analysis — it prevents us from determining the causal correlation between DM and PA. To validate the soundness of our results, we performed a sensitivity test, excluding DM-affected participants identified within the past year. The consistency of our results gives confidence in their robustness. The second limitation refers to the exclusion of participants due to missing variables, which potentially introduced selection bias to our study. Lastly, we relied on patient self-reporting to determine the presence of DM. This approach may inadvertently exclude individuals with undiagnosed DM. Compared to those aware of their DM status, this group may pay less attention to health management and, as a result, have lower PA levels. By utilizing self-reported data alone, the likelihood of overestimating PA amongst DM patients increases, creating the potential for false-negative conclusions.

Our results underscore the necessity of crafting actionable strategies and interventions designed to inspire a higher level of PA engagement among Chinese DM patients. It is paramount that such guidelines and interventive actions are grounded in an understanding of Chinese cultural and societal

TABLE 3. Association of DM with low-level PA at different levels of population characteristics.

Subgroups	Low-Level PA*		
	Non-DM	DM	Interaction *P*-value
Age (years)			
<60	1.00	1.26 (1.00–1.57)	<0.001
≥61	1.00	1.02 (0.93–1.12)	
Sex			
Male	1.00	1.00 (0.86–1.17)	<0.001
Female	1.00	1.06 (0.96–1.18)	
Region			
Urban	1.00	0.93 (0.82–1.05)	<0.001
Rural	1.00	1.20 (1.06–1.36)	
Education level†			
Low	1.00	1.00 (0.89–1.12)	<0.001
Medium	1.00	1.15 (1.00–1.31)	
High	1.00	0.74 (0.47–1.17)	
Occupation			
Employed	1.00	1.49 (1.20–1.86)	<0.001
Retired/unemployed	1.00	0.99 (0.91–1.01)	
Smoking			
Never	1.00	1.02 (0.92–1.12)	0.052
Previous	1.00	1.26 (0.94–1.69)	
Current	1.00	1.07 (0.85–1.33)	
Drinking			
Never	1.00	1.03 (0.93–1.14)	<0.001
Previous	1.00	0.83 (0.55–1.26)	
Current	1.00	1.09 (0.92–1.30)	
Sleep duration (h)			
≤6	1.00	0.97 (0.84–1.11)	0.011
7–8	1.00	1.01 (0.89–1.16)	
≥9	1.00	1.22 (1.01–1.47)	
Other chronic disease history§			
Yes	1.00	1.03 (0.93–1.14)	<0.001
No	1.00	1.09 (0.94–1.26)	

Abbreviation: PA=physical activity; DM=diabetes mellitus.
* All adjusted for variables other than the stratification variable in Table 3;
† Low, medium, and high level of education in CKB refers to primary school and below, secondary school and college and above;
§ Other chronic medical history includes cardiovascular disease, chronic obstructive pulmonary disease, and hypertension.

characteristics, thereby facilitating a more targeted enhancement of PA levels among this patient population.

Conflicts of interest: No conflicts of interest.

Acknowledgements: The participants in the China Kadoorie Biobank and the members of the survey teams in each of the 10 regional centers, as well as the project development and management teams based at Beijing, Oxford, and the 10 regional centers.

Funding: Supported by National Natural Science Foundation of China (82192904, 82192901, 82192900); "Precision Medicine Research" Key Project, National Key Research and Development Program of China (2016YFC0900500); Kadoorie Charitable Foundation in Hong Kong of China.

doi: 10.46234/ccdcw2023.188

Corresponding authors: Canqing Yu, yucanqing@pku.edu.cn; Dianjianyi Sun, dsun1@bjmu.edu.cn.

[1] Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, China; [2] Peking University Center for Public Health and Epidemic Preparedness & Response, Beijing, China; [3] Key Laboratory of Epidemiology of Major Diseases (Peking University), Ministry of Education, Beijing, China.

Submitted: August 09, 2023; Accepted: October 24, 2023

REFERENCES

1. Chinese Diabetes Society. Guideline for the prevention and treatment of type 2 diabetes mellitus in China(2020 edition)(Part 1). Chin J Pract Internal Med 2021;41(8):668 – 95. http://dx.doi.org/10.19538/j.nk2021080106. (In Chinese).
2. Francesconi C, Lackinger C, Weitgasser R, Haber P, Niebauer J. Physical activity and exercise training in the prevention and therapy of type 2 diabetes mellitus. Wien Klin Wochenschr 2016;128 Suppl 2:S141-5. http://dx.doi.org/10.1007/s00508-015-0923-3.
3. Samson SL, Vellanki P, Blonde L, Christofides EA, Galindo RJ, Hirsch IB, et al. American association of clinical endocrinology consensus statement: comprehensive type 2 diabetes management algorithm - 2023 update. Endocr Pract 2023;29(5):305 – 40. http://dx.doi.org/10.1016/j.eprac.2023.02.001.
4. He XW, Pan J, Pan MX, Wang JW, Dong JF, Yuan HD, et al. Dietary and physical activity of adult patients with type 2 diabetes in Zhejiang province of eastern China: data from a cross-sectional study. J Diabetes Investig 2016;7(4):529 – 38. http://dx.doi.org/10.1111/jdi.12458.
5. Zuo MF, Yu QM, Ma X, Chen YC, Wang Y. Analysis of physical activity status of type 2 diabetes patients in community. Chin J Prev Control Chronic Dis 2020;28(11):866 – 9. http://dx.doi.org/10.16386/j.cjpccd.issn.1004-6194.2020.11.016. (In Chinese).
6. Wang FF, Lu M, Wang Y. Analysis of influencing factors on blood glucose control and level of physical activity among patients with type 2 diabetes. Chin J Public Health Manage 2020;36(4):541 – 3. http://dx.doi.org/10.19568/j.cnki.23-1318.2020.04.027. (In Chinese).
7. Chen Y, Fan YG, Leng RX, Mao YM, Liao T, Ye D. Influencing factors for substandard physiques among residents aged 20-69 years in Anhui Province. J Prev Med 2021;33(7):649-55. 10.19485/j.cnki.issn2096-5087.2021.07.001. (In Chinese).
8. Ng SW, Popkin BM. Time use and physical activity: a shift away from movement across the globe. Obes Rev 2012;13(8):659 – 80. http://dx.doi.org/10.1111/j.1467-789X.2011.00982.x.

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Association of DM, DM course, and blood glucose control with low-level PA.

DM conditions	Low-level PA*
Non-DM	1.00
DM	1.04 (0.95, 1.13)
The course of DM	
Non-DM	1.00
≤5 years	0.97 (0.82, 1.14)
5–10 years	0.94 (0.79, 1.12)
>10 years	1.12 (1.00, 1.26)
P_{trend}	<0.001
Blood glucose control	
Non-DM	1.00
Good	1.03 (0.92, 1.20)
Poor	1.05 (0.92, 1.20)

Abbreviation: DM=diabetes mellitus; PA=physical activity; BMI=body mass index.
*Adjusted for age, gender, region, education level, occupation, smoking, drinking, sleep duration, BMI, and other chronic medical history.

SUPPLEMENTARY TABLE S2. Association of DM with low-level PA at different levels of population characteristics.

Subgroups	Low-level PA*		
	Non-DM	DM	Interaction *P*-value
Age（years）			
<60	1.00	1.25 (0.99–1.59)	<0.001
≥61	1.00	1.03 (0.93–1.13)	
Sex			
Male	1.00	1.00 (0.85–1.17)	<0.001
Female	1.00	1.07 (0.96–1.19)	
Region			
Urban	1.00	0.94 (0.83–1.06)	0.001
Rural	1.00	1.20 (1.06–1.36)	
Education level†			
Low	1.00	1.00 (0.90–1.13)	<0.001
Medium	1.00	1.14 (0.99–1.31)	
High	1.00	0.70 (0.44–1.11)	
Occupation			
Employed	1.00	1.43 (1.14–1.79)	<0.001
Retired/unemployed	1.00	1.00 (0.91–1.10)	
Smoking			
Never	1.00	1.02 (0.93–1.13)	0.094
Previous	1.00	1.26 (0.93–1.70)	
Current	1.00	1.04 (0.83–1.31)	
Drinking			
Never	1.00	1.03 (0.93–1.14)	<0.001
Previous	1.00	0.88 (0.57–1.36)	
Current	1.00	1.10 (0.92–1.31)	
Sleep duration (h)			
≤6	1.00	0.96 (0.83–1.11)	0.008
7–8	1.00	1.01 (0.88–1.16)	
≥9	1.00	1.24 (1.02–1.50)	
Other chronic diseases history§			
Yes	1.00	1.03 (0.93–1.15)	<0.001
No	1.00	1.08 (0.92–1.26)	

Abbreviation: PA=physical activity; DM=diabetes mellitus; CKB=China Kadoorie Biobank.
* All adjusted for variables other than the stratification variable in Table 3;
† Low, medium, and high level of education in CKB refers to primary school and below, secondary school and college and above;
§ Other chronic medical history includes cardiovascular disease, chronic obstructive pulmonary disease, and hypertension.

Preplanned Studies

Impact of Daily Step Count on Diabetes Management and Complications Among Elderly Individuals — Jiangsu Province, China, 2020–2022

Peng Yu[1,&]; Xuejian Ni[2,&]; Li Xu[3,&]; Lei Zhang[1]; Ling Cao[1]; Qiyu Chen[1]; Yixin Hu[4]; Kun Qian[4]; Xiaoying Li[1]; Xiaomu Li[1,#]; Jianying Gu[4,#]

Summary

What is already known about this topic?

Current literature underscores the significance of appropriate physical activity in managing diabetes, primarily utilizing self-reported data. Yet, the impact of objectively measured physical activity in older diabetic populations remains unclear.

What is added by this report?

Our research on elderly diabetic patients indicated a correlation between an increased number of daily steps and improved metabolic profiles, as well as a decrease in the incidence of cardiovascular complications.

What are the implications for public health practice?

Elevated daily step counts may confer significant benefits to elderly individuals with diabetes. The use of devices to monitor these steps could serve as a potent cardiovascular marker, and hold great potential as a screening or intervention tool in community-oriented settings.

The prevalence of type 2 diabetes mellitus (T2DM) is notably increasing within the population of older adults. Research has noted a compelling link between elevated levels of physical activity (PA) and enriched functional health, diminished risk of falls, and enhanced cognitive health in older adults (*1*). More specifically, PA quantified in daily step counts emerges as a vital modifiable behavior for diabetes management among the geriatric population. Substantial evidence from various studies substantiates that regular PA can lead to a better prognosis on diabetes. Historically, PA was primarily evaluated through questionnaires, which often yielded higher outputs when compared to device-measured activities (*2*). The advent of movement sensors, such as pedometers, has facilitated more accurate, tangible measurement of PA, in terms of daily step counts. This metric communicated as steps/day is highly translatable, memorable, and readily accessible via modern wearables and smartphones that are now ubiquitous (*3*). The detection and quantification of appropriate PA levels in older adults has become an area of intensified focus as it plays a significant role in estimating and promoting their overall health status (*4*).

In the course of this study, we assembled a geriatric diabetic cohort and undertook an analysis of baseline data collected between 2020 and 2022. Our primary focus was the correlation between daily steps and diabetic complications. To accurately assess step counts, we distributed electronic smart wristbands in three distinct streets in Xiangcheng District, Suzhou City, Jiangsu Province. These were primarily given to the elderly diabetic population during freely provided annual health check-ups, sponsored by the local government (*5*). A total of 1,415 individuals, all 65 years or older and diagnosed with diabetes according to the standards set by the American Diabetes Association (*6*), participated in the study from 2020 to 2022 (305, 964, and 146 cases per year, respectively).

High-sensitivity cardiac troponin T (hs-cTnT), albuminuria, serum creatine, and other laboratory parameters were measured using Roche Cobas 6000. Microalbuminuria (MA) was defined as a urine albumin-creatinine ratio ≥30 mg/g, subclinical myocardial injury (SMI) as hs-cTnT ≥14 ng/L (*7*), and chronic kidney disease (CKD) as an estimated glomerular filtration rate (eGFR) <60 mL/(min·1.73 m^2) using the CKD-EPI equation (*8*). Additional pre-existing conditions such as cancer, chronic obstructive pulmonary disease (COPD), etc. were self-reported by participants through questionnaires, with reference to previous studies (*9*). This research received approval from the Ethics Committee of Zhongshan Hospital, Fudan University [Approval No. B2020-201(3)], and all participants willingly gave consent to partake in this study.

The study employed *t*-tests and chi-squared tests for the evaluation of means and category distributions, respectively, based on variables calculated according to steps per day categories. A linear regression model was utilized to estimate correlations, with adjustments made for key potential confounding variables, which included age, gender, body mass index (BMI), HbA1c, amongst other factors. Covariates adjusted for in the logistic regression consisted of age (categorized, <75 and ≥75), gender, BMI (categorized, <18.5, 18.5–23.9, 24.0–27.9, and ≥28.0), HbA1c (categorized, <7% and ≥7%), and triglycerides (TG) (categorized, <1.7 and ≥ 1.7). Statistical analysis of all data was performed using STATA for Windows (Version 17.0; Stata-Corp, College Station, TX, USA), and two-tailed *P* values less than 0.05 were deemed statistically significant.

