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REVIEW

Big databases and biobanks for studying the links between CKD, cognitive impairment, and dementia

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ABSTRACT

Research on cognitive function in individuals with chronic kidney disease (CKD) is critical due to the significant public health challenge posed by both CKD and cognitive impairment. CKD affects approximately 10–15% of the adult population, with higher prevalence in the elderly, who are already at increased risk for cognitive decline. Cognitive impairment is notably higher in CKD patients, particularly those with severe stages of the disease, and progresses more rapidly in those on dialysis.

This review explores how data from large biobank studies such as the Alzheimer's Disease Neuroimaging Initiative, UK Biobank, and others could be used to enhance understanding the progression and interplay between CKD and cognitive decline. Each of these data sources has specific strengths and limitations. Strengths include large sample sizes and longitudinal data across different groups, and in different settings. Addressing limitations leads to challenges in dealing with heterogeneous data collection methods, and addressing missing data, which requires the use of sophisticated statistical techniques. Combining data from multiple databases can mitigate individual study limitations, particularly via the 'epidemiological triangulation' concept.

Using such data appropriately holds immense potential to better understand the pathobiology underlying CKD and cognitive impairment. Addressing the inherent challenges with a clear strategy is crucial for advancing our understanding and improving the lives of those affected by both CKD and cognitive impairment.

Keywords: biobank, chronic kidney disease, cognitive impairment, dementia, epidemiology

INTRODUCTION

Understanding in the field of pathobiology has been revolutionized by the use of large-scale biobanking providing extensive, multifaceted datasets that enable researchers to uncover complex relationships between various health conditions. These biobanks compile vast amounts of information from large and diverse populations, including genetic profiles, biomarker measurements, clinical assessments, and lifestyle factors. For some biobanks participant information at baseline is linked (with consent) to routine electronic health data, thereby minimizing the cost of collecting follow-up information, whilst others do high-quality systematic repeat assessments of every participant. Such a longitudinal approach is crucial for understanding the progression of chronic diseases and identifying potential causal relationships. Additionally, the large sample sizes inherent in modern biobanks increase the statistical power of studies, enabling the detection of subtle associations that might be missed in smaller cohorts. Big databases also facilitate multidisciplinary research by integrating data from various fields such as genetics, neurology, cardiology, and nephrology. This holistic approach is essential for studying complex conditions that involve multiple organ systems and risk factors.

The impact of big databases and biobanks on medical research is evident from the substantial number of publications that utilize these resources. For instance, the UK Biobank has been cited in over 2 000 peer-reviewed publications since its inception [1]. Similarly, the Alzheimer's Disease Neuroimaging Initiative (ADNI) has resulted in more than 1 500 publications, advancing our understanding of Alzheimer's disease and related conditions [2].

In nephrology, the use of such linked databases has also been significant. The Chronic Renal Insufficiency Cohort (CRIC) Study has contributed to over 200 publications, providing valuable insights into the progression and complications of chronic kidney disease (CKD) [3]. The United States Renal Data System (USRDS), although it does not contain any genetic data, has been cited in numerous studies, with over 1 000 publications leveraging its data to explore various aspects of end-stage kidney disease (ESKD) [4].

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It has been estimated that 800 million of the world's population are affected by some degree of kidney dysfunction [5]. Kidney function declines with age, making CKD a common comorbidity in older people [6]—a group already at heightened risk for cognitive decline [7]. When taking age into account, studies have found that prevalence of cognitive impairment in patients with CKD is still higher than in the general population, with some estimates indicating that more than 50% of individuals with CKD stage 4 or 5 (severe to end-stage renal disease) exhibit some degree of cognitive dysfunction [8]. Epidemiological data suggests that even mild to moderate renal impairment is associated with an increased risk of cognitive decline, including deficits in executive function, attention, and memory [9]. The risk of worsening of cognitive impairment also increases as CKD progresses; patients with ESKD on dialysis experience cognitive decline at a rate that is potentially 2–3 times faster than that of the general population [8]. The risk of developing new-onset dementia appears to be higher in individuals with CKD compared to those with normal kidney function. Longitudinal studies reported that individuals with moderate CKD have a 20–30% increased risk of developing dementia over a follow-up period compared to those without CKD, after adjusting for other risk factors [10–12].

