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Closing the gap in dementia research by community-based cohort studies in the Chinese population

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Summary

China accounts for 1/5 of the global population and China faces a particularly heavy dementia burden due to its rapidly ageing population. Unique historical events, genetic background, sociocultural factors, lifestyle, and the COVID-19 pandemic further influence cognitive outcomes in the Chinese population. We searched PubMed, Web of Science, and Embase for community-based cohort studies related to dementia in the Chinese population, and summarized the characteristics, methodologies, and major findings published over the last 25 years from 39 cohorts. We identified critical research gaps and propose future directions, including enhancing sample representativeness, investigating China-specific risk factors, expanding exposure measurements to the whole life-span, collecting objective data, conducting administer-friendly domain-specific cognitive assessments, adopting pathological diagnostic criteria, standardizing biobank construction, verifying multi-modal biomarkers, examining social and genetic-environmental aspects, and monitoring post-COVID cognitive health, to approach high quality of dementia studies that can provide solid evidence to policy making and promote global brain health research.

Keywords: Dementia; Community-based; Cohort; Chinese population; Cognitive impairment

Introduction

Dementia is a term encompassing a variety of brain diseases that affect memory, thinking, and the ability to perform daily activities.[1] As the aging population grows, the global number of people with dementia is projected to surge to 139 million by 2050, with 70% residing in low- and middle-income countries (LMICs).[1,2] Over the past five years, while basic research has focused on the aetiology and pathophysiology of dementia,[3,4] we also have witnessed significant advancements in disease-

Abbreviations: AHLS, Anhui healthy longevity survey; BABRI, Beijing aging brain rejuvenation initiative; BECHCS, Beijing elderly comprehensive health cohort study; BLSA, Beijing longitudinal study of aging; CCHS-Beijing, Cardiovascular and cognitive health study in middle-aged and elderly residents of Beijing; CHAP, Confucius hometown aging project; CHARLS, The China health and retirement longitudinal study; CHCCS, China Hainan centenarian cohort study; CHNS, The China health and nutrition survey; CLAS, The Chinese longitudinal ageing study; CLASS, China longitudinal aging social survey; CLHLS, Chinese longitudinal healthy longevity survey; COAST, China cognition and aging study; EMCOA, Effects and mechanism investigation of cholesterol and oxysterol on Alzheimer's disease; GBCS, Guangzhou biobank cohort study; HABCS, Healthy ageing and biomarkers cohort study; HALST, The healthy aging longitudinal study in Taiwan; HK-MAPS, Hong Kong memory and ageing prospective study; HMACS, Hubei memory and aging cohort; ILLAN, I-Lan Longitudinal Aging Study; JCICS, Jidong cognitive impairment cohort study; MIND-CHINA, Multimodal interventions to delay dementia and disability in rural China; Mr. OS & Ms. OS, Mr. OS and Ms. OS; PHASE, Panel on health and ageing of Singaporean elderly; PINDEC, The prevention and intervention on neurodegenerative disease for elderly in China; PINE, The population study of Chinese elderly in Chicago; PLAD, The project of longevity and aging in Dujiangyan; RuLAS, The rugao longevity and aging study; SAS, Shanghai aging study; SCHS, The Singapore Chinese health study; SCS, Shunyi cohort study; SEBAS, The social environment and biomarkers of aging study in Taiwan; SLAS, Singapore longitudinal ageing studies; TENC, Tianjin elderly nutrition and cognition; TIGER, Taiwan initiative for geriatric epidemiological research; TIS, Taizhou imaging study; TLSA, The Taiwan longitudinal study on aging; WCHAT, West China health and aging trends study; ZAHCS, Zhejiang ageing and health cohort

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Research in context

Evidence before this study

Despite advances in basic laboratory and clinical research, the natural history, disease burden, risk/predictive factors and diagnostic approaches of dementia can be best revealed through prospective studies conducted in large-sampled population cohorts. The 2024 update of the Lancet Commission proposed a life-course model of risk, suggesting that up to 45% of dementias could be prevented by modifying 14 risk factors. However, most evidence comes from Western populations. Despite numerous surveys in China and the incorporation of cognitive measures in cohort studies, there remains significant gaps in community-based studies exploring dementia's risk factors, aetiology, and progression, especially compared to other populations.

Added value of this study

This scoping review provides insights into the characteristics, methodologies, and findings unique to Chinese community-based dementia cohorts over the last 25 years. It identifies critical research gaps and proposes future directions, including enhancing sample representativeness, investigating China-specific risk factors, using life-span exposure approaches, collecting objective data, conducting domain-specific cognitive assessments, adopting pathological diagnostic criteria, standardizing biobank construction, researching multi-modal biomarkers, examining social and genetic-environmental aspects, and monitoring post-COVID cognitive health.

Implications of all the available evidence

By summarizing the existing gaps in current research in Chinese population, we can address issues relevant not only to China but also to other LMICs. High-quality dementia community-based cohort studies are crucial for providing solid evidence to inform policy-making and promote global brain health research.

modifying therapies for Alzheimer's disease (AD). These developments provide substantial hope for the therapeutic management of dementia.[3,4]

Despite advances in basic laboratory and clinical research, the natural history, disease burden, risk/predictive factors and diagnostic approaches of dementia can be best revealed through prospective studies conducted in large-sampled population cohorts. Community-based cohort studies on dementia epidemiology were first initiated in the 1980s in Europe and the United States.[5,6] These studies illustrated the dementia prevalence rates, and a decreasing trend in incidence over subsequent decades, which may be partially attributable to improvements in risk factor management.[5–9] The 2024 update of the Lancet Commission has proposed a novel life-course model of risk, and demonstrated that up to 45% of worldwide dementias could theoretically be prevented by modifying 14 risk factors.[10] However, most existing evidence came from Western populations.

China, accounting for one-fifth of the global population, faces a particularly heavy dementia burden due to its rapid ageing process.[11] An epidemiological survey reported that 8.4 million older adults in China had dementia in 2020, imposing a significant socioeconomic burden.[12,13] A Markov model projects this number will rise to 66.3 million by 2050.[14] The ageing generation has gone through frequent wars and turmoil over the first half of the 20th century, later the remarkable economic growth after the reform and opening-up,[15] and even COVID epidemic. Such historical events, along with personal experiences, genetic background, sociocultural environment, and lifestyle factors, are likely to impact the health outcomes of different birth cohorts of the population.[16,17] Despite numerous cross-sectional surveys conducted in China, and measures for cognitive function have been gradually incorporated into existing cohort studies, there remains significant gaps in community-based cohort studies designed to further explore the risk factors, aetiology, and progression of dementia, especially in comparison to other populations. By summarizing these gaps, we can address issues relevant not only to China but also to other LMICs, while much more cohort studies of dementia research and subsequent meta-analyses are predominantly conducted in high-income countries (HICs).

In this scoping review, we intended to summarize the characteristics, methodology, and major findings unique to Chinese population from published community-based cohorts with dementia or cognitive impairment as a major outcome. We also proposed challenges and future research directions in this important population health topic.

Methods

Search strategies and selection criteria

We searched PubMed, Web of Science, and Embase to identify articles describing prospective community-based cohort studies with dementia or cognitive impairment as a major outcome in the Chinese population. The search strategy covered publications from January 1, 1982 to June 1, 2024, as there were no reports on this topic before this date in the databases. The search terms used were: (Dementia OR cognitive impairment OR cognitive disorder OR cognitive dysfunction OR cognitive decline OR cognition OR MMSE OR Alzheimer OR AD OR MoCA) AND (cohort OR longitudinal OR follow up OR prospective) AND (population OR community) AND (Chinese OR China)

NOT Patients NOT Trial NOT Hospital NOT Meta NOT Children.

Eligible cohorts were included in the current review if they: 1) are conducted in the Chinese population; 2) are prospective cohorts with at least one wave of follow-up; 3) are population-based or community-based cohorts having measured cognitive function; 4) have detailed documentation including the protocol, profile, and baseline characteristics; 5) have a series of published original articles on cognitive decline, cognitive impairment or dementia.

Two reviewers (XWZ and ZXX) independently screened the titles and abstracts of the retrieved records for inclusion. Discrepancies were resolved through discussion or consultation with a third reviewer (DD). The same reviewers then obtained and assessed the full texts of potentially eligible articles. We identified 2947 eligible articles, among which 39 cohorts met the inclusion criteria. A flow chart of the searching process was shown in Supplementary Figure S1.

Data extraction and analysis

Information collected for each cohort included cohort design, aim, sampling, timeline (baseline and each wave), participants' characteristics, data and bio-sample collection, neuropsychological tests, dementia diagnosis criteria, and key findings. We extracted cohort information from profiles, protocols, or publications with baseline characteristics of the target population.

A panel composed of all authors held discussions to select findings that were consistent with the topic, unique to the Chinese population context, and of high quality for further investigation.

