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ABSTRACT

Early Life Exposure to the Great Chinese Famine (1959–1961) and the Health of Older Adults in China: A Meta-Analysis (2008–2023)

There is mounting evidence indicating that the aging process initiates during early life stages, with in utero the individual's environment playing a significant role. Consequently, it is crucial to understand the enduring effects of early life circumstances on health in old age. In this study, we conducted a meta-analysis to examine the effects of the Great Chinese Famine (1959–1961) on the health of older adults. We also explored potential mechanisms underlying these effects. The complex interplay between early life circumstances, multiple health-related sectors, and healthy aging necessitates a comprehensive life-course approach and strategic interventions to enhance public health in an aging society.

JEL Classification: I14, J14, J13, I18

Keywords: meta-analysis, aging, life course health, famine, early life circumstances

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1. Introduction

The increasing aging population and the prevalence of chronic diseases necessitate a comprehensive life-course approach to address the growing demand for cost-effective prevention, treatment, and long-term care. To achieve healthy aging, it is crucial to understand the factors influencing disease development throughout an individual's life and identify opportunities for effective interventions. This study examines the latest evidence on how early life circumstances impact health in old age, distinguishing between exposures *in utero* and during childhood in various environments. Furthermore, we conduct a meta-analysis utilizing studies on the effects of the Great Chinese Famine (1959–1961) on the health of older adults, discussing potential mechanisms underlying these associations.

Prenatal conditions have a significant impact on healthy aging, as evidenced by numerous studies (1–2). The Fetal Origin Hypothesis suggests that disruptions to the prenatal environment, including maternal and fetal health, social and economic shocks, and environmental pollution, can have long-term consequences on developmental health and well-being. These effects become apparent later in life, with an increased susceptibility to diseases persisting into old age.