Hypertension, diabetes, and cardiovascular disease are key risk factors that contribute to both renal and cognitive decline, and these will increase in most populations as they age, and due to the obesity epidemic. The high prevalence and incidence rates necessitate a proactive approach to research, aiming to elucidate the underlying mechanisms and develop additional preventive and therapeutic strategies. However, the same epidemiological data that highlight the need for research also point to the challenges in conducting research, which we discuss in this review.

Despite progress, several epidemiological questions remain unanswered, such as detailed knowledge of the relationship between CKD and cognitive impairment, the role of genetic factors, and the impact of early interventions on cognitive outcomes. Studies based on these databases can address these questions by leveraging their comprehensive data collection and longitudinal design. For example, the integration of genetic data with clinical and cognitive assessments can help identify genetic predispositions to cognitive decline in CKD patients. Additionally, the large sample sizes and repeated measures can facilitate the study of disease progression and the effectiveness of interventions over time.

In this review, we selected several key cohorts and databases that could be used to investigate the link between CKD, cognitive impairment, and dementia (Table 1 and Fig. 1). Studies were chosen based on their comprehensive data collection, longitudinal design, and relevance to the research focus. We did not discuss electronic health records as in many health settings cognition is not formally captured in routine clinical care, which means that cohort studies and biobanks with cognition assessments are required. Some caveats in studies based on these databases cannot be overemphasized (Table 2). Thus, while the potential for discovery is substantial when leveraging these large-scale databases to study cognitive impairment in relation to CKD and cardiovascular diseases, researchers must approach this task with a clear strategy for overcoming the inherent challenges in such studies.

CHALLENGES IN COLLECTING DATA FOR RESEARCH

Collecting research data involves ethical considerations, participant consent, and specific data-collection tools. Generalizability is often compromised as health-aware individuals are more likely to participate, skewing results. Phenotyping for kidney function and cognition is challenging due to the need for urine and blood samples and the difficulty in testing those with severe cognitive impairment. Confounding and reverse causality can distort observational studies [13], but Mendelian randomization [14] can help. Selection bias occurs when follow-up data is not representative of the initial cohort [15]. Causal inferences may be strengthened by integrating results from several different approaches via epidemiologic triangulation [16], where each approach has different (and assumed to be largely unrelated) key sources of potential bias. Understanding drug effects requires detailed medication histories, which are often incomplete in large databases [17].

We discuss these unavoidable practical issues for some of the large landmark studies in turn, so that more context is provided for how we ended up listing our strengths/limitations for the studies in Table 2.

GENERAL POPULATION STUDIES WITH A CARDIOVASCULAR FOCUS

Framingham Heart Study

The Framingham Heart Study (FHS) is a landmark longitudinal cohort study that has provided a wealth of information on cardiovascular health and disease [18]. It has also contributed to understanding risk factors associated with cognitive decline and dementia [19].

Strengths and limitations of FHS

The FHS has followed participants over several decades, providing valuable data on the natural history of chronic diseases and their progression, including cognitive decline. The study includes multiple generations, which allows for examining genetic and familial factors in relation to cognitive dysfunction and dementia within the CKD population. The FHS has collected a wide range of biomarkers relevant to cardiovascular health and cognitive function, potentially elucidating links between CKD and cognitive outcomes. The study has extensively assessed traditional and emerging risk factors for cardiovascular disease, many of which overlap with risk factors for CKD and cognitive decline (e.g. hypertension, diabetes). The FHS is based on a community-dwelling population, which can increase the generalizability of findings to similar populations.

However, while the FHS has data relevant to CKD, such as hypertension and diabetes, it is not specifically tailored to study CKD. Detailed information on renal function over time may not be as comprehensive as in studies focused on kidney disease. The original FHS cohort was predominantly Caucasian, which may limit the applicability of findings to more diverse populations that might have different risks for both CKD and cognitive dysfunction. Diagnostic criteria for cognitive dysfunction and CKD have evolved over the course of the FHS, which may affect the consistency of diagnoses across different study waves. As an observational study, FHS can identify associations but cannot establish causality. This is particularly important when disentangling the complex relationships between cardiovascular health, CKD, and cognitive function. If kidney function was not a primary focus during certain periods of the study, there might be gaps in the data necessary to make strong connections between CKD progression and cognitive decline. Over time, participants who remain in longitudinal studies like the FHS may differ from those who drop out or pass away, potentially leading to selection bias in studying long-term outcomes like dementia.

Table 1: Summary of some major databases that could be used for exploring the association of CKD with cognitive function.