The participant pool of 1,415 individuals comprised 664 males and 751 females, each averaging 6,370 steps/day (±4,431). A trend emerged wherein those who walked more steps daily were generally younger and demonstrated lower BMIs, diastolic blood pressure, and triglyceride levels. Correspondingly, there was a general decrease in HbA1c levels as daily step counts increased. Interestingly, no significant variances were observed in education level, the proportions of current drinkers or smokers, or residential status in relation to step count. With respect to comorbid conditions, the incidences of cancer, COPD, and MA appeared to decline with increased daily steps, albeit falling short of statistical significance. Importantly, higher daily steps were associated with lower levels of the myocardial injury biomarker hs-cTnT, as well as reduced UACR, an indicator of kidney damage or elevated kidney disease risk. Simultaneously, higher estimated glomerular filtration rates (eGFR) correlated with increased steps/day (Table 1).

The linear correlation analysis results indicated negative correlations between the steps per day, and both hs-cTnT (β=−0.207, r=0.14, *P*<0.001) and the log-transformed UACR (β=−0.0268, r=0.087, *P*<0.001). A positive correlation surfaced with eGFR (β=0.709, r=0.16, *P*<0.001). The correlations involving hs-cTnT and eGFR remained significant even after adjusting for variables such as age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, educational level, and insulin administration. (Table 2).

The results from multivariable-adjusted logistic regressions suggest that, when compared to the first quartile, the odds ratios [95% confidence interval (*CI*)] for self-reported cardiovascular diseases (CVD) (comprising stroke, coronary heart disease, and heart failure) were 0.398 (0.230–0.689), and 0.620 (0.386–0.994) for elevated hs-cTnT — indicating SMI; both showing a statistically significant trend (*P*<0.05, Table 3). In terms of renal complications, such as MA and decreased eGFR (indicative of CKD), the odds ratios (95% *CI*) stood at 0.886 (0.617–1.272) and 0.777 (0.374–1.616) respectively. However, these results did not achieve statistical significance (Table 3).

DISCUSSION

In this study, we explored the correlation between daily step counts and various laboratory parameters as well as complications amongst community-dwelling elderly residents diagnosed with diabetes. Our data indicates that senior residents with diabetes on average took 6,370 steps daily. Interestingly, our analysis also revealed that a higher step count was associated with lower metabolic markers, specifically BMI and TG. Furthermore, a significant association was found between daily step counts and incidence of cardiovascular events, alongside cardiovascular and renal damage indicators.

Pedometers enabled us to evaluate the intensity of physical activity. The recommended daily step count for healthy older adults falls between 7,000 and 10,000, while for individuals with chronic illnesses like diabetes, the suggested range is between 6,500 and 8,500. This recommendation is based on limited evidence. It should be noted that increasing physical activity in the elderly, particularly those with diabetes, necessitates a clinical approach as opposed to a public health strategy. A previous meta-analysis has indicated that PA levels are inversely associated with risks of CVD and T2DM incidence, an association which is also influenced by changes in PA, primarily based on self-reported questionnaires (*10*). However, to the best of our understanding, no prior studies have investigated how physically active levels, objectively measured using devices, impact community-dwelling elderly individuals with diabetes.

Our findings notably suggest that reduced daily step counts could act as potential biomarkers for identifying complications in community-dwelling elderly individuals. These results also offer clinical evidence that a decrease in daily steps among those with diabetes might present new risk factors and biomarkers for the development of cardiovascular disease. To the best of our knowledge, this represents the first study to

TABLE 1. Descriptive characteristics and number of steps walked per day by geriatric diabetes patients.

Variables	Steps/d, *n* (%)					*P* value
	<4,000 (*n*=460, 32.56%)	4,000−7,999 (*n*=506, 35.73%)	8,000−11,999 (*n*=293, 20.72%)	≥12,000 (*n*=156, 10.99%)	Total (*n*=1,415)	
Steps daily	1,774±1,150	5,915±1,129	9,822±1,139	14,954±2,935	6,370±4,431	
Male, *n* (%)	222 (48.26)	236 (46.64)	131 (44.71)	75 (48.08)	664 (46.93)	0.800
Age, mean±SD, years	73.38±5.32	72.12±4.80	70.87±4.28	70.86±3.90	72.13±4.89	<0.001
Very elderly (≥75 years), *n* (%)	159 (34.57)	122 (24.11)	45 (15.36)	26 (16.67)	352 (24.88)	<0.001
Education						0.162
<High school	436 (94.78)	467 (92.29)	270 (92.15)	150 (96.15)	1,323 (93.50)	
≥High school	24 (5.22)	39 (7.71)	23 (7.85)	6 (3.85)	92 (6.50)	
Alcohol						0.874
Never drinker	387 (84.13)	425 (83.99)	238 (81.23)	129 (82.69)	1,179 (83.32)	
Former drinker	17 (3.70)	17 (3.36)	10 (3.41)	4 (2.56)	48 (3.39)	
Current drinker	56 (12.17)	64 (12.65)	45 (15.36)	23 (14.74)	188 (13.29)	
Smoking						0.117
Never smoker	336 (73.04)	362 (71.54)	226 (77.13)	120 (76.92)	1,044 (73.78)	
Former smoker	42 (9.13)	37 (7.31)	27 (9.22)	15 (9.62)	121 (8.55)	
Current smoker	82 (17.83)	107 (21.15)	40 (13.65)	21 (13.46)	250 (17.67)	
Residential status						0.054
Living with family	413 (90.17)	444 (87.92)	275 (93.86)	138 (88.46)	1,270 (89.94)	
Living alone	45 (9.83)	61 (12.08)	18 (6.14)	18 (11.54)	142 (10.06)	
Examination						
BMI, kg/m^2	25.21±3.4	25.16±3.11	24.8±2.95	24.27±2.68	25±3.14	0.006
Waist, cm	86.89±9.37	86.8±9.23	85.5±10.08	84.7±9.55	86.33±9.52	0.027
BMI category						0.010
<18.5 (lean)	6 (1.35)	2 (0.40)	3 (1.03)	1 (0.66)	12 (0.87)	
18.5–23.9 (normal)	158 (35.59)	181 (36.13)	115 (39.52)	76 (50.33)	530 (38.21)	
24–27.9 (overweight)	196 (44.14)	232 (46.31)	139 (47.77)	59 (39.07)	626 (45.13)	
28–42.9 (obesity)	84 (18.92)	86 (17.17)	34 (11.68)	15 (9.93)	219 (15.79)	
SBP, mmHg	146.64±19.66	146.4±17.72	146.23±18.27	146.5±18.31	146.45±18.52	0.993
DBP, mmHg	79.26±10.95	80.22±10.49	78.4±10.09	78.17±10.27	79.3±10.55	0.054
Laboratory						
FBG, mmol/L	8.4±2.65	8.35±2.45	8.45±2.28	8.31±2.31	8.38±2.47	0.928
HbA1C, %	7.47±1.65	7.37±1.53	7.37±1.63	7.13±1.45	7.37±1.58	0.113
TG, mmol/L	1.9±1.26	1.93±1.53	1.77±1.25	1.57±1.10	1.85±1.35	0.020
TC, mmol/L	4.93±1.21	4.99±1.18	4.98±1.17	4.92±1.11	4.96±1.18	0.837
LDL-C, mmol/L	2.83±1.00	2.91±0.96	2.94±0.98	2.87±0.93	2.88±0.97	0.426
HDL-C, mmol/L	1.33±0.30	1.36±0.33	1.39±0.35	1.43±0.33	1.36±0.33	0.002
ALT, U/L	20.66±17.33	21.9±17.32	21.81±14.8	21.15±14.12	21.39±16.52	0.705
AST, U/L	22.92±9.18	23.4±11.86	22.87±10.16	22.16±7.91	23.00±10.29	0.603
UA, μmol/L	336±111.88	323.83±92.26	310.68±87.89	301.92±84.27	322.65±98.05	<0.001
Medication						
Metformin	280 (60.87)	303 (59.88)	170 (58.02)	91 (58.33)	844 (59.65)	0.866
SU	197 (42.83)	231 (45.65)	149 (50.85)	74 (47.44)	651 (46.01)	0.187
Insulin	73 (15.87)	69 (13.64)	27 (9.22)	26 (16.67)	195 (13.78)	0.047

Continued

Variables	Steps/d, *n* (%)					*P* value
	<4,000 (*n*=460, 32.56%)	4,000−7,999 (*n*=506, 35.73%)	8,000−11,999 (*n*=293, 20.72%)	≥12,000 (*n*=156, 10.99%)	Total (*n*=1,415)	
Comorbidity						
Cancer	14 (3.04)	13 (2.57)	7 (2.39)	3 (1.92)	37 (2.61)	0.876
COPD	11 (2.39)	5 (0.99)	1 (0.34)	1 (0.64)	18 (1.27)	0.059
Stroke	60 (13.04)	42 (8.30)	14 (4.78)	9 (5.77)	125 (8.83)	<0.001
Coronary heart disease	24 (5.22)	8 (1.58)	9 (3.07)	3 (1.92)	44 (3.11)	0.010
hs-cTnT, ng/L	11.51±7.78	9.81±6.01	8.96±4.66	8.73±4.79	10.05±6.36	<0.001
SMI	97 (24.49)	74 (16.41)	34 (13.08)	17 (12.14)	222 (17.80)	<0.001
lgUACR, mg/g	3.42±1.39	3.29±1.36	3.12±1.29	3.02±1.3	3.26±1.35	0.007
MA	151 (42.18)	188 (43.62)	97 (38.34)	42 (31.34)	478 (40.65)	0.063
eGFR, mL/(min·l.73 m^2)	88.87±21.4	92.29±19.47	96.49±16.29	97.40±17.05	92.61±19.52	<0.001
CKD	49 (10.65)	43 (8.51)	12 (4.10)	7 (4.49)	111 (7.85)	0.004

Abbreviation: BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; FBG=fasting blood glucose; HbA1c=glycated hemoglobin; TG=triglycerides; TC=total cholesterol; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; RC=remnant cholesterol; ALT=alanine aminotransferase; AST=aspartate aminotransferase; UA=uric acid; eGFR=estimated glomerular filtration rate; SU=sulfonylurea; COPD=chronic obstructive pulmonary disease; SMI=subclinical cardiac injury with hs-cTnT≥14 ng/L; UACR=urinary albumin-to-creatinine ratio; MA=microalbuminuria with UACR≥30 mg/g; eGFR=estimated glomerular filtration rate; CKD=chronic kidney disease, eGFR<60 mL/(min·1.73 m^2).

TABLE 2. Linear regression analysis for the association between daily step count and cardiac and renal damage in elder T2DM patients.

Cardiorenal injury marker	Model 1	Model 2	Model 3
hs−cTnT β (t, *P*)	−0.207*** (−5.11, <0.001)	−0.116** (−3.03, 0.003)	−0.083* (−2.12, 0.034)
lgUACR β (t, *P*)	−0.027** (−2.99, 0.003)	−0.023* (−2.57, 0.010)	−0.013 (−1.45, 0.146)
eGFR β (t, *P*)	0.709*** (6.13, <0.001)	0.377*** (3.44, 0.001)	0.224* (2.04, 0.042)

Note: Model 1: crude model. Model 2: adjusted for age and gender. Model 3: adjusted to account for variables such as age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, education level, and insulin usage.
Abbreviation: T2DM=type 2 diabetes mellitus; lgUACR=log-transformed urinary albumin-to-creatinine ratio; eGFR=estimated glomerular filtration rate; BMI=body mass index; HbA1c=glycated hemoglobin; TG=triglycerides; LDL-C=low-density lipoprotein cholesterol; UA=uric acid.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

evaluate the impact of objectively measured step count in community-dwelling elderly individuals with diabetes and to discuss implications on comorbidity status, backed by a moderately-sized sample. Given the obstacles associated with identifying complications or symptoms in a community setting, utilizing decreased daily step counts as indicators could aid in the early identification of elderly individuals with diabetes who are at an increased risk for cardiovascular disease.

Modern smartwatches now incorporate advanced health monitoring capabilities, equipped with sensors for tracking heart rate, sleep, and physical activity. Leveraging on sophisticated algorithms, these devices provide personalized insights, and can integrate seamlessly with existing healthcare systems, positioning them as vital tools for managing health and lifestyle patterns. Furthermore, these devices engender an ability to accumulate long-term health data, consequently empowering healthcare providers to make more informed decisions. It also fosters seamless communication between families and medical teams, promoting all-inclusive care and support.

This study was subject to some limitations. Due to its cross-sectional design, it is unable to establish a causal connection between daily step counts and the incidence of cardiovascular disease. Furthermore, the pedometers utilized in this research did not gather information concerning the intensity or duration of walking, nor the type of exercise being performed. These omissions may introduce added layers of complexity and expense to the monitoring process, potentially inhibiting access in certain applications.

TABLE 3. Odds ratio (*OR*) and 95% confidence intervals (*CI*s) for cardiac and renal damage according to quartiles of daily step count.

