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Dementia registries around the globe and their applications: A systematic review

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Abstract

Patient registries are valuable tools helping to address significant challenges in research, care and policy. Registries, well embedded in many fields of medicine and public health, are relatively new in dementia. This systematic review presents the current situation in regards to dementia registries worldwide. We identified 31 dementia registries operating on an international, national or local level between 1986-2016. More than half of the registries aimed to conduct or facilitate research, including preclinical research registries and registries recruiting research volunteers. Other dementia registries collected epidemiological or quality of care data. We present evidence of practical and economic outcomes of registries for research, clinical practice and policy and recommendations for future development. Global harmonization of recruitment methods and minimum data would facilitate international comparisons. Registries provide a positive return on investment; their establishment and maintenance require ongoing support by government, policy makers, research funding bodies, clinicians, individuals with dementia and their caregivers.

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1. Introduction

The prevalence of dementia is estimated to double every 20 years from 46.8 million in 2015 to nearly 131.5 million by 2050 [1,2]. The natural history of different dementias, the quality of diagnosis and care, the use of community services and long-term care, the costs of care and the effects on caregivers at a population level are largely unknown or rely on extrapolations from smaller samples. Such data would be beneficial in shaping policy and planning particularly in low and middle income countries where such information is even more wanting. Harnessing innovative approaches for effective prevention, treatment and care, and changes in policy could improve quality of care and quality of life for people with dementia and their families and help to minimize the financial costs of AD and other dementias [3,4]. Clinical registries are one approach to help recruitment for research and monitoring quality of care.

The many definitions and classifications of registries in medicine are typically embedded within broader frameworks and models of public health surveillance and reporting on the quality of health care [5]. In general, in epidemiology the term “register” refers to a “file of data concerning all cases of a particular disease or other health relevant condition in a defined population” and a “registry” is a “system of ongoing registration” [6 p211] (see Appendix 1 for Definitions and Classifications of Registries). The first patient registries were established in Scandinavian countries at the end of the 19th century. The increasing public health concern with chronic diseases during the 1950s led to a proliferation of registries [5]. The Scandinavian countries, such as Denmark, Finland and Sweden, remain world leaders in regards to extensive register networks and linkage of individual-level data from different sources (“an entire country [as] a cohort”) [7 p2398]. For instance, in Sweden in 2012 there were more than 100 healthcare registries [8]. National repositories of patient registries have been set up in Denmark [9], the UK [10] and the USA [11] to improve sharing of information about existing health data collection systems and, where possible, facilitate data sharing. Another type of registry – a research participant registry, aims to recruit people who are at increased risk of a condition, e.g. women with gestational diabetes, persons with family history of a disease [12]. Patient registries inform health policy and contribute to health care value. A 2011 health economics study in Sweden revealed that an annual investment of US$70m in registries could reduce the annual growth in health care spending by 0.6%, with the estimated cumulative return of more than US$7b over ten years – a $10 return on every dollar invested [13].

Despite popularity of registries in many fields of medicine since the 1950s, and their tangible outcomes, registries collecting dementia-related data are relatively new. The first dementia registries, which focused on diagnostic and clinicopathological data on AD, were established in USA, including the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) in 1986. The principal goal of CERAD was to standardize procedures for the evaluation and diagnosis at the Alzheimer Disease Centers (ADCs) [14]. A decade later, in 1999, the NIA funded the National Alzheimer’s Coordinating Center (NACC) [15] to develop and maintain a large database of clinical and neuropathological information collected by the ADCs. Other pioneering dementia registries, such as the IMAGE Project Population-Based Registry of AD in Quebec [16] and the Camberwell Dementia Case

Register in the UK [17], focused on the study of genetic transmission patterns in AD, and the prevalence and natural history of AD.

Dementia registries [18–24] aim to advance dementia research by optimizing clinical trials for interventions in the pre-dementia phase of AD (i.e., preclinical registries), collecting epidemiological data, monitoring the quality of dementia care and recruiting volunteers for dementia studies (Table 1). Interest in dementia registries has been accompanied by expansion of international research consortia on AD, development of comprehensive national databases on healthy aging, international harmonization in sharing longitudinal datasets, and harnessing big data in dementia research [3,25]. There is considerable potential in linking data across health, care, research and administrative systems using electronic health records and dementia registries. Linkage of big data, i.e., “deep” biological and clinical data and “broad” population-based health and health care data, can advance the understanding of progression of dementia and assessing effectiveness of treatments and interventions [4].

Systematic reviews have mapped registries in many areas of health care, such as renal replacement therapy [26] and trauma [27] but not yet for dementia-related data and their applications. Our study aims to address this gap and to present the current situation in the field including the benefits and outcomes of registries, as well as to inform their further development as tools for dementia research, care, prevention, and policy. This systematic review identifies and classifies dementia registries, including AD registries, operating around the world and reviews their characteristics and functions. We describe the outcomes of dementia registries in terms of research, epidemiology, quality of care, policy and service planning, and health economics, and present recommendations regarding practicalities of operating a dementia registry.

2. Method

2.1. Database search

The databases MEDLINE, EMBASE and SCOPUS were searched up until August 2016. There was no restriction on date of publication. The search combined the following terms: “dementia OR Alzheimer’s disease” and “registry OR register OR database” using “AND” relations. Subject headings and truncations were used when appropriate and supported by search engines. Results were limited to English language articles and abstracts published in peer-reviewed journals until August 2016. After removal of duplicates, the literature search in MEDLINE, EMBASE, SCOPUS, yielded 2,349 references. In addition, reference lists of retrieved articles were manually searched to find relevant publications not already covered in the search. An online search using Google search engine for dementia registry websites and grey literature was conducted in August 2016 with search terms used in database searches. Where contact details were provided in retrieved sources, an email was sent to a registry manager asking for additional peer reviewed publications and other resources, such as conference presentations and annual reports. Screening full text articles, combined with online searches and information sent by managers of individual registries yielded 57 dementia registries (38 identified through database search and 19 identified via search by

hand of references, Google and grey literature), 31 of which met the review inclusion criteria presented below (Figure 1).

2.2. Inclusion and exclusion criteria

We included self-identified "dementia registries", i.e., systems of ongoing registration of all cases of dementia in a defined population [6], regardless of the aims of a particular registry. Although definitions based on the aims of registries exist, mostly within national frameworks of quality of health care [28–30] and public health surveillance [31], we adopted a broad approach in order to explore the full range of existing dementia registries.

Our review included registries which a) collected information on patients with a diagnosis of AD/dementia, individuals at risk of developing dementia/AD, caregivers of people with AD/dementia, and/or control subjects without AD/dementia willing to be recruited into dementia studies; b) had been in operation at any time up to August 2016; and c) collected data at an international, national or local/regional/state-wide level. We excluded AD/dementia registries with restricted local coverage, such as hospital/clinic-based and university-based case registries, as higher levels of geographical coverage of a registry are more likely to be more representative of the whole eligible population [32]. We also excluded planned registries which had not been operational over the period covered by the review. To simplify presentation of results and discussion, the general term "dementia registry" (inclusive of AD-specific registries) is used in the text.

2.3. Data extraction

Based on retrieved peer-reviewed publications and grey literature, dementia registries meeting inclusion criteria were further analyzed to obtain information regarding ten characteristics (Table 2). These were the type of registry, registry coverage, language in which data are collected, year registry was established (or where applicable, period covered by registry data collection), most recent number of registered participants, dementia type, diagnostic system, recruitment setting, type of consent procedure, registry population and type of collected data. We included a descriptive review of benefits and outcomes of the dementia registries.

Four categories of dementia registries, related to registry aims, were used in the review, based on the literature on patient/clinical registries [28–30] and dementia registries [20–24]: dementia research registries, epidemiological dementia registries, quality of dementia care registries and dementia research volunteer registries (Table 1). Preclinical dementia research registries, i.e. registries, which aim to optimize conduct of clinical trials for interventions in the pre-dementia phase of AD, were included as a subcategory of dementia research registries.

3. Results

3.1. General overview of dementia registries

Thirty-one registries met inclusion criteria for the review (Table 3). We excluded 24 hospital-based or university-based registries: 14 in the USA, 2 in the UK, 2 in South Korea

and individual registries in Canada, India, Italy, Pakistan, Japan and Taiwan because of their limited geographical coverage and two planned, but not operational national dementia registries (Cuba and the Netherlands). (The list of excluded registries is provided in Appendix 1).