Database	Focus	Strengths	Limitations
Alzheimer's Disease Neuroimaging Initiative (ADNI)	Alzheimer's disease	Comprehensive data collection, standardized protocols, high-quality neuroimaging, public availability	Sample selection, CKD as secondary focus, underrepresentation of CKD stages, adjusting for multiple factors simultaneously may present a challenge, causality limitations, ethnic and genetic diversity, clinical application
Framingham Heart Study (FHS)	Cardiovascular health	Longitudinal data, generational data, biomarker collection, comprehensive risk factor assessment, community-based sample	Not specific to CKD, demographic homogeneity, evolution of diagnostic criteria, causality challenges, missing data on kidney function, potential for selection bias
Chronic Renal Insufficiency Cohort (CRIC) Study	Chronic kidney disease	Targeted population, detailed renal data, longitudinal design, comprehensive data collection, diverse population	Cognitive function as secondary focus, selection bias, potential for missing data, variability of diagnostic criteria for dementia, lack of imaging data
UK Biobank	General health	Large sample size, comprehensive data collection, longitudinal design, diverse population, public availability	Selection bias (volunteer study), observational nature, changes over time not captured, measurement errors, potential for missing follow-up data, resource intensity
Cardiovascular Health Study (CHS)	Cardiovascular health in older adults	Focus on older adults, comprehensive data collection, longitudinal design, diverse population	Specificity to CKD, potential for selection bias, causality challenges, missing data on kidney function
German National Cohort (NAKO) [41]	General health	Large sample size, comprehensive and very extensive data collection, longitudinal design with re-examinations	Potential for selection bias, resource intensity
Atherosclerosis Risk in Communities (ARIC) Study	Atherosclerosis	Focus on atherosclerosis, comprehensive data collection, longitudinal design, diverse population	Specificity to CKD, potential for selection bias, causality challenges, missing data on kidney function
Rotterdam Study	Chronic diseases in the elderly	Focus on the elderly, comprehensive data collection, longitudinal design, diverse population	Specificity to CKD, potential for selection bias, causality challenges, missing data on kidney function
National Alzheimer's Coordinating Center (NACC)	Alzheimer's disease and dementia	Comprehensive data collection, standardized protocols, public availability, focus on dementia	Sample selection, CKD as secondary focus, underrepresentation of CKD stages, confounding factors, causality limitations, ethnic and genetic diversity, clinical application
National Health and Nutrition Examination Survey (NHANES)	General health and nutrition	Representative sample, comprehensive data collection, public availability	Specificity to CKD, potential for selection bias, causality challenges, missing data on kidney function
Tohoku Medical Megabank Organisation (ToMMo)	General health after the Great East Japan Earthquake	Representative sample, comprehensive data collection	Resource intensity, missing data

The Cardiovascular Health Study

The Cardiovascular Health Study (CHS) focuses on risk factors for coronary heart disease and stroke in adults 65 years or older [20] but also includes cognitive assessments and biomarkers relevant to dementia research [21].

The Atherosclerosis Risk in Communities Study

The Atherosclerosis Risk in Communities (ARIC) Study investigates the causes of atherosclerosis and its clinical outcomes [22], including measures of cognitive decline [23].

Strengths and limitations of CHS and ARIC studies

The CHS specifically targets older adults, a population at high risk for both cardiovascular disease and cognitive decline. The ARIC study's focus on atherosclerosis, a common comorbidity in CKD, makes it relevant for studying the interplay between cardiovascular health and cognitive decline in CKD patients. Both studies have collected a wide range of data, including cardiovascular risk factors, cognitive assessments, and biomarkers relevant to dementia research. Both studies have included a diverse population, enhancing the findings' generalizability to different groups.

