

# Developing clinical research infrastructure in Scotland: the Scottish Dementia Clinical Research Network

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In this paper, we look at how the environment for clinical research in dementia developed in Scotland from a position where we were under-performing and had lost key academic leadership. We discuss how a clinician-led research network has improved the scope of research and is leading to a resurgence of interest in using Scotland as a base for developing and undertaking clinical research.

**Keywords:** dementia • infrastructure • protocol development • research register

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## Background of clinical research in Scotland prior to the set up of the Scottish Dementia Clinical Research Network

The Scottish Dementia Clinical Research Network (SDCRN) was set up in August 2008 using funds from the Chief Scientist's Office of the National Health Service (NHS) Scotland for the purpose of improving the number of people with dementia and their carers in high-quality clinical studies with no restriction on type; that is, not solely to randomized, double-blind, placebo-controlled pharmaceutical studies [10].

Scotland has a good record of contributing to basic science research in dementia, social research and psychology-based assessments of people with early dementia. There are two longitudinal birth cohort studies, one of people born in 1921 and the other of those born in 1936, both of which have made a significant contribution to the research literature [1]. There was also a comprehensive, Scotland-wide epidemiological study of early-onset dementia from 1974 to 1988 that determined incidence, both overall [2] and in terms of nonrandom geographical variation [3], and identified a range of socioenvironmental risk factors [4]. However, recruitment into high-quality clinical studies on dementia was historically low. As an example, in the year 2007/2008 only 83 patients were enrolled from Scotland into studies registered on the UK Clinical Research Network portfolio, an index of study quality, with only three from Principal Investigators based in National Health Service secondary care services. Although this is a disappointing figure, it does mean that people with dementia in Scotland are unlikely to have been involved in research, creating an opportunity for research to be developed.

## Demographics of dementia in Scotland

Scotland covers an area of 30,418 miles<sup>2</sup> (78,782 km<sup>2</sup>) and has a current population of 5.3 million people [102], of whom approximately 900,000 are aged over 65 years of age. The 2011 Census revealed that, for the first time, the population aged over 65 exceeded that of the population under 16. The demographics of Scotland include people residing in some of the most deprived and some of the most affluent areas in the UK, with a tendency towards a low life expectancy in the main industrial belt. Life expectancy at birth (2008) was 80.1 years for females and 75.3 years for males. Scotland has traditionally seen net emigration

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of people in younger adulthood or mid-life, but, in rural areas in particular, a net immigration of people post-retirement. To some extent, the former trend has been over-compensated by net immigration from elsewhere in Europe, consequent on the expansion of the European Community, with the overall Scottish population growing by 0.54% per annum. However, the overwhelming majority of people over 65 in Scotland are of white British origin.

### How health & care services are delivered in Scotland

Though interdependent, health services and social-care services are provided and coordinated by separate agencies. Health services are delivered by NHS Scotland and remain free at the point of delivery. Social-care input is subject to means testing and increasingly contracted out to the private sector. Care home provision per capita in Scotland is lower than that of other parts of the UK, though expenditure is higher [5]. In Scotland there has been a considerable increase in the number of people diagnosed with dementia over the last 3–4 years, as a consequence of a national drive under health, efficiency and access targets [103], but the percentage of people with dementia who have a diagnosis remains only approximately 60% of the number predicted by applying EURODEM prevalence figures [6]. Impetus to improve the number of people diagnosed was given a further boost by the ‘Cameron Challenge’ in May 2012 in which the UK Prime Minister, David Cameron, set a series of targets relating to dementia [104]. Improvements in diagnostic rates provide the opportunity to increase the pool of people with dementia who might participate in research studies.

No figures are available that accurately describe the proportions of people with dementia who have Alzheimer’s disease or other subtypes, but Scotland has a reputation for high levels of vascular problems and mortality rates remain high from coronary artery disease and cerebrovascular disease, though these may be decreasing. For example, The Scottish Health Survey demonstrated cerebrovascular disease, which includes cerebrovascular accident/stroke and transient ischemic attack, was responsible for the deaths of 4600 people in Scotland in 2011, though mortality from stroke in the <75s declined from 37.5 deaths per 100,000 in 1995 to 18.8 deaths per 100,000 in 2007 [105]. Approximately 2.9% of men and 2.7% of women over the age of 65 years are living with stroke. In all probability, therefore, the percentage of people with vascular or dementia of mixed Alzheimer’s disease/cerebrovascular disease is higher than in some other western countries.