Outcomes	1,000 steps/day *OR*s (95% *CI*s)				*P* trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
CVD cases/total	65/354 (18.36)	37/354 (10.45)	36/354 (10.17)	25/353 (7.08)	
Model 1	1 (ref.)	0.519 (0.336–0.801)**	0.503 (0.325–0.779)**	0.339 (0.208–0.552)***	<0.001
Model 2	1 (ref.)	0.522 (0.338–0.806)**	0.525 (0.338–0.816)**	0.363 (0.221–0.594)***	<0.001
Model 3	1 (ref.)	0.606 (0.376–0.978)*	0.544 (0.334–0.887)*	0.398 (0.230–0.689)**	<0.001
SMI	75/304 (24.67)	61/303 (20.13)	48/327 (14.68)	38/313 (12.14)	
Model 1	1 (ref.)	0.770 (0.525–1.129)	0.525 (0.351–0.785)**	0.422 (0.275–0.647)***	<0.001
Model 2	1 (ref.)	0.763 (0.509–1.141)	0.599 (0.392–0.915)*	0.524 (0.334–0.823)**	0.003
Model 3	1 (ref.)	0.786 (0.512–1.206)	0.659 (0.424–1.025)	0.620 (0.386–0.994)*	0.035
MA	112/271 (41.33)	128/289 (44.29)	128/310 (41.29)	110/306 (35.95)	
Model 1	1 (ref.)	1.129 (0.807–1.578)	0.998 (0.717–1.390)	0.797 (0.569–1.115)	0.137
Model 2	1 (ref.)	1.106 (0.786–1.555)	1.036 (0.738–1.454)	0.813 (0.576–1.149)	0.220
Model 3	1 (ref.)	1.076 (0.752–1.539)	1.042 (0.732–1.484)	0.886 (0.617–1.272)	0.499
CKD	37/354 (10.45)	37/353 (10.48)	22/354 (6.21)	15/353 (4.25)	
Model 1	1 (ref.)	1.003 (0.620–1.624)	0.568 (0.328–0.984)*	0.380 (0.205–0.706)**	<0.001
Model 2	1 (ref.)	1.024 (0.628–1.669)	0.661 (0.378–1.156)	0.481 (0.256–0.905)*	0.009
Model 3	1 (ref.)	1.350 (0.756–2.409)	0.818 (0.430–1.556)	0.777 (0.374–1.616)	0.282

Note: Model 1: crude model. Model 2: adjusted for age, gender. Model 3: adjusted for variables including age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, education level, and insulin usage.
Abbreviation: CVD=cardiovascular disease, including stroke, coronary heart disease, and heart failure; SMI=subclinical myocardial injury, high-sensitivity cardiac troponin T (hs-cTnT)≥14 ng/L; MA=microalbuminuria; UACR=urinary albumin-to-creatinine ratio, UACR≥30 mg/g; CKD=chronic kidney disease, eGFR=estimated glomerular filtration rate, eGFR<60 mL/(min·1.73 m^2); BMI=body mass index; HbA1c=glycated hemoglobin; TG=triglycerides; LDL-C=low-density lipoprotein cholesterol; UA=uric acid.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

In conclusion, our research suggests a significant inverse correlation between daily step count and cardiovascular disease risk in community-dwelling elderly individuals afflicted with diabetes.

Conflicts of interest: No conflicts of interest.

Acknowledgements: All dedicated health workers in the Xiangcheng District health system, and all participants who took part in the construction of this geriatric diabetes cohort.

doi: 10.46234/ccdcw2023.189

[#] Corresponding authors: Xiaomu Li, li.xiaomu@zs-hospital.sh.cn; Jianying Gu, gu.jianying@zs-hospital.sh.cn.

[1] Department of Endocrinology and Metabolism, Zhongshan Hospital, Fudan University, Shanghai, China; [2] Taiping Community Healthcare Center, Suzhou City, Jiangsu Province, China; [3] Yuanhe Community Healthcare Center, Suzhou City, Jiangsu Province, China; [4] Department of Information and Intelligence Development, Zhongshan Hospital, Fudan University, Shanghai, China.
[&] Joint first authors.

Submitted: July 28, 2023; Accepted: September 12, 2023

REFERENCES

1. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The physical activity guidelines for Americans. JAMA 2018;320(19):2020 – 8. http://dx.doi.org/10.1001/jama.2018.14854.
2. Althoff T, Sosič R, Hicks JL, King AC, Delp SL, Leskovec J. Large-scale physical activity data reveal worldwide activity inequality. Nature 2017;547(7663):336 – 9. http://dx.doi.org/10.1038/nature23018.
3. Garduno AC, Lacroix AZ, Lamonte MJ, Dunstan DW, Evenson KR, Wang GX, et al. Associations of daily steps and step intensity with incident diabetes in a prospective cohort study of older women: the OPACH study. Diabetes Care 2022;45(2):339 – 47. http://dx.doi.org/10.2337/dc21-1202.
4. Jefferis BJ, Iliffe S, Kendrick D, Kerse N, Trost S, Lennon LT, et al. How are falls and fear of falling associated with objectively measured physical activity in a cohort of community-dwelling older men? BMC Geriatr 2014;14:114. http://dx.doi.org/10.1186/1471-2318-14-114.
5. Wei Y, Zhou GQ, Wu XY, Lu XF, Wang XJ, Wang B, et al. Latest incidence and electrocardiographic predictors of atrial fibrillation: a prospective study from China. Chin Med J (Engl) 2023;136(3):313 – 21. http://dx.doi.org/10.1097/CM9.0000000000002340.
6. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2022. Diabetes Care 2022;45(S1):S17-38. http://dx.doi.org/10.2337/dc22-S002.
7. Rubin J, Matsushita K, Ballantyne CM, Hoogeveen R, Coresh J, Selvin E. Chronic hyperglycemia and subclinical myocardial injury. J Am Coll

Cardiol 2012;59(5):484 – 9. http://dx.doi.org/10.1016/j.jacc.2011.10.875.
8. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150(9):604 – 12. http://dx.doi.org/10.7326/0003-4819-150-9-200905050-00006.
9. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China health and retirement longitudinal study (CHARLS). Int J Epidemiol 2014;43(1):61 – 8. http://dx.doi.org/10.1093/ije/dys203.
10. Wahid A, Manek N, Nichols M, Kelly P, Foster C, Webster P, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. J Am Heart Assoc 2016;5(9):e002495. http://dx.doi.org/10.1161/JAHA.115.002495.

Preplanned Studies

Dose-Response Meta-Analysis on Risk of Diabetes in Relation to Red and Processed Meat Consumption — Asian Populations, 2006–2021

Hancheng Yu[1]; Jijuan Zhang[1]; Jinchi Xie[1]; Xianli Li[1]; Youjing Wang[1]; Yijia Yang[1]; Fengshuang Zhou[1]; Meichen Liu[1]; Zhe Zhang[1]; Zhilei Shan[1]; Gang Liu[1]; An Pan[1,#]

Summary

What is already known about this topic?

Red and processed meat consumption has been positively related to an increased risk of diabetes in Western populations. However, the results remain inconclusive within Asian populations.

What is added by this report?

This dose-response meta-analysis of prospective cohort studies conducted in East Asian populations reveals a positive relation between the consumption of processed meat and increased risk of diabetes. Furthermore, a U-shaped association was identified between the consumption of unprocessed red meat and the risk of diabetes.

What are the implications for public health practice?

This research presents substantive evidence advocating for the reduction of processed and unprocessed red meat consumption as a viable strategy for mitigating the risk of diabetes in East Asian populations.

The prevalence of diabetes has seen a swift escalation over the past few years. Global age-standardized prevalence for this disease was projected at 6.1% in 2021, with forecasts implying an upsurge to 10% by 2050 (*1*). Notably, in China, the estimated prevalence of diabetes in adults was 12.4% as of 2018 (*2*), leading to a substantial health and economic impact on the population.

Dietary habits play a crucial role in both the prevention and management of diabetes (*3*). Numerous meta-analyses consistently highlight a strong association between the consumption of unprocessed red meat or processed meat and the increased risk of diabetes among Western populations (*4*–*5*). However, the results are less conclusive in stratified analyses for Asian populations (*5*). Given the significant differences in types and quantities of red and processed meats consumed (*6*), findings from Western demographics may not necessarily hold for Asian populations. Therefore, this meta-analysis examines the relationships between the intake of unprocessed red meat or processed meat and the incidence of diabetes, focusing specifically on prospective cohort studies within Asian populations.

We conducted a thorough search of PubMed, Web of Science, EMBASE, and the Cochrane Library, in addition to perusing the reference lists of retrieved articles up until July 8, 2023, imposing no restrictions on language. Detailed search strategies for each database can be found in Supplementary Table S1 (available in https://weekly.chinacdc.cn/). Briefly, we focused our search on prospective cohort studies examining the link between the consumption of red and/or processed meat and diabetes risk, restricting our sample population to adults located in Asian countries. Information regarding study registration, inclusion and exclusion criteria, and data extraction procedures are elucidated in the Supplementary Methods (available in https://weekly.chinacdc.cn/).

The χ^2 and I^2 tests were implemented to assess the heterogeneity between studies, with a $P_{heterogeneity}$ value <0.10 and I^2>50% denoting significant heterogeneity. If substantial heterogeneity was established, random-effects models were employed to collect hazard ratios (*HR*s) and 95% confidence intervals (*CI*s) for the highest versus the lowest consumption group. If not, fixed-effects models were utilized. The inverse-variance method was invoked to calculate study weights.

Restricted cubic spline regression models were used to configure dose-response relationships between red and/or processed meat consumption and diabetes risk. Publication bias and small-study effects were evaluated using Egger's test and by visually inspecting funnel plots. Statistical significance was noted with a two-tailed test where P<0.05. All statistical analyses were

executed using STATA (version 17.0; STATA Corp., College Station, TX, USA).

In conclusion, we identified a total of 14,125 citations, of which 14,118 were excluded after conducting a thorough examination of the titles, abstracts, or the full text. Finally, seven cohort studies were included in our meta-analysis (Supplementary Figure S1, available in https://weekly.chinacdc.cn/). The populations under study comprised East Asians from China, Japan, and the Republic of Korea, along with Chinese adults living in Singapore. Notably, no study was found from other regions in Asia. Further characteristics of the included studies are demonstrated in Supplementary Table S2 (available in https://weekly.chinacdc.cn/). In six studies, dietary information was garnered through food frequency questionnaires, while a single study employed three consecutive 24-hour dietary recalls.

The assessment included a total of 570,296 participants for the evaluation of both red and processed meat consumption, with a further 243,296 participants for unprocessed red meat, and 251,914 for processed meat. Cases of diabetes reported were 21,316, 13,584, and 14,252 for each category, respectively (Table 1). When comparing the highest and lowest consumption groups, the combined HRs and 95% *CI*s of diabetes were 1.12 (0.98, 1.27) for overall red and processed meat consumption, 1.03 (0.89, 1.20) for unprocessed red meat, and 1.12 (1.06, 1.19) for processed meat consumption (Table 1; Figure 1).

Significant heterogeneity was observed in the associations of total red and processed meat (I^2=73.0%, P=0.011), as well as unprocessed red meat consumption and diabetes risk (I^2=71.1%, P=0.008). However, there was no significant heterogeneity in the association between processed meat consumption and diabetes risk (I^2=40.5%, P=0.135; Table 1; Figure 1). Egger's test detected no evidence of publication bias or small-study effects (all P>0.05; Table 1). Nonetheless, the funnel plots suggested potential publication bias for the associations of both red and processed meat, as well as unprocessed red meat consumption with diabetes risk (Supplementary Figure S2, available in https://weekly.chinacdc.cn).

We observed significant non-linear relations between the consumption of total red and processed meat ($P_{non\text{-}linearity}$=0.015), and unprocessed red meat ($P_{non\text{-}linearity}$<0.001), with diabetes (Figure 2). A J-shaped relationship was found between the consumption of total red and processed meat and the risk of diabetes. An accelerated increase in diabetes risk was noticed when consumption surpassed approximately 40 grams per day. As for the consumption of unprocessed red meat, a U-shaped pattern emerged in relation to diabetes risk, with a linear increase when daily consumption exceeded roughly 40 grams (Figure 2). However, the P value for non-linearity between processed meat consumption and diabetes risk was not statistically significant ($P_{non\text{-}linearity}$=0.065; Figure 2).

DISCUSSION

Our study indicates a significant relation between high processed meat consumption and an elevated risk of diabetes in East Asian populations. Furthermore, non-linear associations were observed between total red and processed meat intake, unprocessed red meat consumption and the risk of diabetes.

A recent meta-analysis revealed no significant association between the consumption of unprocessed red meat (per 100 grams/day increment; pooled *HR*: 0.98; 95% *CI*: 0.72, 1.33) or processed red meat (per 50 grams/day increment; pooled *HR*: 0.96; 95% *CI*: 0.83, 1.10) and type 2 diabetes risk within the stratified analysis of the Asian population (*5*). However, these findings come under scrutiny due to the exclusion of several Asian cohorts with absent dose-

TABLE 1. Meta-analysis of red and/or processed meat consumption and risk of diabetes*.