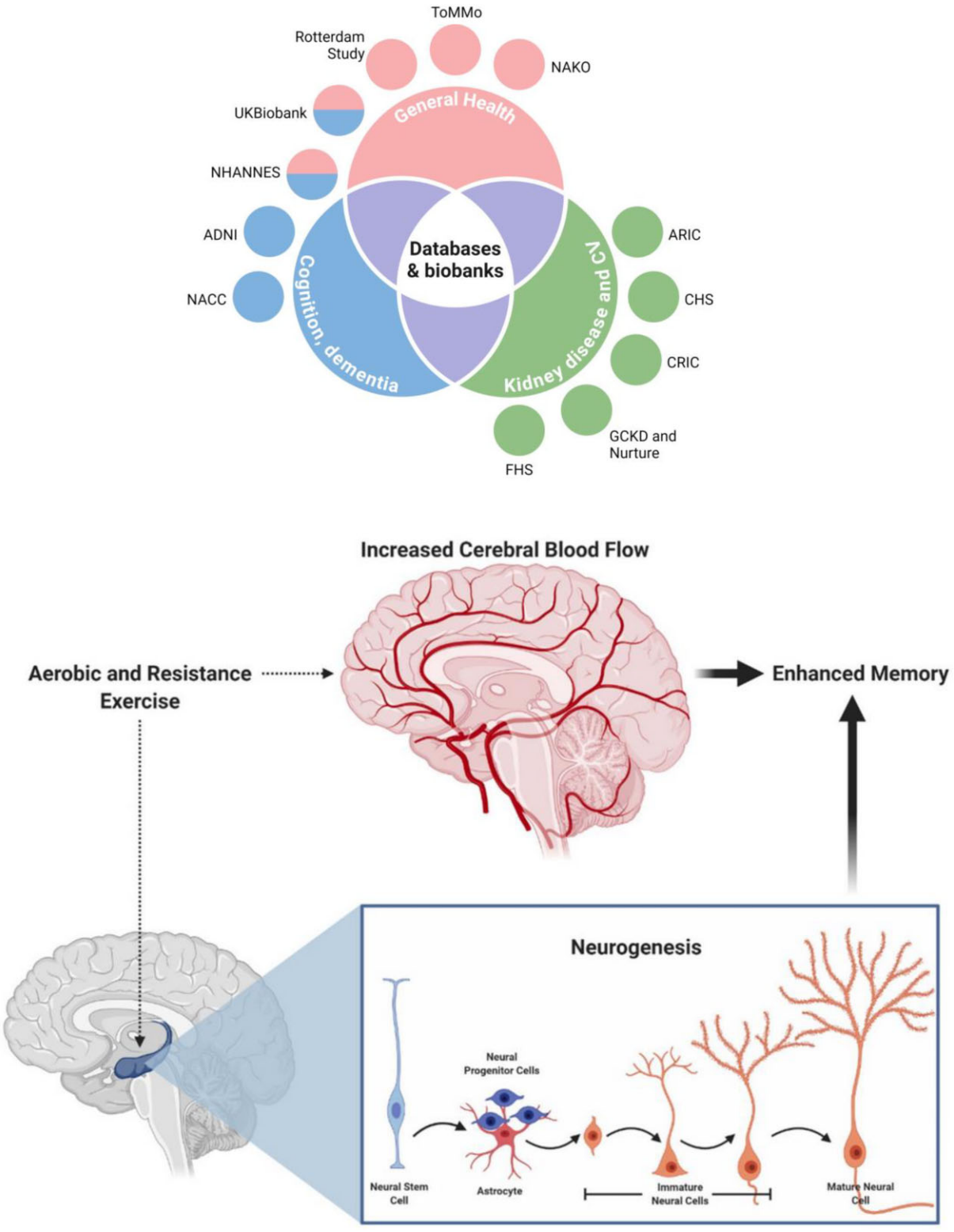

Figure 1: Information available in the databases discussed in this review. The abbreviations are all explained in the main text.

However, they are not specifically tailored to study CKD. Detailed information on renal function over time may not be as comprehensive as in studies focused on kidney disease. Participants may differ from the general population, particularly concerning age, ethnicity, or baseline health status, potentially limiting the generalizability of findings. Self-reported data, commonly used in cohort studies, can be subject to bias and inaccuracies.

The Rotterdam Study

The Rotterdam Study is an ongoing population-based cohort study designed to investigate chronic diseases in the elderly, with

Table 2: Caveats in studies based on large biobanks.

Caveat	Description
Variability in data collection	Different studies have collected and recorded their data in various ways, complicating direct comparisons between datasets. In particular for pharmaco-epidemiology research dates are needed as to when drugs were started/stopped (often missing).
Incomplete datasets	Missing data points can introduce bias or limit the scope of analyses.
Selection bias	Associations seen for participants in long-term health studies may not be replicated in the broader population because of incomplete/selective follow-up of participants.
Complexity in measuring cognitive impairment and dementia	These conditions can be assessed using a variety of tests and biomarkers, and different studies may employ different methodologies, necessitating careful consideration when interpreting results and drawing broad conclusions.
Computational power and data management	Analysing the vast amounts of data within these databases requires significant computational power and expertise in data management.
Sophisticated statistical techniques	The intricate nature of genetic and biomarker information demands sophisticated statistical techniques that are used together with a clear conceptual framework as to which hypotheses are being investigated.

a particular focus on cognitive decline and dementia [24], in relation to various risk factors like cardiovascular health and kidney function.