To investigate the distribution of cohorts and regional disparities within mainland China, we assessed the intensity rank of community-based cohorts in relation to population density and population aging (proportion of the population aged ≥60) at each study site. We first identified the provincial administrative regions covered by each cohort (listed in Table 1) and then counted the number of cohorts in each region. The intensity rank was calculated by dividing the number of cohorts by the population density or the population at each study site, then sorting these values from low to high. The median value of the rank was then divided into low/high categories. Data on population aging (proportion of population aged ≥60) and population density were obtained from the Seventh National Population Census conducted by the National Bureau of Statistics of China.[56]

Results

Characteristics of cohorts

Twenty-eight cohorts were established within mainland China,7 cohorts were based in Hong Kong and Taiwan, and 4 cohorts targeted Chinese populations residing in Singapore and the United States (Fig. 1A, Table 1). The majority of cohorts consisted predominantly of Han ethnicity participants and the WCHAT study additionally recruited participants from multiple ethnicities: Tibetan (20.0%), Qiang (18.1%), Yi (9.1%), and Uyghur (8.3%). Nine cohorts were multi-centre studies in mainland China, while the rest were single-site studies.

To investigate the distribution of cohorts and regional disparities within mainland China, we assessed the intensity rank of community-based cohorts in relation to the population density and the population ageing in each study site (Fig. 1B). Yunnan, Guangxi, Sichuan, Shaanxi, Xinjiang, and Hubei provinces exhibit high intensity of cohort studies in terms of population ageing and density. Whereas Anhui, Henan, Jiangxi, Hunan, and Shanxi in the central region; Hebei, Tianjin, Fujian, and Hainan in the eastern region; along with Liaoning in the northeast still lack of cohort studies matching their population ageing and density.

Random sampling techniques were implemented in 17 (11 of which in mainland China) cohorts, while others (22 cohorts) engaged in voluntary recruitment strategies; 16 studies recruited >5000 participants at baseline, among which CHARLS, CHNS, GBCS, ZAHCS, COAST, PINDEC, and SCHS had samples >10,000 (Table 1).

Enrolled participants were born across 1900s–1960s, with a mean/median age ranging from 57 to 101 years (HABCS enrolled centenarians). These participants lived through significant historical events in China, including Ongoing Industrialization, World War II & Civil War, the Great Leap Forward & Famine, the Cultural Revolution & the Send-Down Movement, Gradualist Reform & Opening, Globalization & Marketization and Covid-19 pandemic[15,57] (Fig. 2). Impoverished conditions and dramatic social shifts during childhood and adulthood may likely influence living conditions and cognitive outcomes in their later life.[16]

Aims and timeline

As depicted in Table 1 and Fig. 3, 14 cohorts were designed with a primary objective on cognition and dementia. The pioneering COAST study, initiated in 2000, has conducted 8 follow-up waves across multiple centres in China. Cohorts established after that were the HK-MAPS (2005) with 3 follow-up waves in Hong Kong, the BABRI (2008) with 6 follow-up waves in Beijing, and the SAS (2009) with 3 follow-up waves in Shanghai. Subsequent studies commenced after 2010 such as CLAS, TIS, EMCOA, PINDEC, JCICS, MIND-CHINA, TENC, and HMACS in mainland China, and TIGER, ILLAN in Taiwan. Seven studies primarily aimed at other geriatric diseases, such as cardiovascular and cerebrovascular diseases (SCS, CCHS-BEIJING, CHAP, and BLSA), osteoarthritis (Mr. OS & Ms. OS) or general geriatric diseases (SCHS, WCHAT), also incorporated cognitive function assessments. Another additional 18

Cohorts	Design aim	Location	Sample method	Sample source	Baseline	Waves	Participants number	Age at baseline, Mean (SD)	Participants characteristics
Mainland China (28)									
Healthy Ageing and Biomarkers Cohort Study (HABCS)[18]	Aging	8 provinces[a]	targeted random sampling	Urban & Rural	2008	4	5599[i]	72–101[j]	Cognitive impairment: 34.6%
The Project of Longevity and Aging in Dujiangyan (PLAD)[19]	Aging	Sichuan	community-eligible-willing person	Rural	2005	2	870	93.6 (3.3)	Cognitive impairment: 64.4% MMSE: 15.0 (5.9)
Chinese Longitudinal Healthy Longevity Survey (CLHLS)[20]	Aging	22 provinces[b]	community-eligible-willing person	Urban & Rural	1998	9	9093 (1998 wave)[g]	92.3 (7.6)	Cognitive impairment: 25.3%; MMSE: 21.4 (9.2)
The Rugao Longevity and Aging Study (RuLAS)[21]	Aging	Jiangsu	community-eligible-willing person	Urban & Rural	2007	5	2251[h]	75.4 (3.9)	Dementia: 2.5% (HDS-R) MCI: 39.9%
The Chinese Longitudinal Ageing Study (CLAS)[22]	Cognition and dementia	Shanghai	randomly selected	Urban & Rural	2011	2	1068	72.8 (8.5)	MMSE: 24.7 (6.2) MoCA: 20.8 (7.3) MCI: 25%, AD: 4.7%, VD: 2.5%, mixed Dementia: 1.3%
Shanghai Aging study (SAS)[23]	Cognition and dementia	Shanghai	community-eligible-willing person	Urban	2009–2010	3	3141	72.3 (8.1)	MCI: 20.1%
Hubei memory and aging cohort (HMACS)[24]	Cognition and dementia	Hubei	community-eligible-willing person	Urban & Rural	2018–2020	2	8221	71.3 (5.4)	SCD: 58.3%; MCI: 26% Dementia: 7.2%
Anhui Healthy Longevity Survey (AHLS)[25]	Cognition and dementia	Anhui	community-eligible-willing person	Urban & Rural	2019	2	5848	71.0 (7.1)	MMSE: 21.5 (6.1) MCI: 34%
Multimodal Interventions to Delay Dementia and Disability in Rural China (MIND-CHINA)[26]	Cognition and dementia	Shandong	community-eligible-willing person	Rural	2017	2	5765	70.9 (5.9)	Dementia: 4.7% AD: 3.1% VD: 1.4% MCI: 24.2%
The Prevention and Intervention on Neurodegenerative Disease for Elderly in China (PINDEC)[27]	Cognition and dementia	Beijing, Shanghai, Hubei, Sichuan, Guangxi, Yunnan	multistage clustered sampling	Urban & Rural	2015	2	24,117	70.5 (7.0)	Dementia: 4.2%; AD: 2.3%
Beijing Elderly Comprehensive Health Cohort Study (BECHCS)[28]	Aging	Beijing	two-stage stratified random sampling	Urban & Rural	2009; 2014	4	4499	70.3 (6.7)	MMSE: 24.3 (5.4) Cognitive impairment: 17%
China Cognition and Aging Study (COAST)[13]	Cognition and dementia	12 provinces[c]	community-eligible-willing person	Urban & Rural	2000	8	46,011	70.3 (7.5)	MMSE: 26.9 (4) Dementia: 6.0%, AD: 3.9%, VD: 1.6%, Other Dementia: 0.5%; MCI: 15.5%
Beijing Longitudinal Study of Aging (BLSA)[29]	Other diseases	Beijing	multi-stage stratified random sampling	Urban & Rural	1992	9	3257	men: 70.1 (9.2); women: 70.2 (8.7)	MMSE: 24 (21–26)
China Longitudinal Aging Social Survey (CLASS)[30]	Aging	30 provinces[d]	multistage stratified sampling	Urban & Rural	2014	3	8553	69.7 (7.3)	CI: 2.18%
Zhejiang Ageing and Health Cohort (ZAHCS)[31]	Aging	Zhejiang	community-eligible-willing person	Rural	2014	4	10,911	69.5	Cognitive impairment: 16.7%
China Hainan Centenarian Cohort Study (CHCCS)[32]	Aging	Hainan	community-eligible-willing person	Urban & Rural	2014–2016	3	1002	69.5 (7.6)	Cognitive decline: 76.6%
Confucius Hometown Aging Project (CHAP)[33]	Other diseases	Shandong	community-eligible-willing person	Urban	2010	2	1538	68.6 (4.9)	MMSE: 26.2 (4.5)
Tianjin Elderly Nutrition and Cognition (TENC)[34]	Cognition and dementia	Tianjin	community-eligible-willing person	Urban	2018	2	4766	67.6 (4.9)	MCI: 10.7%

(Table 1 continues on next page)