The 31 reviewed dementia registries were established in 14 countries, of which 24 were established between 2000 and 2015. They were in Europe (n=15), followed by North America (n=11), South America (n=2) and Asia (n=1). The review identified two international (both preclinical research) registries: a European collaboration (European Prevention of Alzheimer's Dementia; EPAD) and a collaborative project involving countries in North America, South America, Europe, Asia and Australia (Dominantly Inherited Alzheimer Network (DIAN) Expanded Registry). In four countries there was more than one dementia registry - USA (n=10), UK (n=5), Sweden (n=2) and Norway (n=2) - with varying levels of coverage.

The review identified registries with different levels of geographic coverage (international, national and regional/local/state-wide). National dementia registries were established in Argentina, Austria, France, South Korea and Sweden. In Canada, Colombia, Germany and Spain, dementia registries covered specific geographic and/or administrative regions within the country. In Norway, the UK and the USA, there were multiple registries operational on both national and local levels.

In addition, in Norway (initially the South-East and West Health Regions) and in Denmark (initially Copenhagen) local dementia registries over time evolved into national registries, and local registries in the UK (Scotland) and the USA (Arizona) merged with national registry initiatives. The characteristics of dementia registries included in the review are presented in Table 3. Figure 2 captures the registries ranging from the least specific (i.e. health aging/research volunteer registries) to the most specific (AD only registries).

3.2. Research dementia registries

Thirteen dementia registries, including four preclinical research registries, focused on dementia research. Dementia research registries were the first dementia registries ever established: CERAD (data collected over 1986-1994) [14] and NACC (data collection ongoing since 1999) [15] in the USA, IMAGE in Canada (est. 1986, no longer recruiting) [16] and Camberwell Dementia Case Register in the UK (data collected over 1993-1995) [17]. CERAD's aim was to develop standardized assessments for patients with AD based on longitudinal data collected from more than 1,000 dementia patients and almost 500 healthy control subjects recruited by the Alzheimer's Disease Research Centers and university programs in the US. NACC is a central database in the USA collecting standardized information on all patients at the Alzheimer's Disease Centers. Since its inception, NACC collected, first a cross-sectional, retrospective Minimum Data Set (MDS) (n~65,000), and then a prospective, standardized, and longitudinal clinical evaluation data, which still continues, the Uniform Data Set (UDS) (n~35,000); and also detailed neuropathological data, the Neuropathology Data Set (n~15,000 from both MDS and UDS).

Other dementia research registries were established from 2001 onwards in regions of Germany (Bavarian Dementia Survey – BayDem) [33], Norway (Health and Memory Study of Nord-Trondelag) [34], and USA (Wisconsin Registry for Alzheimer Prevention - WRAP) [35], and nationally in Austria (Prospective Dementia Registry Austria – PRODEM) [36] and South Korea (Clinical Research Center for Dementia of South Korea (CREDOS) Study) [37]. Almost half of the research registries were set up as longitudinal cohort studies. BayDem, CREDOS and PRODEM recruited patients with dementia and their caregivers through hospitals, specialist clinics, medical professionals, and aged care services, and collected data on demographics, cognition, function, bio-banking and other data, including BPSD and past medical history. Additionally, BayDem and PRODEM assessed caregiver burden related to dementia. The WRAP longitudinal registry recruited adults with a parent with autopsy-confirmed or probable AD and control participants (parents without AD/dementia) through health professionals, registry website or word of mouth. The WRAP registry collected data of similar type and scope as other longitudinal registry-based studies. Characteristics of research registries differed in the numbers of participants enrolled, diagnostic systems, and type of data collected (see Table 3). All dementia research registries actively seek consent (opt-in) from patients with dementia, and where applicable, their caregivers.

3.3. Preclinical dementia research registries

We identified four registries in this category: the Dominantly Inherited Alzheimer Network (DIAN) Expanded Registry [38], the Alzheimer's Prevention Initiative (API) Colombian Registry [39], the European Prevention of Alzheimer's Dementia (EPAD) project [40] and the Global Alzheimer Platform (GAP) Trial Ready Cohort for Preclinical/Prodromal Alzheimer's Disease (TRC PAD) [41]. Preclinical registries are relatively new having been established from 2008 onwards. They recruit healthy individuals who are at high risk of developing symptomatic AD, including autosomal dominant Alzheimer's disease (ADAD). Drawing on existing national and regional registers, EPAD develops a shared virtual registry, from which individuals are recruited into the Longitudinal Cohort Study and further, a trial of interventions that could delay (or even prevent) the onset of dementia [40]. Similarly, the TRC PAD GAP Cohort of preclinical and prodromal participants is identified primarily through existing dementia registries in USA, including the Alzheimer's Prevention Registry [41]. The API Colombian Registry was established in the region of Antioquia, in close collaboration with the US-based Alzheimer's Prevention Initiative, and GAP TRC PAD is a national project in the USA. DIAN and EPAD are international collaborations.

3.4. Epidemiological dementia registries

Eight registries collected epidemiological data on dementia, two with national coverage (Argentina and France) [42,43] and six which covered a particular region of the country (Italy, Spain and four registries in the USA) [44–49]. The first epidemiological dementia registries were set up in 1988 in USA and had state-wide coverage (New York State and South Carolina) and the other registries were established from 2005 onwards. Three registries identified patients with diagnosis of collaborations. dementia through a process of data linkage; the others identified eligible patients through healthcare services, including specialized clinics and general practitioners. Epidemiological registries focused primarily on

collecting demographic and diagnostic data on patients with dementia/AD. Half of epidemiological registries also collected information on function, cognition, and other information, such as brief medical history, medication, or date of entry into residential care (where applicable). All registries, except for a pilot national registry in Argentina (Cognitive Impairment Centralized Case Registry in Argentina; ReDeCAr) and Registry of Dementia of Girona (ReDeGi), included over 10,000 patients with dementia, with numbers of registrants ranging between 28,000 (West Virginia, since 2011) and 225,938 (South Carolina, since 1988). Epidemiological dementia registries use different models of consent, including mandatory reporting (e.g., West Virginia), waiver of consent (e.g., the French National Alzheimer database) or informed consent (opt-in) (e.g., ReDeCAr and RedeGi).

3.5. Quality of dementia care registries

The review identified four registries collecting data on quality of care for dementia patients clustered in three Scandinavian countries: Denmark [50], Norway (NorKog; Norwegian Dementia Registry) [51] and Sweden (Swedish Dementia Registry – SveDem) [52]; and Swedish PBSD Registry [53]). These registries were established from 2005 onwards and in 2016 all registries collected data on a national level. Two registries (SveDem and the Danish Dementia Registry) evaluate the quality of dementia care based on adherence to national guidelines, using dementia-related quality indicators (eight indicators in Denmark and seven in Sweden). All registries include data on patients with dementia diagnosed and identified through health care and aged care services, including specialized clinics and nursing homes. Except for the Swedish BPSD Registry, all quality of care registries collect data on demographics, dementia diagnosis, function, cognition, as well as other data, such as medication, possession of driving license, and date of entry into residential care (if applicable). The Swedish BPSD Registry focuses on management of behavioral and psychological symptoms of dementia, and collects data using the Neuropsychiatric Inventory [54]. The numbers of registrants in quality of care registers range between approx. 3,500-6,500 (dementia registries in Denmark and Norway collecting data on regional level) and approx. 23,000-59,000 (two national registries in Sweden).

Quality of care dementia registries use various models of consent. The SveDem and the BPSD Registry operate within the framework of Swedish national quality registries [30] and require that patients are informed about collection of their data and have an option of actively opting-out. In Denmark, collection of data in clinical quality databases approved by the Danish National Board of Health, including the National Dementia Registry, does not require consent of an individual patient. In Norway, written informed consent from a patient diagnosed with dementia (or a relative, if the patient is not able to provide consent) is required to include patient's data in the National Dementia Registry.