Strengths and limitations of the Rotterdam Study

The Rotterdam Study specifically targets the elderly [25], a population at high risk for both chronic diseases and cognitive decline. The study collects a wide range of data, including cardiovascular risk factors, repeat imaging, and repeat cognitive assessments [24], and biomarkers relevant to dementia research. The Rotterdam Study follows participants over time, allowing researchers to study the progression of chronic diseases and their relationship with cognitive decline and includes a diverse population, which enhances the generalizability of the findings to different groups.

However, while the Rotterdam Study includes data relevant to CKD, it is not specifically tailored to study CKD. Detailed information on renal function over time may not be as comprehensive as in studies focused on kidney disease.

STUDIES THAT SAMPLE STUDY PARTICIPANTS BASED ON COGNITIVE RISK

Alzheimer's Disease Neuroimaging Initiative

The Alzheimer's Disease Neuroimaging Initiative (ADNI) is a multicenter project that aims to improve clinical trials to prevent and treat Alzheimer's disease (AD) by validating biomarkers for AD clinical trials. It includes neuroimaging, genetic, neuropsychological, and biological markers [26].

The National Alzheimer's Coordinating Center

The National Alzheimer's Coordinating Center (NACC) maintains a database of clinical and neuropathological data from individuals with Alzheimer's disease and other types of dementia collected from Alzheimer's Disease Research Centers across the United States [27].

Strengths and limitations of ADNI and NACC

ADNI collects a wide range of data, including MRI and PET scans, cerebrospinal fluid (CSF) biomarkers, genetic information, and cognitive function tests. The longitudinal nature of the study allows for the observation of disease progression over time, which is essential for understanding the trajectory of cognitive decline in relation to CKD. ADNI provides high-quality neuroimaging data that can be used to assess brain structure and function changes in CKD patients at risk for or diagnosed with AD.

NACC collects a wide range of data, including clinical assessments, neuropathological data, and biomarkers relevant to dementia research. It uses standardized protocols for data collection across various sites, enhancing the reliability and comparability of the data.

The data from ADNI and NACC are available to researchers worldwide, facilitating collaborative studies and a broader understanding of dementia.

The comprehensive approach taken in ADNI and NACC can help to identify multifactorial links between CKD and cognitive dysfunction.

Participants in ADNI and NACC are primarily recruited based on their perceived likelihood of developing Alzheimer's disease, which is a strength, as many other studies tend to not oversample this population, and often people with impaired cognition tend to be lost from follow-up. However, this may mean that participants will not be representative of the general CKD population. The stages of CKD among participants may not be uniformly represented, potentially limiting the understanding of how different stages of kidney dysfunction affect later cognitive decline (collider bias [28]). CKD is not the primary focus of either of these studies; therefore, specific markers of renal function may not be as extensively studied or longitudinally tracked as those for dementia. While ADNI and NACC collect a vast array of data, controlling for all potential mediators of how CKD contributes to worsening cognition (such as electrolyte imbalances, anemia, and hypertension) in the analysis may be challenging. The genetic information collected may not fully represent the diversity seen in the general CKD population. Translating findings from these studies into clinical practice for CKD patients may require additional validation studies focused specifically on the CKD population.

COHORT STUDIES WITH A RENAL FOCUS

Chronic Renal Insufficiency Cohort Study

The Chronic Renal Insufficiency Cohort (CRIC) Study is a long-term study designed to understand the consequences of CKD and to identify factors that may help predict its progression [3, 29]. It focuses specifically on people with varying stages of renal insufficiency.

Strengths and limitations of CRIC

CRIC is specifically designed to study individuals with CKD, making it a very relevant database for examining issues directly related to renal insufficiency, including potential cognitive impacts. The database includes comprehensive information on

kidney function over time, including glomerular filtration rate, proteinuria, and other biomarkers relevant to kidney health. CRIC follows participants over a long period, enabling researchers to study the progression of CKD and its relationship with cognitive decline and the development of dementia. The study collects a wide range of data, including demographics, comorbid conditions, treatments, laboratory values, and outcomes, which can be used to control for confounding variables in analyses. CRIC includes a racially and ethnically diverse population, which enhances the generalizability of the findings to different groups and allows for the study of disparities in health outcomes.