Characteristics	No. of studies	No. of cohorts	No. of cases/ subjects	Pooled *HR*	95% *CI*	*P*	Heterogeneity, I^2 (%)	$P_{heterogeneity}$	*P* for Egger's test
Total red and processed meat†	3	3	21,316/ 570,296	1.12	0.98, 1.27	0.085	73.0	0.011	0.941
Unprocessed red meat†	4	5	13,584/ 243,296	1.03	0.89, 1.20	0.665	71.1	0.008	0.810
Processed meat§	5	6	14,252/ 251,914	1.12	1.06, 1.19	<0.001	40.5	0.135	0.876

* Pooled hazard ratios (*HR*s) and 95% confidence intervals (*CI*s) for diabetes were comparing the highest intake groups to the lowest groups of red and/or processed meat consumption.
† Results from a random-effects model.
§ Results from a fixed-effect model.

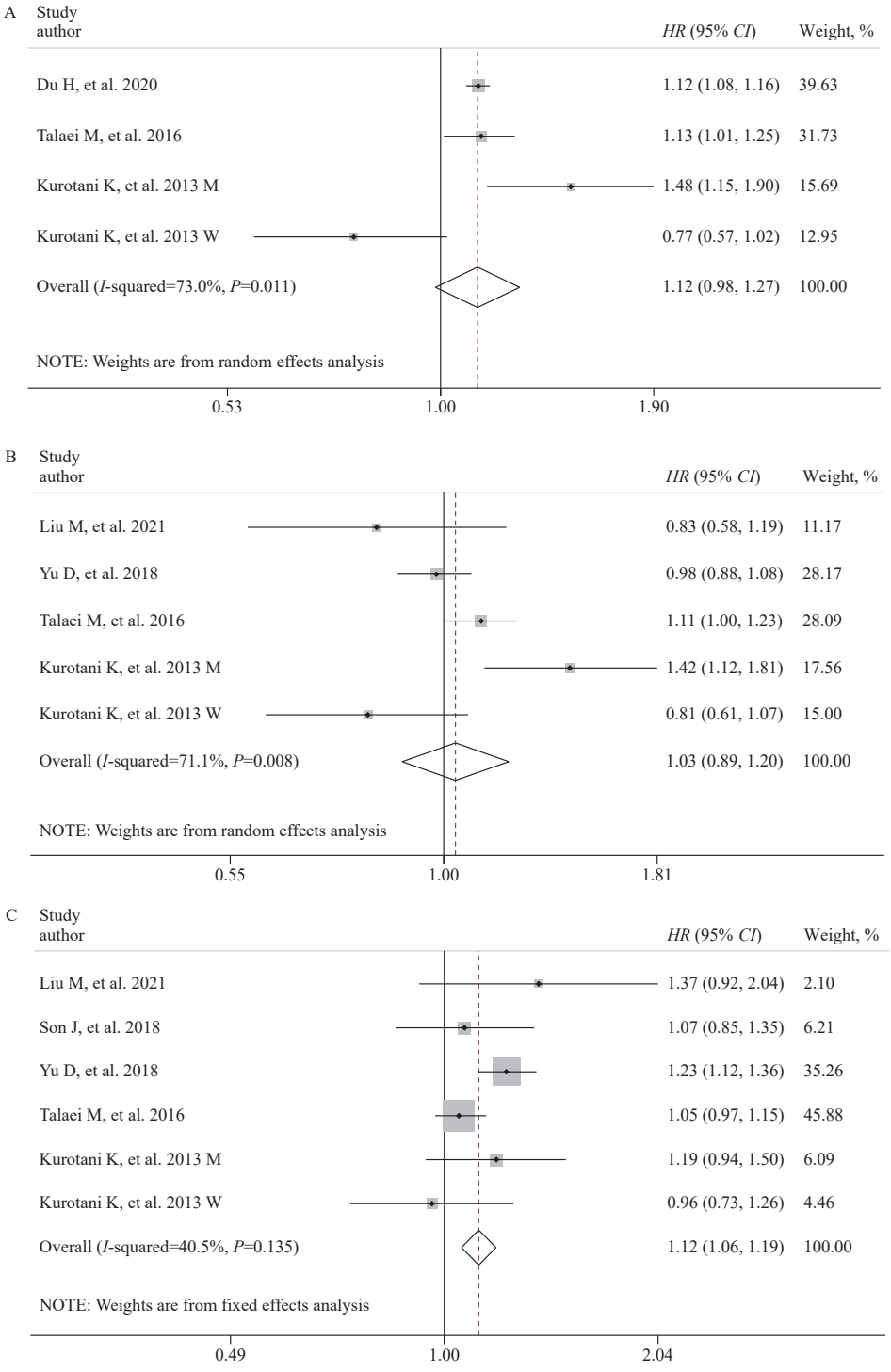


FIGURE 1. Hazard ratios (*HR*s) and 95% confidence intervals (*CI*s) associated with diabetes for the highest versus the lowest consumption categories of (A) total red and processed meat, (B) unprocessed red meat, and (C) processed meat.
Note: (A) 570,296 individuals with 21,316 cases from the China Kadoorie Biobank, the Singapore Chinese Health Study (SCHS) and the Japan Public Health Center-based Prospective Study (JPHC), (B) 243,296 individuals with 13,584 cases from the China Health and Nutrition Survey (CHNS), the Shanghai Women's and Men's Health Study (SW&MHS), SCHS and JPHC, and (C) 251,914 individuals with 14,252 cases from CHNS, the Korean Genome Epidemiology Study, SW&MHS, SCHS and JPHC were included. The black squares represent the study-specific HRs, with the size of each square proportional to the study's weight in the overall meta-analysis; the horizontal lines extending from these squares indicate the respective 95% *CI*s; the open diamond in each graph symbolizes the pooled *HR*, with the diamond's width illustrating the 95% *CI*s for these pooled results.

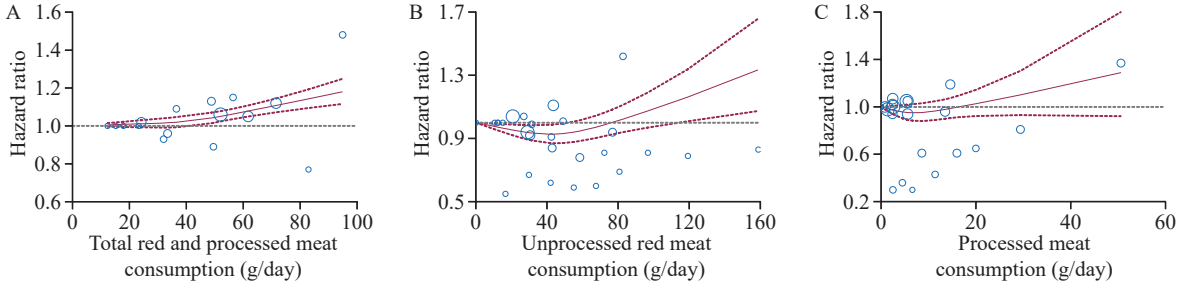


FIGURE 2. Non-linear dose-response relationship (*HR*s and 95% *CI*s) between (A) total red and processed meat ($P_{non\text{-}linearity}$=0.015), (B) unprocessed red meat ($P_{non\text{-}linearity}$<0.001) and (C) processed meat ($P_{non\text{-}linearity}$=0.065) daily intakes and risk of diabetes.

Note: Results from the Singapore Chinese Health Study (SCHS), the Japan Public Health Center-based Prospective Study (JPHC) and the China Kadoorie Biobank were included in (A); SCHS, the China Health and Nutrition Survey (CHNS), JPHC and the Shanghai Women's Health Study (SWHS) in (B); the Korean Genome Epidemiology Study, SCHS, CHNS, and JPHC in (C). The solid line represents the fitted dose-response curve, and the dashed line is the 95% *CI*; the position of each bubble represents the corresponding dose and effect in the included studies, and the size of the bubble represents the weight; the weight of the reference category is considered as half of the minimum weight of other categories.

Abbreviation: *HR*s=hazard ratios; *CI*s=confidence intervals; g=grams.

response data from the meta-analysis. In an attempt to address these limitations, additional data was assimilated from the Shanghai Men's Health Study (SMHS) and the Japan Public Health Center-based Prospective Study (JPHC). This was exclusively for the unprocessed red meat in the extreme-category comparison analysis along with data obtained from the SMHS, JPHC, and the Singapore Chinese Health Study for processed meat (Supplementary Material, available in https://weekly.chinacdc.cn/). After incorporating data from all available Asian prospective cohorts, the current study showed an increased risk of diabetes related to increased consumption of processed meat.

The dose-response investigations have unveiled a U-shaped relationship between the consumption of unprocessed red meat and the risk of diabetes, with the lowest level of risk at about 40 grams per day. This pattern may originate from the potential nutritional benefits of a moderate intake of unprocessed red meat, such as the provision of protein, iron, and various vitamins. Conversely, high consumption of red meat could potentially result in excessive intake of saturated fat, cholesterol, and heme iron, which may negatively impact insulin sensitivity and escalate diabetes risk. The non-significant impact tied to the daily increment of 100 grams of unprocessed red meat, as previously stated in an earlier meta-analysis (*5*), may be partially attributed to the existence of a non-linear dose-response relation. As of 2007, the United States had an average meat consumption of 122.8 kg/year, contrasted with China, Japan, and the Republic of Korea's consumption ranging between 46.1 kg/year and 55.9 kg/year (*6*). Therefore, applying large daily increments, as used in the previous study (*5*), may not be suitable for Asian populations. Notably, certain studies did not have available dose-response data, resulting in these investigations not being included in the dose-response examination. This accounted for a lower number of included studies in this analysis as opposed to the extreme-category comparison analysis, potentially causing discrepancies between the two analyses. For instance, the Shanghai Women and Men's Health Study findings (Supplementary Material) displayed a positive association (*HR* comparing highest to the lowest category: *HR*: 1.23; 95% *CI*: 1.12, 1.36) between processed meat consumption and the risk of diabetes. However, due to data limitations, this study was not incorporated into the dose-response analyses.

In Western populations, an increase in daily consumption of unprocessed red meat by 100 grams and processed red meat by 50 grams was associated with a 36% and 51% escalated risk of type 2 diabetes, respectively (*5*). The variation in correlations between consumption of red and processed meat and diabetes risk in Western and Asian populations could partially be due to various exposure factors such as the quantity and type of meat products (*6*), cooking methods (*7*), and dietary patterns (*8*). For example, the median daily intake of unprocessed red meat and processed meat in an included Chinese cohort was respectively 58.9 grams and 0 grams (*9*), considerably lower than that in the United States (*10*). Nonetheless, there has been an extraordinary surge in the levels of red meat consumption in Asian countries in recent decades due to economic development (*6*,*10*). Accordingly,

findings from the cohorts incorporated in the current study, which were established nearly 20 years ago, may not accurately reflect current conditions. Given the substantial shifts in red meat consumption among Asian populations, there is a continued need for further evidence regarding the association between red and processed meat consumption and diabetes risk.

This study has several limitations. Initially, our capability to conduct sensitivity and subgroup analyses was hindered due to the paucity of prior studies on this topic. Furthermore, a number of studies did not supply the requisite data for accomplishing the dose-response analysis. Another limitation is that most surveys did not collect data concerning potential confounders, such as types of meat consumed and cooking practices. A discordance in diabetes assessment methods (Supplementary Table S2) could introduce potential bias, particularly in the form of misdiagnoses or underdiagnoses among self-reported cases. Moreover, our study population was composed of East Asians, which may limit the extent of generalizability and warrant further exploration into other Asian populations. Therefore, additional research is paramount in further understanding the impact of these factors on the associations between red meat consumption and diabetes risk.

In conclusion, our study reveals an association between higher processed meat consumption and elevated risks of diabetes among East Asian populations. Although there was no identifiable relation observed between moderate unprocessed red meat consumption and increased diabetes risk, elevated consumption levels nevertheless exhibited a heightened risk. This finding warrants further exploration. This study furnishes the most current evidence advocating for the avoidance of processed meat and the reduction of unprocessed red meat consumption, specifically for the prevention of diabetes in East Asian populations.

Conflicts of interest: No conflicts of interest.

Funding: Supported by grants 81930124, 82192902, and 82021005 from the National Natural Science Foundation of China and grant 2022YFC3600600 from the National Key Research and Development Program of China.

doi: 10.46234/ccdcw2023.190

Corresponding author: An Pan, panan@hust.edu.cn.

[1] Department of Epidemiology and Biostatistics, Ministry of Education Key Laboratory of Environment and Health and State Key Laboratory of Environmental Health (incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China.