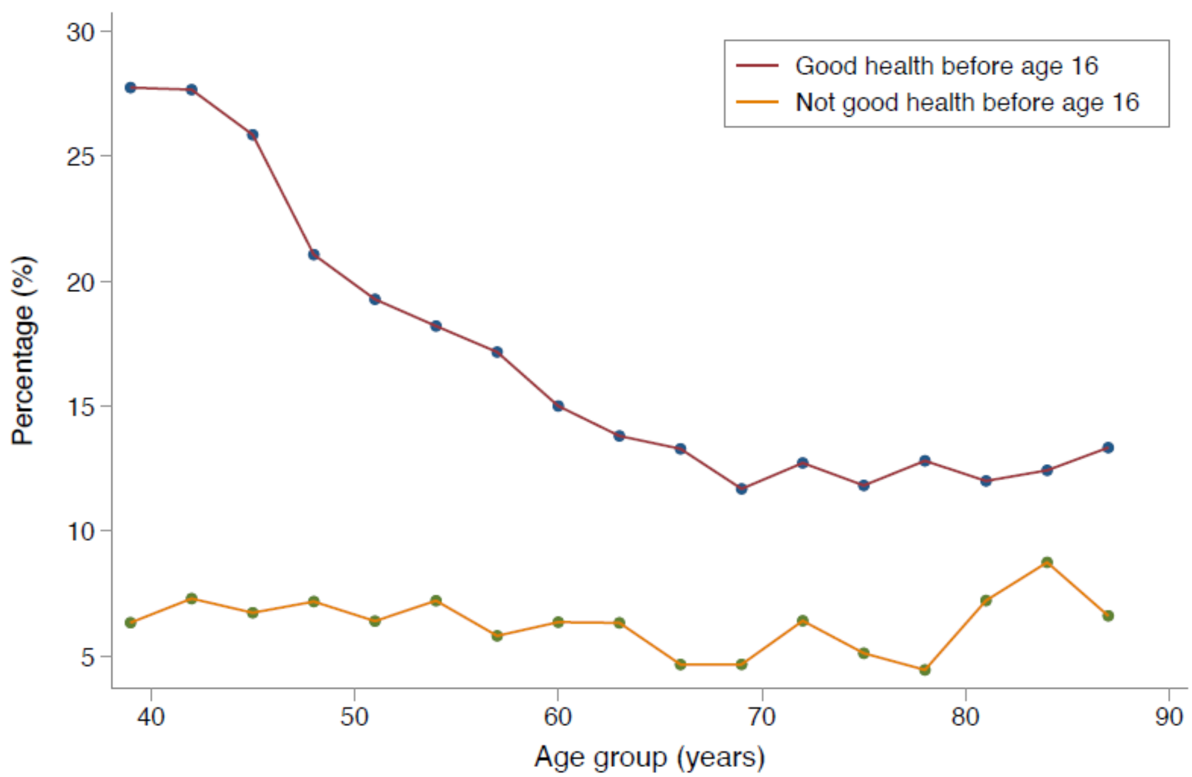

FIGURE 1. Self-rated health among middle-aged and older adults by child health.
Note: In this figure, we included data from the longitudinal survey, ensuring that each respondent is counted only once. If a respondent participated in multiple waves of the survey, we used information from their earliest participation for plotting purposes. The respondents featured in this

figure are middle-aged and older adults. Data: CHARLS National Sample (2011, 2013, 2015)

Abbreviation: CHARLS=China Health and Retirement Longitudinal Study

Childhood represents a critical period during which adverse circumstances can have long-lasting effects on health (3). Figure 1 displays the variation in self-rated health among respondents from the China Health and Retirement Longitudinal Study (CHARLS) national sample over three waves, based on retrospective reports of health status before age 16. The data reveals a significant association between good health before age 16 and a higher likelihood of reporting excellent or very good health after the age of 60, with a difference of 5–10 percentage points. Additionally, various other childhood factors, including traumas and adversity, neighborhood safety and cohesion, education, friendship, parent-child relationship, parenting skills, natural environments, exposure to famine, parental health behaviors, disease infections, access to healthcare, parental socioeconomic status, and home and social environments, have also shown associations with health outcomes in later life.

Multiple risk factors *in utero* and early *childhood* have been identified as contributors to various adverse health outcomes, including but not limited to diminished height, disability, premature mortality, depressive symptoms, schizophrenia, cognitive impairment, metabolic syndrome, frailty, reduced lung function, arthritis, anemia, diabetes, coronary heart disease, stroke, and fatty liver disease.

2. Methods and Data

Numerous studies in China have explored the association between early life risk factors and aging, with a particular focus on exposures to the Great Chinese Famine (1959–1961) (4). It is worth noting that a significant proportion of the Chinese population over the age of 60 today were exposed to the famine during their early years. Both animal and human studies have indicated that the famine may have a substantial long-term impact on the prevalence of chronic diseases. The international literature has extensively documented the link between early-life undernutrition and detrimental health outcomes in later life (5).

We conducted a comprehensive search of publications, including journal articles, degree theses, and conference manuscripts, in various databases such as PubMed, Embase, Chinese Wanfang Data, and Chinese National Knowledge Infrastructure (CNKI) databases. The search was conducted until August 31, 2023. The keywords used for the search were [(China OR Chinese) AND (famine OR undernutrition OR starvation OR malnutrition)] OR great leap forward OR great famine. English language was used for the search in PubMed and Embase, while Chinese language was used for Wangfang and CNKI. For further details, please refer to the Supplementary Materials (available in http://weekly.chinacdc.cn).

The article selection process involved independent review of titles and abstracts by two researchers. Data extraction included information on authors, publication details, analytical methods, study size, exposure definitions, control selections, conditions studied, and reported results. Excel spreadsheets were used to collect this data. Additionally, the researchers independently extracted data on the number of disease events and at-risk populations.

The quality of the literature was assessed using the Newcastle-Ottawa scale, which evaluates three main perspectives: study group selection, comparability of study groups, and identification of relevant exposures or outcomes in case-control or cohort studies. Each perspective was assigned a score of “good”, “fair”, or “poor” based on predefined criteria. Only literature of “good” quality in any perspective was included in the study, with specific criteria of achieving 3 or 4 points in the selection domain, 1 or 2 points in the comparability domain, and 2 or 3 points in the outcome/exposure domain.

The data analysis in this study utilized the 'meta' package (version 6.5-0) in R (version 4.2.3; R Core Team, 2023) as the third-party software. Heterogeneity between studies was assessed using the I^2 statistic and analyzed using the χ^2 test. For $I^2<50\%$, a common-effects model (also known as the fixed-effect model) was employed for the meta-analysis. For I^2 values above or equal to 50%, a random-effects model was utilized. Statistical significance was defined as $P<0.05$.