3.6. Dementia research volunteer registries

Six registries recruited volunteers for dementia studies; four in the UK: Dementia Register (DemReg) - Dementia Research Registry North Thames DeNDRoN and the EVIDEM (Evidence-based Interventions in Dementia) program [55], Scottish Dementia Research Interest Register [56], CHARIOT (Cognitive Health in Ageing Register: Investigational, Observational and Trial studies in dementia research) [57] and Join Dementia Research

(https://www.joindementiaresearch.nihr.ac.uk); and two in the USA: Alzheimer's Prevention Registry [58] and Arizona Alzheimer Registry [59]. These registries were established between 2006 and 2015, and over this time two local volunteer registries, operating in Scotland and Arizona, merged with new national registry initiatives (Join Dementia Research in the UK and Alzheimer's Prevention Registry in the US, respectively).

Depending on the scope of intended dementia research, registries include patients with a diagnosis of dementia, their caregivers and/or healthy volunteers, i.e., individuals without a diagnosis of dementia. Eligible individuals are identified and recruited through primary and secondary care, social and community services, as well as community awareness campaigns, local champions, consumer organizations, user-friendly websites and social media. Registries recruiting through the general population collect, often through their website, demographic and contact information, and sometimes also basic information about medical and family history related to dementia. Registries recruiting via health providers usually collect more detailed data in regards to cognitive and functional status, as well as data on medications and medical investigations, such as imaging.

Depending on the size of the population targeted by the registry, recruitment strategy, and the type of registry population, number of research volunteers recruited to local registries range between 250 (DemReg) and over 25,000 (Arizona Alzheimer Registry). National dementia registries in the UK (Join Dementia Research) and the USA (Alzheimer's Prevention Registry) recruited approx. 16,000 (2015-mid 2016) and approx. 215,000 (2012-mid 2016) research volunteers respectively.

3.7. Benefits and outcomes

Data collected by research registries and related longitudinal studies provide information on etiology and natural history of dementia, and the relative influence of environmental, biological and genetic factors [17,18,37]. Dementia research registries informed diagnostic and therapeutic practice [14,15], and help to assess physical, psychological and economic burden on caregivers [33,36]. Preclinical registries allow testing potential disease-modifying treatments, such as anti-amyloid drugs, in individuals at high risk of AD because of a genetic profile or a biomarker burden [2,40]. Research registry data have also been enriched by linkage to other research or administrative datasets [60]. In addition, the few operating quality of care, research, and volunteer registries actively survey caregivers of people with dementia and collect information on their needs and caregiving burden. Comparison of actual diagnostic and care practices against published recommended practices and quality indicators afforded an opportunity to highlight discrepancies and improve clinical practice [50,52]. Research volunteer registries raise community awareness of dementia research, care and prevention, and provide an opportunity for members of the public, including the "worried well" and caregivers, to participate in studies, and to the long-term knowledge translation resulting in improvement in dementia diagnosis, management and care.

Researchers have benefitted by having access to research-ready, and often prescreened, populations, to assess more accurately the feasibility of the study [55]. In addition, projects such as the Brain Health Registry in the USA (http://brainhealthregistry.org/) and the Neuroscience Research Australia (NeuRA) Research Volunteer Registry (https://

www.neura.edu.au/volunteer/) helped in recruitment of research volunteers for prevention and treatment studies for a broad range of brain disorders, including AD, Parkinson's disease, depression, schizophrenia and post-traumatic stress disorder. Prospective trial participants can have access to information about studies through registry websites or directly by email.

Dementia registries have proved useful epidemiological tools informing planning of services and health care policy, and complementing epidemiological studies, such as the Rotterdam Study [61]. Data linkage with health and/or administrative databases improves registration of people with dementia, although problems remain with sensitivity (i.e., completeness) and specificity of registry data [45]. For instance, the Experimental Registry for Alzheimer's Disease and Other Dementias in Tuscany [45] enabled population-based analytical epidemiological studies and analyses of targeted health and social services for dementia.

Quality of care and epidemiological registries have proved to be important sources for local/national governments, policy makers, and health economists to assist with planning, provision and assessment of outcomes for service delivery in dementia [30]. Registry data have also provided information to calculate the costs of diagnostic procedures for dementia patients. In Sweden in 2010 the estimated average costs of dementia diagnosis per patient based on the registry data were US$968 in primary care and US$1,669 in specialist care [62]. In this context, it is important to consider the representativeness of the population of people with dementia captured by a registry.

4. Discussion

Our review reports the design, operation, recruitment, geographical coverage, and type and number of participants in 31 dementia registries world-wide. More than half of reviewed dementia registries aim at conducting or facilitating research, including clinical trials for interventions in the pre-dementia phase of AD and recruiting volunteers for dementia studies. Other registries collect epidemiological dementia data or data on quality of care. Due to their wide application and purposes, dementia registries facilitate better diagnosis, management and care of people with dementia, as well as caregiver support, across the course of the illness. Consequently, registries can significantly contribute to the reduced cost of dementia and improve standards of diagnosis and care [52]. For instance, an NACC data study comparing clinical diagnosis of AD with neuropathologic results at autopsy reported on inappropriate medication regimen in misdiagnosed patients, which could adversely affect their health outcomes *and* increase healthcare costs [63].

Registries provide well-established infrastructure for recruiting and following patients in randomized clinical trials and other types of studies in every-day healthcare environment [55,64]. They help to reduce barriers to research recruitment and its cost, which are major challenges to successful implementation of national initiatives, such as the US National Plan to Address Alzheimer's Disease aiming to prevent and effectively treat AD by 2025 [19]. Recent developments in the broader field of patient registries also offer new and exciting possibilities for the use of registry data, including dementia registries. An example is a new clinical paradigm – a registry-based randomized controlled trial (RRCT) [64]. Through

inclusion of a randomization module, the RRCT model combines the advantages of a prospective randomized trial and a large-scale clinical registry based on unselected consecutive enrolment. This novel paradigm was successfully applied in cardiology and was completed with over 90% cost saving, compared with a conventional RCT, due to limited number of patient visits, lower patient attrition and use of existing collaborative networks [65].

There is an ongoing need for improvements in the quality of assessment, diagnosis, management and care. The World Health Organisation (WHO) [66] stressed the role of clinical practice guidelines in helping to improve the average quality and consistency of care. Dementia registries are valuable tools for monitoring the uptake and quality of use of clinical practice guidelines in everyday practice. For instance, there have been significant improvements in the quality of dementia care related to operation of the Swedish Dementia Registry (SveDem); between 2011 and 2015. In primary health care centers which joined the registry, the percentage of complete basic investigations increased by 23% and diagnosis of "dementia not otherwise specified" decreased by 15% [67].

Cancer and cardiovascular disease registries have been trailblazers for dementia registries. The models and problems related to registries for cardiovascular diseases may be more closely related to dementia and AD than the model of a cancer registry [22]. The latter are usually successful as treatment usually occurs in hospitals and requires a pathologic or surgical diagnosis, which is available for all cases. Recent developments leading to more explicit understanding of the preclinical phase of AD and other dementias generate unique opportunities, harnessed by innovative registries optimizing conduct of clinical trials for interventions in the pre-dementia phase of AD, such as DIAN, API, EPAD and GAP TRC PAD. Nonetheless, a significant limitation of dementia registries is that over half of people with dementia [2] do not have a formal diagnosis, this being different from registries for research on cancer or stroke. Also, some dementia registries recruit research volunteers, including "worried well" older adults. This is in contrast to registries on other chronic conditions, which include persons with a formal diagnosis.

Despite these many tangible outcomes and significant progress in the field, three major deficiencies in regards to existing dementia registries stand out: no coverage in many countries, limited possibilities of data sharing between existing data collection systems (i.e., interoperability) and lack of available data on the costs of operating dementia registries and their cost-effectiveness.

Dementia registries cluster in North America, mostly the USA, and Western Europe, mostly in Scandinavia and the UK, with only three registries operational in other parts of the world (Argentina, Colombia, and South Korea). This is of concern as about 60% of people with dementia live in low and middle income countries (LMIC), and the proportionate rise in the prevalence of dementia between 2015 and 2050 is expected to be twice as high in these countries than in high income countries (264% and 116%; respectively) [1]. The WHO [66] recommends a range of actions to improve care and services for people with dementia and their caregivers worldwide. These include strengthening of health systems, developing and implementing dementia policies and plans, supporting dementia research, advocacy and

awareness-raising, which can be addressed, among others, by dementia registries. In addition, the recently established WHO Global Dementia Observatory will promote planning and monitoring of strategic objectives, such as establishment of national dementia plans and policies, and will support surveillance systems providing data on the burden of dementia. Development of dementia registries in LMIC countries could support care systems and research, and help to put dementia on public health agenda.