However, while CRIC collects information on cognitive function, this is not the primary focus of the study. This means that the depth of cognitive assessment may not be as extensive as in studies specifically designed to investigate cognitive outcomes. As with any long-term study, there can be attrition over time, leading to missing data that could bias the results if not properly accounted for in the analysis. The criteria used to diagnose cognitive dysfunction and dementia may vary over time and between sites, potentially affecting the consistency and reliability of diagnoses across the cohort. Unlike studies like ADNI, CRIC may not have extensive neuroimaging data available for participants, which could limit the ability to directly assess changes in brain structure or function associated with cognitive decline.

There have been CRIC equivalent renal cohort studies set up in Germany (German CKD study, GCKD) [30] with similar strengths and limitations.

EXAMPLES OF GENERAL POPULATION SAMPLED BIOBANK STUDIES

The National Health and Nutrition Examination Survey

The National Health and Nutrition Examination Survey (NHANES) includes a range of health, nutrition, and laboratory data from a representative sample of the US population collected repeatedly over time [31] that could be leveraged for research on CKD and cognitive impairment [32].

Strengths and limitations of NHANES

NHANES includes a representative sample of the US population and a great deal of effort has gone into investigating representativeness/non-response. NHANES did collect genetic information since its phase II (1991–94), and later phases. The survey collects a wide range of health, nutrition, and laboratory data, which can be used to study the relationship between CKD and cognitive impairment. The data from NHANES is available to researchers worldwide, facilitating collaborative studies and a broader understanding of the intersection between CKD and cognitive impairment.

However, while NHANES includes data relevant to CKD, it is not specifically tailored to study CKD. Because kidney function was not a primary focus during certain periods of the survey, there might be gaps in the data necessary to make strong connections between CKD progression and cognitive decline.

UK Biobank

The UK Biobank is a large-scale biomedical database containing in-depth genetic and health information from half a million UK participants [1, 33]. It includes data on cognitive function and has been used for research into a wide range of diseases, including CKD and cardiovascular diseases.

Strengths and limitations of UK Biobank

The UK Biobank has this large sample size because the original purpose of the study was to understand genetic risk factors for chronic disease, and gene–environment interactions. This allows for the detection of subtle associations that might be missed in smaller cohorts. The database includes a wide range of data, including genetic information [34], biomarker measurements [35], cognitive function tests [36], neuroimaging studies [37], and detailed health and lifestyle information [37]. The UK Biobank collected data at baseline and is continually being updated with new data from electronic medical records. However, changes in lifestyle, environment, and medical practices over time can affect the outcomes and may not be fully captured in routine electronic records. With such a large dataset, researchers might conduct multiple statistical tests, increasing the possibility of finding significant associations by chance (Type I error). Managing and analysing data from such a large cohort requires significant computational resources and expertise, which may not be readily available to all researchers. The longitudinal nature of the UK Biobank allows researchers to study disease progression and outcomes over time. The UK Biobank includes a diverse population, which helps create a more comprehensive understanding of how diseases manifest across different population groups. The data from the UK Biobank is available to researchers worldwide, facilitating collaborative studies and a broader understanding of the intersection between CKD and cognitive impairment.

However, UK Biobank is a volunteer study, and participants in the UK Biobank tend to be healthier, more educated, and of a higher socioeconomic status than the general population, with overall half the mortality of that observed for the general population. This severely limits the generalizability of findings to CKD clinic populations seen in routine care in the UK National Health Service, and there is scope for collider bias [28, 38].

The **German National Cohort study (NAKO)** [30] was modelled on the idea of UK Biobank with 205 000 adults undergoing whole-body imaging and extensive assessments (including cognition, nutrition, renal function) and the microbiome, and with a number of added substudies. Germany has very stringent data protection laws and a very fragmented electronic health data system, which meant that national investment into a high-quality study with repeat follow-up assessments for 30 years was seen as extremely important to inform German public health strategies. There are many strengths to NAKO similar to those of UK biobank, and, because health inequalities in Germany were less extreme than seen in the UK the volunteer bias may be less pronounced.