3. Results

As shown in Figure 2, data from 30 studies could be used for a meta-analysis of overweight and obesity, diabetes, hyperglycemia, metabolic syndrome, schizophrenia, depression, and arthritis. These studies provided data on famine births and post-famine births. Several reports findings for more than one health condition. The forest plot shows effect estimates for health conditions comparing famine births with post-famine births serving as controls.

The meta-analysis findings indicate that there is a significant increase in the odds of overweight [odds ratio (*OR*) 1.14; 95% confidence interval (*CI*): 1.02, 1.27], hyperglycemia (*OR* 1.27; 95% *CI*: 1.13, 1.42), metabolic syndrome (*OR* 1.31; 95% *CI*: 1.18, 1.45), and schizophrenia (*OR* 1.52; 95% *CI*: 1.29, 1.78). However, no significant effects are observed for obesity (*OR* 1.18; 95% *CI*: 0.99, 1.40), diabetes (*OR* 1.32; 95% *CI*: 0.99, 1.75), hypertension (*OR* 1.07; 95% *CI*: 0.92, 1.25), depression (*OR* 1.65; 95% *CI*: 0.98, 2.78), or arthritis (*OR* 1.04; 95% *CI*: 0.86, 1.26). The estimates from both common-effects and random effects models were similar, with the random-effects model having wider 95% *CI*s due to between-study heterogeneity.