There is also significant heterogeneity regarding the aims and characteristics of dementia registries, which rules out comparing registries in different categories, and often even registries within a particular category. Understandably, most registries were set up as individual data collection systems, designed to operate independently and not with the explicit aim of comparing datasets internationally. Nonetheless, as much as possible and feasible, standardization of registries and datasets is the *sine qua non* of truly international initiatives in dementia research in the era of big data. Data harmonization also allows comparisons between countries and regions with and without registries, providing the much needed, and currently limited, data on outcomes and cost-effectiveness of registries. International collaboration is facilitated by standardizing and integrating existing datasets, harmonization of ongoing international research initiatives (i.e., interoperability), and defining international data-sharing guidelines, including the challenges of informed consent [25]. The EPAD project [40] and the International Database for Longitudinal Studies on Aging and Dementia (IDAD) [4] are examples of initiatives aiming at integrating existing international datasets.

Set-up and running costs of existing dementia registries are not publicly available. One estimate from US is that the costs of establishing the Brain Health Registry and Alzheimer's Prevention Initiative were millions of dollar and of maintenance, hundreds of thousands annually (Personal communication, M. Wiener, 2017). EPAD aims to recruit 24,000 participants from existing cohorts/registers (which reduces the costs of recruitment). The total cost of EPAD is €64 million/US$ 68 million over five years which includes €15 million in cash and €21 million in kind from pharmaceutical companies (Personal communication, C. Ritchie, 2017). The virtual EPAD register budget is approximately €1.5 million / US$ 1.6 million over 5 years from the European Union with 20% extra coming from pharmaceutical companies; a major cost is the development of the IT platform. In France the national AD bank derived from memory clinic intake approximately cost about €1.5 million (US$1.6) for data entry annually, €1 million (US$1.06) for development of the software for data base management and €300,000 pa for IT support queries and analyses (Personal communication, K. Ritchie and A. Gabelle, 2017). Based on the French data, a 50-year investment, the required total cost would be approximately US$ 97 million / €91 million, although costs could be 2-3 times higher and will depend on the size of the population covered and the comprehensiveness of the data base and follow-up intervals. While registries offer participants the opportunity to participate in scientific drug trials there is the possibility of 'leakage' to for-profit interests. Ethical guidelines are necessary, and some registries, such as SveDem, choose not to have sponsors from the pharmaceutical industry [52].

The substantial global cost of dementia, estimated at $818 billion [1], calls for development of cost-effective medical and social care interventions and evidence-based prevention

strategies [62]. No study to evaluate the cost-effectiveness of dementia registries was located despite evidence from other areas of medicine, such as hip arthroplasty, cystic fibrosis, cancer, ophthalmology, and rheumatology that patient registries can significantly contribute to lowering the costs of health care [13,68]. For instance, in the USA, a cystic fibrosis registry contributed to the saving of US$23m p.a. in avoided infection-related costs, which equates to approximately 2% of the total costs of care for the condition [13]. Economic evaluation of five clinical quality registries in an Australian review [68] showed a relatively low cost for improvement in clinical practice, resulting in significant positive return on investment. The benefit-to-cost ratios for the return on investment ranged from 2:1 (Victorian Prostate Cancer Registry, net benefit AU$ 2.4 million / approx. US$ 1.8 million / Euro 1.7 million over 2009-2013) to 7:1 (Australia and New Zealand Dialysis and Transplantation Database, net benefit AU$ 49 million / approx. US$ 36.75 million / Euro 34.6 million over 2004-2013). If state-level registries could reach full national coverage, the minimum expected benefit-to-cost ratio was estimated to increase to 4:1 [68]. The Australian review emphasized that registries deliver significant value for money when “correctly implemented and sufficiently mature” [68 p3]. A caveat to drawing conclusions from other disease registries is that dementia unlike many other conditions has no disease modifying treatment yet.

The cost-effectiveness of dementia registries is linked to the need for sustainability in development and operation of registries, and efforts to attract (or leverage) registry resources to facilitate future self-financing. For instance, one of the aims of the EPAD Project is development of a sustainability business plan extending beyond the time frame of the project [69]. The business plan calls for an analysis of relevant public-private partnership collaborative models, and an analysis of stakeholders’ interests and incentives towards sustainability, Continuation of EPAD also requires development of sustainability procedures for the local trial delivery centers infrastructure. Similarly, in the US, the GAP TRC PAD initiative aims to establish a long-term sustainability business model involving two-fold financial support from pharmaceutical companies: upfront investment in the infrastructure and reimbursement based on trial enrollment [70].

5. Limitations

Several limitations of the systematic review are noted. First, the review included self-identified “dementia registries”, regardless of the aims of a registry. While this broad approach allowed exploring all categories of dementia registries, it resulted in heterogeneity. Secondly, to promote clarity, the review presented four mutually exclusive categories of dementia registries; in reality the situation is more complex. Although some registries operate within particular frameworks, which clearly define registry aims, e.g., the Scandinavian registries for the quality of care or the preclinical research registries, other registries, such as the Alzheimer’s Prevention Registry, can be included in more than one category (e.g., a preclinical registry and a research volunteer registry). Thirdly, the review is based on material retrieved through database search of peer-reviewed publications in English and grey literature identified through online searches and contact with registry managers. It is possible that the review excluded some eligible dementia registries not identified through the searches. Nonetheless, the search of resources available in English identified registries

collecting original data in nine languages (Danish, English, French, German, Italian, Korean, Norwegian, Spanish and Swedish).

Fourth, registries vary in regards to the level of detail, completeness, and accuracy of the collected data. While methodology exists to evaluate coverage and accuracy of clinical databases [32] and surveillance systems [71], available data currently precludes such an analysis. Given the variable amount of information on methods used to construct different dementia registries presented in the peer-reviewed and grey literature, our review did not include an evaluation of existing registries. Also, methods of identification of patients with dementia and data collection (e.g., via health care services) may result in incomplete or unrepresentative sampling and limited geographic coverage often restricting the possibility of using registry data to provide estimates of incidence or prevalence [43]. For example, a registry which relies on enrolling patients who use health and aged care services, is more likely to have oversample advanced dementia and underrepresent and underestimate the numbers and needs of people in the earlier stages of dementia [40].

Fifth, we may have missed some studies because of the restriction to “registries” and “databases” since that term may not be used consistently for dementia/AD data repositories. Finally, we excluded hospital/clinic-based and university registries due to their limited geographic coverage. Many low and middle-income countries may successfully rely on these registries as the state/country level infrastructure is lacking.

6. Practicalities of hosting a dementia registry and recommendations

The technical, organizational and logistic challenges of establishing and maintaining registries are substantial. Critical elements in setting up a dementia registry follow [5,28,29]:

1. Ensure sufficient funding and sustainability of a registry.

Registries with good coverage and accuracy most likely will require significant and continuing funding. For instance, in Australia, the cost of establishing a major national registry (50,000 cases reported annually), including the cost of the IT systems, has been estimated in 2013 dollars at AU$ 750,000-1 million (approximately US$ 500,000 - 750,000 / Euro 470,000 – 700,000) and the cost of maintaining such a registry at AU$1-1.5 million p.a. (approximately US$ 0.75-1 million / Euro 470,000- 940,000) [28,72]. Specifically for dementia registries, costs vary depending on the cost of recruiting and screening subjects and of developing, launching and growing the registry. Typically registry costs include the online data system, developing and testing the minimum data-set, publicizing the registry, data-collection and reporting, outcome determination (via follow-up or data-linkage), system maintenance and statistical analysis. Funding is also required to cover the costs of the registry governance, collaboration with stakeholders, ethics approvals, and implementation of quality assurance procedures.

Given the high estimated cost of setting up and operating a dementia registry, including long term commitment of stakeholders and sustainability of funding, the essential question is whether a registry is the best method of collecting the data of interest, whether there are cheaper alternatives, and whether the returns on investment can be realized. Also, given the

involvement of health care staff in data collection as a part of everyday clinical practice, the amount of mandatory information must be restricted to the minimum. The critical question is “can this [data collection] be done in any other way? If the answer is yes, then it is probable that the register is a luxury” [73 p227]; better recoding of routine hospital, specialist, and primary care consultations may be a much cheaper alternative.