Cohorts	Design aim	Location	Sample method	Sample source	Baseline	Waves	Participants number	Age at baseline, Mean (SD)	Participants characteristics
(Continued from previous page)									
Cardiovascular and Cognitive Health Study in Middle-Aged and Elderly Residents of Beijing (CCHS-Beijing)[35]	Other diseases	Beijing	4-stage stratified random sampling	Urban	2013	3	4268	66.9 (9.9)	MMSE abnormal: 13.4%
Beijing Aging Brain Rejuvenation Initiative (BABRI)[36]	Cognition and dementia	Beijing	Multi-stage stratified random sampling	Urban	2008	5	6976	66.2 (61–72)	MCI: 26%
The China Health and Nutrition Survey (CHNS)[37]	Aging	15 provinces[e]	4-stage stratified random sampling	Urban & Rural	1989	11	25,867	64 (59–70)	TICS-m: 12 (7–17)
West China Health and Aging Trends study (WCHAT)[38]	Other diseases	Yunnan, Guizhou, Sichuan and Xinjiang	Multi-stage stratified random sampling	Urban & Rural	2018	6	7439[k]	62.5 (8.3)	(SPMSQ) MCI: 11% Moderate/severe cognitive decline: 4.3%
Guangzhou biobank cohort study (GBCS)[39]	Aging	Guangzhou	community-eligible-willing person	Urban	2003–2008	6	30,430	61.5	MMSE: 29 (3)
Taizhou Imaging study (TIS)[40]	Cognition and dementia	Jiangsu	community-eligible-willing person	Urban & Rural	2013–2018	2	904	59.7 (3.0)	MMSE: 27 (23–29)
Effects and Mechanism Investigation of Cholesterol and Oxysterol on Alzheimer's disease (EMCOA)[41]	Cognition and dementia	Beijing, Shanxi, Shandong	community-eligible-willing person	Urban	2014	3	4573	59	MMSE: 28.1 (2.1) MoCA: 24.8 (3.6) MCI: 37.6%
The China Health and Retirement Longitudinal Study (CHARLS)[42]	Aging	28 provinces[f]	probability-proportional-to-size	Urban & Rural	2011–2012	5	17,708	58.5 (9.2)	TICS-m: 11.0 (4.1)
Jidong cognitive impairment cohort study (JCICS)[43]	Cognition and dementia	Hebei	community-eligible-willing person	Urban	2015	2	5854	57.4 (9.5)	MCI: 5.5%
Shunyi Cohort Study (SCS)[44]	Other diseases	Beijing	community-eligible-willing person	Rural	2013–2014	4	1586	56.7 (10.0)	MMSE: 26.5 (3.2) MoCA: 19.2 (4.9)
Taiwan, Hongkong (7)									
Taiwan Initiative for Geriatric Epidemiological Research (TIGER)[45]	Cognition and dementia	Taiwan	community-eligible-willing person	Urban & Rural	TigerI:2011 II: 2019	6	TIGERI: 600 TIGERII: 605	72.6 (5.2)	Non-demented
Mr. OS and Ms. OS[46]	Other diseases	Hongkong	recruitment	Urban	2001	5	4000	72.5 (5.2)	MMSE: men 26.9 (2.7), women 24.2 (3.9)
Hong Kong Memory and Ageing Prospective Study (HK-MAPS)[47]	Cognition and dementia	Hongkong	randomly sampled from a non-institutionalized population	Urban	2005	3	787	71.4 (6.73)	MCI: 33.5%
The Healthy Aging Longitudinal Study in Taiwan (HALST)[48]	Aging	Taiwan	recruitment	Urban & Rural	2009–2013	2	5664	69.4 (8.2)	MMSE: 26.3 (3.1)
The Taiwan longitudinal study on aging (TLSA)[49]	Aging	Taiwan	three-stage stratified random sampling	Urban & Rural	1989	10	4049	67.6 (8.6)	SPMSQ scores <3: 18.2%
The Social Environment and Biomarkers of Aging Study in Taiwan (SEBAS)[50]	Aging	Taiwan	three-stage stratified random sampling	Urban & Rural	2000	2	1023	66	CI answered incorrectly (potential range 0–24): 7.2 (3.2)
I-Lan Longitudinal Aging Study (ILLAN)[51]	Cognition and dementia	Taiwan	random sampling	Rural	2011	4	1839	63.9 (9.3)	MMSE: 25.6 (4.0)
Other countries (4)									
Panel on Health and Ageing of Singaporean Elderly (PHASE)[52]	Aging	Singapore	random sampling	Urban	2009	3	3572 Chinese	70.2	CI: 13.1%

(Table 1 continues on next page)

Cohorts	Design aim	Location	Sample method	Sample source	Baseline	Waves	Participants number	Age at baseline, Mean (SD)	Participants characteristics
(Continued from previous page)									
The Singapore Longitudinal Ageing Studies (SLAS)[53]	Aging	Singapore	random sampling	Urban	2003	4	2611 Chinese	69.6 (7.4)	Dementia: 2.03%; MCI: 19.38%
The Singapore Chinese Health Study (SCHS)[54]	Other diseases	Singapore	recruitment	Urban	1993	4	63,257 Chinese	55 (49–62)	MMSE: 24.81 (3.89) at 3rd follow
The Population Study of Chinese Elderly in Chicago (PINE)[55]	Aging	USA	recruitment	Urban	2011	2	3159 Chinese	72.8 (8.3)	MMSE: 22.80 (5.39)

TICS-m, Telephone Interview for Cognitive Status-modified; MMSE, mini-mental state examination; SPMSQ, The Short Portable Mental Status Questionnaire. [a]Shandong, Jiangsu, Henan, Hubei, Hunan, Guangdong, Guangxi, Hainan. [b]Beijing, Tianjin, Hebei, Shanxi, Liaoning, Jilin, Heilongjiang, Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong, Henan, Hubei, Hunan, Guangdong, Guangxi, Chongqing, Sichuan, Shaanxi. [c]Sichuan, Yunnan, Guizhou, Tibet, Chongqing, Shaanxi, Gansu, Qinghai, Xinjiang, Ningxia, Inner Mongolia, Guangxi. [d]Except for Hainan, Taiwan, Tibet and Xinjiang. [e]Beijing, Chongqing, Guangxi, Guizhou, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Liaoning, Shaanxi, Shandong, Shanghai, Yunnan, and Zhejiang. [f]Guangdong, Jiangsu, Shandong, Zhejiang, Sichuan, Henan, Hubei, Fujian, Hunan, Shanghai, Anhui, Hebei, Beijing, Shaanxi, Jiangxi, Liaoning, Chongqing, Yunnan, Guangxi, Shanxi, Inner Mongolia, Guizhou, Xinjiang, Tianjin, Heilongjiang, Jilin, Gansu, Ningxia, Qinghai. [g]1998 wave (n = 9093 (1998 wave)); 2000 wave (n = 6368); 2002 wave (n = 9748); 2005 wave (n = 7459); 2008 wave (n = 9459); 2011 wave (n = 1360); 2014 wave (n = 1125). [h]1788 (ageing arm) +463 long-lived participants (longevity arm). [i]Centenarians (1385), Nonagenarians (1350), Octogenarians (1294), Younger elderly (1570). [j]Younger elderly: 72 (68–75); Octogenarians: 84 (82–86); Nonagenarians: 93 (91–95); Centenarians: 101 (100–102). [k]Han 36.2%, Tibetan 20.0%, Qiang 18.1%, Yi 9.1%, Uyghur 8.3%.

Table 1: **Methodology of cohorts in Chinese population.**

studies focused on overall healthy ageing or longevity, with the cognitive evaluation included. Studies like TLSA, CHNS, GBCS, PLAD, CHCCS, SLAS, and HALST primarily aimed at general ageing, physical function, and healthy ageing, while CLHLS and CHARLS adopted a broader approach, examining a wide array of health determinants over the life course in a transitioning society.

Measurement and data acquisition

At baseline, all cohorts collected demographic characteristics, lifestyle and habits, and medical histories. Most cohorts conducted anthropometry and physical examinations (Fig. 4 and Supplementary Table S1). Cranial magnetic resonance imaging (MRI) was administered in cohorts such as COAST, SAS, TIGER, CLAS, ILLAN, TIS, HMACS, SCS, CHCCS (structure MRI), BABRI, and MIND-CHINA (sMRI + fMRI). The Positron Emission Tomography (PET) images, representing molecular pathology in vivo, were collected in COAST (FDG, Aβ), BABRI (FDG, Aβ, tau), SAS (Aβ), and HMACS (Aβ, tau). Some cohorts also administered auxiliary examinations to measure physical functions, such as carotid ultrasound (COAST, ILLAN, TIS, CHAP, SCS, CCHS-Beijing, CHCCS), fundus photography (TIGER, CCHS-Beijing), optical coherence tomography (RuLAS, MIND-CHINA), bone mineral density and dual-energy X-ray absorptiometry (ILLAN, TIS, Mr. OS & Ms. OS), triaxial accelerometer, and pure-tone audiometry (MIND-CHINA).

Biospecimen collection

As indicated in Fig. 4 and Supplementary Table S2, majority of the cohorts have collected and stored specimen, primarily blood samples. Additionally, 13 out of the 39 cohorts preserved urine samples, and a few cohorts collected feces and saliva samples. Other biospecimens procured included cerebrospinal fluid (CSF) (COAST), nails (RuLAS, CHNS, Mr. OS & Ms. OS), hair (WCHAT, CHCCS), gingival crevicular fluid (TIS) and buccal cells (SCHS).

Whole exome sequencing has been conducted by the SCS, CLHLS, and GBCS, while genetic factors e.g. telomere attrition and SNPs associated with ageing have been examined by HALST and SEBAS. The APOE gene, recognized as a genetic factor for sporadic AD, has been genotyped in 12 cohorts, with the prevalence of APOE4 carriers reported between 9.3% and 20.4%. Other AD-related genes investigated include PS1, PS2, APP, ABCA7, TOMM40, PICALM, BDNF, COMT, SORL, MTHFR, and KIBRA.