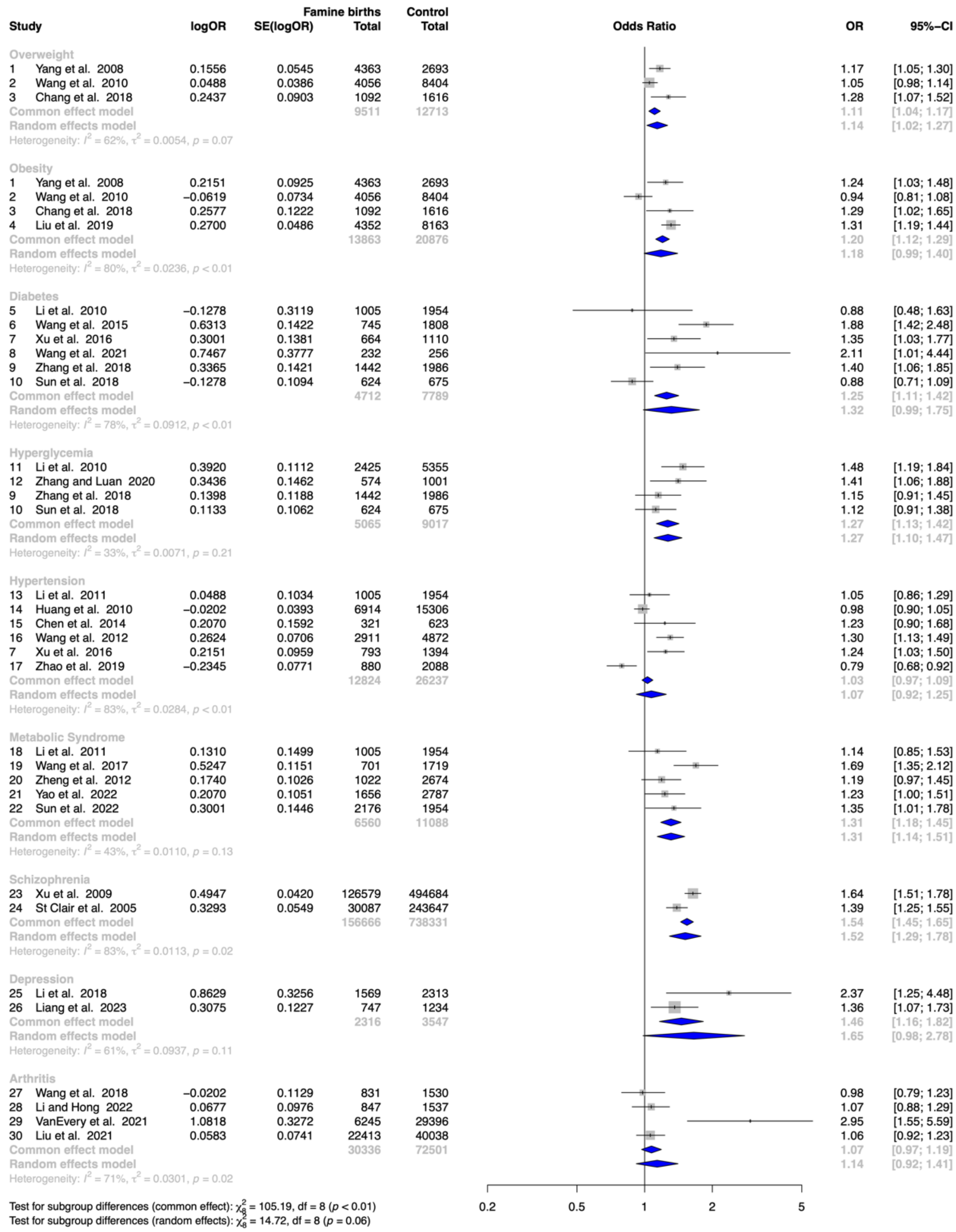

FIGURE 2. Effect estimates on selected health conditions comparing famine births with controls (post-famine births, meta-analysis).

Note: Summary estimates for the Mantel-Haenszel fixed-effects model and DerSimonian-Laird random-effects model are provided. Each outcome is represented by a box and horizontal lines, indicating the odds ratio (*OR*) and 95% confidence intervals (*CI*s). The size of each box reflects the weight of the report for that particular outcome. Diamonds represent the 95% *CI* for pooled effect estimates, centered on the pooled odds ratio of either the fixed-effects model or the random-effects model for each outcome.

4. Discussion

Evidence shows that infancy is often considered the most crucial period for nutrition-related health outcomes later in life in comparison to the prenatal period or childhood. However, there is some indication that adverse events during the first two trimesters of pregnancy may have an even more significant impact on specific health outcomes. Understanding the reasons for these differential effects of malnutrition during this narrow time window in early life would provide valuable insights.

Gender disparities in the long-term health effects of the Great Chinese Famine (1959–1961) have been observed. Female survivors tend to experience poorer health outcomes in adulthood and old age compared to their male counterparts (6–7). This discrepancy may be attributed to the scarring effect, which disproportionately affects women, overpowering the influence of mortality selection. In contrast, mortality selection has a greater impact on male survivors, resulting in relatively less detrimental health consequences (6).

The impact of famine on late-life health is more pronounced among vulnerable groups, such as those who are overweight or obese, reside in severely affected areas, or have lower educational attainment (9). For example, the famine disproportionately affected rural areas in China due to biased food distribution, resulting in higher excess mortality. As a result, rural survivors show smaller long-term health consequences compared to their urban counterparts, reflecting the combined effects of mortality selection and scarring (8). Additionally, rural survivors tend to exhibit null or even positive effects on later-life disease risks, whereas urban survivors are not affected in the same way. This disparity can be attributed, at least in part, to the stronger mortality selection effect observed in rural areas.

Early life exposure to famine, combined with a subsequent nutrient-rich environment later in life, can have negative health consequences in old age, particularly among individuals of high socioeconomic status. In China, two significant historical events, the Great Chinese Famine (1959–1961) and the subsequent economic reform and opening up since 1978, have played a key role in shaping these health risks. Individuals who experienced undernutrition during the Great Chinese Famine may have developed a "thrifty genotype" as a survival mechanism, altering their body's physiological and metabolic function. However, this thrifty genotype can become maladaptive in the context of rapid economic development and increased nutritional abundance in later life, leading to a higher risk of obesity, type 2 diabetes, and coronary heart diseases (10).

The complex interplay of early life circumstances and various health-related factors impact healthy aging, necessitating a comprehensive life-course approach and strategic measures to enhance public health in an aging society. Effective interventions should be implemented early in life, focusing on women of childbearing age and childhood, before disease and disability onset, in order to attenuate the aging process, enhance population health, and improve quality of life in later years.

The implementation of the Healthy China 2030 national initiative since 2016 has highlighted the need for holistic approaches in promoting population health. This includes a shift towards comprehensive life-cycle health management and the adoption of health-in-all policies, as opposed to a narrow focus on disease management. In order to inform policy development and interventions, it is important to consider the substantial scientific evidence linking early life circumstances with health outcomes in elderly populations in China.

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Conflict of interest: The authors have no conflict of interest.