2. Define and document the purpose of the registry.

The intended purpose and available funding determine design and scope of a dementia registry. There are many types of dementia registries, each serving particular purpose(s), and “no single [dementia] registry will be able to solve all problems” [22 p200]. Although categories often overlap, e.g., quality of care registries can provide research data, and epidemiological registries support clinical practice, the purposes of the registry have to be clearly defined and agreed upon by the registry stakeholders. Follow-up procedures, usually annually, need to be made clear at the outset. Also, prespecified indicators of a successful operation of a registry help to assess its effectiveness. For instance, registries monitoring quality of care for dementia patients operating in Scandinavian countries [50–53] monitor and report on adherence to clinical indicators stipulated by national guidelines.

3. Develop leadership/governance structure and registry policies.

Effective operation requires a multidisciplinary set of skills and involvement of a range of stakeholders, including clinicians, researchers, epidemiologists, statisticians, dementia patients and families, policy makers, patient advocacy groups, and regulatory agencies. A registry requires development of policy documents, which provide guidelines regarding ethics, data management, access, and security, communications, publications, reporting, and privacy.

4. Develop adequate infrastructure for data entry, storage and access.

It is recommended that registries use web-based infrastructure, as user-friendly online technology facilitates data collection, processing, and reporting [74]. Use of electronic databases supports data linkage, and where available, allows automatic data capture from existing e-health records and administrative data systems. National legislation and regulations should inform development of registry protocols for safe and secure collection, storage and transmission of electronic data, and address existing limitations of linkage to existing e-health records, such as capture of limited retrospective data and lack of formal diagnosis of dementia in many patients.

5. Identify data sources and data collection procedures.

Collection of data on dementia from multiple, diverse and often dispersed sites, including general practice, memory clinics, independent specialists, and residential aged care facilities, is a significant challenge. This can be addressed by standardizing the process of data collection and data entry through publishing eligibility criteria, metadata, and data dictionaries. A successful registry requires a sustainable workflow model, with minimal disruption, which can be easily integrated into the everyday practice of medical personnel contributing to a registry. The process of data collection must not place an unnecessary

burden or financial cost on patients and other users of health services [28]. Integration of the registry infrastructure with the information and communications technology systems already in place within the national healthcare systems (where electronic health records or administrative systems exist) enables automatic data capture, which significantly reduces the burden of data entry.

6. Define the registry population, including case definition.

Use of reliable and valid diagnostic methods for dementia and/or cognitive impairment, such as DSM [75] or ICD [76], ensures collection of quality data. Depending on the aims, some registries may have a limited geographical coverage, limited time period for data collection, or may focus on particular patient attributes, such as a subtype of dementia or age group.

7. Decide on the type of consent process.

The majority of dementia registries actively seek consent from patients for inclusion of data, i.e., opt-in approach; others use an opt-out approach, in which consent for participation is presumed unless a patient expresses a wish not to participate. The latter can increase participation rate in a registry and to minimize recruitment bias, as data are collected from all groups of patients [77].

8. Decide on the scope of data collection and data collection instruments.

Data elements included in a dementia registry should reflect the goals and resources of the registry. Collected data should be acceptable to patients with dementia, their caregivers, and healthcare personnel, and should keep the burden of response and data collection to the minimum. Data collection instruments should be valid, reliable, and standardized across settings or regions.

9. Set up quality control procedures for a dementia registry.

A registry is only as good as the data it collects; it is essential that the registry data are of high quality and serve the registry purposes. Procedures and policies to ensure completeness and validity of data should be developed before the data collection commences, and reviewed at regular intervals. A range of factors ensures the quality of registry data: adherence to the procedures of data collection, clear definition and structure of data elements, sufficient training of the personnel involved in data collection, and good procedures for handling problems with data, such as data entry errors and missing data.

10. Continually re-evaluate purpose and operation of the registry.

The length of time for the planned operation of a registry should be taken into consideration during the initial stages of its development. In general, registries are long-term data repositories and to achieve their purpose(s), such as monitoring of quality of care or collecting data on the natural history of a disease, data must be collected over an extended period of time. This requires ensuring long-term sustainable funding and infrastructure, ideally, supported by policy makers and local/national governments. Registries with good coverage and accuracy require significant and continuing funding. Although registries can be expensive activities, which require considerable investment, their cost needs to be judged

against improvements in the quality of healthcare and cost savings gained from the collected data. The Swedish government has recognized quality registries as a priority and has sought to increase necessary funding, which reached $US45m p.a. in 2013 [78]. The operation and value of a registry must be routinely examined to ensure that the purpose still holds and is being achieved. If registry objectives are not met, they "should be revised or the register closed. The least successful registers seem to be those which attempt to meet ill-defined needs" [73 p226]. Where applicable, a plan or criteria for closing a registry should be specified at the commencement of the project.

Several registry handbooks have been developed by professional and academic agencies and are freely available online [29,74,79]. These documents contain detailed information regarding setting up and operation of health registries. As the handbooks are based on national frameworks and policies, adaptation to local settings and circumstances may be required. Some countries, such as Australia [80], have developed operating principles for registries, which may inform national/regional dementia registries.

7. Conclusions

Over the last two decades dementia registries have proven to be versatile tools, which have significantly contributed to dementia research, clinical practice and health policy. Recent developments, such as availability of big data, international collaborations calling for harmonization of research projects and datasets, and increasing focus on preclinical stages of AD, create new and exciting opportunities. In addition, development of dementia registries in low and middle income countries could be a part of dementia awareness rising and could provide tools for improvement in research and clinical services in these regions of the world. Although almost 2 in 3 people with dementia in the world live in low and middle income countries, there is a scarcity of registries in these regions.

Given the tangible practical and economic outcomes for research, clinical practice and policy, further development and growth of dementia registries can be expected and should be supported by policy makers, research funding bodies, clinicians and consumers. The recent evolution in clinical research on AD, i.e., trials of candidate drugs in pre-symptomatic at-risk populations, requires engagement of cohorts identified through existing registers or recruited via research volunteer databases. Standardization of procedures including ethical principles and security of privacy and minimum data sets will assist international collaboration and comparisons.

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Appendix 1.: Definitions and Classifications of Registries

The many definitions and classifications of registries [1] are typically embedded within broader frameworks and models of public health surveillance and reporting on the quality of

health care (Box 1). In general, in epidemiology the term “register” refers to a “file of data concerning all cases of a particular disease or other health relevant condition in a defined population” and a “registry” is a “system of ongoing registration” [2 p211]. Different terms, such as “patient registries”, “clinical registries”, “clinical data registries”, “disease registries”, and “medical registries” have been used internationally to describe registries focused on health information. Terms such as “clinical databases”, “outcomes registries”, “quality registries”, “clinical quality registries”, have been used in reference to registries aiming specifically at clinical audit, i.e., “the routine assessment of the quality of care of health care providers” [3 p131]. In addition, “patient-powered patient registries” (also called “patient-generated”, “patient-run”, “patient-powered, and participant controlled” registries) are data sets managed or controlled by patients and family members affected by a particular medical condition, who also set the research agenda, and decide on the translation and dissemination of the study outcomes based on the collected data [4](Workman, 2013).

Box 1.

Examples of frameworks and models of public health surveillance and reporting on the quality of health care

The US Agency for Healthcare Research and Quality

The US Agency for Healthcare Research and Quality (AHRQ) defines a patient registry as an “organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes” [5 p13]. According to the AHRQ, there are three categories of patient registries: a) disease or condition registries where inclusion is related to a diagnosis of a disease or a condition, b) product registries, which include patients exposed to a health care product, such as a drug or a device, and c) health service registries, which relate health outcome to exposure to healthcare services. Many registries are a combination of these three categories.

The Framework for Australian Clinical Quality Registries

In Australia clinical registers are defined as “databases that systematically collect health-related information within an overall governance and management structure on individuals who are: treated with a particular surgical procedure, device or drug, e.g. joint replacement; diagnosed with a particular illness, e.g. stroke; or managed via a specific healthcare resource, e.g. treated in an intensive care unit.”[1] Similarly to the US AHRQ, three (overlapping) categories of clinical registries are described: a) condition/disease registries (collecting diagnostic details on patients with specific disease/condition), b) drug/device/product registries (monitoring safety of devices/drugs/products, such as blood), and c) clinical quality registries (monitoring outcomes and reporting on quality of care).