To date, COAST, SAS, MIND-CHINA, and HMACS have tested AD pathology-related biomarkers, including plasma Aβ40, Aβ42, total tau (t-tau), phosphorylated tau (p-tau), and neurofilament light (NfL). Notably, COAST has also reported AD biomarkers tested in CSF samples.

Neuropsychological tests and cognitive diagnosis

A comprehensive battery of neuropsychological tests was administered to assess both global and domain-specific cognitive functions in COAST, BABRI, SAS, TIS, CLAS, HMACS, EMCOA, TENC, MIND-CHINA, HK-MAPS, ILLAN, SCS, SLAS, and PINE (Fig. 4 and Supplementary Table S3). Global cognition was evaluated using the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), AD8, and Short Portable Mental Status Questionnaire (SPMSQ). Domain-specific cognition was assessed across memory (e.g. Auditory Verbal Learning Test, Fuld Object Memory Evaluation, Complex Figure Test, Digit Span Test,

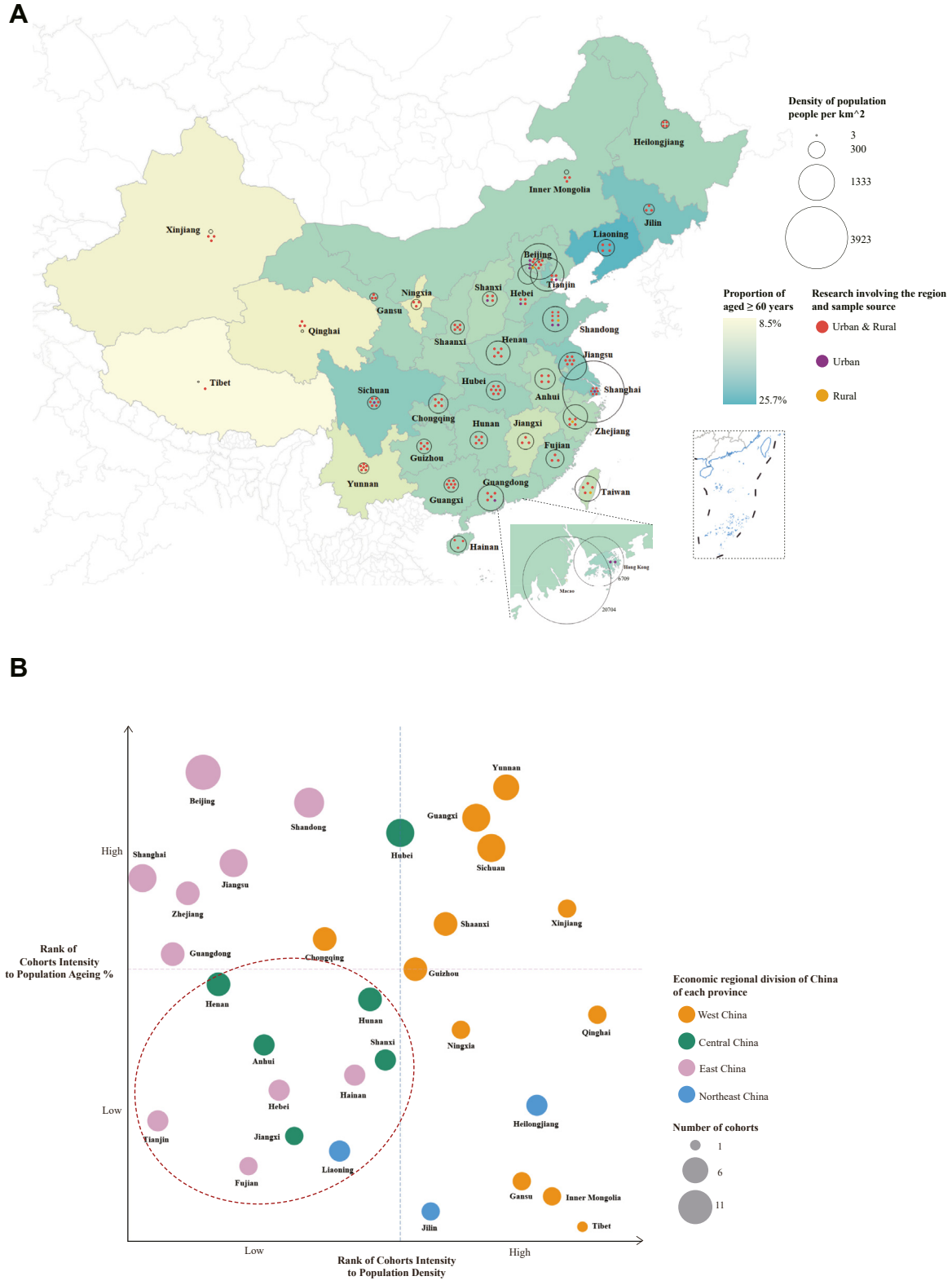

Fig. 1: **A.** The distribution of cohorts and sample source. Data of Population ageing (proportion of aged ≥60 y) and population density are from the National Bureau of Statistics of China; **B** To investigate the distribution of cohorts and regional disparities within China, we assessed the intensity rank of community-based cohorts in relation to the population density (X-axis) and the population ageing (proportion of the population aged ≥60) (Y-axis) in each study site.

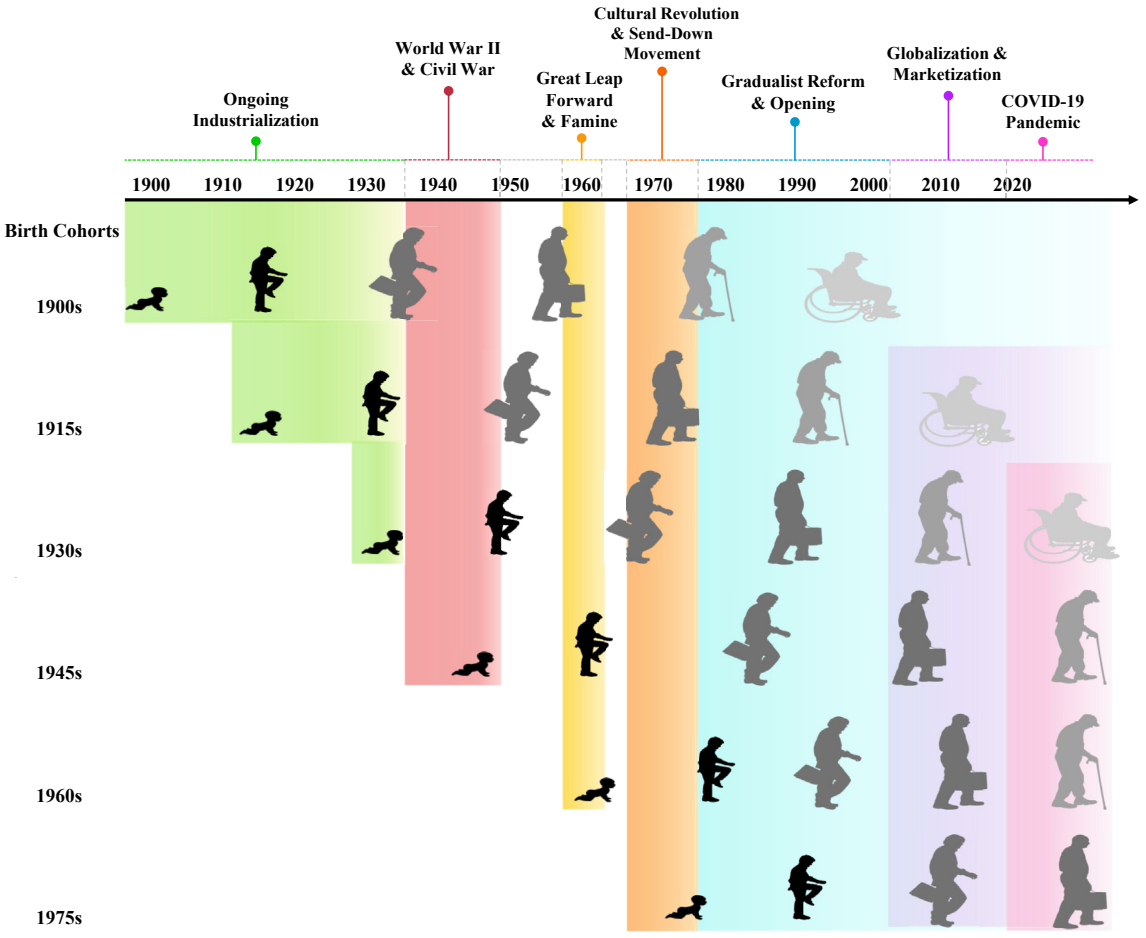

Fig. 2: Influence of major social changes on cognition outcomes and dementia risk factors in different birth cohorts and the lifespans since the 20th century in China.

and Delayed Word Recall Test), attention (e.g. Trail Making Test A, Clock Drawing Test, Complex Figure Test, and Digit Span forward and backward), language (e.g. Modified Common Objects Sorting Test, Verbal Fluency Test, Boston Naming Test, and Verbal Paired Associates Task), visuospatial ability (e.g. Stick Test, Symbol Digit Modalities Test, Complex Figure Test, and Clock Drawing Test), and executive function (e.g. Conflicting Instructions Task, Trail Making Test-B, Stroop Test, and Picture Completion). Some studies also conducted tests and questionnaires to assess the levels of activity of daily living (Activities of Daily Living functional scales), depression (Centre for Epidemiologic Studies Depression Scale, Geriatric Depression Scale, Geriatric Mental State Examination, and Patient Health Questionnaire-9), anxiety (Self-rated Anxiety Scale, Geriatric Anxiety Inventory), and neuropsychiatric symptoms (Neuropsychiatric Inventory).