Submitted: August 25, 2023; Accepted: October 30, 2023

REFERENCES

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2023;402(10397):203 – 34. http://dx.doi.org/10.1016/S0140-6736(23)01301-6.
2. Wang LM, Peng W, Zhao ZP, Zhang M, Shi ZM, Song ZW, et al. Prevalence and treatment of diabetes in China, 2013-2018. JAMA 2021;326(24):2498 – 506. http://dx.doi.org/10.1001/jama.2021.22208.
3. Ley SH, Hamdy O, Mohan V, Hu FB. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. Lancet 2014;383(9933):1999 – 2007. http://dx.doi.org/10.1016/S0140-6736(14)60613-9.
4. Schwingshackl L, Hoffmann G, Lampousi AM, Knüppel S, Iqbal K, Schwedhelm C, et al. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. Eur J Epidemiol 2017;32(5):363 – 75. http://dx.doi.org/10.1007/s10654-017-0246-y.
5. Shi WM, Huang X, Schooling CM, Zhao JV. Red meat consumption, cardiovascular diseases, and diabetes: a systematic review and meta-analysis. Eur Heart J 2023;44(28):2626 – 35. http://dx.doi.org/10.1093/eurheartj/ehad336.
6. Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98(4):1032 – 41. http://dx.doi.org/10.3945/ajcn.113.062638.
7. Liu G, Zong G, Wu KN, Hu Y, Li YP, Willett WC, et al. Meat cooking methods and risk of type 2 diabetes: results from three prospective cohort studies. Diabetes Care 2018;41(5):1049 – 60. http://dx.doi.org/10.2337/dc17-1992.
8. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care 2011;34(6):1249 – 57. http://dx.doi.org/10.2337/dc11-0442.
9. Liu MY, Liu CZ, Zhang ZX, Zhou C, Li QQ, He PP, et al. Quantity and variety of food groups consumption and the risk of diabetes in adults: a prospective cohort study. Clin Nutr 2021;40(12):5710 – 17. http://dx.doi.org/10.1016/j.clnu.2021.10.003.
10. Wang HH. The perspective of meat and meat-alternative consumption in China. Meat Sci 2022;194:108982. http://dx.doi.org/10.1016/j.meatsci.2022.108982.

SUPPLEMENTARY MARERIAL

Supplementary Methods. Registration, Study Selection, and Data Extraction

Registration and study selection

This study was registered in the International Prospective Register of Systematic Reviews database (identifier CRD42023423339) on May 16, 2023. In adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (*1*), study selection, data extraction, and quality assessment were independently conducted by three authors (H-CY, J-JZ, and J-CX). Any discrepancies were resolved via discussion or by consulting another author (AP). The exclusion criteria for the studies were as follows: 1) if the research did not constitute an epidemiological study; 2) if the research did not employ a prospective design; 3) if the research was unrelated to red or processed meat; 4) if the research was not conducted in the general population; 5) if the research did not originate from Asian countries; and 6) if the research was only available in the form of conference abstracts. Although the inclusion of intervention studies was initially intended, no eligible intervention studies were identified during the screening process. In this meta-analysis, "Asian populations" represent the populace residing within the geographical confines of Asia. However, two studies originating from Iran (*2*–*3*) were eliminated due to the significant variations in dietary habits concerning types of red and processed meat influenced by religious customs. Notably, in East Asian countries, pork consumption surpasses other forms of red meat (*4*), whereas it is almost non-existent in Iran.

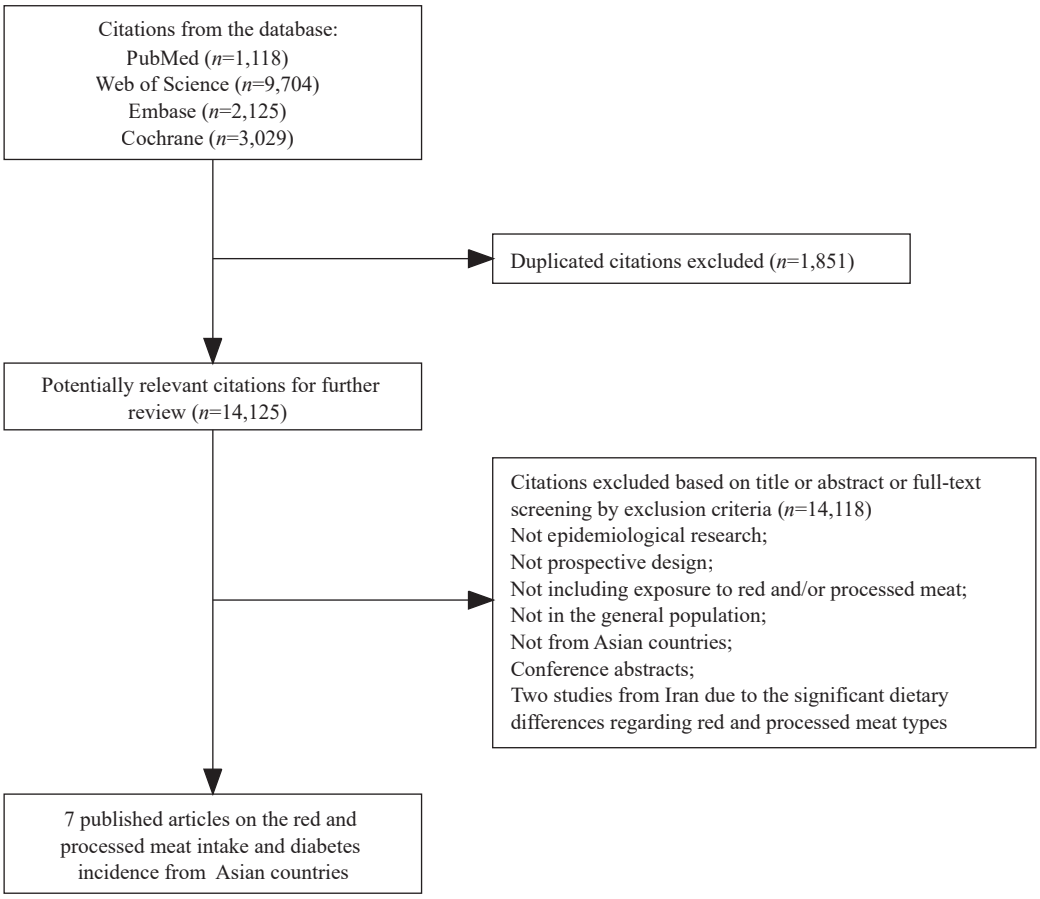
Data extraction

This research paper includes details such as the authors' information, publication year, cohort names, participants' native countries and count, age, assessment of exposures and outcomes, follow-up period (or person-year), acquisition of red and processed meats, covariates incorporated in fully adjusted models, hazard ratios (*HR*s) with corresponding confidence intervals (*CI*s), and specific diabetes cases per group, all of which were extracted (Supplementary Table S2). In instances wherein intake categories were left undefined, we estimated the median by assuming that the distance from the lower boundary to the median reflects the adjacent category with a defined range.

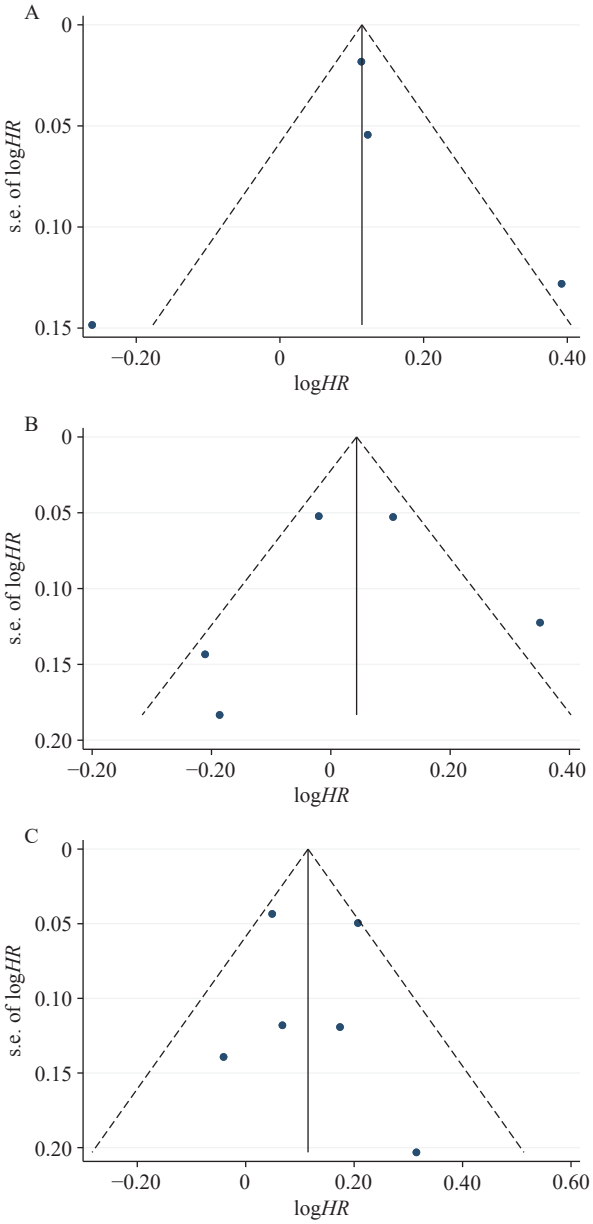
The study encompasses red and processed meat, namely all mammalian meat such as beef, pork, and lamb, and meat products treated through methods like salting, curing, fermentation, smoking, or with added preservatives. The term 'unprocessed red meat' specifically refers to raw, unaltered mammalian meats including beef, pork, and lamb. On the other hand, 'processed meat' includes all meat products that have been modified using salting, curing, fermentation, smoking, or the application of chemical preservatives to boost flavor or enhance preservation.

We made use of the Newcastle-Ottawa Scale to gauge the quality of the study (Supplementary Table S2), with a score of >6 denoting high quality (*5*). Eventually, there were three studies of total red and processed meat (*6*–*8*), four studies of unprocessed red meat (*6*–*7*,*9*–*10*), and five studies of processed meat (*6*–*7*,*9*–*11*) that furnished the data required to compute the pooled relative ratios and confidence intervals.

Three studies of total red and processed meat (*6*–*8*), four studies of unprocessed red meat (*6*–*7*,*9*,*12*), and four studies of processed meat (*6*–*7*,*9*,*11*) furnished the information necessary for dose-response analyses. Considering the relatively low diabetes incidence (about 2%) in the included study with odds ratios (*7*), we assumed that odds ratios closely resemble the *HR* estimates. Hence, no transformations were performed.



SUPPLEMENTARY FIGURE S1. Flow chart of study selection.



SUPPLEMENTARY FIGURE S2. Funnel plots of risks of diabetes associated with the highest versus lowest consumption categories of (A) total red and processed meat, (B) unprocessed red meat, and (C) processed meat.
Abbreviation: s.e.=standard error; *HR*=hazard ratio.

SUPPLEMENTARY TABLE S1. Search strategies used for each database.