### Development of SDCRN & Scottish Dementia Research Interest Register

Following retirement of the only Chair in Old Age Psychiatry in Scotland, in 2008, there has been no academic department of old age psychiatry. Although there was interest and expertise in dementia, delirium and cognitive ageing in three of the four Scottish academic centers of Geriatric Medicine (Dundee, Edinburgh and Glasgow), the majority of people with dementia were under the clinical care of old age psychiatry. Many research projects were of small scale with limited sample size and concentrated on clinical topics, such as factors influencing cholinesterase inhibitor use [7–9] and nursing homes [10]. This led to difficulties in dissemination of findings and limited adoption of the study findings into practice, though the longitudinal birth cohort studies, concentrated in two areas – Grampian (population 450,000) and Lothian (population 880,000), were much larger. The goal of the SDCRN was to expand potential recruitment across Scotland and to act as a catalyst for the generation and development of large, better quality clinical studies. Three key components were recognized as essential to achieve this goal:

- A well-characterized resource of potential participants in clinical studies;
- Trained and experienced clinically based researchers;
- External funding of dementia research.

Since there was an absence of academic old age psychiatry in Scotland, involving NHS-based clinicians in the specialty was key to the success of the Network. Hence, unlike many networks, its development has not been hosted in an academic department but has been dependent on clinical leadership working in tandem with academic staff from outwith old age psychiatry. Although this presents challenges in the development of research projects from scratch, it has the advantage of the clinicians having direct access to caseloads of people with dementia who might be willing to participate in research projects. This was the background for the creation of the Scottish Dementia Research Interest Register, addressing the first of the components needed to achieve the goal.

### Description of the Register

Details of the Scottish Dementia Research Interest Register have been published previously [11]. Briefly, referrals of people with dementia and/or carers are identified by local clinical teams who continue to provide mainstream services. Referrals are then allocated to a locally appointed Clinical Studies Officer (most commonly, but not exclusively, psychiatric nurses), who then obtain demographic information, including a medical history concentrating on vascular risk factors and record current medication

use. Cognitive assessments included the Addenbrooke's Clinical Examination – Revised [12], and the Clinical Dementia Rating [13], with information on activities of daily living obtained from the Instrumental Activities of Daily Living/Personal Self-Maintenance Scales [14]; and information on behavior and carer distress obtained from the Neuropsychiatric Inventory [15].

All information is collected electronically using custom-designed software, and as soon as is practical, transferred to a secure server. Internet usage among older people in Scotland is growing but far from universal and several areas have no internet access at all. Mobile network coverage is also limited and a purely web-based system would be impractical. However, no data are stored on local computers. Ethical permission was obtained from the Scotland Multi-centre Research Ethics Committee, which specializes in research studies that include adults who are incapable of giving informed consent.

Data are anonymized on the site of the secure server at the Health Informatics Centre in Dundee, Tayside (Scotland). Monthly extracts are released in SPSS (International Business Machines Corp., NY, USA) format, which can only be accessed by a password protected site from which no patient identifiable information can be exported. However, feasibility assessments for studies based on inclusion and exclusion criteria can be undertaken by the restricted group of SDCRN staff with access to that safe-haven file storage.

### Improving access to research participants

Following an appropriate feasibility assessment (currently free of charge) researchers are given access to the names of potential recruits, providing studies have ethical approval and funding. Inclusion and exclusion criteria are passed via SDCRN staff to the Health Informatics Centre who then decode the anonymized data and forward names of potential participants to a Safe Haven site, which means that lists of patients cannot be printed, emailed, shared or copied. For larger studies, names are provided under a staged-release system to ensure that potential participant fatigue is minimized. Researchers agree to store any study information securely, under the International Conference on Harmonization's GCP guidelines and they sign to state that these data are only used for the current study. This prevents local researchers building up potential recruitment databases for other studies, which would be a potential breach of Data Protection legislation. Accrual rates are provided to the SDCRN on a regular basis from researchers accessing the service.

We record active studies and monitor recruitment into them. Currently, 25 studies are active, with an overall recruitment of 553. In 2011/12, 38% of people whose names were forwarded to research agreed to participate in that researcher's study.

The SDCRN were able to invite all the registrants at one moment in time, in 2011, to participate in a study to see what kind of research they would value with some interesting and unexpected results [16].

In perspective, however, Dementia Challenge is to have 10% of people with dementia recruited into a dementia study. Even with the presence of the Network this is a highly challenging target.

### Developing protocols for research

In the absence of academic Old Age Psychiatry Departments and in an environment where psychiatrists' time is increasingly contracted to the provision of direct clinical care, opportunities for the development of individually led research projects are restricted. In addition, prior to 2008, the history of Scottish centers engaging with larger centers elsewhere in the UK was poor. Challenges for SDCRN were, therefore, first, to encourage engagement of Scottish psychiatrists into the wider research community and second to develop Scottish-led clinical research projects.