In cohorts specifically designed for cognition and dementia research, cognitive or dementia diagnoses were made predominantly according to established diagnostic criteria, i.e. the DSM-IV for dementia, NINCDS-ADRDA/NIA-AA criteria for AD, and Petersen's criteria for mild cognitive impairment (MCI). In cohorts not primarily aimed to cognitive dementia, professional diagnoses were only conducted in SLAS, CHCCS, and SCS. The vast majority of these studies utilized cut-off scores from MMSE, MoCA, AD8, or SPMSQ to define cognitive impairment, dementia, or MCI.

Major findings unique to Chinese populations

The methodology, strengths, and applications of prospective community-based cohorts have led to key findings focusing on disease burden, natural history, risk and predictive factors, and diagnostic approaches for dementia.[6] Most Chinese cohort studies have verified the general risk factors for dementia predominantly identified in Western populations and have shown similar results for many of the risk factors proposed in

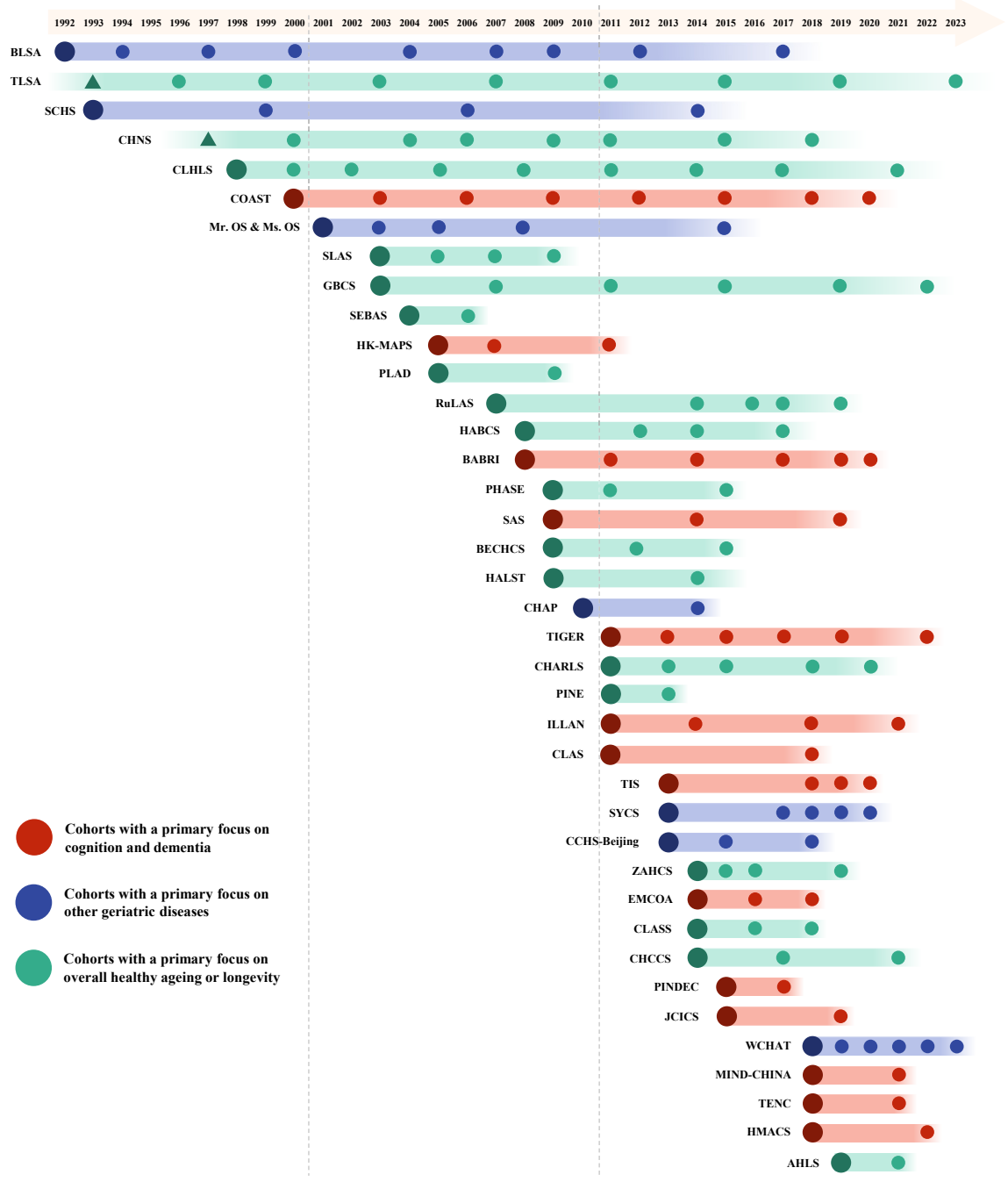

Fig. 3: Timeline of included cohorts. The initiate of this cohort and the waves of each follow-up are indicated by a circle. TLSA and CHNS didn't measure cognitive function at the beginning of the cohort, so the initiate of the cognitive function measurement was indicated by a triangle.

the 2024 update of the Lancet Commission,[10] such as hearing loss,[58,59] high cholesterol,[41,60] physical inactivity,[61] diabetes,[62] smoking,[63,64] hypertension,[65,66] obesity,[67,68] excessive alcohol consumption,[63,64] social isolation,[69] and visual loss.[70] A study utilizing data from the CHARLS found similar individual weighted PAFs (IW-PAFs) for these modifiable risk factors, while lower educational attainment and depression were identified as the most significant modifiable risk factors, contributing average IW-PAFs of 11.3% and 7.61%, respectively.[71] These figures are notably higher than those reported in Western populations,[10] revealing potential

Fig. 4: Overview of the data collection of each cohort.

differences that may include socioeconomic, cultural, and ethnic factors. Considering these aspects, we described the major findings unique to the Chinese context.

Disease burden

The COAST, SAS and PINDEC reported dementia (DSM-IV criteria) prevalence rates ranging from 5.1% to 13%, with 3.2%–6.9% for AD, 0.5%–1.6% for VD.[13,23,27,72] The COAST, SAS, and BABRI reported the prevalences of MCI (NIA-AA or Petersen's criteria) among old adults ranging from 15.5% to 20.1%, with amnestic MCI ranging from 10.1% to 13.2%.[13,23,36] The COAST showed prevalence distribution with the lowest prevalence in the south of China and the highest in the west,[13] while the CHARLS showed high dementia prevalence and concentrated spatial autocorrelation in North China, with a low–low cluster in East and South China.[73] Notably, these studies have maintained gender and rural-urban balance, and found that the incidence of dementia and MCI was significantly higher among women than men and in rural areas than in urban areas.[13,23,36,40] The WCHAT study[38] found that ethnic minorities Yi (34.6%), Tibetan (20.8%), Qiang (16.6%), Uighur (16.6%) and other minority (21.8%) groups in western China exhibited a higher prevalence of cognitive impairment (AD8 score ≥2 or SPMSQ score ≥3) than the Han population (11.2%), presenting a unique ethnic diversity.[74] Although data from Western populations indicate that dementia incidence rates are decreasing,[75] SAS also highlighted an increasing trend of dementia prevalence and incidence, and a decreasing trend of dementia mortality across 20 years in a cohort with older adults living in urban Shanghai.[76,77]

Few published studies on the progression of MCI were from Chinese populations. The SAS found that the conversion rate from MCI to dementia was 6.0 per 100 person-years, while the reversion rate to normal cognition was 7.8 per 100 person-years.[78] The CHARLS demonstrated that over 50% of cognitively normal participants were likely to progress to MCI after seven years, whereas participants with cognitive impairment had a 54.2% probability of transitioning to normal cognitive status.[79] Older age, APOE ε4 status, less

education, low MMSE scores, depression, metabolic syndrome, and cardiovascular risk factors were associated with an increased risk of progression to worse cognitive status.[64,78–81]

Educational attainment

Education level is a critical risk factor for cognitive decline.[76,82] In comparison to Western countries, China has a larger population with low educational attainment, particularly in women and rural residents.[83,84] A cross-national comparative study demonstrated that population-level differences in educational attainment explained approximately 50%–90% of the observed differences in cognitive function scores between LMICs (China, Mexico, and India) and HICs (United States and England).[85] The CHARLS revealed that low education contributed the most IW-PAFs for new-onset dementia in Chinese population.[71] Secular trends in dementia prevalence and incidence conducted by the SAS showed that the dramatic rise in the number of people with dementia over the past 20 years is most likely to occur in low-educated populations,[76] underscoring that low educational attainment is a crucial factor in the prevention and management of dementia in Chinese populations.