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ONLINE SUPPLEMENTARY MATERIAL

Search Strategy and Research Selection

We searched publications including journal articles, degree theses and conference manuscripts in databases including PubMed, Embase, Chinese Wanfang Data, and Chinese National Knowledge Infrastructure (CNKI) until August 31, 2023. The search terms included [(China OR Chinese) AND (famine OR undernutrition OR starvation OR malnutrition)] OR great leap forward OR great famine. English was used as the search language for PubMed and Embase, while Chinese was used for Wanfang and CNKI.

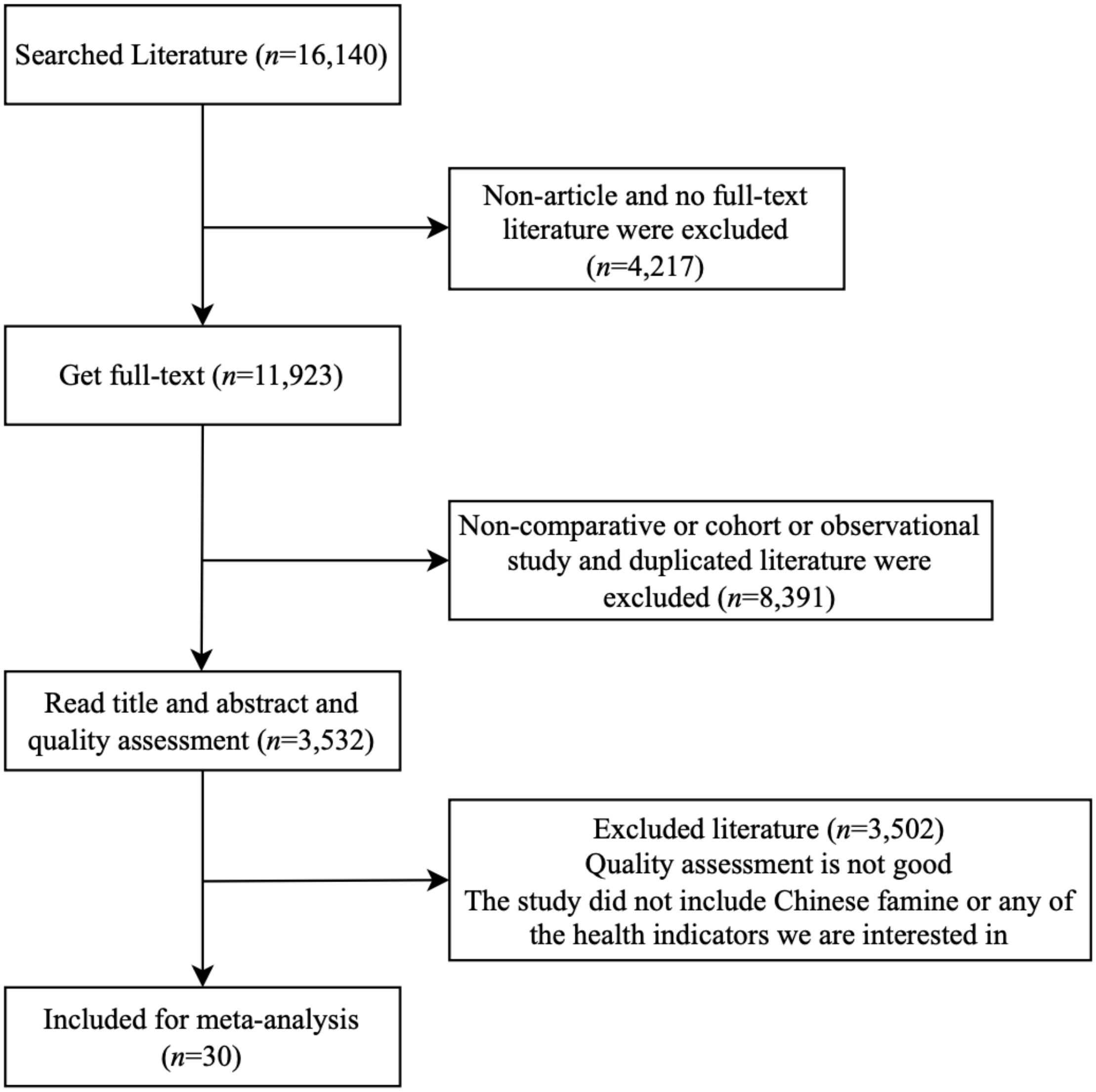
The inclusion criteria for our study were as follows: 1) Chinese famine was considered as an exposure or risk factor; 2) the primary outcome of interest was long-term health status or chronic disease; 3) comparable methods were used to assess outcomes for different birth cohorts with and without famine experience; 4) the study population, study design, and analyses were appropriately described; and 5) only literature of "good" quality, as determined by any criteria of the Newcastle-Ottawa scale, was included in our study.