[1] http://www.med.monash.edu.au/sphpm/depts-centres-units/registries/index.html

The Framework for Australian Clinical Quality Registries further defines Australian clinical quality registers as “organisations that systematically monitor the quality (appropriateness and effectiveness) of health care, within specific clinical domains, by routinely collecting, analysing and reporting health-related information. The information is used to identify benchmarks, significant outcome variance, and inform improvements in healthcare quality” [6 p7].

The Swedish Patient Data Act

The Swedish Healthcare Quality Registries have been defined as “an automated and structured collection of personal data that were initiated with the purpose to systematically and continuously develop and safeguard quality of care. A national or regional quality registry refers to a quality registry in which personal data have been collected from several caregivers and which allows for comparisons within healthcare at a national or regional level” [7 p108].

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Appendix 2.: Hospital-based and university-based dementia registries.

Canada

University of Western Ontario Dementia Study Registry [1]

India

Nizam’s Institute of Medical Sciences Hospital Dementia Registry [2]

Italy

Treviso Dementia (TREDEM) Registry [3]

Japan

Hyogo Institute Hospital for Aging Brain and Cognitive Disorders Registry [4]

Pakistan

Shifa International Hospital, Islamabad Registry [5]

South Korea

Konkuk Dementia Registry, Konkuk University [6]

Hyoja Dementia Registry, Hyoja Geriatric Hospital [7]

Taiwan

Lin-Shin Dementia Registry Project [8]

UK

Maudsley Biomedical Research Center Dementia Case Registry at King's Health Partners [9]

Newcastle and Tyneside Area Case Register [10]

USA

Alzheimer's Disease Prevention Registry, Duke University [11]

Alzheimer's Disease Patient Registry, Prototype Alzheimer's Collaborative Team (PACT) [12]

Boston University Alzheimer's Disease Center Registry [13]

East Boston Alzheimer's Disease Registry [14]

Massachusetts Alzheimer's Disease Research Center at Massachusetts General Hospital Registry [15]

Mayo Clinic Alzheimer's Disease Patient Registry [16]

Rhode Island Hospital Alzheimer Prevention Registry [17]

University Alzheimer Center, Case Western Reserve University and University Hospitals of Cleveland Registry [18]

University of California at Los Angeles Alzheimer's and Dementia Care Program Registry [19]

University of Iowa Prototype Alzheimer's Disease Registry [20]

University of Pittsburgh Alzheimer's Disease Patient Registry [21]

University of Rochester Alzheimer's Disease Research Center Neuropathology Database [22]

University of South California Alzheimer's Disease Research Center Registry [23]

University of Washington Alzheimer's Disease Patient Registry [24]

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Patient registries are valuable tools helping to address significant challenges in research, care and policy. Registries, well embedded in many fields of medicine and public health, are relatively new in dementia. This systematic review presents the current situation in regards to dementia registries worldwide. We identified 31 dementia registries operating on an international, national or local level between 1986-2016. More than half of the registries aimed to conduct or facilitate research, including preclinical research registries and registries recruiting research volunteers. Other dementia registries collected epidemiological or quality of care data. We present evidence of practical and economic outcomes of registries for research, clinical practice and policy and recommendations for future development. Global harmonization of recruitment methods and minimum data would facilitate international comparisons. Registries provide a positive return on investment; their establishment and maintenance require ongoing support by government, policy makers, research funding bodies, clinicians, individuals with dementia and their caregivers.

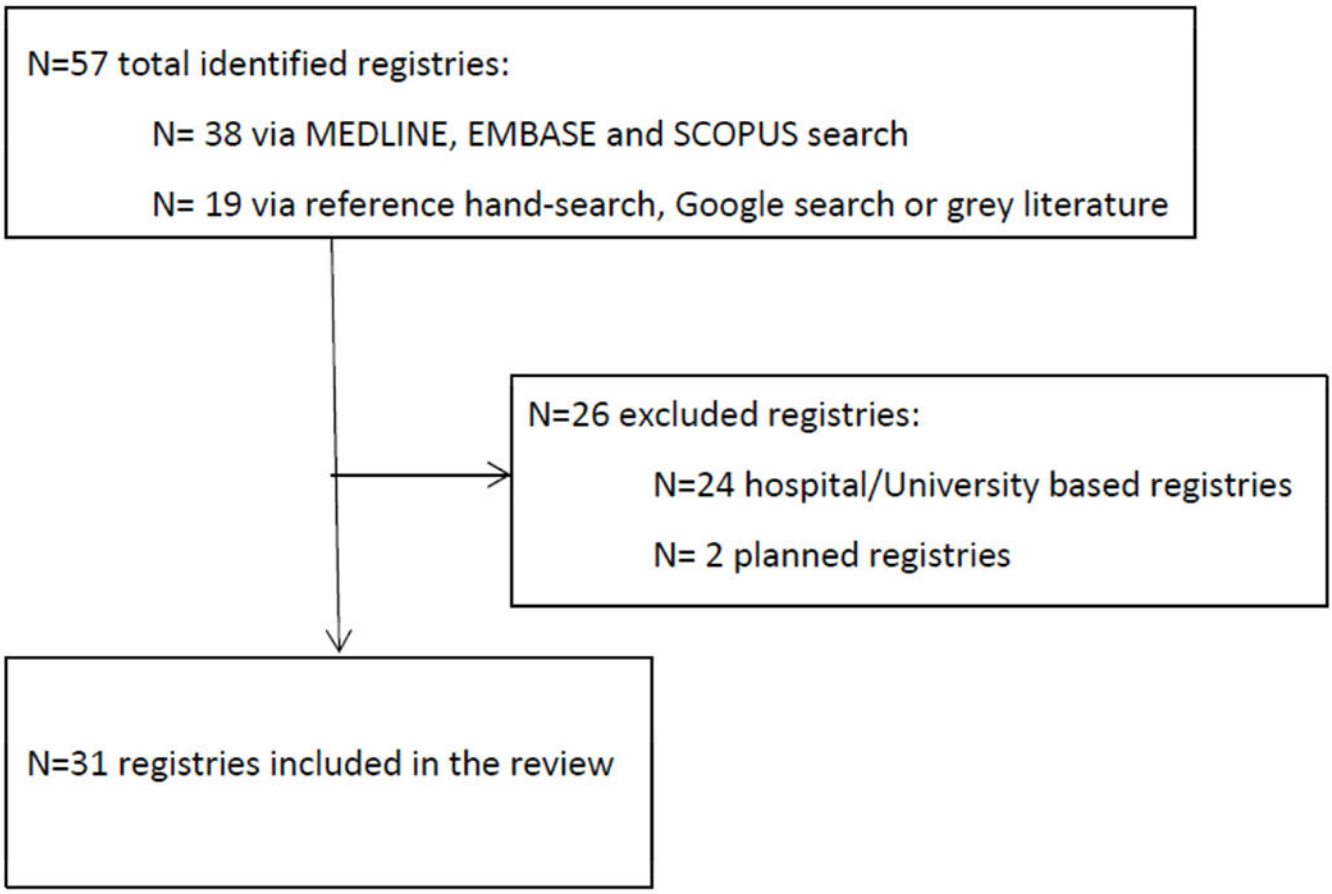

Figure 1.
Study inclusion and exclusion criteria flowchart.