The SAS and the TIS indicated that higher education was associated with a slower rate of cognitive decline among participants living in disadvantaged rural environment,[82] and highlighted the additive effects of education and neighbourhood environment on cognitive decline in older adults. The SAS also demonstrated that the built-environment with educational and community cultural facilities in the neighbourhoods was associated with a better cognition in older adults.[86] These results emphasize the importance of providing such facilities to maintain cognitive health, especially for low-educated populations in less-developed areas.

Chinese lifestyle

The COAST highlighted that a combination of a healthy lifestyle profile (healthy diet, regular physical exercise, active social contact, active cognitive activity, and abstaining from smoking or drinking) may significantly slow memory decline, even in individuals carrying the APOE4 allele.[64] The CHARLS and AHLS revealed that engaging in traditional Chinese games such as playing cards or Mah-jong was significantly associated with enhanced memory and a decreased risk of dementia.[87,88]

The Chinese diet is distinct from other countries, characterized by heavy consumption of rice, pork, and fish, and lower intake of wheat and whole grains, but undergoing a rapid westernization these years, including increases in consumption of red meat, processed meat, and sugar-sweetened beverages.[89–91] Excessive dietary salt, commonly consumed in Chinese cuisine, was linked to impaired cognitive function and an increased risk of cognitive impairment in older adults.[92] The CHNS reported that the Chinese Food Pagoda based on the Chinese Dietary Guidelines, and a "vegetable-pork" diet with high intakes of legume products, vegetables, fruits, nuts, pork, fish, and plant oil were associated with better cognitive function among older Chinese adults.[90,93]

Environmental exposures

The CLHLS demonstrated a correlation between extended exposure to $PM_{2.5}$, ozone, and extreme weather conditions (e.g. heatwaves) and an increased incidence of cognitive impairment in 22 provinces.[94,95] This finding was further supported by the TIGER study, which revealed that prolonged exposure to $PM_{2.5}$, PM_{10}, or co-exposure to PM_x and NO_2 adversely affects global cognition, verbal fluency, and executive function over a 4-year follow-up.[45] The CHARLS uncovered that females and individuals residing in Middle China appear more susceptible to the deleterious effects of PM_x and NO_2 on cognitive decline.[96,97] Moreover, the CLHLS found a synergistic interaction of air pollution, residential greenness or lack of green space, and heatwave exposure on cognitive impairment in older adults.[95,98] Both the CHARLS and CLHLS highlighted the adverse impact of traditional Chinese household solid-fuel burning on cognitive decline, and underscored the importance of promoting clean fuel alternatives and encouraging the adoption of well-ventilated cooking devices in Chinese households.[99–101]

In addition, the CHARLS indicated that rural participants without access to tap water exhibited lower cognitive scores.[102] Furthermore, the CLHLS revealed that individuals who consume unboiled water faced a higher risk of cognitive impairment (HR: 1.27).[103] Compared to drinking well water, drinking tap water during childhood and around age 60 was associated with a reduced incidence of cognitive impairment in later life (HR: 0.67 and 0.74).[103] These results suggest an urgent need to expand the use of clean tap water across China, especially in rural areas.

Psychological symptoms

Prevalence rates of depression and anxiety symptoms among Chinese community-dwelling older adults were reported as 4.5–15.5% and 12.8–33.3% from the CHARLS, CLHLS, CLASS and CLAS.[30,104–106] Such psychological factors played a crucial role in cognitive performance and subsequent progression.[30,104,105,107–109]

The high IW-PAFs for depression (averaging 7.61%), as identified in the CHARLS, indicate its unique and significant role in cognitive health among Chinese populations.[71] Severe depressive symptoms were associated with worse cognitive performance[105] and moderately faster cognitive decline in episodic memory.[110] The CHARLS using group-based trajectory model showed that individuals with increasing depressive symptoms exhibited the fastest decline in global cognitive function

and episodic memory.[111] Conversely, the alleviation of depressive symptoms was a reversible factor that might slow down cognitive decline in the older adults,[107] highlighting the priority for interventions among individuals with depressive symptoms. A study using multi-cohort data verified that anxiety increased the risk of subsequent cognitive decline in non-dementia individuals,[104] although further data is needed to confirm the impact of anxiety in cognitive performance in Chinese populations.

Migration

The PINE study, conducted in the Greater Chicago area, aimed to enhance the understanding of immigration as a life-course experience, in relation to cognitive trajectories among older Chinese immigrants in the United States.[55] Moving to areas with vastly different cultural backgrounds, Chinese older adults often experience racial discrimination and lack of acculturation, which is related to older age, more offspring, lower income, shorter time living in the United States, worse overall health status, lower quality of life, and even suicide ideation.[112–114] These circumstances may potentially increase the risk of cognitive impairment.[112,113,115] Additionally, limited education and living in ethnic enclaves, such as Chinatown, may further contribute to poor cognitive outcomes.[115–117]

The development of the market economy and globalization has led to rapid urbanization in China, triggering large-scale cross-regional population migration, especially rural-to-urban internal migration.[15] The CHARLS showed that individuals who migrated from rural to urban areas had higher cognitive scores compared to rural non-migrants.[118] Furthermore, migrating to urban areas predicted better cognition among those born in rural areas.[119] These findings provide a rare perspective on the impact of social change and economic urbanization on late-life cognitive function.

Biomarker research

Some cohort studies tested the emerging AD blood-based biomarkers over the past five years and verified their ability to indicate and predict AD in Chinese populations, comparable to findings in Western populations. The MIND-CHINA study indicated that plasma Aβ, t-tau, and NfL varied across the AD clinical spectrum, with plasma NfL being particularly indicative of the clinical stages of AD.[120] The large-sample COAST study demonstrated that plasma Aβ42, p-tau181, and NfL were significantly associated with their CSF equivalents and can predict AD before clinical onset in Chinese populations.[121] The SAS reported associations between plasma p-tau217, p-tau181, and NfL with long-term cognitive decline and increased dementia risk.[122] Specifically, plasma p-tau217 was verified as an early predictor of dementia and AD onset with comparable importance to age and neuropsychological tests according to machine learning algorithms.[123] Furthermore, these biomarker profiles were also associated with multimorbidities.[122,124] Since renal function (measured by estimated glomerular filtration rate) may influence the concentrations of plasma NfL and p-tau181, interpreting AD biomarkers in the general ageing population should be done cautiously.[124]

Blood samples were also used to investigate other biomarker of dementia like those related to inflammation and metabolism.[125,126] The HABCS revealed that higher serum level of fibrinogen was negatively associated with cognitive function, independent of APOE genotypes and prior cerebrovascular events in dementia-free older adults.[126] The SEBAS identified a relationship between high blood uric acid levels and reduced risks of MCI among older adults, highlighting the potential protective role of uric acid against cognitive decline.[125] The SAS demonstrated that higher serum levels of glutamine and O-acetyl-glycoproteins were associated with an increased risk of dementia through metabolomics analysis.[127] A panel of five metabolites was found to predict incident dementia with an area under the receiver-operating characteristic curve of 0.72.[127]

Moreover, the TIS employed metagenomic sequencing of the gut microbiota, and revealed a potential role for short-chain fatty acids and lactic acid in the association between gut microbiota and cognitive function.[128] These findings provided valuable clues of microbiome biomarkers for dementia and suggested that alterations in gut microbiota composition may influence cognitive health.[128]

Challenges and future directions

The current landscape of dementia research in Chinses populations, while growing, faces several challenges. Accordingly, future directions need to address issues related to sample representativeness, risk factors, exposures, data collection, cognitive assessments, diagnosis, biobanks, immigrations, and post-COVID considerations (Fig. 5).