Exclusion criteria: publications on the impact of famine, undernutrition, starvation, malnutrition, or the great leap forward on educational achievements or economic outcomes were not included.

Data Extraction

The titles and abstracts of the articles were independently reviewed by two researchers simultaneously. Data regarding author and publication details, analytical methods, study size, exposure definitions, control selection, studied conditions, covariates, and reported results were extracted. Excel spreadsheets were utilized for data collection, and two researchers independently gathered information on the number of disease events and at-risk populations.

SUPPLEMENTARY FIGURE S1 Flowchart of literature retrieval and screening.



SUPPLEMENTARY TABLE S1. Summary of research features.

Ref No.	Authors	Analytical methods	Study size (famine births/total births)	Conditions studied	Covariate
(1)	Yang et al., 2008	Time control	4363/7056	Overweight	Yes
(2)	Wang et al., 2010	Time control	4056/12460	Overweight	Yes
(3)	Chang et al., 2018	Time control	1092/2708	Overweight	Yes
(1)	Yang et al., 2008	Time control	4363/7056	Obesity	Yes
(2)	Wang et al., 2010	Time control	4056/12460	Obesity	Yes
(3)	Chang et al., 2023	Time control	1092/2708	Obesity	Yes
(4)	Liu et al., 2019	Time control	4352/12515	Obesity	Yes
(5)	Li et al., 2010	Double difference	1005/2959	Diabetes	Yes
(6)	Wang et al., 2015	Time control	745/2553	Diabetes	Yes
(7)	Xu et al., 2016	Time control/ double difference/ instrumental variable	664/1774	Diabetes	Yes
(8)	Wang et al., 2021	Time control	232/488	Diabetes	Yes
(9)	Zhang et al., 2018	Time control	1442/3428	Diabetes	Yes
(10)	Sun et al. 2018	Time control	624/1299	Diabetes	Yes
(11)	Li et al., 2010	Time control	2425/7780	Hyperglycemia	Yes
(12)	Zhang and Luan, 2020	Time control	574/1575	Hyperglycemia	Yes
(9)	Zhang et al., 2018	Time control	1442/3428	Hyperglycemia	Yes
(10)	Sun et al. 2018	Time control	624/1299	Hyperglycemia	Yes
(13)	Li et al., 2011	Double difference	1005/2959	Hypertension	Yes
(14)	Huang et al., 2010	Double difference	6914/22220	Hypertension	Yes
(15)	Chen et al., 2014	Time control	321/944	Hypertension	Yes
(16)	Wang et al., 2012	Time control	2911/7783	Hypertension	Yes
(7)	Xu et al., 2016	Time control/ double difference/ instrumental variable	793/2187	Hypertension	Yes
(17)	Zhao et al., 2019	Time control	880/2968	Hypertension	Yes
(18)	Li et al., 2011	Double	1005/2959	Metabolic	Yes

		difference		Syndrome	
(19)	Wang et al., 2017	Time control	701/2420	Metabolic Syndrome	Yes
(20)	Zheng et al., 2012	Time control	1022/3696	Metabolic Syndrome	Yes
(21)	Yao et al., 2022	Time control	1656/4443	Metabolic Syndrome	Yes
(22)	Sun et al., 2022	Time control	2176/4130	Metabolic Syndrome	Yes
(23)	Xu et al., 2009	Time control	126579/621263	Schizophrenia	Yes
(24)	St Clair et al., 2005	Time control	30087/273734	Schizophrenia	Yes
(25)	Li et al., 2018	Matching/Time control	1569/3882	Depression	Yes
(26)	Liang et al., 2023	Time control	747/1981	Depression	Yes
(27)	Wang et al., 2018	Time control	831/2361	Arthritis	Yes
(28)	Li and Hong, 2022	Time control	847/2384	Arthritis	Yes
(29)	VanEvery et al., 2021	Time control	6245/35641	Arthritis	Yes
(30)	Liu et al., 2021	Time control	22413/62451	Arthritis	Yes

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