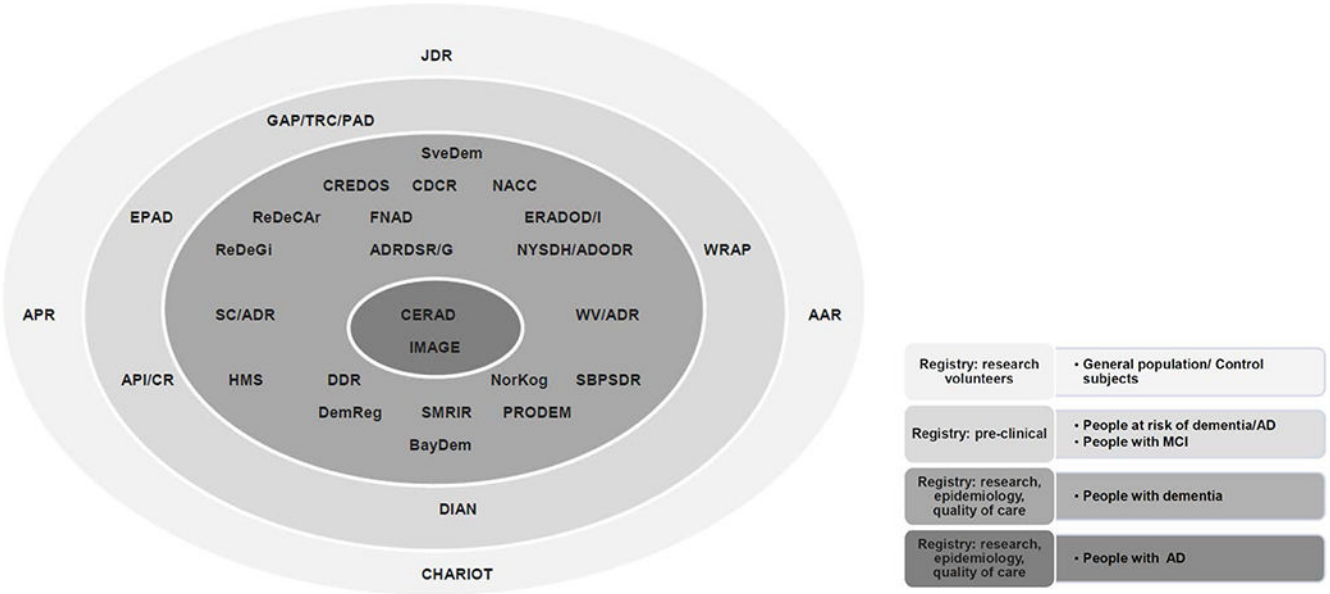

Figure 2.

Populations captured in existing dementia registries.

AAR - Arizona Alzheimer Registry; AD/RDSR/G - AD/Related Dementia State Registry (Georgia); API/CR - Alzheimer's Prevention Initiative Colombian Registry; APR - Alzheimer's Prevention Registry; BayDem - Bavarian Dementia Survey; CDCR - Camberwell Dementia Case Register; CERAD - Consortium to Establish a Registry for Alzheimer's Disease; CHARIOT - Cognitive Health in Ageing Register; CREDOS - Clinical Research Center for Dementia of South Korea; DemReg - Dementia Research Registry North Thames DeNDRoN/EVIDEM; DDR - Danish Dementia Registry; DIAN - Dominantly Inherited Alzheimer Network; EPAD - European Prevention of Alzheimer's Dementia; ERADOD/I - Experimental Registry for AD/other Dementias in Italy; FNAD - French National Alzheimer Database; GAP/TRC/PAD - Global Alzheimer Platform Trial Ready Cohort for Preclinical/ Prodromal AD; HMS - Health and Memory Study of Nord-Trøndelag; JDR - Join Dementia Research; IMAGE - IMAGE Project Population-Based Registry of AD; NACC - National Alzheimer's Coordinating Center; NorKog - Norwegian Dementia Registry; NYSDH/ADODR - New York State Department of Health AD/Other Dementias Registry; PRODEM - Prospective Dementia Registry Austria ; ReDeCAr - Cognitive Impairment Centralized Case Registry in Argentina; ReDeGi - Registry of Dementia of Girona; SC/ADR - South Carolina AD Registry; SveDem - Swedish Dementia Registry; SBPSDR - Swedish Behavioural and Psychological Symptoms of Dementia Registry; SMRIR - Scottish Dementia Research Interest Register; WV/ADR - West Virginia AD Registry; WRAP - Wisconsin Registry for Alzheimer Prevention

Table 1.

Aims and categories of dementia registries

Category of registry	Aims
Dementia research registry	• To support research into causes and risk factors for dementia. • To provide data on the natural history of dementia, determinants of progression, and their implications for clinical management. • To develop and measure effectiveness of interventions to reduce the risk and incidence of dementia, its treatment and management. • To evaluate and refine the diagnostic criteria for dementia, to standardize and validate screening instruments and diagnostic tests.
Subcategory: Preclinical dementia research registry	• To optimize conduct of clinical trials in preclinical stages of AD/dementia, to accelerate cohort development and trial recruitment.
Epidemiological dementia registry	• To collect epidemiological data on the prevalence, incidence, and risk of dementia.
Quality of dementia care registry	• To monitor the quality of dementia care. • To provide information on utilization and cost of health and aged care services and carer support, and to inform planning and development of dementia services.
Dementia research volunteer registry	• To identify people with dementia, their carers, and healthy volunteers who are willing to be involved in research studies and clinical trials.

Table 2.

Data elements included in the review

Category	Data elements
Type of registry	dementia research registry (including a preclinical dementia research registry), epidemiological dementia registry, quality of dementia care registry, dementia research volunteer registry
Registry coverage	international, national, local/state-wide
Language of collected data	Language of collected data
Year registry was established (or where applicable, period covered by data collection)	year, time period
Number (N) of registered participants	N (most recent)
Dementia type	dementia, AD (if other, specify)
Diagnostic system	ICD, DSM, NINCDS-ADRDA, not applicable
Recruitment setting	health care services, awareness campaign/general population, data linkage, other
Consent	opt-in, opt-out, other, info not available (if other, specify)
Registry population	patients with a diagnosis of AD/dementia, carers, family members of people with AD/dementia, individuals at risk of developing dementia/AD, normal (i.e., no diagnosis of dementia/AD) control subjects
Type of collected data	cognition, demographics, function, imaging and other biomarker measures, other (e.g., caregiver burden, BPSD symptoms)

DSM - Diagnostic and Statistical Manual of Mental Disorders; ICD - International Classification of Diseases; NINCDS-ADRDA – the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria

Table 3.

Characteristics of dementia registries

Registry name (country)	Coverage	Language of collected data	Established in year	N (most recent)	Dementia type	Diagnostic system	Recruitment setting	Consent	Registry population	Type of collected data
Dementia research registry										
Prospective Dementia Registry Austria (PRODEM) (Austria) (Seiler et al., 2012)	National	German	2008 (ongoing)	N=500+ (2014)	Dementia	DSM-IV	HCS	Opt-in	PWD, C	Cog, Dem, Funct, IBM, Other
the IMAGE Project Population-Based Registry of AD (Canada) (De Braekeleer et al., 1989)	Local (Quebec)	French	1986 (no longer recruiting)	N=194 (definite) N=206 (probable) N=211 possible (1996)	AD	NINCDS-ADRDA	HCS	Opt-in	PWD	Cog, Dem, Funct, IBM, Other
Bavarian Dementia Survey (BayDem) (Germany) (previously: the Erlangen Dementia Registry) (Schaller et al., 2015)	Local (Bavaria)	German	2012 (ongoing)	N=91 (2012-2014)	Dementia	ICD-10	HCS	Opt-in	PWD, C	Cog, Dem, Funct, Other
Health and Memory Study of Nord-Trøndelag (Norway) (Bergh et al., 2014)	Local (Nord-Trøndelag)	Norwegian	Data for 1995-2011	N=1,434	Dementia	ICD-10	HCS	Opt-in	PWD	Cog, Dem, Funct, IBM, Other
Clinical Research Center for Dementia of South Korea (CREDOS) Study (Park et al., 2011)	National	Korean	2005 (ongoing)	N=2,967 (2005-2012)	Dementia	NINCDS-ADRDA/ DSM-IV	HCS	Opt-in	PWD, C	Cog, Dem, Funct, IBM, Other
Camberwell Dementia Case Register (UK) (Holmes, 1996)	Local (Camberwell)	English	Operating 1993-1995	N=530	Dementia	NINCDS-ADRDA/ DSM-III-R	HCS	Opt-in	PWD, C	Cog, Dem, Funct, IBM, Other
Consortium to Establish a Registry for Alzheimer's Disease (CERAD) (USA) (Fillenbaum et al., 2008)	National	English	Operating 1986-1994	N=1,094 (AD), N=463 (control)	AD	NINCDS-ADRDA	HCS	Institutional Review Board approval	PWD, NC	Cog, Dem, Funct, IBM, Other
National Alzheimer's Coordinating Center (NACC) Database (USA) (Beekly et al., 2004)	National	English	1999 (ongoing)	N=74,397 (MDS), N=33,900	AD/related disorders	NINCDR or DSM	HCS	Institutional Review Board approval	PWD	Cog, Dem, Funct,