Representativeness: from geographical disparity to mega dataset

Geographical disparities within China present significant challenges in data harmonizing, with variations in natural and social environments, lifestyles, and economy development. Cohort studies were still limited in some less developed provinces where the ageing population is increasing rapidly (Fig. 1B). The development of networks covering representative of the national population, especially rural and minority areas are essential for the multi-centred collaboration aiming for "mega" datasets. The utilization of medical registration is another efficient way towards this integration, providing a standardized set of diagnostic criteria and

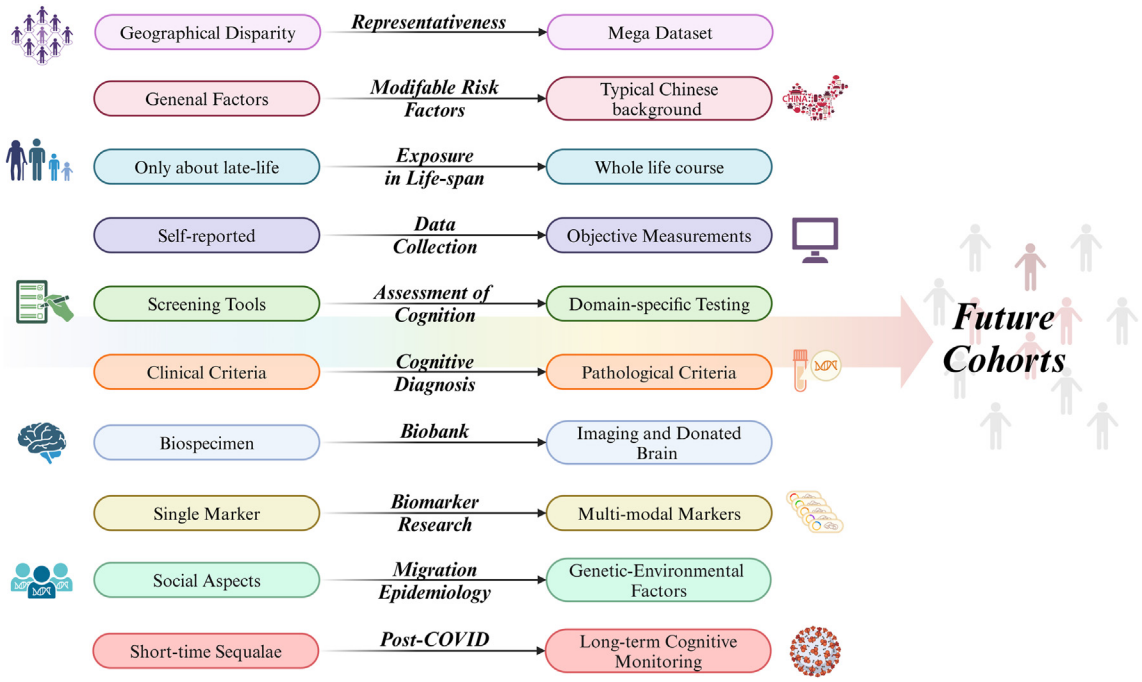

Fig. 5: Merging the gaps and future directions in dementia research in Chinese population.

capturing the data from a wider spectrum of health services.[5,129] Additionally, harmonizing Chinese cohorts with international studies on global data platforms (e.g. The Program on Global Aging, Health, and Policy,[130] 10/66 Dementia Research Group[131]) will enhance contributions to dementia research globally.

Modifiable risk factors: from general to typical Chinese background

China's long history and unique cultural background present unique diets, exercise patterns and other health-related behaviours that have not been sufficiently studied.[87,88,132,133] Traditional Chinese diets not only differ from Western diets and also vary across provinces. For instance, spicy foods, bean curd, river fish, vinegar, rice wine, tea, and Chinese herbal tonics (e.g. ginseng) may impact cognitive health. Forms of physical exercise e.g. tai chi and square dancing, and leisure activities e.g. mah-jong and Chinese chess, may also be associated with cognitive maintenance. Future research should focus on the cognitive protection role of the above-mentioned typical Chinese lifestyle factors and the underling mechanisms would be valuable.

Exposures: from late-life to a whole life course

Social-environmental factors, spanning from early life to adulthood, significantly contribute to health disparities among individuals.[16,17,57,134,135] Recognizing the multifaceted nature of these influences, adopting a life course approach, rather than focusing solely on late-life stages, may provide a comprehensive understanding of how various factors synergistically impact health outcomes over extended periods.

Participants in the current Chinese cohort studies were born in the early 1900s and lived through significant historical events in China (Fig. 2). In contrast to their counterparts in developed societies, many older Chinese adults experienced impoverished conditions and dramatic social shifts during childhood and adulthood, which may have influenced their living conditions and cognitive outcomes later in life.[16,17] Longitudinal and population-based studies, within and across generations and birth cohorts, collect a wide range of individual, biological, social, and environmental data over decades, making life course research possible. The CHARLS life history survey, developed using the English Longitudinal Study of Ageing (ELSA) and the Survey of Health, Ageing and Retirement in Europe (SHARE) life histories as a base, was conducted in 2014 and retrospectively collected information on the life history of all living respondents.[136] This unique context in China sheds light on the early life histories of individuals across different life stages and their impacts on future cognitive conditions and other dementia risk factors. Such insights can guide population-based and high-risk prevention strategies for dementia from early life to late life.

Data collection: from self-reported to objective measurements

Previous studies on the risk factors for dementia have predominantly concentrated on variables related to demographics, lifestyle, and chronic diseases, primarily

collecting data through self-reported questionnaires, such as dietary patterns or nutrient intake from Food Frequency Questionnaires, sleep disorder from Pittsburgh sleep quality index[137] and physical activities data from lifestyle questionnaires.[13,87,88,93,132,133,138,139] The use of objective recording metrics, such as sleep devices and wrist accelerometers, offers a more accurate and comprehensive method to document the sleep patterns and daily activities of older adults.[26] Despite their potential, these metrics face challenges in terms of validation, calibration, and data interpretation, as well as acceptability, adherence, and privacy concerns.

Assessment of cognition: from screening to domain-specific testing

Most Chinese cohort studies used the cut-off values of MMSE and MoCA to define dementia and MCI[140] (Supplementary Table S3). However, MMSE and MoCA are more screening tools than diagnostic instruments in population studies. With optimal cut-offs, the sensitivity and specificity of the Chinese version of MMSE used in screening for dementia were initially reported as 85.2% and 92.7%, respectively.[141] The sensitivity of the MoCA was 80.5% for MCI and 96.9% for dementia, and the specificity of 82.5% for identifying cognitive normalcy in Chinese populations.[140] As the basis of the clinical diagnosis of MCI (with subtypes) and dementia, assessment of global and domain-specific cognition requires a comprehensive neuropsychological tests battery.[142,143] However, only a few Chinese cohort studies are capable of conducting comprehensive cognitive assessments. A major obstacle is the lack of professional psychometrists and neuropsychologists, particularly in resource-poor areas in China. Digital neuropsychological testing emerges as a significant innovation, especially in remote areas where conventional testing is unfeasible.[144,145] This approach can potentially reduce costs, save manpower of cognitive assessments, and enhance the feasibility of longitudinally repeated testing.[144–146] However, there is a pressing need for the standardization and validation of digital neuropsychological tests in Chinese populations.[145]

Another concern is the cultural and sociolinguistic differences that are often overlooked in reported studies.[147,148] Given the diverse dialects, low levels of education, and significant socio-linguistic differences, the Chinese population is not homogeneous culturally, genetically, linguistically, and sociologically.[148,149] This diversity, even within the Han population, affects the sensitivity and validity of cognition assessment and dementia diagnosis when directly using cognitive tests validated in Western populations.[149] Cognitive assessment in the Chinese context may require linguistic adaptation and cultural standardization, particularly with dialects, extending to cognitive and memory tests.[147] While bilingual clinicians in Hong Kong have developed resources for Cantonese-speaking users, standardized tests for other Chinese dialects remain underdeveloped, though some are in progress.[148–150] Additionally, testing instruments for individuals with low education or illiteracy need to be developed, as approximately one-third of the Chinese population aged ≥40 years still have less than primary education, which puts them at higher risk of dementia in the future.[151]

Cognitive diagnoses: from clinical to pathological criteria

Most Chinese community-based studies used Petersen's criteria, DSM-IV, and NINCDS-ADRDA criteria for the diagnosing MCI, dementia, and AD, respectively. These criteria are primarily based on the cognitive performance and clinical symptoms. Due to lack of detailed examination, limited pathologic profiling, and absence of neurologists and neuropsychologists in community-based studies, most cohorts cannot characterize dementia subtypes or aetiologies, such as AD, vascular dementia, Lewy body dementia, frontotemporal dementia, and mixed dementia.[152] Challenges in diagnosis include between-clinician variability and diagnostic drift over time, especially in syndromes without definite neurobiological or pathological underpinnings.[152] Consequently, findings are often presented as if they are representative of patients with dementia as a whole. Emerging biomarkers in recent years offer promising research directions.

AD is the most common type of dementia, characterized by Aβ and tau pathology. The biological definition of AD proposed by the NIA-AA has shifted the focus of risk factor research towards protein-level AD pathological biomarkers.[153] In clinical settings, Aβ pathology can be detected through amyloid PET scans and CSF analysis of Aβ42 or the Aβ42/Aβ40 ratio; tau pathology can be evaluated via tau PET scans or CSF p-tau levels.[154–158] However, PET scans require specialized equipment and are costly, while CSF analysis necessitates invasive procedures such as lumbar puncture and hospitalization.[154] Both tests can only be conducted in qualified hospitals, which restricted their uses in large-scale population screening. With the rapid evolving of the AD blood biomarkers, especially the recent revised criteria for diagnosis and staging of AD,[159] exploring AD pathological changes and diagnosing AD in the population-based level is becoming feasible. Improving the convenience of blood sample collection (e.g. dried blood spots[160]) and reducing costs will be a prerequisite for blood biomarker testing in cohort studies, especially in LMICs.