Database	Search strategies
PubMed	#1(red meat[MeSH Terms] OR meat products[MeSH Terms] OR red meat*[Title/Abstract] OR meat product*[Title/Abstract] OR processed meat*[Title/Abstract] OR beef[Title/Abstract] OR pork[Title/Abstract] OR hot dog*[Title/Abstract] OR salami*[Title/Abstract] OR veal[Title/Abstract] OR sausage*[Title/Abstract] OR lamb*[Title/Abstract] OR goat*[Title/Abstract] OR bacon[Title/Abstract] OR mutton[Title/Abstract] OR ham[Title/Abstract] OR luncheon meat*[Title/Abstract] OR pastrami*[Title/Abstract] OR diet pattern[Title/Abstract] OR diet quality[Title/Abstract]) AND (intake*[Title/Abstract] OR consumption*[Title/Abstract] OR diet*[Title/Abstract]) AND (diabetes mellitus[MeSH Terms] OR T2DM[Title/Abstract] OR Type 2 Diabetes[Title/Abstract] OR blood glucose[MeSH Terms] OR fasting glucose[Title/Abstract] OR glycated hemoglobin[Title/Abstract] OR glycemic control[Title/Abstract] OR insulin resistance[MeSH Terms] OR impaired glucose regulation[Title/Abstract] OR impaired fasting glucose[Title/Abstract] OR impaired glucose tolerance[Title/Abstract] OR hyperglycemia[Title/Abstract])
	#2systematic review[Publication Type] OR systematic review[Title/Abstract] OR meta-analysis[Publication Type] OR meta-analysis[Title/Abstract] OR review [Publication Type] OR review [Title/Abstract] OR meta analysis[Title/Abstract]
	#1 NOT #2 Filters: Humans
Web of Science	#1(TS=(red meat*) OR TS=(meat product*) OR TS=(processed meat*) OR TS=(beef) OR TS=(pork) OR TS=(hot dog*) OR TS=(salami*) OR TS=(veal) OR TS=(sausage*) OR TS=(lamb*) OR TS=(goat*) OR TS=(bacon) OR TS=(mutton) OR TS=(ham) OR TS=(luncheon meat*) OR TS=(pastrami*) OR TS=(diet pattern) OR TS=(diet quality)) AND (TS=(intake*) OR TS=(consumption*) OR TS=(diet*)) AND (TS=(diabetes mellitus) OR TS=(T2DM) OR TS=(Type 2 Diabetes) OR TS=(blood glucose) OR TS=(fasting glucose) OR TS=(glycated hemoglobin) OR TS=(glycemic control) OR TS=(insulin resistance) OR TS=(impaired glucose regulation) OR TS=(impaired fasting glucose) OR TS=(impaired glucose tolerance) OR TS=(hyperglycemia))
	#2TS=(systematic review) OR TS=(meta-analysis) OR TS=(review) OR TS=(meta analysis)
	#1 NOT #2
Embase	#1('red meat'/exp OR 'processed meat'/exp OR 'smoked meat'/exp OR 'red meat*':ti,ab,kw OR 'meat product*':ti,ab,kw OR 'processed meat*':ti,ab,kw OR beef:ti,ab,kw OR pork:ti,ab,kw OR 'hot dog*':ti,ab,kw OR salami*:ti,ab,kw OR veal:ti,ab,kw OR sausage*:ti,ab,kw OR lamb*:ti,ab,kw OR goat*:ti,ab,kw OR bacon:ti,ab,kw OR mutton:ti,ab,kw OR ham:ti,ab,kw OR 'luncheon meat*':ti,ab,kw OR pastrami*:ti,ab,kw OR 'diet pattern':ti,ab,kw OR 'diet quality':ti,ab,kw) AND (intake*:ti,ab,kw OR consumption*:ti,ab,kw OR diet*:ti,ab,kw) AND ('diabetes mellitus'/exp OR T2DM: ti,ab,kw OR 'Type 2 Diabetes':ti,ab,kw OR 'glucose blood level'/exp OR 'fasting glucose':ti,ab,kw OR 'glycated hemoglobin':ti,ab,kw OR 'glycemic control':ti,ab,kw OR 'insulin resistance'/exp OR 'impaired glucose regulation':ti,ab,kw OR 'impaired fasting glucose':ti,ab,kw OR 'impaired glucose tolerance':ti,ab,kw OR hyperglycemia:ti,ab,kw)
	#2'systematic review'/exp OR 'systematic review':ti,ab,kw OR 'meta analysis'/exp OR meta-analysis:ti,ab,kw OR 'review'/exp OR review:ti,ab,kw OR 'meta analysis':ti,ab,kw
	#1 NOT #2
Cochrane	#1 (red meat* or meat product* or processed meat* or beef or pork or hot dog* or salami* or veal or sausage* or lamb* or goat* or bacon or mutton or ham or luncheon meat* or pastrami* or diet pattern or diet quality):ti,ab,kw
	#2 MeSH descriptor: [Red Meat] explode all trees
	#3 MeSH descriptor: [Meat Products] explode all trees
	#4 (intake* or consumption* or diet*):ti,ab,kw
	#5 (#1 or #2 or #3) and #4
	#6 MeSH descriptor: [Diabetes Mellitus] explode all trees
	#7 MeSH descriptor: [Insulin Resistance] explode all trees
	#8 (T2DM or Type 2 Diabetes or blood glucose or fasting glucose or glycated hemoglobin or glycemic control or impaired glucose regulation or impaired fasting glucose or impaired glucose tolerance or hyperglycemia):ti,ab,kw
	#9 #5 and (#6 or #7 or #8)
	#10 MeSH descriptor: [Systematic Review] explode all trees
	#11 MeSH descriptor: [Meta-Analysis] explode all trees
	#12 MeSH descriptor: [Review] explode all trees
	#13 (systematic review or meta-analysis or meta analysis or review):ti,ab,kw
	#14 #9 not (#10 or #11 or #12 or #13)

SUPPLEMENTARY TABLE S2. Characteristics of the studies included in the meta-analysis*

Study	No. of participants	Age (years)	Endpoints (no. of cases)	Follow-up period	Exposure and assessment method (exposure)	Outcome assessment	Daily consumption (exposure)	Year of recruitment	Covariates in fully adjusted model	Quality score
Liu et al. (2021) CHNS, China (*9*)	16,117	Mean: 43.0 (SD: 15.2)	DM (1,088)	Median: 9.0 years; 158,018 person-years	Three consecutive 24-hour dietary recalls (unprocessed red meat, processed meat)	Self-reported	Median: 58.9 g (unprocessed red meat); median: 0 g (processed meat)	1997	Age, sex, BMI, waist circumference, smoking and drinking status, systolic blood pressure, diastolic blood pressure, education, region, occupation, physical activity, urban residence, as well as total energy, and 12 food groups were mutually adjusted.	6
Du et al. (2020) CKB, China (*8*)	461,036	Mean: 51.2 (SD: 10.5); 35–74 years	DM (14,931)	Mean: 9 years; 4.5 million person-years	Laptop-based FFQ (total red and processed meat)	Linkages with chronic disease registries and national health insurance claim databases	Mean: 55.1 g (total red and processed meat)	2004–2008	Age, sex, region, education, income, smoking, alcohol consumption, physical activity, family history of diabetes, and fresh fruit consumption, two main dietary exposure variables, and BMI.	9
Yu et al. (2018) SWHS & SMHS, China (*10*)	64,802 Women and 53,117 men	40–74 years	T2DM (6,111)	Mean: 11.5 years (13.6 years for women; 8.8 years for men).	Semiquantitative FFQ (unprocessed red meat, processed meat)	Self-reported diagnosis	NA	1996–2000 (women); 2002–2006 (men)	Total energy intake, education, income, smoking, alcohol drinking, leisure-time exercise, family history of diabetes, history of hypertension, history of dyslipidemia, and, in women, menopausal status, BMI, and all eight food groups were mutually adjusted.	6
Son et al. (2018) KoGES, Republic of Korea (*11*)	8,618	40–69 years	T2DM (668)	62,130 person-years	Semiquantitative FFQ (processed meat)	Self-reported interviews	Median: 0 g (processed meat)	2001–2002 and 2005–2006	Age, sex, educational level, monthly household income, and residential area, smoking, physical activity, BMI, alcohol intake, energy intake, consumption levels of dietary fat, crude fiber, sodium, fruit and vegetable, current use of antihypertensive and antihyperlipidemic medications.	7
Talaei et al. (2017) SCHS, Singapore (*6*)	45,411	Mean: 55.2 (SD: 7.6); 45–74 years	T2DM (5,207)	Mean: 10.9 years; 494,741 person-years	Semiquantitative FFQ (total red and processed meat, unprocessed red meat, processed meat)	Self-reported interviews	Median of Q1–Q4 (total red and processed meat): 12.3 g, 24.2 g, 33.4 g, 48.8 g; median of Q1–Q4 (unprocessed red meat): 10.5 g, 20.7 g, 29.0 g, 43.5 g; median of Q1–Q4 (processed meat): 0 g, 1.4 g, 2.57 g, 5.39 g	1993–1998	Age, sex, dialect, year of interview, and educational level, BMI, physical activity level, smoking status, alcohol use, baseline history of self-reported hypertension, adherence to the vegetable-, fruit-, and soy-rich dietary pattern, and total energy intake, heme iron intake	8

Continued

Study	No. of participants	Age (years)	Endpoints (no. of cases)	Follow-up period	Exposure and assessment method (exposure)	Outcome assessment	Daily consumption (exposure)	Year of recruitment	Covariates in fully adjusted model	Quality score
Kurotani et al. (2013) JPHC, Japan (*7*)	63,849	45–75 years	T2DM (1,178)	Max: 5 years	Self-administered FFQ (total red and processed meat, unprocessed red meat, processed meat)	Self-reported interviews	Men: median of Q1–Q4 (total red and processed meat): 17.9 g, 36.5 g, 56.4 g, 94.9 g; median of Q1–Q4 (unprocessed red meat): 15.1 g, 31.4 g, 49.0 g, 82.7 g; median of Q1–Q4 (processed meat): 0 g, 2.4 g, 5.6 g, 14.6 g; women: median of Q1–Q4 (total red and processed meat): 15.2 g, 32.0 g, 49.5 g, 82.9 g; median of Q1–Q4 (unprocessed red meat): 12.3 g, 26.9 g, 42.4 g, 72.2 g; median of Q1–Q4 (processed meat): 0 g, 2.4 g, 5.6 g, 13.5 g	1990 and 1993	Age, public health center area, BMI, smoking status, alcohol consumption, total physical activity, the history of hypertension, coffee consumption, the family history of diabetes, Mg intake, Ca intake, rice intake, fish intake, vegetable intake, soft drink consumption and energy intake	6
Villegas et al. (2006) SWHS, China (*12*)	70,609	Mean: 51.7 (SD: 8.97); 40–70 years	T2DM (1,972)	Mean: 4.6 years; 326,625 person-years	FFQ (unprocessed red meat, only for dose-response)	Self-reported type 2 diabetes identified through the baseline and follow-up surveys	Median: 42.6 g (unprocessed red meat)	1997–2000 (women)	Age, energy intake, BMI, WHR, smoking, alcohol consumption, physical activity, vegetable intake, income level, education level, occupation status, hypertension, and chronic disease	6

Abbreviation: CHNS=China Health and Nutrition Survey (China); CKB=China Kadoorie Biobank (China); SW(M)HS=Shanghai Women's (Men's) Health Study (China); KoGES=Korean Genome Epidemiology Study (Republic of Korea); SCHS=Singapore Chinese Health Study (Singapore); JPHC=Japan Public Health Center-based Prospective Study (Japan). DM=diabetes mellitus; T2DM=type 2 diabetes mellitus; FFQ=food frequency questionnaire; g=grams; Q=quartile; SD=standard deviation; NA=not applicable.

REFERENCES

1. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62(10):1006 – 12. http://dx.doi.org/10.1016/j.jclinepi.2009.06.005.
2. Esfandiar Z, Hosseini-Esfahani F, Mirmiran P, Azizi F. Diet quality indices and the risk of type 2 diabetes in the Tehran Lipid and Glucose Study. BMJ Open Diabetes Res Care 2022;10(5):e002818. http://dx.doi.org/10.1136/BMJDRC-2022-002818.
3. Hosseini-Esfahani F, Beheshti N, Koochakpoor G, Mirmiran P, Azizi F. Meat food group intakes and the risk of type 2 diabetes incidence. Front Nutr 2022;9:891111. http://dx.doi.org/10.3389/FNUT.2022.891111.
4. Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98(4):1032 – 41. http://dx.doi.org/10.3945/ajcn.113.062638.
5. Cook DA, Reed DA. Appraising the quality of medical education research methods: the medical education research study quality instrument and the Newcastle-Ottawa Scale–Education. Acad Med 2015;90(8):1067 – 76. http://dx.doi.org/10.1097/ACM.0000000000000786.
6. Talaei M, Wang YL, Yuan JM, Pan A, Koh WP. Meat, dietary heme iron, and risk of type 2 diabetes mellitus: the Singapore Chinese health study. Am J Epidemiol 2017;186(7):824 – 33. http://dx.doi.org/10.1093/aje/kwx156.
7. Kurotani K, Nanri A, Goto A, Mizoue T, Noda M, Oba S, et al. Red meat consumption is associated with the risk of type 2 diabetes in men but not in women: a Japan Public Health Center-based Prospective Study. Br J Nutr 2013;110(10):1910 – 8. http://dx.doi.org/10.1017/S0007114513001128.
8. Du HD, Guo Y, Bennett DA, Bragg F, Bian Z, Chadni M, et al. Red meat, poultry and fish consumption and risk of diabetes: a 9 year prospective cohort study of the China Kadoorie Biobank. Diabetologia 2020;63(4):767 – 79. http://dx.doi.org/10.1007/s00125-020-05091-x.
9. Liu MY, Liu CZ, Zhang ZX, Zhou C, Li QQ, He PP, et al. Quantity and variety of food groups consumption and the risk of diabetes in adults: a prospective cohort study. Clin Nutr 2021;40(12):5710 – 17. http://dx.doi.org/10.1016/j.clnu.2021.10.003.
10. Yu DX, Zheng W, Cai H, Xiang YB, Li HL, Gao YT, et al. Long-term diet quality and risk of type 2 diabetes among urban Chinese adults. Diabetes Care 2018;41(4):723 – 30. http://dx.doi.org/10.2337/dc17-1626.
11. Son J, Lee Y, Park K. Effects of processed red meat consumption on the risk of type 2 diabetes and cardiovascular diseases among Korean adults: the Korean Genome and Epidemiology Study. Eur J Nutr 2019;58(6):2477 – 84. http://dx.doi.org/10.1007/s00394-018-1799-6.
12. Villegas R, Shu XO, Gao YT, Yang G, Cai H, Li HL, et al. The association of meat intake and the risk of type 2 diabetes may be modified by body weight. Int J Med Sci 2006;3(4):152 – 9. http://dx.doi.org/10.7150/ijms.3.152.

Perspectives

Risk Factors for Diabetes and Cardiovascular Complications in the Chinese Population

Chun Dou[1,2]; Dong Liu[1,2]; Tiange Wang[1,2,#]

Type 2 diabetes, a major noncommunicable disease, is typified by hyperglycemia, which stems from insulin resistance and dysfunction of pancreatic β-cells (*1*). Prior multi-ethnic studies hypothesized that type 2 diabetes among Caucasians was primarily driven by insulin resistance, whereas in East Asians, it was predominantly a consequence of β-cell dysfunction (*2*). Apart from the apparent genetic variations, obesity has been identified as the main factor responsible for the pathophysiological differences in diabetes between Caucasians and East Asians (*3*). Notably, China has seen a considerable increase in obesity cases in congruence with substantial changes in lifestyle and urbanization over the last four decades. In a recent population-based national cohort study, we showed that insulin resistance, rather than β-cell dysfunction, had a significant role in the pathological progression of diabetes within the Chinese population (*1*). This correlation was particularly pronounced among obese adults (*1*).