Registry name (country)	Coverage	Language of collected data	Established in year	N (most recent)	Dementia type	Diagnostic system	Recruitment setting	Consent	Registry population	Type of collected data
				(UDS) (2016) **						IBM, Other
Wisconsin Registry for Alzheimer Prevention (WRAP) (USA) (Sager et al., 2005)	Local (Wisconsin)	English	2001 (ongoing)	N > 1,500 (2016)	AD	NINCDS-ADRDA	HCS	Opt-in	FAM, NC	Cog, Dem, Funct, IBM, Other
Preclinical dementia research registry										
Alzheimer's Prevention Initiative (API) Colombian Registry (Lopera et al., 2013; Reiman et al., 2011)	Local (Antioquia)	Spanish	2010 (ongoing)	N=2,092 (2010-2012)	Autosomal Dominant AD	n/a	HCS	Opt-in	FAM	Cog, Dem, Funct, IBM, Other
European Prevention of Alzheimer's Dementia (EPAD) (Ritchie et al., 2016)	International	International project	2015 (ongoing)	Aim: N=24,000 (registry) N=6,000 (longitudinal cohort) N=1,500 (trials)	AD	n/a	Other	Opt-in	AT-RISK	Cog, Dem, Funct, IBM, Other
Global Alzheimer Platform (GAP) Trial Ready Cohort for Preclinical/Prodromal Alzheimer's Disease (TRC PAD) (USA) (Cummings et al., 2016)	National	English	2013 (ongoing)	Aim: N=1,000 (preclinical) N=1,000 (prodromal)	AD	n/a	Other	Opt-in	AT-RISK	Cog, Dem, Funct, IBM, Other
Dominantly Inherited Alzheimer Network (DIAN) Expanded Registry (Morris et al., 2012; Moulder et al., 2013)	International	International project	2008 (ongoing)	N = 336 (2013)	Autosomal Dominant AD	n/a	HCP, AC/GP	Opt-in	FAM	Cog, Dem, Funct, IBM, Other
Epidemiological dementia registry										
Cognitive Impairment Centralized Case Registry in Argentina (ReDeCAr) (Allegri, 2011)	National	Spanish	2010 (pilot)	N=292 (2010)	Dementia	DSM-IV-TR/ICD-10	HCS	Opt-in	PWD	Cog, Dem, Funct, Other
French National Alzheimer Database (Anthony et al., 2014)	National	French	2009 (ongoing)	N=760,120 (since 2009)	AD/related disorders/ Mild cognitive impairment	ICD-10	HCS	Not required	PWD	Cog, Dem, Funct, Other
Experimental Registry for AD/other Dementias (Italy) (Francesconi et al., 2007)	Local (Tuscany)	Italian	Data for 1999-2005	N=47,889	Dementia	ICD-9	DL	Info not available	PWD	Dem, Other

Registry name (country)	Coverage	Language of collected data	Established in year	N (most recent)	Dementia type	Diagnostic system	Recruitment setting	Consent	Registry population	Type of collected data
Registry of Dementia of Girona (ReDeGi) (Spain) (Garre-Olmo et al., 2009)	Local (Girona)	Spanish	2007 (ongoing)	N=4,314 (2007-2012)	Dementia	DSM-IV-TR	HCS	Opt-in and opt-out	PWD	Cog, Dem, Funct, Other
AD/Related Dementia State Registry (USA) (Weeks Leonard et al., 2016)	State-wide (Georgia)	English	2014 (ongoing)	N=112,430 (2013)	AD/related dementias	ICD-9, ICD-10	DL	Not required	PWD	Dem, Other
New York State Department of Health AD/Other Dementias Registry (USA) (Lillquist, 2004)	State-wide (New York)	English	1988 (ongoing)	Info not available	AD/ dementia	ICD-9-CM	HCS	Info not available	PWD	Dem, Other
South Carolina AD Registry (USA) (Macera et al., 1991)	State-wide (South Carolina)	English	1988 (ongoing)	N=225,938	AD/related disorders	ICD-9-CM	DL	Info not available	PWD	Dem, Other
West Virginia AD Registry (USA) (Schreurs, 2010)	State-wide (West Virginia)	English	2011 (ongoing)	N= 28,000 (2015)	AD/related disorders	ICD-9-CM, ICD-10-CM	HCS, DL	Not required	PWD	Cog, Dem, Funct, Other
Quality of dementia care registry										
Danish Dementia Registry * (Johannsen et al., 2011)	National	Danish	2005 (ongoing)	N=6,576 (2007-2012)	Dementia	ICD-10	HCS	Not required	PWD	Cog, Dem, Funct, Other
Norwegian Dementia Registry * (NorKog) (Persson et al., 2015)	National	Norwegian	2013 (ongoing)	N=3,633 (2014)	Dementia	ICD-10	HCS	Opt-in	PWD, C	Cog, Dem, Funct, IBM, Other
Swedish Dementia Registry (SveDem) (Religa et al., 2015)	National	Swedish	2007 (ongoing)	N=58,823 (2016)	Dementia	ICD-10	HCS	Opt-out	PWD	Cog, Dem, Funct, Other
Swedish Behavioural and Psychological Symptoms of Dementia (BPSD) Registry (Mayer et al., 2014)	National	Swedish	2010 (ongoing)	N=23,311 (2015)	Dementia	ICD-10	HCS	Opt-out	PWD	Dem, Other
Dementia research volunteer registry										
CHARIOT (Cognitive Health in Ageing Register: Investigational, Observational and Trial studies in dementia research) (UK) (Larsen et al., 2015)	Local (London)	English	Data for 2011-2014	N > 25,000 (2016)	Dementia	n/a	HCS	Opt-in	NC	Dem, Other
Scottish Dementia Research Interest Register (SMRIR) (UK) (Russ et al., 2015)	Local (Scotland)	English	2008 (2015: merged with JDR)	N=1,427 (carers), N=1,401	Dementia	n/a	HCS, Other	Opt-in	PWD, C	Cog, Dem, Funct, Other

Registry name (country)	Coverage	Language of collected data	Established in year	N (most recent)	Dementia type	Diagnostic system	Recruitment setting	Consent	Registry population	Type of collected data
				(patients) (2014)						
Dementia Register (DemReg) - Dementia Research Registry North Thames DeNDRoN and the EVIDEM (Evidence-based Interventions in Dementia) programme (UK) (Illife et al., 2011)	Local (North Thames)	English	2009 (ongoing)	N=~ 250 (2010)	Dementia	ICD-10, DSM-IV, other	HCS	Opt-in	PWD	Cog, Dem, Funct, Other
Join Dementia Research (JDR) (UK) (https://www.joindementiaresearch.nihr.ac.uk/	National	English	2015 (ongoing)	N > 20,000 (2016)	Dementia	n/a	AC/GP	Opt-in	General population	Dem, Other
Alzheimer's Prevention Registry (APR) (USA) (https://www.endalznow.org/)	National	English	2012 (ongoing)	N > 200,000 (2016)	AD	n/a	AC/GP	Opt-in	General population	Dem, Other
Arizona Alzheimer Registry (USA) (Saunders et al., 2014)	State-wide (Arizona)	English	2006 (2012: merged with APR	N=1,182 (2006-2011)	Cognitive impairment, dementia	n/a	AC/GP	Opt-in	General population	Cog, Dem, Funct, Other

*Originally established as a local registry;

**MDS = Minimum Data Set, UDS = Uniform Data Set

Recruitment setting: DL = data linkage, AC/GP = awareness campaign/general population, HCS = health care setting, Other

Registry population: AT-RISK = individuals at risk of dementia/AD, C = carers, FAM = family members of patients with dementia/AD, PWD = patients with dementia/AD, NC = normal (i.e., no diagnosis of dementia/AD) control subjects

Type of data: Cog = Cognition, Dem = Demographic, Funct = Function, IBM= Imaging and other biomarker measures, Other, including caregiver burden, quality of life, behavioural and psychological symptoms of dementia