Biobank: from biospecimen to donated brain

Cognitive-related research often requires substantial investment in biobank, including infrastructure, sample storage, advanced analytical technologies, and professional managers, which are undeveloped in most Chinese cohort studies.[161] Therefore, increasing funding

from government grants, private sector partnerships, and international collaborations, as well as implementing training programs to develop capacities in biobank management and operations should be prioritized to support cohort studies. Additionally, there is a cultural reluctance or knowledge gap towards medical procedures that involve blood draws or other invasive techniques, such as lumbar puncture, which are often necessary for collecting high-quality biospecimens.[161]

A promising new field in dementia research is the integration of imaging biobanks.[162] High-throughput computing harnesses advanced imaging technologies to generate diagnostic images, from which radiomic features can be extracted. These features serve as non-invasive biomarkers, representing a frontier in biobank when correlated with biosamples and clinical information.[163] However, CT/MRI/PET scans should be administered in clinical facilities with large-scale equipment. High quality imaging needs longer scanning time to perform sequences to meet research requirements. These are challenges for community-based cohort studies, especially in remote or resource-poor areas.

Neuropathological studies can offer deep insights into the mechanisms underlying various cognitive disorders and neurodegenerative diseases.[164,165] Such studies utilizing donated brain were initiated in Western population, notably the Nun Study[166] and the Brains for Dementia Research.[165] Community-based neuropathological studies were mostly in developed countries, including the Hisayama study in Japan,[167] the Cognitive Function and Ageing Study[168] and the Cambridge City over –75s Cohort Study[169] in the UK, the Honolulu-Asia Aging Study,[170] and the Cache County Study on Memory and Aging[171] in the US. China's human brain bank has remained in its infancy, although the China Brain Bank Consortium has been developed in recent years. Currently, obtainable brain tissue is limited to individuals with end-of-life and severe diseases, and seeking brain donation consent from participants within existing longitudinal cohorts is a promising approach forward.[164] This limitation is primarily due to Chinese cultural traditions emphasizing the integrity of the body after death, posing challenges to brain donation.[164] Public education campaigns may help shift cultural perceptions and improve the accessibility of brain tissue for dementia research.

Biomarker research: from single modal to multimodal

Blood biomarker testing offers advantages such as being non-invasive, more acceptable to participants, and easier to obtain samples, making it more feasible for widespread clinical practice and population screening.[154,172,173] Cohort studies in western populations, such as the BioFINDER, ESTHER, Rotterdam study, Framingham Heart Study, and the Baltimore Longitudinal Study on Aging have assessed concentrations of biomarkers including Aβ40, Aβ42, p-tau181, p-tau217, p-tau231, t-tau, GFAP, and NfL.[174–180] These studies have validated the utility of these biomarkers for disease detection and prediction in population cohorts. However, in China, only COAST, SAS, and MIND-CHINA have published results related to AD biomarkers.[120–122,124,181] Among these, p-tau217, which was found to have the best predictive efficacy for AD in BioFINDER, has also been reported in the SAS.[122,174,178] There is currently no evidence in Chinese population-based cohorts for p-tau231 and GFAP. Furthermore, most Chinese cohort studies have primarily explored the cross–sectional association between blood biomarkers and dementia/AD, with limited research on the relationship of baseline blood biomarkers with subsequent incident AD or their predictive values for AD onset by prospective follow-ups.

Previous biomarker study in community cohorts usually considered single modal markers—the core Aβ and tau. However, other non-amyloid/non-tau–related proteins involved in innate and adaptive immunity, blood–brain barrier dysfunction, vascular pathology, and limbic-associated TAR DNA-binding protein encephalopathy (LATE), often, contribute to cognitive impairment or dementia in the population and provide evidence of the systemic pathogenesis.[182,183] In this context, multi-modal biomarker profiles AT_1T_2NISV, as suggested by the Alzheimer's Association Workgroup, merit depiction and deeper exploration at a population level.[159] Other non-amyloid/non-tau–related proteins involved in innate and adaptive immunity, blood–brain barrier dysfunction, vascular pathology, and central insulin resistance providing evidence of the systemic pathogenesis of dementia. With the evolution of omics technology, such as Genomics, Proteomics, Metabolomics, Transcriptomics, and Radiomics, novel biomarkers would be explored to update the current biomarker framework.

Migration epidemiology: from social aspects to genetic-environmental factors

A prominent issue in China is internal migration. The late 1970s marked the beginning of the Gradualist Reform & Opening (Fig. 2), accompanied by rapid urbanization, triggered large-scale cross-regional population migration.[15] This resulted in a spatial pattern where the Southeast China absorbed population while provinces in central and western China (e.g. Anhui, Hubei, Jiangxi, and Hunan) experienced outflows.[15] This significant rural-to-urban internal migration trend induced the profound changes in living environments and social psychology of the migrated population. Additionally, the large-scale migration of young rural populations to cities has led to an increase in "empty-nest families" and "empty nester" who lives alone. The lack of care and increased loneliness, can lead to physical and psychological vulnerability, potentially promoting the

cognitive health disparity of older adults in less developed rural areas. This aspect warrants further attention in future research.

Immigrate epidemiology offer a unique opportunity to understand the interaction between genetic and environmental factors in the development of dementia. Sharing the same genetic background but living in different circumstances allows researchers to disentangle the effects of environment from those of heredity. Chinese immigrants, particularly those in developed countries, present an ideal population for such studies.[55,115] PINE has already provided critical insights into how lifestyle, socioeconomic status, cultural practices, and access to healthcare contribute to cognitive health and the risk of dementia.[112,113,115] Effects of different environmental exposures on cognitive ageing may be further evaluated by comparing cognitive health outcomes between Chinese individuals living in China and those who have migrated to other countries. Moreover, different stages of migration, such as the age at migration, length of time in the immigrate country, and level of acculturation, can further elucidate the interplay between genetics and environment.[117]

Post-COVID: from short-time sequalae to long-term cognitive monitoring

The pandemic of COVID-19 has been noted as a major public health event that significantly threatened the health of the older population. Worse cognitive performance was prevalent in older adults following COVID-19 infection.[184] A Chinese study longitudinally followed a large-sample older COVID-19 survivors from 6 months to 2.5 years, and reported a higher risk of progressive cognitive decline,[185,186] especially in those with severe COVID-19.[187] Besides this hospital-based study, another study reported a 15.6% prevalence of self-reported cognitive impairment within 2 years after COVID-19 among 1000 community residents, nearly of whom were older adults.[188] Unfortunately, none of the 39 community-based cohort studies in the current review reported the cognitive sequalae, although these cohorts had cognitive data from before and after the COVID-19 epidemic, which should provide a unique opportunity to explore the impact of COVID-19 on cognitive function and validate the "brain fog hypothesis" or "infectious hypothesis" (severe infections may represent a risk factor for dementia or accelerate the progression of dementia pathology) in Chinese older adults.[189] Additionally, the psychological and social factors associated with prolonged lockdowns, such as isolation, fear, depression, and anxiety, may also exacerbate cognitive decline, and are worth further investigation. The ongoing prospective community-based cohort studies also provide opportunities to monitor the long-term cognitive trajectory of Chinese populations affected by the COVID-19 pandemic and to determine if COVID-19 could modify the overall burden of dementia in the future.

Limitations

This review has certain limitations. Firstly, we only reviewed literature in English, because translation discrepancies can result in inconsistencies between the cohort names in the original articles in Chinese and their English versions, leading to repeated inclusion. Future evaluations will provide a more comprehensive integration of information from both Chinese and English databases. Secondly, some cohorts include different populations based on study objectives, and several cohorts dynamically enrolled samples across different waves. For consistency in summarizing sample characteristics, we selected the baseline wave data from each cohort. This approach may limit the accuracy of our summary of sample size and corresponding characteristics. Future systematic review could employ a more comprehensive approach to account for varied sampling methods in each cohort. Thirdly, we cannot obtain reliable data on all established cohorts that have had follow-ups but remain unpublished. Including such cohorts would introduce substantial bias and reduce the reproducibility of our review. Consequently, we used standardized and widely-used search databases to include established cohorts with published follow-up data, thereby enhancing discussion and reproducibility. Furthermore, this review identified gaps by discussing the differences between cohorts in the Chinese population and Western populations, but not assessd the reliability of the evidence or systematically compared those findings.

Conclusion

This scoping review provides insights into the characteristics, methodologies, and major findings of published Chinese community-based cohorts over the last 25 years, with dementia as the main research outcome. We also identified critical research gaps and proposed future directions including enhancing sample representativeness, investigating China-specific risk factors, using life-span exposure approaches, collecting objective data, conducting domain-specific cognitive assessments, adopting pathological diagnostic criteria, standardizing biobank construction, researching multi-modal biomarkers, examining social and genetic-environmental aspects, and monitoring post-COVID cognitive health, to approach high quality of dementia studies that can provide solid evidence to policy making and promote global brain health research.

Contributors

DD conceptualised this Review. XZ, ZX, and DD wrote the first draft. All authors were involved in draft revisions and approving the final draft for submission. All authors approved the final manuscript and accept responsibility for the decision to submit for publication.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Copilot in order to improve readability and language of the work. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101465.

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