The **Tohoku University Tohoku Medical Megabank Organization (ToMMo)** was founded to establish an advanced medical system to foster the reconstruction from the Great East Japan Earthquake. ToMMo has set up a biobank on 150 000 healthy Japanese participants that combines both medical and genome information during the process of rebuilding the community medical system, as well as supporting health and welfare in the Tohoku region. It provides a rich cross-sectional resource of information (including whole-genome sequencing) on a non-European population study.

JOINT USE OF DIFFERENT SOURCES OF INFORMATION TO TRIANGULATE RESEARCH FINDINGS

Triangulation of findings is a concept that was introduced into etiological epidemiology because there was a recognition that it

is impossible to have a single perfect study [16]. As can be seen from the examples above, whenever data are collected, there are strengths and limitations to data collection and follow-up, which inevitably run the risk of having some degree of bias [16].

Combining data from multiple databases allows researchers to create a more diverse and representative sample that better reflects the broader population. Pooling data from multiple sources increases the overall sample size, enhancing the study's statistical power. When data from multiple studies are combined, researchers can cross-validate findings across different datasets. If a particular association is observed in multiple independent datasets, it is more likely to be a true finding rather than an artifact of a random finding in a single study. Hence, studies bridging across large databases collected at various institutions abound. By limiting to studies dealing with dementia, a study based on the ADNI cohort and the Amsterdam Dementia Cohort tried to define unbiased cut-points in the CSF for t and p tau. Four CSF t- and p-tau distributions and three corresponding cut-points were identified in both cohorts. Increasingly high tau subgroups were characterized by a steeper decline in minimental state and higher progression risk to Alzheimer's dementia [39]. Another study compared patterns of Alzheimer's atrophy between the ADNI cohort and a cohort of a European, public/private consortium developed for AD biomarker discovery (AddNeuroMed), focusing on the prediction of conversion from mild cognitive impairment to Alzheimer's disease dementia [40]. The list of international studies based on large databases is even larger in cardiology, oncology, and the obesity and diabetes area.

For our question, integrating data from studies with different focuses (e.g. cardiovascular health in FHS, cognitive function in ADNI, renal function in CRIC) can provide a more holistic view of the interactions between CKD, cognitive impairment, and dementia. Utilizing longitudinal data from multiple studies (e.g. FHS, ARIC, Rotterdam Study) can help trace the progression of cognitive decline over time and identify potential causal relationships. These possibilities are compactly presented in Table 3.

Ultimately, after narrowing down potential candidate associations, we do require a clinical trial for the benefit of patients with CKD and cognitive impairment, in order to investigate whether associations are modifiable through intervention.

Table 3: Potential synergies in joint use of databases.

Research focus	Databases	Potential synergies
Lifestyle and environmental factors	NHANES, UK Biobank, FHS, NAKO, ToMMo	Understanding the impact of lifestyle and environmental factors on cognitive decline in CKD patients. Combining data from these databases can provide insights into how lifestyle modifications can mitigate cognitive decline.
Longitudinal studies	FHS, ARIC, Rotterdam Study	Long-term tracking of cognitive function and kidney health. These databases provide extensive longitudinal data that can help in understanding the progression of cognitive decline in CKD patients over time.
Ethnic and genetic diversity	UK Biobank, NACC, NHANES, ToMMo	Exploring the role of ethnic and genetic diversity in cognitive impairment among CKD patients. These databases offer diverse populations that can help in identifying genetic and ethnic disparities in cognitive health.

CONCLUSION

In summary, databases offering extensive data, including genetic profiles, biomarker measurements, and cognitive function tests, are a reality, and these databases can help elucidate the progression and interplay between cognitive problems and CKD. These databases' diversity and longitudinal nature enhance the robustness and generalizability of findings. The challenges in utilizing these databases include variability in data collection methods, incomplete datasets, and selection bias. The complexity of measuring cognitive impairment and the need for sophisticated statistical techniques further complicate research efforts. Despite these challenges, the potential for discovery is substantial, provided researchers adopt an upfront clear strategy for overcoming these obstacles. Integrative multidimensional studies across multiple data sources will facilitate the identification of novel risk factors and biomarkers, and provide deeper insights into disease mechanisms. The success of such studies underscores the potential of leveraging large databases to advance our knowledge and develop effective preventive and therapeutic strategies across a wide range of health conditions.

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DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

CONFLICT OF INTEREST STATEMENT

None declared.

APPENDIX

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