The interplay between environmental dynamics, socioeconomic status (SES), lifestyle practices, and a distinct genetic backdrop results in specific patterns of health preservation and disease onset within the Chinese population. As a result, the risk triggers and origins of diabetes and associated cardiovascular complications among this demographic may not fully align with the international expert consensus, which is primarily informed by findings from European and North American populations. This perspective collates current evidence concerning the profiles of diabetes risk factors and associated cardiovascular complications in the Chinese community, paying special attention to age-linked risk profiles and gene-environment interplays (Figure 1). It also recommends potential avenues for future research, concentrated on developing precise and effective prevention and intervention strategies to arrest the surge of diabetes and cardiovascular complications.

Profiles of Risk Factors for Diabetes

Large-scale epidemiological studies have demonstrated that factors such as aging, sex, SES, lifestyle choices, dietary habits, psychological health, and metabolic disturbances collectively or individually contribute to the onset of diabetes and weight gain (*4–8*). A prospective evaluation involving 93,781 adults within China's Cardiometabolic Disease and Cancer Cohort (4C) Study, with a robust follow-up period equivalent to 337,932 person-years, revealed that the incidence of diabetes progressively rose, from a base rate of 5.1% in adults aged between 40–55 years to a striking 10.0% in seniors aged 75 or older (*4*).

Further analysis from this study exposed a series of age-specific diabetes risk profiles. Intriguingly, metabolic risk factors such as obesity, prediabetes, hypertension, and dyslipidemia, although remained accountable for most newly diagnosed diabetes cases across all age groups, showed a marginally decreasing correlation with age (*4*). A similar age-related decline was also observed for socioeconomic risk factors such as lower levels of education (*4*). In contrast, the prominence of lifestyle-induced diabetes risks, specifically below 6 hours or above 8 hours of daily sleep, amplifies distinctly with age (*4*). This insight underscores the need for strategizing risk management methods based on age groups, to devise more cost-effective prevention and management strategies against diabetes.

In the past ten years, there has been increasing evidence suggesting that exposure to endocrine-disrupting chemicals (EDCs), which are human-made chemicals capable of mimicking, blocking, or interfering with hormones, contributes to impaired glucose regulation and increased risk of type 2 diabetes in Chinese adults (*9–12*). An observational cohort study conducted in Shanghai, China, followed 2,336 participants over a 4-year period, revealing sex-specific correlations between heightened urinary bisphenol A (BPA) levels and impaired glucose homeostasis (*9*). This correlation includes elevated fasting plasma glucose levels and β-cell dysfunction, independent of multiple covariates and body mass index (BMI) in non-diabetic women, but not in men (*9*). Interestingly,

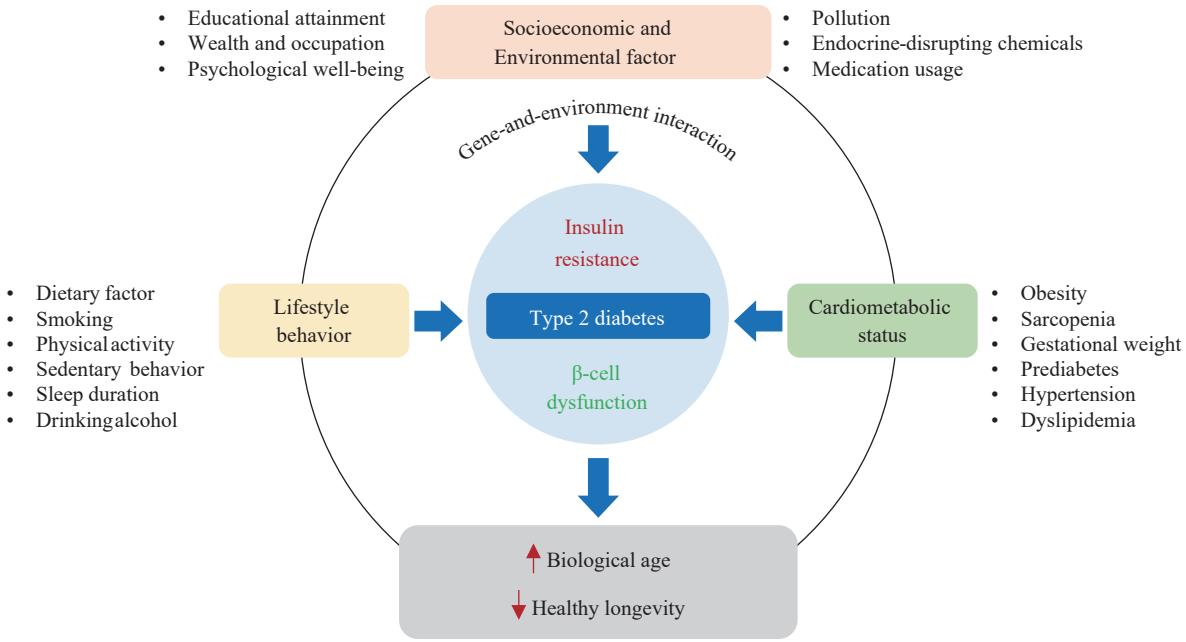


FIGURE 1. Profiles of risk factors for diabetes and the role of diabetes in healthy longevity.
Note: Type 2 diabetes is principally typified by two pathologic characteristics: insulin resistance and β-cell dysfunction. Beyond genetic predisposition, main diabetes risk factors encompass socioeconomic and environmental factors, lifestyle behaviors, and cardiometabolic status. Type 2 diabetes not only poses as a risk factor for cardiometabolic disruptions but also operates as a facilitator in the pathogenic pathway, subsequently leading to accelerated biological aging and impacting healthy longevity.

within the same study group, although no significant association was found between BPA exposure and diabetes risk, high urinary BPA concentrations were positively linked to a significant rise in fasting glucose levels in adults with a greater genetic predisposition to diabetes (*12*).

Encouragingly, substantial evidence of gene-environment interactions suggests that a genetic predisposition to diabetes or obesity may not diminish the metabolic benefits of maintaining a healthy lifestyle (*13*). In fact, individuals with a higher genetic predisposition might glean even more benefits from adhering to healthier lifestyles, evident through improvements in physical activity as well as dietary patterns, and even weight loss (*6–8*,*13*). A gene-environment interaction analysis, conducted using 20-year follow-up data from the Nurses' Health Study and the Health Professionals Follow-Up Study, showed that while genetic variations in BMI and body fat percentage were correlated with long-term weight increases, the positive impact of physical activity on weight loss was more pronounced in individuals with a high genetic susceptibility to obesity (*6*). Furthermore, within these same population cohorts, comprehensive evidence has underscored the interactions between healthy dietary patterns [such as the alternative healthy eating index (AHEI) 2010 and dietary approach to stop hypertension (DASH), which advocate for increased consumption of fruits, vegetables, and whole grains, as well as restricted intake of sugar-sweetened beverages, red or processed meats, and trans fats] and the genetic predilection to obesity in relation to long-term weight change (*7–8*), indicating that individuals with a higher genetic predisposition to obesity will likely witness greater weight loss through adherence to these healthful dietary patterns (*8*).

In a manner consistent with findings observed among individuals of European descent, a population-based study of 1,180 women with gestational diabetes from the Tianjin Gestational Diabetes Mellitus Prevention Program examined the interactions between the zinc transporter-8 gene (*SLC30A8*) genotype and gestational weight gain in relation to postpartum glycemic changes (*14*). The study found that optimal gestational weight control is particularly beneficial for Chinese women possessing the high-diabetes-risk *SLC30A8* genotype, as it can reduce the potential of developing hyperglycemia following pregnancy (*14*). These findings involving gene-environment interactions suggest that healthy lifestyle behaviors such as regular physical activity, a balanced diet, and maintaining an ideal weight can help mitigate the

adverse effects of genetic susceptibility to diabetes or obesity, underscoring potential tailored approaches for precision health.

Diabetes as a Risk Factor for Cardiovascular Disease and Its Impact on Longevity

Cardiovascular disease (CVD) is recognized as the most significant complication associated with diabetes and the leading cause of mortality for those who have diabetes. A prospective, nationwide analysis of 139,925 participants without CVD at baseline, drawn from the 4C Study, revealed that metabolic risk factors were largely responsible for 52.4%, 47.2%, and 37.8% of the population-attributable risk percentages for CVD event development in adult age groups: 40 to <55 years, 55 to <65 years, and 65 to <75 years, respectively (*15*). Within these demographic divisions, hypertension and diabetes emerged as the most prominent metabolic risk factors (*15*). Interestingly, among individuals aged 75 years or older, the primary risk factors for CVD transitioned to inappropriate sleep duration, lower education, hypertension, and diabetes (*15*). The age-specific risk factor profiles imply differential mechanisms underlying CVD development across different age groups, offering valuable insights to inform the development of age-specific preventive strategies and interventions.

Insulin resistance and its association with obesity have been identified as pivotal factors in the onset of CVD and cardiometabolic disorders in middle-aged and elderly Chinese adults (*16*). A prospective analysis of 111,576 participants from the 4C Study showed that, in comparison to adults with normal glucose tolerance, the hazard ratios (HRs) for CVD associated with the highest quartile of the homeostatic model assessment for insulin resistance (HOMA-IR) stood at 1.61 [95% confidence interval (*CI*): 1.30 to 2.00] for adults with diabetes and 1.23 (95% *CI*: 1.07 to 1.42) for adults with prediabetes (*16*). Notably, individuals with prediabetes who were both insulin-resistant and obese demonstrated increased CVD risks (*16*). Conversely, in adults with diabetes, the CVD risk linked to insulin resistance was consistent, irrespective of obesity (*16*).

Moreover, another analysis from the 4C Study indicated that adults with either prediabetes or diabetes presenting five or more ideal cardiovascular health metrics (ICVHMs), including non-smoking status or a smoking cessation period exceeding 12 months, a BMI below 23 kg/m^2, the achievement of physical activity targets (equal to or exceeding 150 minutes/week of moderate intensity, 75 minutes/week of vigorous intensity, or 150 minutes/week of moderate or vigorous intensity), daily consumption of at least 4.5 cups of fruits and vegetables, total cholesterol levels below 200 mg/dL (untreated), blood pressure readings below 120 mmHg/80 mmHg (untreated), and optimal glycated hemoglobin levels (less than 5.7% for prediabetes or less than 6.5% for diabetes), exhibited no significant excess risk or lower risk of CVD when compared to individuals with normal glucose tolerance (*17*).

Recent Mendelian randomization (MR) studies have validated previous observational findings that diabetes and insulin resistance are risk factors for cardiometabolic diseases (*18–19*). Contrasting with conventional epidemiological studies, MR analysis employs genetic variants, determined at conception and randomly allocated to individuals, as instrumental variables. This enables inference of causal relationships between phenotypes and significantly reduces the possibility of reverse causality and bias arising from known or unknown confounders. A two-sample MR study, utilizing genome-wide association study (GWAS) summary statistics, proposed that diabetes diagnosed at various age ranges (<50, 50–60, 60–70, and >70 years) has equivalent causal effects on CVD and related cardiometabolic diseases (*18*). This suggests that genetically defined diabetes subtypes, classified by age at diagnosis, may not infer differential CVD risks (*18*). Another MR study revealed causal links between insulin resistance (as evidenced by fasting insulin) and six cardiometabolic diseases [type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), hypertension, coronary heart disease (CHD), myocardial infarction (MI), and small vessel stroke] (*19*). It further suggested that insulin resistance serves as a mediating factor in the causal relationships between sarcopenia-related traits and five aforementioned cardiometabolic diseases (type 2 diabetes, NAFLD, hypertension, CHD, and MI) (*19*). More specifically, insulin resistance is accountable for approximately 7% to 34% of the causal effects of grip strength or appendicular lean mass on diabetes, NAFLD, hypertension, CHD, and MI (*19*).

Several studies have demonstrated causal relationships between diabetes and both biological aging and longevity in humans (*20–21*). In a recent MR study, type 2 diabetes was conclusively identified as a causative risk factor for biological aging (*20*). This link was identified by two reliable DNA methylation-

based indicators known as GrimAge acceleration and PhenoAge acceleration, which provide useful insights into potential interventions for reducing age-related morbidity and promoting healthy longevity (*20*). Importantly, type 2 diabetes also acts as a mediator in the causal pathway connecting broader environmental risk factors, such as SES, and human longevity (*21*). A recent comprehensive MR study, using GWAS summary statistics from over 1,000,000 European-ancestry individuals, found that genetically predicted elevated levels of SES, including higher educational attainment, household income, and occupational status, were positively associated with both a longer parental lifespan and individual longevity (*21*). Among these, educational attainment exhibited an independent effect. In the causal pathways, type 2 diabetes was found to mediate approximately 7.50%, 21.98%, and 47.33% of the effects of education on parental lifespan, and on the 90th and 99th percentile of individual longevity, respectively (*21*).