The distribution of SDCRN staff around Scotland enabled the majority of the Scottish population to be accessed, which may help to reduce any sense of future recruitment fatigue from centers in which research is undertaken regularly. In addition, the co-ordination of these staff by SDCRN allows us to distribute potential sites around the country. In 2012, a dementia-themed call was announced by the National Institute for Health Research, with UK£22 million of research funding awarded to a total of 21 projects led by UK researchers [106]. Although none of these projects originated in Scotland, three have invited participation from Scottish sites and one further major study will also have a Scottish site. We have also been successful in securing sites for two major studies led by pharmaceutical companies, one of which is interventional. The profile of Scotland as a potentially fruitful ground for clinical research has unquestionably grown as result of the presence of the SDCRN.

We have also undertaken a commitment to develop Scottish-led clinical studies. This has been done by setting up small groups of interested personnel to generate and refine research ideas into which we provide guidance of protocol writing, sample size calculation, potential statistical analyses, dealing with ethical issues, and grant application – all with a view to improving the portfolio of clinical research across Scotland. We have identified a number of groups with common interests, which we expect to see translated into potential multicenter projects over the next year or two. Finally, we have been able to potentially expand some local projects that had inadequate sample size for appropriate statistical power and the ability of the SDCRN to engage staff on multiple sites considerably reduces the cost of such multicenter studies.

### Conclusion

From a low starting point, the SDCRN has made substantial progress in developing an environment for clinical research in dementia in Scotland, from which we are now beginning to see some results. We have overcome ethical and practical problems associated with the development of a research interest register that provides a database of people who have consented to be approached for research studies. We have ensured that researchers have access to people in urban and rural areas, maximizing the chances of projects being completed to time. We have established groups for the development of further research protocols and stimulated research across disciplines. We now have a sound base from which future developments can be established.

### Future perspective

Further impetus to the development of clinical research in Scotland was supplied by the creation of an Alzheimer's Scotland Clinical Research Fellow in 2010, and the opening of the Alzheimer's Scotland Dementia Research Centre in Edinburgh in 2012, jointly funded by the University of Edinburgh and Alzheimer Scotland. This Centre acts as a hub for resources such as statistical information that can be made available to researchers across Scotland. The Clinical Research Fellow works closely with SDCRN and the work of the Alzheimer's Scotland Dementia Research Centre dovetails with the work of the SDCRN.

As the profile of clinical research in dementia in Scotland grows, we anticipate increasing opportunities for jointly working with colleagues in the UK through networks in England, Wales and Northern Ireland, and one Scottish center has become a member of the European Alzheimer's Disease Consortium, thus, allowing scope for engagement in international studies or in the development of international multicenter protocols.

We are currently collaborating with the dementia and neurodegenerative disease network [107], our counterpart in England, on a development to better involve care homes in dementia research. The name of the initiative is Enabling Research in Care Homes and the aim is to improve care homes' input and confidence in dementia

research by supporting, assisting and helping care homes to deliver research.

For too long, clinical research in dementia in Scotland has been a weak link in an otherwise strong research community. In recent months, we have tried to address this by provisionally agreeing to set up the Scottish Dementia Research Consortium, which includes research from all disciplines – from basic science through translational medicine, clinical research and social research, with potential links to researchers in related fields, particularly those associated with vascular disease. Seeing this come to fruition would be a natural stepping stone towards the goal of meeting the Dementia Challenge laid down by David Cameron and securing the widespread engagement of people with dementia and their carers' in dementia research. Additionally, we have created the role of Research Associate to allow people who do not have time to actively participate in dementia research to promote the work of SDCRN and other research and thus engage the more widespread community in the promotion and development of dementia research studies.

Our belief is that the more people who participate in dementia research, the more studies we will see undertaken, the quicker these studies will be done and the faster positive results will be translated into clinical practice for the benefit of people with dementia and their carers. Ultimately, this has been, and will continue to be, the primary *raison d'être* for the SDCRN and any potential Scottish Research Consortium that we hope to see emerge.

### Disclosure

*The views expressed in this publication are those of the authors and not necessarily those of Scottish Ministers or the Chief Scientist's Office.*

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### Executive summary

- The UK Prime Minister, David Cameron, has issued a challenge that 10% of people with dementia should be involved in clinical studies.
- The Chief Scientist's Office of the National Health Service Scotland has funded the Scottish Dementia Clinical Research Network to provide infrastructure to enable opportunities for clinical research to be expanded in Scotland.
- A key resource of the Scottish Dementia Clinical Research Network is the Scottish Dementia Research Register, which now has over 1000 patients and 1000 carers registered with consent to be approached by researchers.
- Plans are in place to expand research in care homes and to develop a consortium that improves collaboration with research communities.

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