The primary socioeconomic risk factor for diabetes, according to the 4C study, was lower educational attainment. This demographic represented more than 10% of the risk factor for the disease in adults younger than 65 years (*4*). While an increase in ICVHMs was inversely related to the risk of CVD in populations with both high and low levels of educational attainment, there was no evidence supporting the interaction between these two factors in prediabetic or diabetic individuals (*17*). Insights from the Prospective Urban Rural Epidemiology study, which included 154,169 adults from 20 countries, suggest that country income levels affect socioeconomic gradients in CVD and mortality rates (*22*). The HRs for major CVD events, when comparing lower to higher education levels, ranged from 1.23 (95% *CI*: 0.96 to 1.58) for individuals in high-income countries to 2.23 (95% *CI*: 1.79 to 2.77) for those in low-income countries (*22*). Consequently, the socioeconomic context of the study population and the generalizability and reliability of existing evidence are vital considerations in interpreting the impact of risk factors on diabetes and cardiovascular complications. This will promote a nuanced comprehension of diabetes etiology and aid in building more effective prevention and intervention strategies.

Future Prospects and Challenges in Diabetes Research and Prevention

Given the escalating concerns regarding the diabetes epidemic and its impact in China, both the Diabetes Prevention and Control Action and the Healthy Diet Campaign within the Healthy China Initiative (2019–2030) underscore the importance of delivering education (e.g., health knowledge and nutritional awareness), intervention, and standard health management to the broader population and individuals with diabetes (*23–24*). Notably, numerous MR studies primarily rely on GWASs conducted on individuals of European descent; consequently, care must be exercised when generalizing the findings. While it is critical to collate and analyze global datasets, as they can showcase the gamut of risk factors in varied socioeconomic circumstances and offer predictions for future trajectories, it is equally crucial to formulate and implement strategies tailored specifically toward the Chinese population.

Emerging technologies are propelling diabetes research into new arenas, encompassing climate change, environmental exposure, nutrition and longevity, the human gut microbiome, multi-omics, and artificial intelligence models (*25–30*). There is an abundance of scientific inquiries that warrant further examination. First, understanding the intersection of climate change (e.g., global warming) and traditional risk profiles. Second, conducting in-depth assessments of EDC impacts. Third, investigating the intermediary role of the gut microbiome in metabolically healthy longevity. Fourth, establishing a medical research database specifically for the Chinese population. Fifth, initiating ground-breaking research in novel drug development and biotechnologies for metabolic diseases. Sixth, integrating multi-omics and artificial intelligence algorithms into medical services.

Conflicts of interest: No conflicts of interest.

Funding: This work was supported by the grants from the National Natural Science Foundation of China (82022011, 81970706), the "Shanghai Municipal Education Commission–Gaofeng Clinical Medicine Grant Support" from Shanghai Jiao Tong University School of Medicine (20171901 Round 2), and the Innovative Research Team of High-Level Local Universities in Shanghai.

doi: 10.46234/ccdcw2023.191

[#] Corresponding author: Tiange Wang, tiange.wang@shsmu.edu.cn.

[1] Department of Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2] Shanghai National Clinical Research Center for Metabolic Diseases, Key Laboratory for Endocrine and Metabolic Diseases of the National Health Commission of the PR China, Shanghai Key Laboratory for Endocrine Tumor, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

Submitted: July 18, 2023; Accepted: September 05, 2023

REFERENCES

1. Wang TG, Lu JL, Shi LX, Chen G, Xu M, Xu Y, et al. Association of insulin resistance and β-cell dysfunction with incident diabetes among adults in China: a nationwide, population-based, prospective cohort study. Lancet Diabetes Endocrinol 2020;8(2):115 – 24. http://dx.doi.org/10.1016/S2213-8587(19)30425-5.
2. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. Diabetes Care 2013;36(6):1789 – 96. http://dx.doi.org/10.2337/dc12-1235.
3. Møller JB, Pedersen M, Tanaka H, Ohsugi M, Overgaard RV, Lynge J, et al. Body composition is the main determinant for the difference in type 2 diabetes pathophysiology between Japanese and Caucasians. Diabetes Care 2014;37(3):796 – 804. http://dx.doi.org/10.2337/dc13-0598.
4. Wang TG, Zhao ZY, Wang GX, Li Q, Xu Y, Li M, et al. Age-related disparities in diabetes risk attributable to modifiable risk factor profiles in Chinese adults: a nationwide, population-based, cohort study. Lancet Healthy Longev 2021;2(10):e618 – 28. http://dx.doi.org/10.1016/S2666-7568(21)00177-X.
5. Wang TG, Lu JL, Xu Y, Li M, Sun JC, Zhang J, et al. Circulating prolactin associates with diabetes and impaired glucose regulation: a population-based study. Diabetes Care 2013;36(7):1974 – 80. http://dx.doi.org/10.2337/dc12-1893.
6. Wang TG, Huang T, Heianza Y, Sun DJY, Zheng Y, Ma WJ, et al. Genetic susceptibility, change in physical activity, and long-term weight gain. Diabetes 2017;66(10):2704 – 12. http://dx.doi.org/10.2337/db17-0071.
7. Wang TG, Heianza Y, Sun DJY, Zheng Y, Huang T, Ma WJ, et al. Improving fruit and vegetable intake attenuates the genetic association with long-term weight gain. Am J Clin Nutr 2019;110(3):759 – 68. http://dx.doi.org/10.1093/ajcn/nqz136.
8. Wang TG, Heianza Y, Sun DJY, Huang T, Ma WJ, Rimm EB, et al. Improving adherence to healthy dietary patterns, genetic risk, and long term weight gain: gene-diet interaction analysis in two prospective cohort studies. BMJ 2018;360:j5644. http://dx.doi.org/10.1136/bmj.j5644.
9. Wang B, Li M, Zhao ZY, Lu JL, Chen YH, Xu Y, et al. Urinary bisphenol A concentration and glucose homeostasis in non-diabetic adults: a repeated-measures, longitudinal study. Diabetologia 2019;62(9):1591 – 600. http://dx.doi.org/10.1007/s00125-019-4898-x.
10. Wang TG, Li M, Chen B, Xu M, Xu Y, Huang Y, et al. Urinary bisphenol A (BPA) concentration associates with obesity and insulin resistance. J Clin Endocrinol Metab 2012;97(2):E223 – 7. http://dx.doi.org/10.1210/jc.2011-1989.
11. Ning G, Bi YF, Wang TG, Xu M, Xu Y, Huang Y, et al. Relationship of urinary bisphenol A concentration to risk for prevalent type 2 diabetes in Chinese adults: a cross-sectional analysis. Ann Intern Med 2011;155(6):368 – 74. http://dx.doi.org/10.7326/0003-4819-155-6-201109200-00005.
12. Bi YF, Wang WQ, Xu M, Wang TG, Lu JL, Xu Y, et al. Diabetes genetic risk score modifies effect of Bisphenol A exposure on deterioration in glucose metabolism. J Clin Endocrinol Metab 2016;101(1):143 – 50. http://dx.doi.org/10.1210/jc.2015-3039.
13. Wang TG, Xu M, Bi YF, Ning G. Interplay between diet and genetic susceptibility in obesity and related traits. Front Med 2018;12(6):601 – 7. http://dx.doi.org/10.1007/s11684-018-0648-6.
14. Wang TG, Liu HK, Wang LS, Huang T, Li WQ, Zheng Y, et al. Zinc-associated variant in *SLC30A8* gene interacts with gestational weight gain on postpartum glycemic changes: a longitudinal study in women with prior gestational diabetes mellitus. Diabetes 2016;65(12):3786 – 93. http://dx.doi.org/10.2337/db16-0730.
15. Wang TG, Zhao ZY, Yu XF, Zeng TS, Xu M, Xu Y, et al. Age-specific modifiable risk factor profiles for cardiovascular disease and all-cause mortality: a nationwide, population-based, prospective cohort study. Lancet Reg Health West Pac 2021;17:100277. http://dx.doi.org/10.1016/j.lanwpc.2021.100277.
16. Wang TG, Li M, Zeng TS, Hu RY, Xu Y, Xu M, et al. Association between insulin resistance and cardiovascular disease risk varies according to glucose tolerance status: a nationwide prospective cohort study. Diabetes Care 2022;45(8):1863 – 72. http://dx.doi.org/10.2337/dc22-0202.
17. Wang TG, Lu JL, Su Q, Chen YH, Bi YF, Mu YM, et al. Ideal cardiovascular health metrics and major cardiovascular events in patients with prediabetes and diabetes. JAMA Cardiol 2019;4(9):874 – 83. http://dx.doi.org/10.1001/jamacardio.2019.2499.
18. Ye CJ, Kong LJ, Wang YY, Lin H, Wang SY, Zhao ZY, et al. Causal associations between age at diagnosis of diabetes and cardiovascular outcomes: a Mendelian randomization study. J Clin Endocrinol Metab 2023;108(5):1202 – 14. http://dx.doi.org/10.1210/clinem/dgac658.
19. Ye CJ, Kong LJ, Wang YY, Zheng J, Xu M, Xu Y, et al. Causal associations of sarcopenia-related traits with cardiometabolic disease and Alzheimer's disease and the mediating role of insulin resistance: a Mendelian randomization study. Aging Cell 2023;22(9):e13923. http://dx.doi.org/10.1111/ACEL.13923.
20. Kong LJ, Ye CJ, Wang YY, Hou TZC, Zheng J, Zhao ZY, et al. Genetic evidence for causal effects of socioeconomic, lifestyle, and cardiometabolic factors on epigenetic-age acceleration. J Gerontol: Ser A 2023;78(7):1083 – 91. http://dx.doi.org/10.1093/GERONA/GLAD078.
21. Ye CJ, Kong LJ, Wang YY, Dou C, Zheng J, Xu M, et al. Mendelian randomization evidence for the causal effects of socio-economic inequality on human longevity among Europeans. Nat Hum Behav 2023;7(8):1357 – 70. http://dx.doi.org/10.1038/S41562-023-01646-1.
22. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. Lancet Glob Health 2019;7(6):e748 – 60. http://dx.doi.org/10.1016/S2214-109X(19)30045-2.
23. Wang WJ. Interpretation of the diabetes prevention and control action of the healthy China initiative 2019-2030. China CDC Wkly 2020;2(9):143 – 5. http://dx.doi.org/10.46234/ccdcw2020.039.
24. Wang LS, Wang HJ, Wang ZH, Jiang HR, Li WY, Wang SSZ, et al. Interpretation of healthy diet campaign in healthy China initiative 2019-2030. China CDC Wkly 2021;3(16):346 – 9. http://dx.doi.org/10.46234/ccdcw2021.092.
25. Bogar K, Brensinger CM, Hennessy S, Flory JH, Bell ML, Shi C, et al. Climate change and ambient temperature extremes: association with serious hypoglycemia, diabetic ketoacidosis, and sudden cardiac arrest/ventricular arrhythmia in people with type 2 diabetes. Diabetes Care 2022;45(11):e171 – 3. http://dx.doi.org/10.2337/dc22-1161.
26. Lind PM, Lind L. Endocrine-disrupting chemicals and risk of diabetes: an evidence-based review. Diabetologia 2018;61(7):1495 – 502. http://dx.doi.org/10.1007/s00125-018-4621-3.
27. Longo VD, Anderson RM. Nutrition, longevity and disease: from molecular mechanisms to interventions. Cell 2022;185(9):1455 – 70. http://dx.doi.org/10.1016/j.cell.2022.04.002.
28. Zhou WY, Sailani MR, Contrepois K, Zhou YJ, Ahadi S, Leopold SR, et al. Longitudinal multi-omics of host–microbe dynamics in prediabetes. Nature 2019;569(7758):663 – 71. http://dx.doi.org/10.1038/s41586-019-1236-x.
29. Kreitmaier P, Katsoula G, Zeggini E. Insights from multi-omics integration in complex disease primary tissues. Trends Genet 2023;39(1):46 – 58. http://dx.doi.org/10.1016/j.tig.2022.08.005.
30. Singhal K, Azizi S, Tu T, Mahdavi SS, Wei J, Chung HW, et al. Large language models encode clinical knowledge. Nature 2023;620(7972):172 – 180. http://dx.doi.org/10.1038/s41586-023-06291-2.

Indexed by Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), PubMed Central (PMC), Scopus, Chinese Scientific and Technical Papers and Citations, and Chinese Science Citation Database (CSCD)

The inauguration of *China CDC Weekly* is in part supported by Project for Enhancing International Impact of China STM Journals Category D (PIIJ2-D-04-(2018)) of China Association for Science and Technology (CAST).

CCDC weekly

Vol. 5 No. 45 Nov. 10, 2023

Published since November, 2019

Responsible Authority
National Health Commission of the People's Republic of China

Sponsor
Chinese Center for Disease Control and Prevention

Editing and Publishing
China CDC Weekly Editorial Office
No.155 Changbai Road, Changping District, Beijing, China
Tel: 86-10-63150501, 63150701
Email: weekly@chinacdc.cn

Printing
Beijing Kexin Printing Co., Ltd

CSSN
ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1